Intestinal permeability

Editor,—We read with interest the paper by Dr Orishi and colleagues (Gut 1995; 36: 891–6) investigating intestinal permeability and the immune response to enteric bacterial antigens in patients with inflammatory bowel disease. Their finding of an increased systemic concentration of antibodies to lipid A in patients with colitis as compared to controls, is in agreement with studies showing increased titres of antibodies to the endotoxin core, 1 to peptidoglycan-polysaccharide complexes,2 and to a variety of enteric bacteria3 in these diseases.4 The study by Dr Orishi and colleagues,5 however, does not provide the same evidence of increased intestinal permeability in these patients. Their study was carried out in patients with colitis, and not in controls, and the results are not comparable.6

The study by Orishi and colleagues also proves the point that the pattern of antibody response to enteric antigens is different in patients with Crohn’s disease from those with ulcerative colitis. 1 There is an increase in the systemic concentration of IgG to endotoxin core/lipid A in patients with Crohn’s disease but not in those with ulcerative colitis. Systemic IgM concentration to endotoxin core/lipid A is not increased in patients with either disease. With regard to IgA, we similarly found that the plasma concentration of IgA to the endotoxin core was increased (although not significantly) in patients with Crohn’s disease (107.3–20.5 median units) and ulcerative colitis (93.0–24.2) in comparison with healthy controls (61.3–15.7). We are unable, as yet, to explain these differences.7 The mechanism of increased intestinal permeability in patients with Crohn’s disease needs further study.

Lactulose has been shown to eliminate systemic endotoxinemia in a hapten induced rat model of colitis and has been suggested as treatment for patients with inflammatory bowel disease.8,9 The mechanism of the anti-endotoxin action of lactulose is not clear, as lactulose treatment did not have any significant effect on the faecal count of Gram negative bowel bacteria in the experimental model of colitis.8 It has generally been assumed that lactulose is fermented rapidly by colonic bacteria and that colonic absorption after oral administration would be minimal.10 Their study is also interesting with regard to treatment for impaired gut barrier function. Lactulose has been shown to eliminate systemic endotoxinemia in a hapten induced rat model of colitis and has been suggested as treatment for patients with inflammatory bowel disease.9,11 The mechanism of the anti-endotoxin action of lactulose is not clear, as lactulose treatment did not have any significant effect on the faecal count of Gram negative bowel bacteria in the experimental model of colitis.8 It has generally been assumed that lactulose is fermented rapidly by colonic bacteria and that colonic absorption after oral administration would be minimal.10

2 Sartor RB, Cleland DR, Akkalis CG, Schwab JH. Serum antibody to bacterial cell wall peptidoglycan in inflammatory bowel disease patients. Gastroenterology 1985; 88: 1517A.

Reply

Editor,—We thank Mr Keith Gardiner and his colleagues for their comments.

We are aware of the anti-endotoxin action of lactulose. In our study, however, we used lactulose as a marker of intestinal permeability. Anti-lipid A antibody concentrations were not influenced by lactulose with an anti-endotoxin action, because anti-lipid A antibody concentrations were measured just before lactulose administration. Lactulose may be useful in both evaluation of disease activity and treatment in diseases with an increasing intestinal permeability and endotoxemia, such as inflammatory bowel disease, alcoholics in a therapeutic phase of Crohn’s disease, the continuous administration of lactulose may be interesting. We look forward to further study on this subject.

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Hydatid disease

Editor,—We read with interest the leading article by Dr D L Morris (Gut 1994; 35: 1517–8). We agree with the points concerning treatment of the hydatid disease, however, we are in disagreement with Dr Morris’ statement ‘there are two forms of echinococcus that affect the liver of humans, E granulosus and E multilocularis’.1 Rausch and Bernstein in 1972 described a new species of echinococcus named E vogeli.2 Furthermore E vogeli was found to be the aetiologic agent of the hydatid disease in several patients from Colombia, Venezuela, Equador, and Panama, most of them showing hepatic involvement by the disease.3 More recently, we had the opportunity to study nine patients with hydatid disease, seven of them from the Brazilian Amazon region; eight of nine showed extensive involvement of the liver.4 Another study of six additional patients from the state of Acre (Amazon region) showed severe involvement of the liver.5 (Menehelli et al, unpublished data). All of these patients showed pathological findings that allowed us to establish the diagnosis cystic echinococcosis.6 Subsequently new cases of this neotropical hydatidosis have been detected in Brazil by Ferreira et al and by D’Alessandro et al (unpublished data). It seems that the disease is an extensive distribution in South America, mainly in the Amazon region. All patients we studied had extensive involvement of the liver making a surgical approach impossible. We found that albendazole is effective for the treatment of the disease.7 Thus we consider that we have enough evidence to say that there are at least three species of echinococcus that affect the liver of humans: E granulosus, E multilocularis, and E vogeli. Moreover there is a possibility, although rare at the moment, that E oligarthrus, may also cause hepatic disease in humans.

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Gastric mucus viscosity and Helicobacter pylori

Editor,—The article in Gut by Markesich et al reports that H pylori infection does not cause reduction in the viscosity of human gastric mucus gel (Gut 1995; 36: 527–9). The findings contradict the results of our three studies,1–3 and misquote the source of materials with which the work was carried out.1,2 Contrary to the authors’ assumption, we never used commercially obtained mucin and the work included human gastric mucus, as well as its purified mucin.4,5 Furthermore, our assays of H pylori enzymatic activities were carried out with enzyme enriched protein fraction under well defined conditions.6 These studies showed that H pylori through its mucolytic enzyme activities is capable of exerting a detrimental effect on gastric mucus gel viscosity.7 The viscosity data presented by Markesich et al were obtained directly on gastric juice samples from patients with and without H pylori infection, and do not provide any information on the mucolytic enzyme activities of the bacterium, nor for that matter on

1 Rausch RL, Bernstein JJ. Echinococcus vogeli sp n (Cestoda; Taeniidae) from the bush dog Speothos venaticus (Lund), E Echinococcus Parish 1923; 25: 35–4.
the effect of other degradative enzymes present in the samples. Hence, the results obtained by Markesich et al are not comparable to that of ours.1 2 3 4 Studies with gastric juice performed by others5 however, showed lower viscosity values for \( H \) pylori positive patients than that of \( H \) pylori negative patients. Also hydrophobicity measurement data totally argue against the conclusions reached by Markesich et al.

There may be several reasons for the different results obtained by Markesich et al. The most important are the lack of control for the peptic activity during the processing and the most likely method for the preparation of the measurements. As such, the ‘mucus gel’ samples obtained after the centrifugation in both cases represent only the undegraded mucus, as the degraded one would remain in the supernatant. Hence, the viscosity measurements on the materials prepared from patients with and without \( H \) pylori infection were carried out only on the undegraded insoluble mucus gel. No reference of any sort was made to the sample concentration (for example, mg protein/ml). The conditions used for ‘mucus gel preparation’ (for example, centrifugation 10 000 rpm for 15 min) would result in the insoluble fraction consisting of some undegraded mucus, cell debris, and other particulate matter. Consequently, this kind of material would give very high and erroneous viscosity values, as is the case in this study.

We would also like to point out that the study by Markesich et al, in contrast with their contention, represents typical in vitro experiments, and unless a method is devised to take the viscosity measurements directly in the stomach, the claim is not valid.

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7 Goggin PM, Marrero JM, Spychal RT, Jackson KS, Northfield TC. Surface hydrophobicity of gastric mucosa in \( H \) pylori infection: effect of clarification and eradication. Gastroenterology 1992; 103: 1486–90.

Copper associated childhood cirrhosis

EDITOR.—The report of copper associated childhood cirrhosis by Horslen et al (Gut 1994; 35: 1497–500) is of considerable interest. But I take issue with one small point. The authors cite a case reported by Bartók et al1 in 1971 as an instance of idiopathic hepatic copper toxicity. A glance at the original publication arouses doubts whether another diagnosis might be correct. Early last year, through the courtesy of Professor J Ormos of the University of Szeged, I was sent a block of liver tissue from that case (see Figures). Stainable copper in large amounts was present, but other findings – using both immunohistochemical and standard techniques – confirmed my suspicion that the underlying disease was \( \alpha \)-antitrypsin deficiency. This diagnosis had been recognised and published in the Hungarian literature;1 I was not aware of this when I asked for tissue.

In any event, it is time that this patient’s case no longer be invoked as an instance of non-Indian copper associated childhood cirrhosis or idiopathic hepatic copper toxicosis. Given parental consanguinity, a she of course may have had \( \alpha \)-antitrypsin deficiency and another defect involving copper handling, but this is speculation.

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