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EFFECT OF DIETARY FAT ON METHOTREXATE INDUCED MUCOSAL INJURY IN THE RAT. J.A. Vanderhoof, M.D., JHY Park, Ph.D., D. Blackwood, B.S., H. Mohammadpour, B.S.
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We have previously shown that dietary linoleic acid stimulates small bowel mucosal growth following intestinal resection. To determine if linoleic acid may also be important in recovery from mucosal injury, such as occurs in infectious diarrhea, 70 male weanling Sprague-Dawley rats (50 g) were pair-fed a low fat (0% safflower oil, 42 rats) or a normal fat (1% safflower oil, 28 rats) diet for 34 d. Mucosal injury was then induced using methotrexate (MTX), 2.5 mg/kg/d x 3 d, after which animals were pair-fed either a normal fat (1% safflower oil), low fat (0% safflower oil), or high fat (10% safflower oil) diet. Half were killed 3 days later, the other half 12 days later. Mucosal protein (mg/cm bowel):

% Fat	Pre/Post MTX	0/0%	0/1%	0/10%	1/1%	1/10%
Jejunum 3 d	4.28±0.74	4.47±0.61	4.51±0.70	3.60±0.53	2.71±0.17	
Jejunum 12 d	5.35±0.42	6.73±0.46	6.00±0.36	6.98±0.69	6.15±0.31	
Ileum 3 d	5.44±0.46	6.14±0.35	5.70±0.73	5.41±0.79	4.93±0.61	
Ileum 12 d	4.61±0.17	5.29±0.24	5.51±0.34	6.39±0.69	6.62±0.10	

In general, changes in mucosal wt. and DNA content paralleled these findings. Histology showed comparable changes. Measurement of glucose and leucine uptake by intestinal sacs failed to show differences between dietary groups. Feeding large quantities of linoleic acid to rats following mucosal injury appeared to exacerbate damage to the jejunum at 3 days, this being the site of greatest injury caused by MTX. By day 12, a trophic effect of the high fat diet was apparent, especially in the ileum. The role of linoleic acid as a substrate for both mucosal leukotriene and prostaglandin synthesis may be a factor in these findings.

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DEVELOPMENT OF Cl SECRETION IN ADRENALECTOMIZED NEWBORN RAT STOMACH

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We previously demonstrated that rat gastric HCl secretion that develops from the end of gestation drops to zero by postnatal day 12 when absence of H⁺K⁺ATPase activity and neutral NaCl absorption are observed. Rapid increase of HCl secretion after day 12 follows elevation of plasma corticosterone. Is development of Cl secretion after day 12 induced by corticosterone? This question was examined in adrenalectomized (Ad) newborns. Pups were Ad on day 8 and gastric mucosa mounted in Ussing chamber on day 15. Unidirectional and net ³⁶Na and ³⁶Cl fluxes were measured under short-circuit conditions and compared to those of non-operated and sham-operated newborns. Ad was checked on day 15 by RIA of plasma corticosterone.

Ad significantly reduced short-circuit current without modification of tissue conductance. Reduction of unidirectional fluxes of both Na and Cl was observed with slight decrease in Na net absorption but a significant increase in neutral Cl net secretion. We conclude that Ad does not prevent Cl secretion development in 15 days old newborn. In vivo, development of Cl secretion after day 12 is not likely induced by corticosterone.

3

CHANGES IN JEJUNAL EPITHELIAL MORPHOLOGY & KINETICS DURING SUCKLING & WEANING IN THE GROWING GUINEA PIG

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Weaning, the nutritional adaptation from milk to solid diet, demands changes in GI function. We measured jejunal mucosal morphology and kinetics during suckling and weaning to determine if the marked changes seen in the altricial rat also occur in the precocial guinea pig (CP). 79 animals were studied. Groups of at least 3 CPs aged 1, 7, 14, 21 and 28 d were given IP colchicine at time 0, and killed at 20 to 30 min intervals. Tissue was taken 5 cm from the pylorus, fixed and bulk stained with Schiff reagent. Jejunal morphology was measured by microdissection and crypt cell production rate (CCPR) by a metaphase arrest technique. There was a 40% decline in villus ht. from 986 µm to 618 µm (p<0.001), and 25% increase in crypt depth, from 148 µm to 199 µm (p<0.01), during the first 2 wks. After an initial decline there was an increase in crypt: villus (C:V) ratio from 6.7 to 8.2, and in CCPR from 3.9 to 5.6 cells/crypt/hr from 14 d onwards (p<0.001). These changes represent a proliferative response of jejunal epithelium during the 3rd & 4th postnatal weeks, accounted for by increase in the depth and number of crypts, and CCPR, leading to increase in net villus influx. In contrast with the rat in which abrupt changes in epithelial morphology, function and kinetics occur around d 21 at the time of cessation of suckling, in the CP they are gradual and follow weaning by some days. The CP, which in many respects more closely resembles man than rat, is a more suitable animal model for our understanding of human GI maturation and perinatal nutritional adaptation.

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ADENOVIRUS 12 INFECTION AND COELIAC DISEASE

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It is noteworthy the region of amino acid sequence homology between A gliadin and the early region Elb protein of human adenovirus 12 /Ad 12/. The encounter of immune system with Elb protein produced during viral infection may be important in the pathogenesis of coeliac disease /CD/ because of immunological cross reactivity. We have investigated the prevalence of neutralising antibody to Ad 12 among children with treated CD /16 girls, 7 boys, mean age: 8,7 years, range: 4.0 – 13.9 years/. 23 age-matched children served as controls. Serial two fold dilution of sera were incubated with the same volume of 20 TCID₅₀ of Ad 12 at 37°C for two hours, then the mixtures were added to the test tubes containing of HEp2 cell culture. The cytopathic effects were examined after five to six days incubation. Reciprocal neutralising antibody titres greater than 4 arbitrarily were regarded as positive. 12 of 23 treated coeliac children had neutralising antibody to determinants on the structural hexon protein of Ad 12. In contrast such antibody was present in only 5 of 23 controls /p<0.05/. No correlation was found between the neutralising antibody titres and the time elapsed from diagnosis of CD. The role of Ad 12 in the pathogenesis of CD may be possible on the basis of our results.