47 PROTRACTED DIARRHOEA AND AUTOIMMUNE ENTEROPATHY: A GENERALISED AUTOIMMUNE GUT DISORDER WITH A COMMON HLA HAPLOTYPE

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In children with protracted diarrhoea, circulating enterocyte auto-antibodies (Ec Ab's) and an enteropathy, diarrhoea may persist despite therapy. We have examined the colon endoscopically in 17 such patients. Multiple biopsies were studied histologically, and by immunocytochemistry for HLA class II expression and T cell populations, and compared with histologically normal colon from control subjects. In addition, in view of the probable autoimmune nature of the diarrhoea HLA typing was done. 14/17 patients had a colitis characterised endoscopically by oedema and patchy erythema throughout the colon, and histologically by an inflammatory infiltrate of lymphocytes and plasma cells without crypt dysplasia, goblet cell changes or epitheloid granulomas. Class II (DR complex) expression was absent in both surface and crypt colonocytes of histologically normal colon (controls and 3/17 patients), but aberrant expression of DR molecules was seen in the 14 patients with a colitis. DR + ve lamina propria lymphomononuclear cells were present in patients and controls. Intraepithelial T cells were increased in 1 of 2 patients examined, and were CD8 + ve. On peripheral blood HLA typing patients were predominantly HLA CW7 (67%), DR3 (58%) and commonly B8 (38%). Our data shows that the HLA type in children with autoimmune enteropathy is consistent with that seen in other autoimmune diseases, and in over 80% intestinal inflammation extends to the colon where colonocytes may perpetuate the disease by acting as antigen presenting cells.

48 6 HOURS POST-PRANDIAL pH MONITORING: AN ADEQUATE TEST FOR GASTRO-OESOPHAGEAL REFLUX IN CHILDREN AND INFANTS

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24 hour ambulatory pH monitoring is the "gold" standard for detecting gastro-oesophageal reflux (GOR) but requires an overnight admission. In children there are few studies of abbreviated pH monitoring suitable for day patient use. Some have suggested that in infants GOR is mostly post-prandial thus abbreviated post-prandial pH monitoring may be a suitable test for reflux. Others believe that in infants most GOR occurs when asleep. We have investigated 100 patients (20<6 months) by 24 hour (24) and 6 hour post-prandial (6PP) ambulatory pH monitoring using a naso-oesophageal probe with its tip 1cm above the lower oesophageal sphincter and a Synectics Digitrapper. 55 patients were investigated for vomiting, 17 with feeding problems, and 28 with respiratory symptoms. 69 were endoscoped and 22 had oesophagitis. Acid exposure time was calculated as the proportion of time with pH below 4. A total acid exposure time greater than 5% was found in 71/100 on 24 and 61/100 on 6PP with a correlation of r=0.7. There were 10 false negatives 3 with >10% reflux. Those with severe reflux (>20% 20/71) were detected in both tests. In those under 6/12, 13/20 refluxed on 24 and 12/20 on 6PP. Only 3/20 had significantly more reflux in the sleep period. The data indicates that 6PP is as good as 24 at predicting severe reflux and an adequate prediction of the degree of acid reflux in both infants and children for those with moderate reflux. GOR did not occur significantly more frequently during sleep in infants under 6/12 of age.

49 PERSISTENT TACHYGASTRIA IN SEVERE NAUSEA AND VOMITING

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The integrated action of smooth muscle cells, polypeptide hormones and the enteric nerves is required for normal motor activity which may also undergo modulation by the central nervous system. Nausea and vomiting may result from disorder of such controls of antral and duodenal contraction. We have previously shown (Ped. Res. 24: 409; 1988) that disordered activity can be detected non-invasively by recording antral electrical control activity (ECA) from bipolar skin electrodes. We have recorded ECA in 22 children with a history of vomiting (age 6.1±4.2 yrs), 4 with anorexia (9.6±5.8 yrs) and 15 control subjects (12.1±5.3 yrs). A running spectral analysis of overlapping 128 second segments of the recording was performed using an auto-regressive modelling method on a personal computer. In all controls, anorexics and 18/22 vomiters, a dominant frequency of 3cpm which slowed on feeding was seen. In 4 who were nauseated and vomiting, a tachygastria of 6cpm was persistently present, which resulted in uncoupling of electrical and mechanical activity. These patients either suffered from local smooth muscle disease, or CNS disorder, or enteroenteric reflex activity, (subacute obstruction) or an altered humoral environment (post-operative ileus). Our data shows that persistent tachygastria associated with severe resistant vomiting may not only be due to smooth muscle disease as has previously been reported but also to abnormality of the other control factors.

50 SIMULTANEOUS NON-INVASIVE MEASUREMENT OF GASTRIC EMPTYING AND ANTRAL MOTOR ACTIVITY USING APPLIED POTENTIAL TOMOGRAPHY

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Contraction of smooth muscle may be detected electrically as spike potentials or electrical response activity (ERA) but requires difficult highly invasive methods. We have previously shown that gastric antral electrical control activity (ECA) can be recorded from skin electrodes (Ped Res 24:409; 1988) and now have devised a means of simultaneously measuring antral contractions and their functional correlate gastric emptying. Applied potential tomography (APT) is a new non-invasive technique which yields sequential images of resistivity of the stomach via skin electrodes and has been used to measure gastric emptying of liquid and semi-solid meals and acid secretion. As during smooth muscle contraction changes in resistivity occur APT will detect them. In 7 control subjects we assessed emptying of two different test meals and the presence and frequency of ERA and ECA. Gastric emptying profiles were computed and ½ emptying times ($t_{\frac{1}{2}}$ derived). $T_{\frac{1}{2}}$ for 5% dextrose were 15 mins, median, range 13-22 and for OXO 34 mins, range 25-43. ERA was present continuously during emptying and there was good correlation between ERA and ECA (2.8 ± 0.25 vs 3.2 ± 0.4 cp.m). APT not only measures gastric emptying, and our results are similar to other studies, but also allows simultaneous study of control and response aspects of antral muscle contraction. This method should prove useful in the detection of defects of gastric motor activity in children and for monitoring interventional therapies when repeated studies are required.

51 INTERLEUKIN 1β PRODUCTION BY COLONIC MUCOSA FROM CHILDREN WITH CROHN'S DISEASE

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Intereukin 1β (IL-1) is a mediator of many of the biological activities important in inflammation. It is still controversial whether there is increased activity of IL-1 in Crohn's disease (CD). Mucosal biopsies taken at colonoscopy from 5 children with CD and 5 control patients were studied. All children had presented with chronic diarrhoea, and in all 5 with CD a histological diagnosis had been made. 3 of the 5 were on immunosuppressive treatment with Prednisolone. The colonic histology was normal in 3 control children, but 2 had a mild non-specific colitis (NSC). 3 colonic biopsies were taken from each child, 2 was snap frozen and stored and 2 were cultured for 24 hours in 2 mls of standard culture medium. After 2 hours, LPS (50 µg/ml) was added to one of the biopsies. After 24 hours the biopsies and supernatants were havested and stored. An ELISA assay, with a sensitivity of 400-1000 µg/ml was used to measure the concentration of IL-1β in the supernatant. In supernatants from normal controls no IL-1B was detected but in 3/5 with CD it was present (0.05, 1.42, 1.7 µg/ml) and in 1 with NSC (1.1). Following stimulation with LPS, IL-1B was present in all with CD and 1 with NSC. In 3/5 with CD it rose markedly (0.2 - 0.8, 0.4 - 1.6, 0.5 - 1.4). In conclusion IL-1β secretion was detected in CD and NSC. The phenomenon was enhanced by LPS and may not be specific to the inflammation of CD.

52 EVALUATION OF INTESTINAL FUNCTION IN AIDS.

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A longitudinal (9 to 14 months) evaluation of the intestinal function has been performed in 5 children with AIDS (age range 3 months - 9 years).

Diarrhea was observed in two children. One showed 5 episodes of acute, self-limiting diarrhea. The other was diagnosed as having cow's milk protein intolerance and had 5 episodes of diarrhea, 4 of which as a consequence of cow's milk protein ingestion.

All the tests were performed by published methods, while on a normal stool pattern. d-xylose and iron oral loads were positive in 2 out of 3 patients tested. The determination of steatocrit showed steatorrhea in 4/5 cases. Fecal leucocytes were present in 1/3 and increased fecal α1 antitrypsin was found in 2/4. Search for enteric pathogens, including Criptosporidia, was always negative. One child carried a Giardia in her stools. Determination of antigliadin IgG and IgA was positive in 4/4 and 2/4 patients respectively; 2 had intermediate levels of IgA. Although diarrhea was observed in only 2 children and was always mild, several tests indicated an impairment of intestinal function in all cases, suggesting a frequent involvment of upper intestinal function associated with AIDS. The increase in antigliadin IgG and IgA antibodies might be related to alterations of the intestinal permeability and/or to the immunological derangement.