† 614 NATURAL HISTORY & PATHOPHYSIOLOGY OF ENTEROCOLITIS IN PIEBALD LETHAL MOUSE MODEL OF HIRSCHSPRUNG'S DISEASE. Prem Puri & Takao Fujimoto. Children's Research Centre, Our Lady's Hosp. for Sick Children, Crumlin, Dublin 12, Ireland.

A breeding colony of piebald lethal mice was established in order to study the natural history of congenital megacolon in this mouse model of Hirschsprung's disease and to investigate mucosal defense mechanisms and secretory functions in enterocolitis complicating congenital megacolon. In experiment 1, 214 mice were studied, 53 of which had congenital megacolon (S^1/S^1). All S^1/S^1 mice died at 3-11 wks of age showing two distinct patterns of mortality. 64% of mice became acutely ill at 3-4 wks of age and died while the remainder died at 9-11 wks. The former group of mice exhibited clinical & histopathological evidence of severe enterocolitis while the latter group had massive abdominal distension & classical megacolon. In experiment 2, S^1/S^1 mice were sacrificed at the time of acute illness. Significant histological & immunohistochemical differences were seen in the ganglionic colon between piebald mice with early clinical onset of acute illness & piebald mice with the classical clinical picture of congenital megacolon. In the former group of mice the number of immunocytes in lamina propria was significantly higher than control mice ($p<0.001$), immunoglobulin producing cells were equally distributed throughout the lamina propria & IgA containing cells were the most abundant cell type in the colon. In the latter group of mice, immunocyte responses were significantly low & the distribution of immunocytes markedly different with the immunoglobulin producing cells being located only at the deep layer of lamina propria. While there was marked depletion of neutral mucin & sulphomucins in both groups of mice, depletion of sulphomucin which is the dominant mucin of distal colon was more severe in piebald mice with the classical clinical picture of congenital megacolon. The existence of two such populations each of which reflects different clinical form of enterocolitis provides an exciting model for investigation of the causes of development of enterocolitis complicating congenital megacolon.

●615 MECHANISMS OF INTESTINAL IMMUNITY TO ROTAVIRUS ENTERITIS: CHARACTERISTICS OF PERSISTENT INFECTION IN SEVERE COMBINED IMMUNODEFICIENT (SCID) MICE. M. Riepenhoff-Talty, T. Dharakul, I. Uhnoo, P. Chegas, H. Barrett and P.L. Ogra. SUNY at Buffalo, Depts. Pediat. and Microbiol., Children's Hospital, Buffalo, NY and Univ. Hospital, Div. Infect. Dis., Uppsala, Sweden.

Using ELISA and fluorescent antibody assays, we followed shedding and replication of mouse rotavirus (MRV) in groups of suckling, adult, and lactating female SCID, and age matched normal (control) mice. The mice were infected, with orally administered live MRV, or spontaneously via ingestion of virus containing feces from infected pups. Suckling normal and SCID mice were infected with MRV with development of disease in a predictable manner. However, SCID infants exhibited more severe disease and persistent viral shedding in the feces. Although normal adult mice could not be infected with the virus, SCID adults developed infection in about 5-10% of villous enterocytes, but with little or no clinical disease. Significantly, these animals continued to shed virus in feces intermittently 4 to 5 months (to date) after primary infection. No MRV specific secretory antibody activity was induced in the intestine in SCID mice. However, such infected adults manifested significant resistance to subsequent attempts at reinfection with high dose of virus ($8x10^5$ ID50) administered orally. The virus recovered from the SCID mice was highly infectious when re-inoculated in susceptible suckling animals. These data suggest that the virus and host may have achieved a "steady state" in the gut in immunodeficient animals, implying that factors other than rotavirus-specific serum and secretory antibody or T cell function are important in controlling virus replication in the gut.

▲616 TISSUE AMINO ACID RESPONSES TO PARENTERAL NUTRITION. Audelio Rivera, Jr., Jatinder Bhatia, David K. Rassin. The University of Texas Medical Branch at Galveston, Department of Pediatrics.

We have previously described significant differences in plasma amino acids, bile flow and biliary bile acid output between animals infused either glucose or glucose+amino acids. The present study was undertaken to determine liver, bile and brain amino acid responses to the infusion of these various nutrients. Adult male Sprague-Dawley rats (225-325g) were cannulated via the jugular vein and infused with either glucose (GLU) or glucose+amino acids (TPN) or were chow-fed (CHOW). After 5 days of the respective regimens, bile was collected for 4h, animals were killed and brain and liver obtained. The GLU animals received 164 (SD 7) kcal/kg/d, whereas TPN animals received 9.4 (0.5)g AA and 154 (8) kcal/kg/d. Both GLU and TPN animals lost weight and CHOW animals gained weight. In general, the tissue amino acid patterns were similar to those in plasma; most individual amino acids were different among groups in liver and bile whereas only threonine, valine and isoleucine concentrations were different among the groups in the brain. Essential to non-essential amino acid ratios (markers of protein nutritional status) were: 0.59, 0.51 and 0.36 in the plasmas; 0.18, 0.11 and 0.09 in the livers; and 0.29, 0.29 and 0.22 in the bile of TPN, CHOW and GLU animals respectively. The branch chain amino acids are actively accumulated in the liver from the plasma and then appear to be passively tranported down a concentration gradient into the bile. Thus, the amino acid responses to these nutritional manipulations indicate that tissues (primarily the liver) may be susceptible to the trophic and toxic effects of amino acids.

617 PATHOGENESIS OF HYPOGLYCEMIA IN CHILDHOOD DUMPING SYNDROME. Scott A. Rivkees, John D. Crawford, Pediatric Endocrine Unit, Massachusetts General Hospital and Harvard Medical School, Boston, MA.

Reports of pediatric patients with dumping syndrome (DS) are few and the mechanisms of disturbed glucose homeostasis have not been studied. We evaluated 3 children presenting with severe hypoglycemic reactions secondary to DS; Pt 1 developed DS after fundoplication at 30 mo of age. Pt 2 diagnosed at 4 mo of age, had central hypoventilation, Hirschsprung's Disease,and generalized autonomic dysfunction. Pt 3 was 6 mo old when diagnosed and developed DS from malplacement of a feeding gastrostomy tube. Blood glucose levels during and after 2-5 meals in each child showed hyperglycemia-375±97 mg% (m±SD) 30 min postprandially and hypoglycemia-35±10 mg% >120 min later. Swings in glucose were proportional to volume of meals. Insulin and glucagon levels were followed during a single meal challenge test during which glucose rose to 356±59 mg% 30 min postprandially and fell to 32±11 mg% at 150±30 min. Hormonal analyses indicated (1) inappropriate early release of glucagon(300 pg/ml @ 15 min) in Pt 1, (2) exuberant early release of insulin (max 190±15 uU/ml) resulting in rapid fall in glucose in all patients, (3) prolonged cellular glucose uptake in the absence of circulating insulin leading to hypoglycemia in Pt 2, and (4) inadequate glucagon response to hypoglycemia resulting in sustained hypoglycemia in Pts 1 and 2. These data indicate that gross disturbances of the insulin-glucagon axis attend childhood dumping syndrome.

† 618 EVIDENCE THAT 1,25 DIHYDROXYVITAMIN D_3 IS BIOACTIVE IN THE FETAL SHEEP INTESTINE. Richardus Ross, Mei Chen, Jane Florer (Spon. by R.C.Tsang). U. of Cincinnati Med. Ctr, Dept. Pediatrics, Cincinnati, OH

Intestinal calcium binding protein (iCaBP) is the best known molecular expression of the hormone 1,25 dihydroxyvitamin D (1,25) and its synthesis in response to 1,25 requires the presence of specific 1,25 receptor macromolecules (1,25R). In rats, the developmental appearance of the 1,25R, iCaBP and its responsiveness to 1,25 occur around weaning. To test the hypothesis that in the fetal sheep, where there is evidence for a role of fetal 1,25 in mineral metabolism, there would be prenatal appearance of intestinal 1,25R and iCaBP, we isolated cytosolic intestinal 1,25R from samples of fetal (F:n=8) and maternal (M:n=5) small intestinal mucosa at 138d of gestation (term=145d). 1,25R were characterized by sedimentation coefficient (Sed), Scatchard analysis of saturation binding data and DNA-cellulose affinity chromatography (DNAcell). The following results were obtained:

	Sed	Kd (nM)	Nmax (fm/mg pro)	DNAcell elution (MKC1)
F	3.5	0.12±0.02	62±6	0.16
M	3.5	0.23±0.07	619±213	0.16

Gel filtration of F and M intestinal mucosal cytosols revealed a high affinity calcium binding protein in the 12,000 molecular weight region that demonstrated decreased anionic charge when bound to calcium (Ca) with the following elution profile on DEAE-A25 chromatography: (-Ca:elution at 0.2M NaCl / +Ca:elution in void volume). The purified apoprotein exhibited an acidic PI of 5.2 on isoelectric focusing. Conclusion: These data suggest that 1,25 is biologically active in the ovine fetal intestine.

▲619 TOTAL PARENTERAL NUTRITION (TPN) IN INFANCY AFFECTS AMYLASE AND LIPASE BUT NOT TRYPSIN SECRETION Thomas M. Rossi, Ping-Cheung Lee, Emanuel Lebenthal, SUNY at Buffalo, International Institute for Infant Nutrition and Gastrointestinal Disease, Children's Hospital, Buffalo, New York 14222

During prolonged fasting, the absence of enteric stimulation might lead to pancreatic hypofunction or atrophy. The ability of the pancreas to respond to exogenous secretagogues following fasting in conjunction with TPN in infancy is not known. In addition, while severe degrees of malnutrition (M) are known to adversely affect pancreatic structure and function (PF), it is unknown whether infants presenting with chronic diarrhea and first degree M could have alterations in PF. The results of pancreozymin-secretin tests were analyzed in the following patient groups: 7 infants receiving TPN for >6 weeks for severe diarrhea in association with short bowel syndrome or intractable diarrhea; 17 infants exhibiting first degree M and chronic diarrhea and 12 controls (age matched well nourished infants with chronic diarrhea). No significant difference was found among the 3 groups in the volume of fluid collected following either cholecystokinin or secretin. The content and concentration of amylase and lipase were lower in those receiving TPN following secretin ($p<0.05$). Peak specific activity and total trypsin and protein content were similar in all groups

The findings indicate that fasted infants receiving TPN retain their ability to respond to pancreatic secretagogues. However, the enzyme output is affected differently. Amylase and lipase exhibit an attenuated response whereas that of trypsin is maintained. No impairment in exocrine pancreatic secretion was found in infants suffering mild M.