

739 INDIRECT EVIDENCE FOR IMMATURETY OF GALLBLADDER AND BILE DUCTULAR WATER REABSORPTION IN THE NEWBORN DOG.

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Bile secretion in the dog is immature at birth and develops during postnatal life (Hepatology 2:717). To determine whether the developmental changes in secretory activity are associated with age-related changes in bile composition, electrolyte levels in plasma, gallbladder bile and hepatic bile were measured in anesthetized suckling puppies of 0-3 (n=3), 7-21 (n=5) and 28-42 (n=8) days of age and fed (n=4) and 24-hr fasted (n=4) adult dogs. Plasma concentrations (meq/l) of sodium (140-148), chloride (101-111), and bicarbonate (20-27) were the same in all animals. Gallbladder bile volume (ml/kg) was similar among puppies (0.2-1.7 mean=0.74) and fed adult animals (0.67±0.3), but significantly higher in fasted dogs (1.13±0.3). Gallbladder bile acid content was 65±11, 89±17, 144±27, 146±42, and 318±46 µeq/kg in these respective groups. Gallbladder sodium concentrations increased with age (176±14, 188±17, 217±18, 252±12, and 279±15 meq/l), whereas bicarbonate (43±9, 32±6, 14±7, 11±4 and 6±2 meq/l) and chloride levels (55±16, 33±11, 24±7, 16±7 and 6±2 meq/l) decreased. In spontaneously secreted hepatic bile, sodium levels increased (161±6, 167±8, 184±10, 176±12, and 179±12, meq/l) and chloride decreased (96±5, 87±9, 80±8, 74±9, and 60±14 meq/l) with age. Bicarbonate concentrations were similar in puppies of different ages (23±4, 22±4, and 19±6 meq/l), but higher in adult dogs (38±7 and 32±7 meq/l). Bile acid concentrations in these respective groups were 30±10, 14±4, 19±7, 49±7 and 78±12 meq/l. ¹⁴C-erythritol bile-to-plasma ratio also increased with age in the puppies (1.02±0.05, 1.05±0.08 and 1.24±0.11). In adult dogs, the solute ratio was higher in fasted (1.70±0.24) than fed (1.38±0.14) animals. These results support the view that, in the dog, the gallbladder and the biliary epithelium share a common mechanism for water reabsorption (Na-coupled Cl transport), and suggest that such a mechanism is immature at birth and develops during postnatal life.

740

STRUCTURAL ALTERATIONS IN ILEAL EPITHELIUM INDUCED BY L-TRYPTOPHAN S. Teichberg, R.A. Wapnir, M. Zdanowicz, B. Roberts, F. Lifshitz, North Shore Univ. Hosp. and Cornell Univ. Med. Coll., Depts. of Peds. and Labs, Manhasset, N.Y.

Alterations in ileal epithelium and villus structure during L-tryptophan (Trp) exposure were studied *in vivo* in rat ileal loops. The mucosal surface of 20 cm loops was infused for 2.5 and 30 min with isotonic Tris buffer (pH 7.3) and NaCl (140 mM) containing either 20 mM Trp, 20 mM glycine (Gly) or no amino acid. Phenol red was used to monitor water transport. Horseradish peroxidase (HRP) was added in the lumen or i.v. 5 min prior to the experimental treatment. Tissue was then examined by light and electron microscopy. After 2.5 min in Trp there were numerous large vacuoles seen in the serosal side of the apical epithelial cells. The vacuoles appeared as if derived from basolateral plasma membrane; many vacuoles were labeled with HRP injected i.v. prior to luminal Trp and there was detachment of membrane from the basal lamina. By contrast, the mucosal side of the cells was unaffected and the barrier to luminal HRP was intact. Villi and epithelium in Gly and buffer controls were unaltered. After 30 min of luminal Trp, there was marked extrusion of epithelium from the apical villus region and the luminal permeability barrier to HRP was lost. Net water transport was also inhibited by Trp (Trp = 190±09 ul/min/cm; Gly = 1.03±.11 p<.01; buffer = 94±.09 p<.01). Overall, our observations indicate that Trp alters the ileal apical epithelium and induces water malabsorption. The transport change may be linked to internalization of basolateral membrane, thereby removing transport proteins from their normal loci.

741

VITAMIN E LEVELS IN SMALL FOR GESTATIONAL AGE NEWBORNS. Vrinda Telang, Warren Rosenfeld, Hugh Evans. Downstate Medical Center, Interfaith Medical Center, Brooklyn, New York. (Sponsored by Harry S. Dweck).

Small for gestational age (SGA) newborns are frequently denied adequate nutrition during intrauterine development. The fat stores of a full term, SGA newborn are less than that of a preterm newborn of the same weight. This may result in deficiencies of essential nutrients, especially of fat soluble, lipid stored vitamins. We measured serial serum Vitamin E levels in 29 SGA and AGA neonates (G.A. 30-41 wk) in the first week of life, using Hashim's spectrophotometric micro-method. The results are tabulated below.

	Vitamin E (mg/dl)			
	N	Day 1	5	7
Full term AGA	7	0.94	1.01	1.23
Full term SGA	9	1.14	0.80	0.76
Preterm AGA	8	0.69	0.70	0.98
Preterm SGA	5	0.99	0.82	1.36

Statistical analysis using the chi square test revealed no significant differences in the Vitamin E levels in SGA newborns as compared to the control group.

The data of this small sample suggest a trend of lower serum levels of Vitamin E in full term, SGA versus full term AGA babies, although no similar trend was observed in the preterm infants.

742

THE INFLUENCE OF BREAST OR FORMULA FEEDING ON SERUM LIPOPROTEINS IN THE NEWBORN. Denis Tenenbaum, Philippe Gambert, Philippe d'Athis, Sylvie Meunier, Christian Lallemand, Jean-Louis Nivelon, Centre Hospitalier Universitaire, Hopital d'enfants, Dijon, France (Sponsored by Richard M. Cowett)

Breast milk contains more cholesterol and saturated fatty acids than commercially prepared formula. To evaluate the influence of feeding on serum lipoproteins, 43 normal term infants were studied on the first day prior to feeding and on the 6th day after birth. Twenty-two were breast fed and 21 were formula fed. Total cholesterol (TC) was measured by enzymatic analysis, HDL cholesterol (HDL C) after precipitation of light proteins with concanavalin A, and LDL apoprotein B (LDL apo B) by electroimmunodiffusion in the presence of mono specific antibody against apolipoprotein B. LDL+VLDL cholesterol (LDL+VLDL C) was obtained by the difference between TC and HDL C. On the first day there were no differences between the two groups. The results are shown for day six:

Group	TC gm/l	HDL C gm/l	LDL apo B gm/l	LDL+VLDL C gm/l
Breast	1.16±0.19	0.24±0.09	0.67±0.25	0.92±0.21
Formula	1.01±0.19*	0.31±0.11*	0.46±0.12**	0.71±0.19**
(M±SD)		*p<0.025	**p<0.001	by Two Way ANOVA

The breast fed group had significantly higher concentrations of TC, LDL+VLDL C, and LDL apo B and a significantly lower concentration of HDL C compared to the formula fed group. We conclude that the choice of oral intake will influence the serum concentrations of lipoproteins in the immediate newborn period.

743

ALANINE INHIBITION OF BILE FLOW: STUDIES OF MECHANISMS IN PERFUSED RAT LIVER. William R. Treem, David A. Piccoli, John B. Watkins. Univ. PA Sch. of Med., Children's Hosp. of Phila., Div. of Gastroenterology

We have shown that L-alanine (ALA) inhibits taurocholate (TC) uptake in perfused rat liver (Gastro 86:1283). To determine whether this effect mediates changes in bile flow, we studied the influence of ALA on bile flow, TC secretion rate and clearance (CLR) of markers of canalicular bile flow (Erythritol) and membrane permeability (Inulin). After an initial 30' bile collection, livers of male Sprague-Dawley rats were perfused with recirculating KRB buffer (control), or KRB + 5 mM ALA. TC was infused in varying concentrations. Bile was collected and perfusate sampled. Control and experimental groups were similar in body weight, pre-perfusion bile flow rate, oxygen consumption, perfusion pressure, and flow rate.

RESULTS: Data from the lowest TC infusion rate are shown.

0.25µM/min TC Infusion	Control	ALA	P
Bile flow (ul/min/100 gm)	5.87 ± 0.55	4.64 ± .29	p < .001
CLR-Eryth (ul/min/100 gm)	7.31 ± 2.16	7.02 ± 1.95	N.S.
CLR-Inulin (ul/min/100 gm)	.97 ± .18	.65 ± .18	p < .01

Higher TC infusion rates (0.5-1.0 µM/m) yielded results consistent with the data shown. Over a range of TC infusion conc. (5-400 µM), maximum TC secretion rate was not changed by 5 mM Ala (1.073 ± .078 vs 1.065 ± .061 µM/min/100 gm).

CONCLUSIONS: 1) ALA decreases bile flow rate at all TC infusion concentrations. 2) TC secretion rate is not decreased by ALA. 3) The clearance of Inulin but not of Erythritol is altered by the presence of ALA. 4) These results suggest that ALA inhibition of bile flow is mediated by net changes in canalicular membrane water flux.

744

SIALYLATION AND FUCOSYLATION OF LECTIN BINDING SITES IN RAT INTESTINAL MICROVILLUS MEMBRANES (MVM). Ramon Torres-Pinedo, Akhtar Mahmood. University of Oklahoma Health Sciences Center, Department of Pediatrics, Oklahoma City, Oklahoma.

The MVM of rat small intestine undergoes progressive desialylation and fucosylation during postnatal development. In this study, we assessed the role of this process on the terminal reactivities of MVM glycans. Purified MVM of 3-21 day-old and weaned rats were delipidated and treated with 1u of neuraminidase (Clostridium perfringens) or 0.5 u of fucosidase (bovine epididymis). The delipidated-desialylated (DDSM) and delipidated-defucosylated (DDFM) membranes (4.0 µg protein) were incubated with ¹²⁵I-labeled lectins (peanut, wheat germ, Ulex I), and the bound radioactivity measured by collecting the membranes on Millipore filters. Nonspecific binding was measured in the presence of 0.15 M specific sugars. From suckling to weaning periods: a) the binding of WGA to neuraminidase-sensitive sites decreased by 40% (p<0.01), while that of UEA₁ to fucosidase-sensitive sites increased by 13-fold (p<0.001); b) the binding of PNA to DDSM fell by 51% (p<0.02), while binding to DDFM rose by 3.7-fold (p<0.01). Next, the membrane preparations were treated with pronase (30 u), the supernates (30,000 g x 20') applied to PNA or WGA affinity columns, and the bound proteins eluted with 0.2 M lactose or N-acetylglucosamine, respectively. By SDS-PAGE, the main protein fractions were in the MW region of the mucin-type glycoproteins (260-340 K). Thus, the lectin binding properties of O-glycans in mucins of rat MVM seem to be developmentally controlled through a shift from terminal sialylation to fucosylation.