415 EFFECT OF CIMETIDINE ON PANCREATIC REPLACEMENT THERAPY IN THE MALDIGESTION OF CYSTIC FIBROSIS.

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The aim of this study was to evaluate fat and nitrogen absorption in cystic fibrosis when pancreatic replacement therapy was administered with cimetidine, an H_2 receptor antagonist and acid secretory inhibitor. Ten patients (mean age 13.9 yrs.) who had steatorrhea while taking large doses of enzymes were studied. Pancreatic insufficiency was confirmed by poor responses to secretin and CCK stimulation. Celiac sprue as a cause for malabsorption was eliminated by small intestinal biopsy. Calories were supplied as 40% fat, 20% protein, and 40% carbohydrate. Viokase and Cotazym^R were supplied at the rate of 1 tablet per 15 gms. of dietary fat. Cimetidine was given ½ hour before meals at low (L-50 mg), medium(M-100 mg), and high(H-150 or 200 mg) doses. Fecal fats and nitrogens were quantitated while enzymes alone (E) and enzymes with cimetidine (E&C) were given. Results were as follows:

(x̄±SEM	Fecal Fat (gm/24 hr)	%Fat Absorption for 72 hours	Fecal Nitrogen (gm/24 hr)
E	25.3±9.4	77.1±5.7	4.5±2.0
E&C-L	21.4±10.2	80.2±6.6	3.7±2.1
E&C-M	19.7±8.3	81.0±7.3	3.8±2.0
E&C-H	16.6±7.5*	83.6±5.2*	3.4±1.6

*P<.05 compared to E.

When pancreatic enzymes were administered with the highest dose of cimetidine, steatorrhea was significantly reduced.

416 EFFECT OF DIETARY PROTEIN CONCENTRATION UPON THE OCCURRENCE OF HYPONATREMIA IN LOW BIRTHWEIGHT INFANTS

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Association of hyponatremia (serum Na+ <130 meq/1) with variation of diet protein and electrolyte concentration was studied in 3 groups of 10 newborns (b.wt. <1500 gms, 21 AGA, 9 SGA) with the following protocols: I-SMA 20 kcal/oz (0.65 meq Na+ & 1.5 gm protein/100 ml); II-SMA 20 HP (0.65 meq Na+ & 2.1 gm protein/100ml) and III-SMA 27 kcal/oz (0.85 meq Na+ & 2.1 gm protein/100ml). Patients entered the study at mean 10.3 days and were fed 120-130 kcal/kg/d. Significant persistent hyponatremia did not occur although Group I-3 patients, Group II-5 patients, and Group III- 4 patients had one or more sporadic episodes with peak frequency Groups II & III at the 2nd & 3rd weeks of study.

SERUM SODIUM - WEEKS OF STUDY

	1	2	3	4	5	6	7	8
I	134.9	135.3	133.5	132.6	134.3	132.0	130.3	133.7
S.E.M.±	1.5	1.3	1.4	1.2	2.2	1.1	2.0	1.3
II	135.9	131.9	131.1	132.1	132.6	132.0	135.3	134
S.E.M.±	1.6	1.0	1.0	1.5	1.5	.5	.6	---
III	133.2	133.1	129.7	134.1	134.6	131.2	138.3	132.5
S.E.M.±	1.5	1.3	1.3	1.0	.6	2.4	1.3	1.5

No specific therapy was given for ↓Na+; rate of weight gain from start of study (gm/d) were: I-19.4, II-21.0, III-23.3. Increase of formula protein concentration had no significant effect on the incidence of ↓Na at the volume and calories utilized, weight gain was appropriate in all groups with Na intake of 1.13-1.28 meq/kg/d.

417 HISTOLOGIC CRITERIA FOR DIFFERENTIATION OF ACQUIRED MONOSACCHARIDE INTOLERANCE (AMI) AND GLUTEN SENSITIVE ENTEROPATHY (GSE).

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AMI is a condition of infants under a year of age characterized by chronic acidic diarrhea, severe failure to thrive, total carbohydrate intolerance (including glucose) and no correlation with gluten content of the diet. Histological changes observed on small bowel biopsy range from moderate to severe villous atrophy. GSE, a condition seen in children in the similar age group, has some similar clinical features and villous atrophy. In order to define histologic criteria to differentiate the clinical conditions, mucosal biopsies were studied from 9 AMI, 6 GSE and 14 age matching controls ranging from 2 to 30 months. No quantitative differences were found by light microscopy in the thickness of the mucosa, villous height, crypt depth & villi/crypt ratio between AMI and GSE. Quantitative differences were observed in mitotic index (MI) (# of mitotic figures/100 crypt cells): 3.7 ± 1 in AMI vs 7.5 ± 4 (GSE), $p < 0.01$. Maximum mitotic migration (MMM) along the crypt walls (expressed as the fractional migration of the most distant mitotic figure from the base of the crypt along the crypt column) was 0.5 ± 0.1 (AMI) vs 0.8 ± 0.1 (GSE), $p < 0.01$. The interepithelial lymphocyte court (ILC) was 12 ± 2 (AMI) vs 45 ± 26 (GSE), $p < 0.001$. The diagnosis of AMI and GSE can be made by light microscopy using: MI, MMM and ILC. Support: Venezuelan Nat. Acad. of Sciences, NIH.

418 RED CELL PEROXIDE-HEMOLYSIS (RCPH) IN CHRONIC MALABSORPTION: REVERSAL BY FATFREE PARENTERAL NUTRITION.

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While investigating the adequacy of vitamin supplementation in fat-free parenteral nutrition (FFPN), 13 children with malabsorption showed abnormal susceptibility of RC's to H_2O_2-hemolysis while plasma Vit E levels were in the range appropriate for age. By day #15 of FFPN, the RC's were resistant to peroxide. RCPH-rates and the biochemical parameters were (mean ± SEM):

	N	day#1PN	day#15PN	postPN day#7
RCPH% @ 60 mins	13	42 ± 3	10 ± 3	6 ± 2
Vit E ug/dl	13	360 ± 80	470 ± 70	610 ± 100
GSH.Px U/dl RC	3	303	516 (day#7)	---
Vit E/Tot Lipid	13	0.63	0.91	1.05

RCPH @ 60 mins correlated with RC lipid-peroxides ($r=0.88$), but not with Vit E. When RC Glutathione Peroxidase (GSH.Px) was measured in 4 children, high RCPH-rates were initially associated with low GSH.Px in 3 children with malabsorption. One week of FFPN raised the GSH.Px and abolished RCPH. In one child, interruption of FFPN for 5 days because of sepsis resulted in a dramatic rise in RCPH, unrelated to plasma Vit E. The correlation between GSH.Px and RCPH ($r=-0.86$) shows that provision of adequate aminoacids and calories is associated with increased GSH.Px activity perhaps through early enzyme induction, and suggests a dominant role for GSH.Px in degradation of hydroperoxides.

419 EFFECT OF D-GALACTOSE ON THE FLUID LOSS IN SOYBEAN PROTEIN (SBP) INTOLERANCE.

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The mechanism of intestinal fluid loss in SBP intolerance is not known. The possibility of absorptive disturbances was examined in 82 symptomatic infants. Stool composition, oral absorptive tests and mucosal disaccharidases ruled out absorptive impairment in most infants. The possibility of a secretory disturbance was examined in 10 infants by the intestinal perfusion method. 0.142 M NaCl, 5 mM D-glucose (A) and 0.142 M NaCl,5 mM D-galactose (B) were perfuse in the proximal jejunum following soy protein-sucrose feeding. Net water, Na and Cl secretion occurred during perfusion of A and changed to net water and ion absorption during perfusion of B ($p < .001$). The effect of D-galactose was then tested clinically by substituting lactose for sucrose in the soy formula. Symptoms of intolerance ceased immediately. Re-examination of the water and ion fluxes after 1 mo. of SBP-lactose feeding showed equal rates of absorption during perfusions of A and B. It was postulated that D-galactose, but not D-glucose, inhibited and SBP-mucosal surface interaction underlying the mechanism of fluid loss. This assumption finds support on the known specificity of soybean protein (glycinin) for galactosyl receptors in membrane glycoproteins.

420 ENHANCED JEJUNAL MACROMOLECULAR ABSORPTION INDUCED BY SECONDARY BILE SALTS.

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This study concerns the deleterious effects of secondary bile salts, taurodeoxycholate (TDCh) and deoxycholate (DCh), particularly on small intestinal macromolecular absorption. Rat jejunal segments (30-40 cm) were perfused in vivo with an isotonic NaCl-glucose solution (pH 6.9) containing 0.5 g% of horseradish peroxidase (HRP) a macromolecular tracer, with 5mM TDCh or DCh or without bile salts (C). After 30 and 60 min serum HRP levels and cytochemical HRP localization were determined. Both TDCh and DCh induced a greater absorption of HRP than C: at 30 min TDCh .157+.005, DCh .439 +.080 vs C .082 +.010, and at 60 min TDCh .381 + .061, DCh 1.001 + .138 vs C .114 +.011 (data = u/ml means + SEM, $p<.001$). The most striking absorption of HRP was with DCh. Under light and electron microscopy HRP was demonstrable in the intercellular spaces between enterocytes, in the basement membranes, and capillaries of the lamina propria of the jejunum. In contrast, in C, HRP was confined to the microvillar brush border and endocytotic structures of enterocytes. DCh also produced ultrastructural damage including swollen mitochondria and vacuolization of membrane systems whereas TDCh did not alter the intestinal epithelium. These results indicate that high concentrations of secondary bile salts enhance macromolecular absorption and induce functional damage to the jejunal epithelium. Deconjugated bile salts are the most injurious.