letters, book reviews


Experimental colitis is ameliorated by inhibition of nitric oxide synthase activity

EDITOR,—We congratulate Rachmilewitz and colleagues for their paper discussing the effects of nitric oxide synthase inhibition on experimental colitis in the rat (Gut 1995; 37: 247-55). Using a rat model of colitis induced by 30 mg trimetobenzenesulphonic acid in 0.5 ml 5% ethanol (TNBS/E) we have similarly shown the importance of the L-arginine-nitric oxide pathway in mucosal inflammation. L-arginine given by mouth, the biosynthetic precursor of nitric oxide, promoted the inflammatory response in experimental colitis. Administration of Nω-nitro-L-arginine methyl ester (L-NAME) to the arginine supplemented diet reduced both colonic inflammation and weight loss. In accordance with Rachmilewitz and colleagues, we have also found that oral administration of L-NAME in man, as an oral solution (500 mg/l) or as an enema, (1 g/l) reduced colonic inflammation in this model of colitis.

Bacteria, bacterial products, and cytokines may all promote the expression of calcium independent nitric oxide synthesis in the colonic mucosa. There is evidence that enteric bacteria and their products can penetrate the gut mucosal barrier in patients with inflammatory bowel disease and in experimental models of colitis. 2 Increased faecal concentrations of tumour necrosis factor have also been shown in both IBD and TNBS/E induced colitis. 3 In addition we have recently shown that administration of an anti-tumour necrosis factor antibody reduces the inflammatory response in this model of colitis. 4 It is therefore possible that these bacterial products may also exert a pro-inflammatory action in patients with IBD by the induction of nitric oxide synthesis.

We agree with the authors that modulation of nitric oxide synthase activity may have therapeutic potential in IBD. As shown by Rachmilewitz and colleagues L-NAME given by mouth has potent hypertensive effects, which may limit its usefulness in the treatment of patients with chronic IBD. Topical administration of L-NAME in intestinal fluid, may confer beneficial anti-inflammatory effects with reduced cardiovascular complications.


Reduced NO synthase activity in patients with colitis

EDITOR.—We were interested to read the thought provoking paper on heartburn in patients with colitis, in which the authors hypothesised that the heartburn described by 48% of colitis patients eligible for review was related to gastro-oesophageal reflux disease (GORD) and documented on manometry a relative reduction in basal lower oesophageal sphincter pressure in such patients (Gut 1995; 37: 305-8).

They themselves note that there are many alternative causes for heartburn in patients with colitis and that treatment with anti-reflux surgery or medical treatment is appropriate before the time of treatment by surgical myotomy.

Following an initial study examining the need for an antireflux procedure during laparoscopic Heller’s cardiomyotomy, 1 we have not found that colitis patients undergoing such surgery have a protocol that includes pre and postoperative 24 hour pH monitoring. The 12 patients who have undergone preoperative 10 day pH monitoring had a normal composite DeMeester score of 0.45 (range 0.2-16.8) (upper limit of normal 14.72 at pH threshold <4) only one patient showed abnormal oesophageal acidity at this stage. Postoperatively in 10 patients the mean DeMeester score increased to 6.00 (range 2.19-19.6) with two patients lying outside the normal range, one of whom had probably had an inadequate myotomy.

Preoperative significant reflux was extremely uncommon and these results do not support the hypothesis that the heartburn experienced by patients with colitis is due to acid reflux. Even after a myotomy completely dividing the lower oesophageal sphincter very few patients showed significant GORD despite their aperistaltic oesophagus and it seems likely that factors such as the reflux of food into the stomach can effectively prevent reflux in most patients. A survey of 75 reports reviewing 5002 patients with colitis revealed an average incidence of postoperative GORD of 8.6%. 4 It is improbable that this large number of patients refluxed significantly before their development of their colitis as speculated by your authors.


Heartburn in patients with colitis


The explosion in information technology has revolutionised the way knowledge is sought and processed, but in a manner that reduces the impact of pictorial images on education. The role of the classic textbook as pivotal to teaching is increasingly challenged by
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