590 ALTERED BINDING KINETICS OF CHOLERA TOXIN TO DEVELOPING RAT MUCOSA Wayne I.Lencer, Shu-Heh Chu, W.Allan Walker Hvd.Med.Sch., MGH & CHMC, Comb.Prog.Ped.G.I., Boston, Ma.

Children suffer a disproportionate share of the morbidity attributed to enterotoxigenic diarrhea. Receptor density on cell surfaces is known to effect the action of Cholera Toxin (CT). We hypothesize that structural changes during development in enterocyte membranes will modulate the binding and enterocyte response to CT. A complete randomized block design was used to compare the binding kinetics of CT to developing rat enterocyte microvillus membrane (MVM) prepared from newborn (NB), two week (2wk), four week (4wk) and adult (AD) animals. Enrichments of sucrase and lactase ranged from 9 to 22 fold. Saturation binding isotherms were generated on twelve independent samples (3 blocks) under conditions shown to be at steady state and reversible. Scatchard analysis suggested positive cooperative binding to a single class of receptor and the isotherms were analyzed using both the Hill-Waud and Michaelis-Menton function. The Hill-Waud model explained significantly more of the observed data ($P<.05-.001$). Receptor density varied significantly by age (ANOVA $F=4.62$ $P=.013$) as did the "half" dissociation constant (K_h) (ANOVA model: $F=6.28$ $P=.022$ Age: $F=7.48$ $P=.019$). Neither receptor concentration nor membrane "purity" confounded these observations. Changes in binding affinity (K_a) paralleled changes in K_h. We conclude that receptor density and "affinity" change with postnatal age. We speculate that developmental differences in receptor density and binding affinity may partially explain the enhanced morbidity due to toxigenic diarrhea in children.

591 TRYPSIN UPTAKE AND INHIBITION IN NEWBORN AND ADULT RATS. J.Levine,S.Hager,M.Davidson. SUNY at Stony Brook, Schneider Children's Hospital, New Hyde Park, NY

We previously demonstrated increased trypsin levels and trypsin-α2-macroglobulin (α2-MG) complexes in human newborns. In this study, we studied intestinal trypsin uptake and inhibition in 2-week old and adult rats. Plasma was obtained 2 hrs. after oral bolus bovine trypsin and analyzed for trypsin activity using P-tosyl-L-arginine methyl ester (TAME) and for trypsin-α2-MG complexes using gradient polyacrylamide gel electrophoresis (PAGE) and scanning densitometry. Plasma samples were also separated by column chromatography, reconcentrated and subjected to TAME. Finally, plasma before and after column separation was exposed to increasing concentrations of trypsin and analyzed for α2-MG complexes. Results:

	TAME	200kD Fraction	α2-MG Fraction
2-week old	13.6	66%	6%
Adult	6.7	50%	5%

TAME activity (ΔOD/h/ml) was increased in 2-week old compared to adult rats ($p<0.01$). Using PAGE, we could not demonstrate the presence of α2-MG complexes in either group. Trypsin added in vitro did not form α2-MG complexes until α2-MG was separated from smaller proteins by column chromatography. Finally, the majority of TAME activity in both 2-week and adult rats was found in the plasma fraction corresponding to proteins of 200kD. The α2-MG fraction accounted for <10% of plasma TAME activity. Conclusions: 2-week old rats have increased trypsin uptake compared to adults. Unlike humans, the increased uptake is not accompanied by increased α2-MG complexes. In rats, inter-α-inhibitor (200kD) appears to be responsible for a major portion of TAME activity and also prevents trypsin binding to α2-MG.

●592 JEJUNAL CARNITINE (C) LEVELS AND ABSORPTION IN HUMANS B U. K. Li, Mark L. Lloyd, Austin L. Shug and Ward A. Olsen. (Spon. by Grant Morrow) Dept. of Pediatrics, Ohio State Univ., Columbus Children's Hospital, Columbus, OH and Depts. of Medicine and Neurology, Univ. of Wisconsin, Madison, WI

We previously characterized human duodenal uptake of C in vitro as a combined active (K_T 558 μM) and passive system (Gastro 91:10, 1986). To ascertain the response to physiologic or pharmacologic doses, serial intrajejunal and plasma levels were measured for 6 hr after either a hamburger meal [200 μmol free C (FC); 139 μmol short-chain acyl ester (SCAC)] or an oral dose of L-C (50 mg/kg). In vivo jejunal absorption was studied by the triple-lumen perfusion technique.
RESULTS: Fasting luminal levels were 9 μM FC and 15 μM SCAC. The meal raised these fractions to 209 μM FC and 130 μM SCAC at 1 hr reflecting its composition but did not affect plasma levels. The drug dose sharply increased jejunal levels to 20,660 μM FC and 3,780 μM SCAC at ½ hr falling to near baseline by 6 hr. The SCAC portion remained between 14-25% possibly representing mucosal metabolism. Although plasma FC levels doubled to 67 μM at 3-4 hr, the SCAC portion remained between 18-23%. Preliminary in situ perfusions indicate that net C flux was 58 nmol/min/30 cm gut segment at 20 μM and 484 nmol/min/30 cm at 200 μM; thus demonstrating net absorption at fasting and meal concentrations.
CONCLUSION: Absorption of C occurs predominantly by active transport under physiologic conditions and by passive diffusion during drug administration. The presence of considerable SCAC under both conditions suggests that its absorption is of potential physiologic significance.

593 IN VITRO UTILIZATION OF LACTOSE BY THE FECAL FLORA DIFFERS IN BREAST-(BR) AND BOTTLE-FED (BO) INFANTS. Carlos H. Lifschitz, May Chen, Robert J. Shulman, Meyer Wolin, and Buford L. Nichols. USDA/ARS Children's Nutrition Research Ctr, Dept Pediatr, Baylor Coll of Med, Houston, TX and State of NY Dept of Health.

The capacity of the fecal flora of BR (n = 4) and BO (n = 6) infants to degrade lactose in vitro and the effects of pH and the type of acid used to adjust pH were studied. Freshly passed stools from infants 0.25-6 mo old were analyzed for H_2, lactic (LA), acetic (Ac), and propionic (PA) acids, glucose, and pH before and after they were homogenized and incubated anaerobically for 1 hr with 1.25% lactose (L) at pH 6.8 or 5.5. pH was adjusted by addition of HCL or Ac.

	H_2		LA		Ac		PA		Glucose	
					μmol/g feces					
	BR	BO	BR	BO	BR	BO	BR	BO	BR	BO
Pre-inc*	-	-	20(30)†	8(5)	83(45)	105(51)	7(7)	17(8)	6(6)	1(2)
+L‡	11(5)	20(6)	163(52)	115(32)	305(90)	330(78)	9(11)	43(13)	6(9)	14(3)
+L +HCl§	3(2)	6(2)	164(54)	98(38)	283(115)	273(46)	8(10)	33(11)	5(6)	40(23)
+L +Ac§	3(3)	1(1)	146(27)	96(39)	208(113)	268(61)	7(8)	46(37)	7(9)	49(25)

* pre-incubated stool; †mean (SD); ‡postincubation, pH 6.8; §postincubation, pH 5.5. Preliminary results indicate that the fecal flora of BR infants differs in its metabolism of L and in its response to low pH. Stool incubates of BO infants resulted in more H_2, Ac, PA, and glucose than those of BR infants, who accumulated LA. Glucose accumulation increased in BO infants at pH 5.5, while it remained unchanged in BR infants. Ac used to adjust pH to 5.5 inhibits H_2 production in BO infants to a greater extent than does HCl; this difference was not observed in BR infants. Conclusion: These findings may imply a relationship between the type of feeding and the consequent metabolism of malabsorbed carbohydrate by the colonic flora in vivo.

594 WHO GETS IRON DEFICIENCY ANEMIA (IDA) IN INFANCY? B. Lozoff, Abraham W. Wolf, Elias Jimenez, Case Western Reserve University School of Medicine, Cleveland, and Hospital Nacional de Ninos, Costa Rica

The purpose of the proposed study was to identify nutritional and social influences on IDA in infancy. A community project in Costa Rica on the behavioral effects of IDA provided an unusual opportunity to examine such influences, since the 191 12-to 23-month-old infants were all healthy, with birth weights≥ 2.5kg, without previous iron therapy, and living in a country in which breast feeding was the norm and iron-fortified formula or cereal extraordinarily rare. Factors that were hypothesized to effect IDA (defined as a Hb< 10.5 g/dl and a low ferritin and either a high FEP or low transferrin saturation) were grouped conceptually into five stages on the basis of their remote to immediate influence on IDA: family background, neonatal factors, age and sex, caregiving conditions, and current physiologic status of the child, using weight/length percentile and whole blood lead level. Structural modeling (LISREL) was used to develop and test a model of direct and indirect effects. Direct effects were that infants with IDA had lower birth weights ($p=0.03$), consumed greater amounts of cow's milk/day ($p=0.01$), were breast fed for shorter times ($p=0.02$), had poorer home environments (HOME scale) ($p=0.01$), and had their grandparents in the home ($p=0.02$). Indirect effects were that the lower the mother's IQ the poorer the quality of home and the more likely for grandparents to be living in the household; younger mothers were more likely to live with their parents. These results suggest that preventing and treating IDA requires not only appropriate doses of medicinal iron but also attention to feeding practices and disadvantaged conditions in the home environment.

595 GASTROINTESTINAL MANIFESTATIONS OF CONGENITAL ACQUIRED IMMUNODEFICIENCY SYNDROME IN CHILDREN. Steven R. Martin, Samuel Nurko, Stephen J. Chanock, Kenneth McIntosh, and Harland S. Winter, Harvard Univ., Children's Hosp., Dept. of Medicine (Div of GI/Nutrition, Infectious Disease), Boston.

The GI manifestations of AIDS are not well characterized in children. We reviewed 9 children with congenitally acquired HIV. Clinical symptoms began at a mean age of 7.5 months (3wks-22mos); HIV seropositivity was confirmed at a mean of 20 months (3.5 mos - 5.5 yrs). Seropositive status was present at the time of study or death for a mean of 11.8 months. RESULTS: 6 of the 9 children had diarrhea and failure to thrive all within the first 9 mo. of life. Stool cultures contained possible pathogens in 6 (1 candida; 1 enterovirus and candida; 2 pseudomonas aeruginosa and candida; 1 pseudomonas and entero-virus; 1 giardia and rotavirus). 3 patients had secretory diarrhea 1 responding to Loperamide. Rectal biopsy showed non-specific colitis in 1; 2 others were normal. 4 patients with diarrhea had small bowel biopsies; 2 were abnormal (1 invasive CMV; 1 non-specific inflammation) Virus-like particles, distinct from CMV, were seen in both by electron microscopy. Five patients had severe failure to thrive and responded to aggressive nutritional therapy, (2 enteral feeds; 3 requiring TPN). CONCLUSIONS: Differences from experiences in adults with HIV infection include: 1) The spectrum of enteric infections; 2) The timing and severity of the diarrhea and growth failure; these may be related to the immaturity of infants'immune function 3) Aggressive nutritional therapy is important in the rehabilitation of these children.