hydrolyzing lactose in adult life are carrying a mutation derived from natural selection. In regions where malabsorption in adults is prevalent, lactose-free milk should be given to children so as to avoid diarrhea related to lactose intolerance.

A metabolic and anatomic study of a case of Noonan's syndrome with intestinal lymphangiectasia. H. LAWRENCE VALLET, PHILLIP G. HOLTZAPPLE, WALTER R. EBERLEIN, WILLIAM C. YAKOVAC, THOMAS MOSHANG, JR., and ALFRED M. BONGIOVANNI. *Univ. of Pennsylvania Sch. of Med., The Children's Hosp., Philadelphia, Pa.*

Major cardiovascular anomalies and cutaneous lymphatic defects have been described in both Noonan's and Turner's syndrome.

A 6½ year old male presented with anasarca, chylous pleural effusions, cutaneous lymphatic leakage, ascites and hypoproteinemia. Studies revealed findings consistent with the diagnosis of intestinal lymphangiectasia and a major thoracic lymphatic vessel leak. Investigations included X-ray studies of small bowel, Cr^{51}-chloride turnover, stool fat analysis, small bowel biopsy, and effusion studies for electrolytes, cells, lipoprotein electrophoresis and chylomicron analysis. Low lymphocyte counts and immunoglobulins were also found.

Medium chain triglycerides and a low fat diet corrected the protein loss but a seemingly mild pre-existing cardiac lesion worsened, and dictated the need for corrective pulmonary valve surgery. He died following this procedure.

Post mortem studies revealed severe defects in most of the mesenchymal components of cardiovascular organogenesis. Large lympho-venous shunts were present in the lung, liver and pancreas.

The lymphatic defects in these patients may not be as benign as once believed, and may be a major cause of failure to thrive.

Transmissible gastroenteritis in piglets (TGE). A model for study of acute viral diarrhea. MARY KELLY, DANIEL G. BUTLER, and J. RICHARD HAMILTON, *Research Inst., Hosp. for Sick Children, Univ. of Toronto, Toronto, Ont., Can.*

We studied a specific viral gastroenteritis (TGE) in piglets in order to explore the pathogenesis of acute infectious diarrhea. We compared 23–26 day old piglets infected orally with TGE virus, with pair fed non-infected litter mates. Infected pigs lost weight; fecal weight, Na^+, K^+ and Cl^- excretion increased significantly; fat excretion did not increase. Serum concentrations of Na^+, K^+ and Cl^-, Mg^{++} and Ca^{++} did not differ between groups. After 40 hours the pigs were killed. Although a mucosal lesion characterized by diffuse villous and epithelial cell damage occurred in some infected pigs, the groups did not differ significantly with respect to actual villous dimensions. In infected pigs the following changes in specific enzyme activity occurred: Na^+-K^+-ATPase and Mg^{++}-ATPase decreased significantly in proximal jejunum only; alkaline phosphatase decreased in proximal and mid-jejunum; sucrase decreased in mid-jejunum and ileum. There was no change in activity of any of these enzymes in proximal or distal colon. Mucosal protein content was the same in both groups. Our results suggest a relationship between proximal intestinal Na^+-K^+-ATPase activity and the diarrhea of acute viral enteritis.

Group	Stool Wt. (g/24 hr)	Stool Na (mEq/24 hr)	Enzyme activity—proximal jejunal mucosa (mean units/g. protein)			
	M. S.E.	M. S.E.	Na^+-K^+-ATPase	Mg^{++}-ATPase	Alk. Phos.	Sucrase
Control	36.3±9.4	0.9±0.6	1.35 × 10^3	1.09 × 10^3	8.43 × 10^3	0.74
Infected	261.5±74.4	22.0±6.1	0.92 × 10^3	0.74 × 10^3	3.61 × 10^3	0.38
P	<.05	<.01	<.01	<.05	<.01	>.05

Hereditary pancreatitis (HP) without amino-aciduria: Two new kindred. ALLEN LAPEY, JOHN KATTWINKEL, PAUL A. DI SANT' AGNESE, and LEONARD LASTER. *NIH, Bethesda, Md.*

HP, an autosomal dominant disorder with incomplete penetrance has been reported in 13 families and is characterized by chronic relapsing pancreatitis leading to pancreatic insufficiency, pancreatic calcifications, and at times diabetes. In 3 of the original families lysine-cystine amino-aciduria was present in some members regardless of pancreatic involvement.

Our West Va. kindred (total 55 members) had 8 definite and 12 suspected cases of pancreatitis, mean age of onset 5 yrs.: 7 of 8 definite cases had pancreatic lithiasis, in 3 instances before 13 yrs. of age. Our Tenn. kindred (total 110 members) had 9 definite and 12 suspect cases, mean age of onset 14 years, with 6 of 9 definite cases presenting calcifications. There was striking variation in age of onset from 18 mos. to 35 yrs. Steatorrhea and pancreatic deficiency tended to be a late complication but they were found as early as 20 yrs. of age. There was no good clue as to what brought on acute attacks.

In both kindred fecal fat, pancreatic enzymes, and serum amylase and lipase were assessed. Serum lipids and parathyroid function by calcium infusion were normal. All urinary amino acids were determined in 7 patients and 9 relatives and were normal in all instances.

HP is a generally unrecognized cause of pancreatitis in childhood and important in the differential diagnosis of recurrent abdominal pain and pancreatic lithiasis (e.g., from cystic fibrosis). It is speculated that two different genetic types of HP exist with and without amino-aciduria.

Recurrent pleural effusion: A complication of pancreatitis in childhood. FREDERIC B. KOPEL, IRWIN GRIBETZ and HAROLD GROTSKY. (Intr. by Alex J. Steigman). *The Mount Sinai Sch. of Med., New York, N. Y.*

While pleural effusion as a complication of pancreatitis has been described in adults, this entity has not been noted, in the English literature, in children. We have recently uncovered chronic pancreatitis as the cause of recurrent pleural effusions in an 8-year-old Puerto Rican male whose presenting complaint at another hospital was recurrent substernal and epigastic pain radiating to the left shoulder. Exhaustive investigation, including cultures of the pleural fluid, skin tests for typical and atypical mycobacteria and fungi, lupus preparations, bronchography and thoracotomy with pleural biopsy, failed to reveal the cause of the recurrent pleural effusions. Substernal pain recurred, and the initial complaint of epigastric pain was only then appreciated. Pleural fluid showed an amylase concentration of more than 1000 Somogyi units/100 ml at a time when the serum amylase content was 335 units/100 ml (normal = 30–180 units). Pancreatic stimulation with secretin (Boots) 1 unit/kg resulted in a 1 hour output of 25 ml or 1.4 ml/kg (normal = 2 ml/kg), and a maximal

amylase concentration of 29 mEq/L (normal = 90 mEq/L), consistent with chronic pancreatitis. There was no family history of pancreatitis. Lipoprotein electrophoresis and urinary amino acid excretion were normal. Tests for mumps complement-fixing antibodies were negative. Pancreatitis should be considered as a possible cause of pleural effusion in childhood. Pleural-fluid amylase levels should be obtained in all children with unexplained pleural effusions.

Depressed plasma retinol-binding protein (RBP) in cystic fibrosis (CF). FRANK REES SMITH, BARBARA A. UNDERWOOD, CAROLYN R. DENNING, and DEWITT S. GOODMAN. *Columbia Univ. Coll. of Phys. and Surg., N. Y. N. Y.*

Decreased plasma levels with normal or increased liver stores of vitamin A were reported previously in CF patients orally supplemented with water-miscible vitamin A. These findings suggested a defect in the mechanism by which vitamin A is transported from the liver in patients with CF. Plasma levels of RBP, the specific carrier protein for vitamin A, have been measured by radioimmunoassay in 69 samples from 49 CF patients and in 96 normal age-matched controls. Mean RBP levels (± SEM) in CF, 24.4 ± 1.3 μg/ml, were significantly ($p < .001$) lower than in normal controls, 37.3 ± 1.3 μg/ml. In normal children 14 years and under, plasma RBP and vitamin A levels showed a significant ($p < .001$) correlation with age; in contrast no age-related rise was observed in CF children of comparable age. Saturation of RBP with vitamin A was less than normal ($p < .004$), and the levels of plasma prealbumin (the protein normally complexed with RBP) were decreased ($p < .001$) in the CF group 15 years and older compared with controls. Depressed plasma RBP levels were not correlated with plasma G.O.T. or albumin levels. These results suggest that a defect in the hepatic production and/or secretion of RBP occurs in CF.

Severe gastrointestinal hemorrhage (GIH) after "therapeutic" doses of aspirin (ASA) in normal children. J. LAWRENCE NAIMAN, GARRETT BERGMAN, and PHILIP PHILIPPIDIS. *St. Christopher's Hosp. for Children and Temple Univ. Sch. of Med., Philadelphia, Pa.*

Although gastrointestinal hemorrhage (due to gastritis) associated with the abuse of ASA-containing preparations by adults is well recognized, its importance as a cause of severe GIH in children has not been well appreciated, either in the literature or practice of pediatrics. From 1965–1970 we observed 12 children from 3 months to 14 years of age in whom severe hematemesis and/or melena followed ordinary (antipyretic) doses of ASA. Hemoglobin concentrations were decreased in all, with levels below 7 gm% in 3 patients; RBC morphology and reticulocytosis suggested acute blood loss. Studies of hemostasis (prothrombin time, partial thromboplastin time, platelet count, and Ivy Bleeding time) were normal. Gastrointestinal roentgenograms revealed no lesions. Laparotomy in one patient yielded negative results. A history of ASA ingestion had been recorded initially in several patients, but the possibility of an etiologic relationship between ASA and GIH was not considered until the above studies had been reported as normal. Discontinuation of ASA, observation of serial Hb levels and iron prophylaxis has sufficed in the management of this self-limited iatrogenic problem. Our experience with these cases suggests the need to re-evaluate current pharmacologic practices regarding ASA therapy in children.

Irritable bowel syndrome in childhood: The nature of the rectal mucosa correlating proctoscopy, dissecting microscopy and histologic appearances, IAN S. E. GIBBONS, ALEXANDER NEDWICH, HENRY D. APPLEMAN and GIULIO J. BARBERO. *Hahnemann Med. Coll. and Hosp., Philadelphia, Pa.*

We have previously described non-specific proctoscopic findings in children with this syndrome. A further 59 patients ranging in age from 2 to 17 years have been studied. Rectal suction biopsy specimens were examined in buffered formalin, using a dissecting microscope. Serial sections were scrutinized histologically. Mucus was present covering specimens from 17 cases. In 29 patients a single vessel surrounding the cryptal offices was regular and distinct, but consisted of duplicated regular vessels in 19 and irregular disoriented capillaries in 11. Forty biopsies showed aggregations of lymphoid tissue, represented by pale areas over which vessel architecture is lost. Volcanic cone-like openings to the crypts were seen in 51. The muscularis mucosa appeared granular and glistening white in 50 cases, but was greyish yellow in four children with severe symptoms. In 5 children histology was normal but in the others a pattern emerges. Goblet cells are increased in size and number. The glands vary in size, with ballooning, angulation and loss of parallel vertical formation. As a result the intercryptal space narrows, and "ghosts" of disintegrated entire glands appear. Compared with inflammatory colitis there is a decrease in cell population. Mucophages may appear in large clusters or invade the muscularis. Dissecting microscopy shows anatomical variation of vessels in 50%. Histology demonstrates an increase in mucus secreting cells and a diminution of cell population in the lamina propria.

Radioiodinated rose bengal and oral cholestyramine: Identification of patent extra hepatic biliary pathways. J. R. POLEY, E. I. SMITH, D. J. BOON, and C. W. SMITH. *Children's Memorial Hosp., Univ. of Okla. Med. Ctr., Oklahoma City, Okla.* (Intr. by H. D. Riley, Jr.)

The precise preoperative determination of patent vs. obstructed extrahepatic biliary pathways in infants with persistent cholestatic jaundice remains a major problem. The detection of an abnormal low-density serum lipoprotein (LP-X) in infants with extrahepatic biliary obstruction seemed helpful (J. R. Poley et al, Gastroenterology 58:983, 1970). However, a small percentage of infants with "neonatal hepatitis" are LP-X-positive. To further characterize the LP-X-positive infant, we have combined the ^{131}I-Rose Bengal (IRB) test with oral cholestyramine, a nonabsorbable polymer with strong cationic binding sites. We proposed that iodine (IRB) should bind to cholestyramine in the intestine preventing enterohepatic cycling of IRB thus increasing fecal excretion of label. To test this, we have studied seven infants with persistent cholestatic jaundice aged 3–6 months and compared results of the JRB test prior to, after 15–18 days and during cholestyramine, 4 gm/day. In three LP-X-positive infants, there was no change in excretion of label with cholestyramine and all three had impassable extrahepatic biliary pathways. Conversely, the excretion of label in the remaining four patients (two LP-X-positive) increased from a mean of 6% (range 5–8%) to a mean of 28% (range 19–36%) with cholestyramine; patency of the extrahepatic bile ducts was demonstrated in two by operative cholangiogram. The other two were not operated upon and their jaundice cleared subsequently. In vitro studies simulating intestinal conditions demonstrated ready binding of IRB to cholestyramine.