

Ever since the demonstration of the "swan-neck" lesion (shortening and narrowing of the neck of the proximal tubule) in cystinosis by nephron microdissection, it has been a source of speculation. The prenatal or postnatal onset of the lesion and its role in the pathogenesis of cystine storage have been debated. To study this problem, renal function tests, kidney biopsies, and renal tissue amino acid analyses were performed on two cystinotic infants at six and 12 months of age. At six months, the infants showed a generalized aminoaciduria, proteinuria and glucosuria but not hypophosphatemia, hypokalemia or polyuria; and they were pitressin responsive. Renal biopsies did not show the "swan-neck" lesion by light microscopy or nephron microdissection. However, electron microscopy revealed vacuolization and previously undescribed ultramicroscopic crystals in the epithelial cells of the neck region of the proximal tubule. The unbound cystine concentration in the kidney biopsies was three-fold greater than in controls. At 12 months of age the infants exhibited hypokalemia, hypophosphatemia, polyuria and subnormal pitressin responses. Typical "swan-neck" lesions were demonstrated by nephron microdissection. The unbound cystine concentration was ten times normal levels. These studies indicate the "swan-neck" lesion in cystinosis is an acquired rather than congenital defect and it follows rather than precedes cystine storage.

Paramedical personnel in evaluating children with renal disease.

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During the past four years we have utilized the Clinical Laboratory Patient Service Assistant to help us evaluate children with renal disease. She arranges, conducts and calculates all studies, except for performing the renal biopsy. This has permitted us to evaluate 450 children with renal disease, including 2,000 complete series of renal function studies and 300 renal biopsies.

Previously, this diagnostic work-up required 5.5 hospital days. The Clinical Lab. Patient Service Assistant has permitted us to evaluate each patient in the outpatient dept. in 7 hours (overnight hospitalization required for renal biopsy). The studies include two 12-hour urine collections in the recumbent and ambulatory positions (done prior to coming to the hospital), concentrating and diluting capacity, urine culture and urinalysis, creatinine and urea clearance, tubular resorption of phosphate, blood gases, appropriate serological studies and blood chemistries, and a water load test. An intravenous pyelogram and voiding cystogram can be done before and after the studies are completed, respectively.

The Clinical Laboratory Patient Service Assistant has permitted us to decrease hospitalization time, decrease expenses to the family for lodging, decrease cost to the insurance carrier and the time of confinement in the hospital. She represents a familiar friend to the children with renal disease whom we follow.

Body composition in uremic children and the effects of chronic hemodialysis. CAROL J. WILSON, DONALD E. POTTER, JEAN L. HARRAH, MACARIO BUZON, and MALCOLM A. HOLLIDAY. *Univ. of Calif., San Francisco, and San Francisco Gen. Hosp., Calif.*

Chronically uremic children seldom grow normally; growth while on extended hemodialysis is usually not adequate. In order to delineate more precisely the components of this growth failure and the changes in body composition with chronic

dialysis, 46 simultaneous measurements of total body water and of extracellular water (ECW) were determined in 24 children aged 2-17 yrs. The data were divided into two groups: uremic children dialyzed <3 mos and those dialyzed >6 mos. Published data of Cheek for healthy children of similar age were used for comparison. In the uremic children body weight (BW) and height (Ht) were below normal for age. ECW was significantly higher in both groups for Ht and BW, and its fluctuations tended to confuse interpretation of weight changes. In both groups, cell mass (CM), derived from calculated intracellular water, was low in relation to BW and Ht. While on dialysis, Ht, BW, and CM tended to increase; CM as per cent BW did not change, and increases in CM with Ht were less rapid than in normals. Correlation between changes in CM with change in Ht was low. Nutritional status was a factor in rate of increase in CM and in Ht. Although normal linear growth velocity may be observed on dialysis, catch-up growth is uncommon. Growth occurred without restoration of the normal relationship of CM to Ht. These studies have proved useful in defining the character of body composition in uremic children and in evaluating changes in body composition in individual patients with time, variations in caloric intake, and with growth.

#### GASTROENTEROLOGY AND ENZYMOLOGY

Growth of the small intestine in IUGR and normal rat pups.

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Small intestinal growth was compared in intra-uterine growth-retarded (IUGR) pups, obtained from rats fed a diet containing 6% protein during pregnancy and normal (N) control pups. All pups were delivered by C-section at term and nursed with normal foster mothers (7-9 pups/litter). At birth mean body weight in IUGR (27 pups) was 4.3g and in normals (28 pups) 6.3g. Mean small intestinal weight (mg) in IUGR pups was less than in normals (IUGR = 105, N = 140,  $p < 0.01$ ). The intestinal length (cm) was also shorter in the IUGR pups (IUGR = 19.7, N = 21.1,  $p < 0.01$ ). The intestinal hypotrophy (relative low weight/cm) in IUGR pups was more marked in its distal one-third than in the more proximal segments. By age 8 days body weight (16g) and intestinal weight (470mg) were similar in the two groups. However, in the IUGR group hypotrophy was still noted in the distal one-third of the intestine. At this age intestinal length was greater in IUGR pups than in normals (IUGR = 36.4, N = 34.1,  $p < 0.05$ ). Intestinal tissue water and protein contents were similar in IUGR pups and normals. However, protein content (% wet wt.) in the middle one third of the intestine was higher at 8 days than at birth (IUGR, N: 0 days = 14.5, 14.6, 8 days = 16.8, 16.2;  $p < 0.01$ ).

Thus the relatively more rapid body growth in IUGR pups was associated with a similar rapid growth of the small intestine which was more prominent in the proximal than in the distal segments. The higher protein content in the mid-gut at 8 days compared to that at birth suggests a better functional capability of this segment at 8 days than at birth.

Mechanism of antigen absorption from the small intestine. W. ALLAN WALKER, RICHARD CORNELL, LAURA M. DAVENPORT and KURT J. ISSELBACHER. *Harvard Med. Sch., Mass. Gen. Hosp., Boston, Mass.* (Intr. by J. Warshaw).

Evidence exists that the intestine is permeable to antigenic macromolecules. The mechanism of absorption and factors af-

fecting antigen uptake are largely unknown. Studies relating molecular size to the clearance of macromolecules from intestinal loops suggest a diffusion phenomenon. However, the uptake of horseradish peroxidase and fluorescent-labelled gamma globulin by epithelial cells is affected by metabolic inhibitors suggesting an energy-dependent process. To clarify mechanisms of antigen absorption the uptake of horseradish peroxidase (HRP) (M.W. 40,000) and two C<sup>14</sup>-dextrans (M.W. 15,000 and 60,000) were studied in rat everted gut sac preparations. Electron micrographs showed that HRP progressed from membrane-bound structures within epithelial cells into the intercellular space and finally into the lamina propria. Absorption of HRP was five times greater in the jejunum than in the ileum and jejunal uptake was inhibited by S-13, an uncoupling agent. Large weight dextran was absorbed at three times the rate of small weight dextran at equivalent concentrations. Experiments performed at 0° or under nitrogen reduced the absorption of the large weight dextran to that seen with smaller weight dextrans. These studies suggest that the uptake of some antigens occurs by an energy-dependent pinocytotic mechanism. The uptake appears to be greater in the jejunum than the ileum and the jejunal absorption shows a more marked energy-dependency. The energy dependent uptake of the larger dextran suggests a mechanism for absorption of macromolecules other than diffusion. (Work supported by grants from The John A. Hartford Foundation, Inc.)

#### Role of bile acids in fat absorption in low birth weight infants.

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Low birth weight (L.B.W.) infants absorb fats with greater difficulty than normal term infants. The possible role played by intestinal bile acid concentrations (B.A.C.) in this defect was studied. Seventeen L.B.W. infants aged 10 to 34 days weighing 1540-2300 Gm. (mean-1790) were intubated and duodenal contents were aspirated for a period of one hour starting between 2-3 hours after feedings of unsaturated fat formula. Aspirates were kept on ice and were subsequently assayed for lipase activity and total B.A.C. (Method of Iwata). Concurrent 48 hr. stool collections were analyzed for fat. Lipase activity was normal in all infants (6.5-16 I.U./ml.). In infants with duodenal B.A.C. below 2mM/L (critical micellar concentration) coefficients of fat absorption were 48%-77% (normal 80%). In 7 of 8 infants with levels greater than 2mM/L, fat absorption was above 80%. Attempts to correlate ages or weights of the infants with levels of fat absorption did not yield consistent relationships. However, when age of the infants was related to total B.A.C., 10-19 day old infants (12) showed a mean value of  $2.07 \pm 1.3$  mM/L, compared to 20-34 day old infants (7) with a mean of  $5.8 \pm 2.7$  mM/L. Control babies of three weeks to 8 mos. of age (8) had a mean B.A.C. of  $6.8 \pm 2.7$ . Four younger L.B.W. infants were restudied after 2-3 weeks and showed a three-fold rise in B.A.C. Conclusions from these preliminary studies indicate that L.B.W. infants display lower levels of duodenal B.A.C. than do older and larger infants. There is a good inverse correlation between B.A.C. and steatorrhea.

Enhanced calcium and magnesium absorption in premature infants by feeding formulas containing medium chain triglyceride (MCT). PHIENVIT TANTIBHEDHYANGKUL and SAMI A. HASHIM

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Thirty-four premature infants were divided into three groups of comparable weight and fed three formulas differing only in fat composition. Group 1 (control) corn oil, oleo, and coconut oil (39:41:20); Group 2: MCT, corn oil, and coconut oil (40:40:20); Group 3: MCT and corn oil (80:20). Formula feeding was begun within 1 week after birth and continued throughout hospital stay. In all groups two 5-day stool collections were made early and late during the study and analyzed for fat, Ca and Mg. Mean absorption values  $\pm$  SE for the three groups of infants are:

Group	Ca Absorption: % of dietary Ca		Mg Absorption: % of dietary Mg	
	early period	late period	early period	late period
Control	29.5 $\pm$ 3.7	39.1 $\pm$ 4.1	56.1 $\pm$ 4.2	58.4 $\pm$ 4.5
40% MCT	60.1 $\pm$ 4.0	64.3 $\pm$ 3.3	66.0 $\pm$ 4.6	64.6 $\pm$ 2.7
80% MCT	75.0 $\pm$ 2.9	81.2 $\pm$ 3.0	83.6 $\pm$ 2.2	87.5 $\pm$ 2.7

In the MCT groups Ca absorption was significantly increased when compared with control ( $p < .001$ ). The 80% MCT group absorbed more Ca than the 40% MCT group ( $p < .01$ ). When the 80% MCT group was compared with the 40% MCT and control groups, significantly higher Mg absorption was observed ( $p < .005$ ). There was a positive correlation between improvement in fat absorption and both Ca and Mg absorption. The results indicate that calcium and magnesium absorption can be improved in premature infants by administration of MCT-containing formulas.

Congenital defect in folic acid absorption. PEDRO J. SANTIAGO-BORRERO, RAFAEL SANTINI, ENRIQUE PÉREZ-SANTIAGO and NORMAN MALDONADO (Intr. by Antonio Ortiz). *University Hospital, Univ. of Puerto Rico Sch. of Med., San Juan, Puerto Rico.*

A caucasian girl was noted to have persistent diarrhea and progressive pallor since age of two months. Hematologic evaluation at 3 months revealed anemia of 6.0 gm/100 ml and severe megaloblastic erythropoiesis. She failed to respond to oral treatment with folic acid, but she had a prompt hematologic and gastrointestinal response with folic acid I.M. She remained free of anemia and diarrhea and kept growing and developing adequately while receiving parenteral therapy with folic acid. Anorexia and severe stomatitis and glossitis developed regularly three to four weeks after the administration of 15 mg of folic acid I.M. Evaluation at age 11 yrs., 3 weeks after the last dose of folic acid I.M., revealed a normal girl except for moderate stomatitis and glossitis and some hypersegmented PMN leukocytes. Her serum and whole blood folates were 2.0 and 60 ng/ml, respectively, and the serum B-12 was 500 pg/ml. Intestinal absorption tests were normal. Gastric and jejunal biopsies revealed normal mucosa. Folic acid and citrovorum factor absorption tests with 5 mg doses showed flat curves. Forty mg. of folic acid orally also failed to produce an increase in serum folate or to control the early signs and symptoms of folic acid deficiency. The clearance of folate after the administration of 5 mg. of folic acid intravenously was normal, but the urinary excretion of folate was unusually low (100  $\mu$ gm) in 8 hours. Studies for the presence of a folate inhibitor in the plasma were negative. These studies demonstrate an alteration in the