CLINICAL CORRELATES OF NECROTIZING ENTEROCOLITIS (NEC). Ivan D. Frantz III, Philippe L'Heureux, Rolf R. Engel, Arnold S. Leonard and Carl E. Hunt. Depart. of Pediatrics, Radiology and Surgery, Univ. of Minnesota, Minneapolis.

Of 720 newborns admitted to our NICU in a recent 38-month period, 54 (7.5%) developed NEC. In an attempt to better define the etiology of NEC, the acute course of these patients was compared to 98 control patients matched for birth weight. Survival was 37% in NEC as compared to 65% in control patients. The frequency of RDS (74%) and of perinatal asphyxia (32%), hypotension (20%) and hypothermia (20%) was comparable in the two groups. Stool cultures showed no predominance of a single organism in either group. Although DIC (48%) and sepsis (38%) both occurred three times as often in NEC patients as in controls, their onset usually coincided with, rather than preceded, the onset of NEC. On the day of life that NEC occurred, all 54 NEC patients and 63% of controls were receiving formula feedings, both at 80 cal/kg/day. 96% of NEC patients had umbilical arterial (UA) catheters and 78% were still in place within 24 hours of onset of NEC; 73% of controls had UA catheters. Average duration of UA catheters was 7.7 days in NEC as compared to 5.4 days in controls (P=.05). 69% of NEC and 43% of control patients (P=.05) had UV catheters. NEC patients were indistinguishable from controls prior to the onset of NEC. Although our data does not define one single etiology of NEC, the high incidence of formula feedings in NEC patients does suggest that formula feedings may be related to the etiology of NEC as well as to the extent of intramural gas.

GASTROINTESTINAL ENDOSCOPY IN INFANTS AND CHILDREN. Wallace A. Gleason, Francis J. Tedesco, James P. Keating, Paul D. Goldstein, Washington Univ. Med. Sch., Dept. of Ped. & Med., St. Louis, Missouri. (Intr. by Philip R. Dodge)

Thirty children ranging from 2 to 17 years of age have undergone 32 gastrointestinal endoscopic procedures. A variety of flexible fiberoptic instruments were utilized. The recently available Olympus GIF-P (tip diameter 7.2 mm) appears to be a significant advancement for upper gastrointestinal endoscopy. Preparation and anesthesia for the cases varied with the age of the child and the nature of the procedure. A definitive diagnosis was made solely by upper gastrointestinal endoscopy in 6 of 6 procedures performed for upper gastrointestinal bleeding, 2 of 6 for ulcer-type pain, 0 of 2 for gastric outlet obstruction, 1 of 4 for possible esophagitis, and each procedure performed for single cases of dysphagia, pre-pyloric mass, possible esophageal varices, and antral deformity in a patient with regional enteritis. A definitive diagnosis was made solely by colonoscopy in 1 of 5 patients with possible inflammatory bowel disease and 0 of 1 patient with lower gastrointestinal bleeding; 4 of 4 polypectomies were successful. Non-diagnostic or normal examinations almost invariably yielded valuable information. There were no significant complications. Our experience suggests that gastrointestinal endoscopy is a safe and valuable procedure which offers promise as a sensitive diagnostic tool in infants and children.

INTESTINAL PHOSPHATE TRANSPORT IN FAMILIAL HYPOPHOSPHATEMIA. F.H. Glorieux, R. Travers, E.E. Delvin, McGill Univ., Shriners Hosp., The Genetics Unit, and C.L. Morin, R. Poirier, Univ. of Montreal, Ste-Justine Hosp., Dept. of Pediatrics, Montreal, Canada. (Intr. by J.R. Ducharme)

Renal inorganic phosphate (Pi) transport is impaired in familial hypophosphatemic rickets (FHR). Short et al. (Science,179,700,1973) have reported that the mutation was also expressed in the gut. We have examined Pi uptake in vitro by jejunal mucosa from 7 (4 female, 3 male) FHR mutants (from 5 pedigrees) and 6 controls. Peroral samples were incubated for 5 to 40 minutes in TRIS buffer, pH 7.4 with substrate concentrations from 0.003 to 3 mM. Pi uptake was concentrative and energy dependent reaching mean distribution ratios for ^{32}P of 4.2±0.9 in controls and 5.0±0.5 in patients after incubation with 0.003 mM ^{32}Pi for 40 minutes. Incorporation of Pi in the organic pool was rapid and equilibrated after 10 minutes at a $^{32}Pi/^{32}P$ total ratio of 0.5, at all substrate concentrations, in both groups. Only one mediated transport system for Pi was present in control subjects, with a Michaelis constant ≈0.2 mM and a maximum velocity ≈0.7 mmoles per liter per 40 minutes. Similar kinetic values were obtained in the group of FHR patients. These observations do not support the thesis that a significant defect for Pi uptake is present in the jejunal mucosa of FHR mutants.

MECHANISMS OF INTESTINAL ENZYME RELEASE. Hermann Goetze, Joel W. Adelson, Hans B. Hadorn (Intr. by Fima Lifshitz) Dept. of Pediatrics, Univ. of Bern (Switzerland), North Shore Univ. Hosp., Manhasset, N.Y.

The effects of gastrointestinal hormones on small intestinal enzyme release were investigated using perfusion experiments of upper small intestinal segments in rats. Aliquots of the perfusates were ultracentrifuged (130,000gx60 min.) to study their solubility. Supernatants were incubated with rat bile to investigate the effect of bile acids on enzyme activity. Following intravenous injection of 1U Cholecystokinin (CCK-PZ) or 2.5ug Pentagastrin, the output of enterokinase, sucrase and Alkaline Phosphatase (AP) in the perfusate increased markedly. After CCK-PZ 8.5% of the total mucosal enterokinase activity was released, the amounts of sucrase and AP (0.2% and 0.25% respectively) were smaller. The specific activity of enterokinase was higher in the perfusate, that of sucrase and AP was higher in the mucosa. Perfusion with 1 mM Dinitrophenol inhibited the CCK-PZ mediated enterokinase release but did not effect sucrase or AP release. Enterokinase was liberated after CCK-PZ in soluble form whereas sucrase and AP were mostly insoluble. In vitro addition of bile activated enterokinase but did not effect sucrase or AP activity. The data suggests that enterokinase in contrast to sucrase and AP is actively secreted and further activated by bile. Following CCK-PZ administration, the simultaneous presence of enterokinase, bile acids and Trypsinogen results in optimal protein hydrolysis.

JUVENILE WILSON'S DISEASE: HISTOLOGICAL AND FUNCTIONAL CORRELATIONS DURING PENICILLAMINE THERAPY. Richard J. Grand and Gordon F. Vawter. Harvard Medical School, Departments of Medicine and Pathology, Children's Hosp. Med. Ctr., Boston.

Clinical improvement and cupruresis occur during penicillamine(PCN) therapy for Wilson's Disease(WD), but long-term effects of the drug on hepatic morphology are virtually unknown. We studied 6 patients(pts) with WD (diagnosed at 7-24 yrs) who were clinically asymptommatic at follow-up(f/u) liver biopsy 2-7 yrs after onset of treatment. By comparison to pre-treatment biopsies (3 pts), there was marked reduction in portal fibrosis in 1 (7 yr f/u) and significant but less impressive decreases in 2 (2 yr f/u). Portal inflammation was greatly diminished in all 3, with periportal necrosis still present in 1 (2 yr f/u). None had complete restitution of normal architecture. At f/u, 3 pts on therapy for 3,5 or 7 yrs (without initial biopsy) had dense portal cirrhosis; in 2, portal lymphocytic infiltration was prominent; in 1, there was marked fatty change. Hepatocellular non-bilirubin pigment was abundant in 5/6 f/u specimens. Hepatic Cu^{++} levels were 80-750 µg/g (nl<50) and did not correlate with the degree of pigment deposition or healing. Liver function reverted to normal in 5/6 pts; serum Cu^{++} levels fell 50% and remained low. Hypoceruloplasminemia persisted in all. K-F rings faded or disappeared. One pt has hepatic dysfunction, cirrhosis and K-F rings despite therapy. The data show that morphological improvement occurs in some PCN-treated pts with WD, but that this is not predicted by function tests. Sequential biopsies are needed to evaluate fully the extent of healing.

EFFECT OF TOTAL PARENTERAL ALIMENTATION(TPA) ON RAT SMALL INTESTINE. William C. Heird, H.L. Tsang, Roger Macmillan, Ruth Kaplan, and Norton S. Rosensweig. Columbia Univ. Col. Phys. & Surg., Depts. Pediatrics & Medicine and Babies Hospital and St. Lukes Hosp. Center, New York.

Rats were killed on day 0 and after 3, 7, 10 and 14 days of TPA, isocaloric rat chow feedings(IC), or starvation. In each group the small intestine was removed for determination of its total weight(TW), mucosal weight(MW), mucosal protein(MP), mucosal DNA, and mucosal glycolytic enzyme activities. Both TPA and IC rats were in positive N balance; weight gains were 5 and 3.5gm/d, respectively. Starved rats lost 10 gm/d. In IC rats, none of the variables changed significantly over 14 days. In TPA rats, both TW and MW decreased by 40% within 3 days, after which no further changes occurred. Both mucosal protein and DNA of TPA rats were 40% lower by 3 days and remained at this level. TW and MW of starved rats decreased by 63% over 10 days; while both mucosal protein and DNA decreased 65%. In contrast to the changes during TPA, all variables fell continuously, during starvation. Mucosal Protein: DNA ratios remained constant in all groups, suggesting a decrease in the total number of cells. Specific activities of pyruvate kinase and both fructose-1-phosphate and fructose-1,6-diphosphate aldolases remained constant in all 3 groups, but because of decreased mucosal protein and DNA contents, total intestinal activity of all enzymes was significantly decreased. These findings show that although increases in body weight can be achieved with TPA, it does not adequately maintain intestinal cell mass.