MATHEMATIC MODELING OF ROSE BENGAL KINETICS: DIAGNOSTIC AID IN NEONATAL OBSTRUCTIVE HEPATIC DISEASE. Charles E. Mize, Shelley I. Saffer, and Stephen A. Szygenda. Univ. Tex. Health Sci. Ctr. (Southwestern), Dept. of Ped. & Comp. Sci., Dallas

Rose Bengal transport through the hepatobiliary system has been modeled as a stochastic process, with a computer-aided simulation program to generate the model's parameters from kinetic data in infants with obstructive jaundice. Blood, urine, liver & fecal compartments are the key model features, and the percentages of Rose Bengal transferred (transfer parameters) among these compartments over a period of time are found. This system's advantages are 1)use of maximum information content of ^{131}I-Rose Bengal data (urine and stool appearance, plus plasma decay), b)analysis of less data than needed in classic compartmental analysis,and c)subclassification of disease not otherwise available presurgically. The solutions generated include the expected hours (before ending up in urine or feces) in (1)blood or (2)liver, and the probability that Rose Bengal will eventually terminate in (3) urine or (4) feces. Further information derives from ratios of the transfer parameters, e.g. (5)p(liver→ blood)/p(liver→ feces) For example:

Status	(1)	(2)	(3)	(4)	(5)
Idiopathic Hepatitis	10 hr	77 hr	0.22	0.78	4.2
Post-Hepatitis	5 hr	53 hr	0.28	0.72	3.2
Extrahepatic Aplasia	55 hr	949 hr	0.81	0.19	74.0

The model provides results agreeing with pathologic status confirmed by laparotomy/cholangiogram and/or clinical course.

Hepatic Changes in Young Infants with Cystic Fibrosis. Ella H. Oppenheimer and John R. Esterly. Depts. of Pathology, Johns Hopkins Univ. and Univ. of Chicago, Chicago, Illinois.

Histologic changes in the liver which are diagnostic of cystic fibrosis are not frequently recognized during infancy. In a retrospective study of 47 patients surviving up to 3 months of age, only 5 cases of typical focal biliary cirrhosis were identified. In an additional 11 cases, extra or intrahepatic ducts were prominent because of focal mucus accumulations, in these cases there were diffuse nonspecific alterations, including clinical jaundice or cholestasis with bile thrombi, apparent prominence of portal triads with fibrosis or inflammation, and minimal bile duct proliferation. Similar nonspecific lesions were present in 14 cases in the absence of excess stainable mucus in bile ducts or liver. In only 17 of the young infants (36%) was the liver entirely normal.

Diagnostic focal biliary cirrhosis was present in 5 of 32 infants who survived from 3 to 12 months and in 18 of 67 older infants, children, and adolescents, but the diffuse nonspecific changes were absent in the older age groups.

These observations suggest that bile ducts containing mucus alone or in combination with bile may be a possible precussor of focal biliary cirrhosis. The frequency of diffuse changes (cholestasis, bile thrombi, or jaundice) also suggests the possibility of proximal obstruction which is transient.

MICRONODULAR CIRRHOSIS IN ABETALIPOPROTEINEMIA: POSSIBLE EXACERBATION BY MEDIUM CHAIN TRIGLYCERIDE (MCT) FEEDING. John C. Partin, Jacqueline S. Partin and William K. Schubert. Children's Hospital Research Foundation. Cincinnati, Ohio. 45229.

Electron microscopical (EM) and lipid histochemical studies have been made of liver biopsies from 3 abetalipoproteinemic (AB-LP) and 2 hypobetalipoproteinemic (HypoB-LP) children. All AB-LP livers were enlarged and grossly fatty (38% lipid, 91% triglyceride [TG]). By EM, endogenous triglyceride particles were absent. Trans-Golgi vesicles and circum-Golgi smooth endoplasmic reticulum were absent. Most lipid vacuoles were non-membrane-bounded. This Golgi lesion has not been seen in other childhood fatty livers. One AB-LP infant was biopsied at 10, 12, 24, 30 and 38 months, before, during and after treatment with a low-fat MCT diet. During the interval of observation, he had persistent elevation of transaminases and he developed severe micronodular cirrhosis. Alcoholic hyalin (AH) appeared in hepatocytes after MCT treatment; mitochondrial dense bodies increased in size and density. Eight months after MCT was stopped, AH was greatly reduced and mitochondrial dense bodies normalized. It is speculated the alcoholic hyalin was related to accumulation of acetate from MCT-fatty acids in the face of defective TG secretion in a manner biochemically analogous to hepatic ethanol metabolism. MCT should be used cautiously in AB-LP infants until more data is available. Support: NIH #RR-123

MACROPHAGES AND THE PROTECTIVE ACTION OF BREAST MILK IN NECROTIZING ENTEROCOLITIS. Jane Pitt, Barbara Barlow, William C. Heird and Thomas V. Santulli, Columbia Univ. Col. of Physicians and Surgeons, Babies Hosp., Depts. of Ped. and Surgery, New York City.

An experimental model of necrotizing enterocolitis in newborn Sprague-Dawley rats has previously been described (Barlow et al., APSA 1974). It was found that newborn rats exposed to daily hypoxia all succumbed to this disease within two to five days if fed artificial formula (F) but not if fed breast milk (BM). These studies were undertaken to determine the protective factors in BM.

In vitro, BM killed 99% of 10^7/cc Klebsiella in two hours, while frozen breast milk (FBM) killed none and F supported bacterial growth. The Klebsiella used was one which produced peritonitis and sepsis in the experimental model. FBM and F lack the 10^6/cc macrophages (mØ) present in BM. FBM plus 10^6/cc rat peritoneal mØ or rat peripheral white cells or rat BM mØ also killed these organisms in vitro. In the experimental model, all rats died if fed F, 90% died if fed FBM and 20% died if fed F plus peripheral white cells. These studies suggest the importance of the mØ in milk as cells capable of killing potential bacterial pathogens and of preventing necrotizing enterocolitis in the appropriate stressed animal.

A FRESH LOOK AT NECROTIZING ENTEROCOLITIS. Richard A. Polin, Paul F. Pollack, Barbara Barlow, Thomas V. Santulli, William C. Heird. Columbia Univ. Col. Phys. & Surg., Depts. Ped. and Surg., and Babies Hospital, New York City.

Prematurity, asphyxia, infection, and feeding--singly or in combination--have been cited as etiologies of necrotizing enterocolitis. To further define the relative importance of each factor, the clinical courses of 55 patients seen between 1954 and 1973 were reviewed. In most cases the diagnosis of NEC was confirmed at operation or postmortem examination. Other patients included had radiographic evidence of intramural air in addition to other symptoms consistent with the diagnosis. Only 8 of the 55 patients had a gestational age greater than 38 weeks. Three of these had severe cyanotic CHD; others developed NEC at an older age (14-42 days) after a prolonged period of diarrhea. Antenatal complications were documented in 60% of the group; 26% had low Apgar scores and/or asphyxia. Forty infants had symptoms or signs of sepsis. Blood cultures were positive in 36 patients; in 97% of these, the isolated organism was a gram negative baccilus. Thrombocytopenia and/or abnormal clotting profiles were present in 72% of the patients. Abdominal x-rays were normal in only 4% of the patients; intramural pneumatosis was seen in 47%, free air in 23%, and non-specific abnormalities in the remainder. Every patient with intramural pneumatosis or free air, radiographically or on direct examination, had been fed. These findings suggest that all the cited factors play a role in development of NEC.

INTESTINAL ENTEROKINASE (EK) DEFICIENCY IN 2 SIBLINGS. A. Prasad, J.C. Haworth and B. Hadorn. Depts. of Ped., Universities of Manitoba, Winnipeg, Canada and Berne, Switzerland.

EK is a key enzyme for protein digestion since it catalyses the conversion of trypsinogen to trypsin, which in turn activates other pancreatic proteolytic zymogens. 2 cases of EK deficiency are described. A male infant developed diarrhea, vomiting, anemia, and generalized edema due to hypoproteinemia within a few weeks of birth. Weight gain was poor. Formula change to Nutramigen resulted in temporary improvement but at age 4 months he was very malnourished. Cystic fibrosis was excluded. Duodenal juice showed no proteolytic enzyme activity but amylase and lipase were present. Following the In vitro addition of porcine EK to the juice, normal trypsin and chymotrypsin activity was observed. Duodenal mucosa had no EK activity. The patient was treated with pancreatic extract and began to thrive. At 3 1/2 years he is growing normally and no longer needs pancreatic therapy. His older sister also had diarrhea, anemia, hypoproteinemia and poor weight gain in early infancy. She was fed Nutramigen and recovered. Her duodenal juice and mucosa showed the same abnormality as that of her brother. EK deficiency, which may result in variable clinical expression, is treatable and should be looked for in infants with unexplained vomiting, diarrhea, anemia and hypoproteinemia.