89 REGULATION OF INTESTINAL SUCRASE EXPRESSION IN SUCKLING MOUSE INTESTINE.

Michael H. Hart, David Rohwer, Richard Harty.Depts of Pediatrics and Medicine, Creighton Univ. Sch. of Medicine, Univ. of Nebr. Med. Center, Omaha, NE.

Intestinal disaccharidase expression in the developing post-natal animal is under a complex system of regulatory mechanisms involving pre-programmed genetic timing as influenced by circulating humoral factors, paracrine factors, and luminal nutrients. The aim of this study was to examine the relative contribution of circulating glucocorticoids and pre-programmed genetic expression of sucrase and lactase in a suckling mouse between post-natal days 13 and 15. We examined primary jejunal and ileal organ culture explants in serum-free medium at 0-2 hours and 22-24 hours of organ culture, respectively. Animals were studied at days 13, 14, and 15, with an additional group of adrenalectomy animals who underwent adrenalectomy on day 13 with organ culture at day 15. The results of sucrase activity are shown below.

	Jejunum		Ileum	
	0-2 Hours	22-24 Hours	0-2 Hours	22-24 Hours
Day 14	0	.045 ± .007*	0	.039 ± .009*
Day 15	.055 ± .007	.049 ± .010	.018 ± .002	.027 ± .002*
Day 15 Adx	.027 ± .002+	.024 ± .005+	.015 ± .001	.015 ± .002+

* = p <.05 from 0-2 hr. controls. + = p <.05 from non-Adx controls.

In summary, day 14 tissues in organ culture for 24 hours reached the same level of expression in organ culture of serum-free media as in the intact animal on day 15. In addition, adrenalectomy on day 13 did not abolish the time-dependent expression of sucrase. However, the magnitude of expression in the basal state was diminished. We speculate that normal quantitative expression of intestinal disaccharidase in the 15-day suckling mouse is dependent upon a combination of intrinsic timing in conjunction with circulating glucocorticoids.

90 GROWTH FOLLOWING BOWEL RESECTION FOR CROHN'S DISEASE IN CHILDHOOD

Evans CM, Kirk JMW, Leaf AA, Lamkin VA, Savage MO, Walker-Smith JA.
St Bartholomew's Hospital, London, UK.

42 children requiring surgery for Crohn's disease before 17 yrs of age were studied to determine the effect of bowel resection on their growth and pubertal development. Height, weight, pubertal status and bone age were recorded by an auxologist for at least 1 yr post-operatively (mean 3.12 yrs). 20 (48%) were below the 3rd centile for height at surgery, and 13 (31%) had pubertal delay of 2 yrs or more. 6 cases had a small bowel resection, 22 right hemicolectomy, and 14 sub-total colectomy (8 with ileostomy). The children were divided into 3 groups according to pubertal status at surgery - group A (prepubertal), group B (breast/genitalia stages 2+3), and group C (stages 4+5). Mean annual growth velocities (GV, cm/yr) for the 12 months before and after surgery were:

	Gp A (n=18)		Gp B (n=14)		Gp C (n=10)	
	Pre	Post *	Pre	Post *	Pre	Post †
Males	1.85	7.40	2.81	8.20	3.32	4.50
Females	1.64	9.08	2.23	7.14	2.87	3.09

* p < 0.0001 † p = N.S.

Groups A+B showed a highly significant increment in GV after surgery, and pubertal acceleration was seen in 8 of the 13 with delay. GV correlated well with weight gain, and inversely with disease activity index and serum C-reactive protein. Poor growth in the first year post-operatively was a predictor of early disease relapse. GV varied little with site of disease or the type of operation performed. These findings suggest that surgery has an important role in the management of growth failure in CD, but should be performed before puberty becomes too advanced.

91 CEREAL BASED ORS AND CEREAL BASED FOOD CURES CHILDHOOD DIARRHOEA AND IMPROVES NUTRITION

Molla AM, Molla Ayesha, Bhutta ZA.
ICDDR,B & The Aga Khan University Hospital

Food based oral rehydration salt made from 50gm of rice and electrolytes as in WHO ORS was given a trial in 150 age matched children (6m to 3yrs) with acute diarrhoea due to rotavirus, E. Coli and V. Cholerae. WHO ORS was used as control. Cereal ORS reduced the stool output and vomiting by 45 to 50% and 60 to 65% respectively. Subsequent field application demonstrated significant reduction of duration, and weight gain (3 days vs 7 days and 44g vs 16g per month, P < .001). In later studies a traditional weaning diet known as "Khitchri with yoghurt" (K-Y diet) made of Rice, Lentils oil and yoghurt was fed to 37 children, aged 65m to 36m, with persistent diarrhoea for 14 days. Another 36 age matched children receiving soya formula served as control. After one week K-Y diet was added to the soya group. Children fed the K-Y diet demonstrated significantly greater weight gain (468 ± 75 vs 68 ± 286/gm/wk, P< 0.005) and reduce stool output (64 ± 75 vs 38 ± 16/g/Kg/d, P< 0.05). Similar change in the weight and stool volume was seen in the soya group after addition of K-Y diet in the second week. We recommend that complex carbohydrate based ORS is superior for treatment for diarrhoea. Similarly, a traditional diet based on rice, lentils and yoghurt is an effective dietary therapy for persistent diarrhoea and offers major nutritional advantages.

92 IMMUNOHISTOCHEMICAL ASSESSMENT OF THE SMALL INTESTINE IN CHILDREN WITH CONGENITAL HUMAN IMMUNODEFICIENCY VIRUS INFECTION.

Winter HS. Comb. Prog. Ped. Gastro. and Nutr., The Children's Hospital, Boston, MA.

Seven children (< three years of age) with congenital HIV were evaluated for failure to thrive. All had a history of diarrhea, but none had chronic symptoms or enteric pathogens identified by ova and parasite examination and bacterial culture of stool. An intact, columnar-lined epithelium with normal appearing villus architecture was found in 5/7 biopsies of the small intestine. In the other two children, mild focal villus shortening was noted. The lamina propria was mildly hypercellular. The characterization of lymphocyte phenotype and MHC class II antigen distribution was done with monoclonal antibodies (Leu 4, Leu 3a, OKT8, anti-TCR delta, anti-TCR beta, anti-IgG, anti-IgA, anti-IgM, anti-HLA-DR, anti-HLA-DP, and anti-HLA-DQ) and an avidin-biotin complex immunohisto- chemical staining technique. Results: The lamina propria contained increased Leu 4 (CD3) positive cells which were primarily OKT8 (CD8) and TCR-beta positive. TCR-gamma positive cells were rare in the intra- epithelial population of lymphocytes. The surface epithelium strongly expressed MHC Class II antigen DR and in 4/7 it weakly expressed DP. No epithelial expression of DQ was detected. Conclusion: In the small intestinal mucosa of children with HIV, abnormal T cell phenotype and enhanced MHC Class II antigen expression of the surface epithelium precedes injury.

93 EVIDENCE FOR REGION-SPECIFIC REGULATION AND CORTISONE INDUCTION OF SIALYLTRANSFERASE mRNA EXPRESSION IN THE DEVELOPING INTESTINE.

W. Allan Walker, Boris V. Zemelman, C. Keith Ozaki, Shu-heh W. Chu. Harvard Medical School and The Children's Hospital, Boston, MA 02115, USA.

The immature intestinal epithelium is characterized by increased sialyltransferase (ST) activity that controls the sialylation of glycoproteins and glycolipids. Cell-surface sialic acid with specific glycosidic linkages may serve as a receptor determinant for certain viruses, bacteria and their toxins, and thereby may increase the host susceptibility in neonates. Further study of the rat small intestine reveals that developmental changes in ST activity occurred primarily in the distal (ileal), but not in the proximal (jejunal) region. Furthermore, the Galβ1,4GlcNAc α2,6-ST activity, but not the Galβ1,4GlcNAc α2,3-ST activity, was the major ST activity under developmental regulation. Northern blots of total RNA prepared from the proximal and distal small intestine of neonatal and adult rats were probed with a cDNA clone encoding the rat liver α2,6-ST (a gift of Dr. James C. Paulson, UCLA). The data show that α2,6-ST mRNA expression was age-dependent and regionally specific, with the highest level of mRNA expressed in the immature distal gut. Cortisone, a known transciption modulator, when injected into suckling rats, induced expression of ST mRNA only in the distal intestine. A parallel induction of distal ST activity by cortisone was also noted. This study indicates that the levels of ST activity are well correlated with the levels of ST mRNA and suggests that developmental variation in the intestinal ST activity is mainly caused by the control of the steady state levels of ST mRNA.

94 GLYCOSYLATION OF LACTASE-PHLORIZIN HYDROLASE (L-Ph) IN RAT SMALL INTESTINE DURING DEVELOPMENT.

Edmond H.H.M. Rings, Hans A. Büller, Dasja Pajkrt, Robert K. Montgomery, Richard J. Grand.
Divisions of Pediatric Gastroenterology and Nutrition, New England Medical Center, Tufts University, Boston, USA, and Academic Medical Center, University of Amsterdam, Amsterdam, The Netherlands.

Age-specific changes in glycosylation of rat intestinal L-Ph were analyzed using enzyme immunoprecipitated from microvillus membranes (MVM) of suckling, weaning, and adult rats, and carbohydrate moieties were examined by lectin affinity binding, metabolic labeling, and neuraminidase treatment. Lectin binding indicated the presence of N-linked and O-linked oligosaccharide chains containing mannose and galactose throughout development. An age dependent shift in sialic acid and fucose was demonstrated during the period of weaning; no fucose was detectable in L-Ph until after 20 days of age, while sialic acid was reduced in adult L-Ph. The presence of sialic acid in suckling, and fucose in adult, intestine was confirmed by metabolic labeling with appropriate radioactive precursors. SDS-PAGE analysis of immunoprecipitated L-Ph from proximal and mid small intestine demonstrated two bands of approximately 220 kDa and 130 kDa in all age groups. In the distal part of the adult small intestine, L-Ph appeared as two bands of similar size to those found in the proximal and mid portions. In contrast, during the suckling and weaning period, these distal bands were approximately 225 and 135 kDa. [^{35}S]-methionine labeling and fluorography of newborn intestine confirmed these observations. This size difference was virtually eliminated by neuraminidase treatment. These data indicate that the core structure of MVM L-Ph, consisting of both N-linked and O-linked oligosaccharides, remains constant during development, although terminal sugars shift from predominantly sialic acid during the suckling period to fucose in adulthood. This alteration in glycosylation of the protein occurs in a different pattern from the post-weaning decline in L-Ph specific activity. Consequently, age dependent changes in glycosylation cannot account for the decrease in L-Ph specific activity observed during development.