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Tumour necrosis factor and platelet activating factor in stool during salmonellosis

EDITOR.—We read with interest the work of Harendra de Silva *et al* (*Gut* 1993; 34: 194-8) reporting interleukin 6 and tumour necrosis factor (TNF) in the stool of children with *Shigella dysenteriae* infection. We are particularly interested by data reporting the absence of TNF in the stool of patients with *Salmonella* infection.

Platelet activating factor (PAF) is a phospholipid mediator implicated in gastric ulceration and ischaemic bowel necrosis.¹ Tumour necrosis factor generates PAF production in human monocytes.² A close relation has been reported between PAF and TNF in the gastrointestinal tract where PAF mediates TNF induced damage.^{3,4} Platelet activating factor and TNF have been reported in the stool of patients with inflammatory bowel disease.^{5,6} Furthermore PAF is released in the stool of patients with bacterial (*Salmonella*, *Clostridium difficile*) but not with viral (rotavirus, adenovirus) or parasitic (*Cryptosporidium*) diarrhoea.⁷ The lack of TNF in the stool of patients with *Cryptosporidium* or rotavirus may be related to the absence of a faecal PAF. The lack of TNF in the stool of patients with salmonellosis is, however, surprising and suggests, for the first time, that in some gut inflammatory states TNF is not essential for the amplification or initiation, or both of PAF release. To confirm this hypothesis it could be of interest to assess faecal TNF concentrations, for example during *Clostridium difficile* colitis. The lack of TNF and interleukin 6 in the stool of patients with salmonellosis strengthens the putative role of PAF in the ulceration and inflammation seen in the gastrointestinal tract of these patients.

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Oroileal transit of 5-aminosalicylic acid

EDITOR.—We read with much interest the elegantly performed study by Goebell *et al* (*Gut* 1993; 34: 669-75) concerning the fate of 5-aminosalicylic acid (5-ASA) from Salofalk in the small intestine. The study elucidates some important aspects on the bioavailability of 5-ASA (pH of the gut lumen, the intestinal transit time).

We would like to comment, however, on the interpretation of the results. The authors conclude, that 30% of the ingested dose passed the ileum in solution, which is similar to the results from ileostomates on Salofalk.¹ Another 10% was found in the urine, and it is therefore concluded that 60% reach the colon in unreleased form. The design of the study does not permit this conclusion because the localisation of undissolved tablets was not assessed. In fact, some tablets could still be retained in the stomach. As the authors point out, the gastric retention time is highly variable.

Moreover, when the Salofalk tablet dissolves, its content of 5-ASA is released within 30 minutes,² so mean values showing that 1.5%

of the content is released in the duodenum, 5.7% in the jejunum, and 12.7% in the ileum are misleading. Individual data for the six subjects would yield more accurate information.

We have studied ileostomy patients during steady state treatment with different 5-ASA preparations.¹ The subjects were given 2 g 5-ASA daily (two tablets of Salofalk (250 mg) four times daily, 400 mg Asacol five times daily, and Pentasa 500 mg four times daily) half an hour before the meals, as suggested by Goebell *et al*, and the concentration of 5-ASA was measured in the ileostomy output for 24 hours. Despite the dose being given four-five times daily, only one-two peak concentrations were seen for Asacol and Salofalk, and a lower but steady concentration during Pentasa (Figure), emphasising the importance of the size of the drug formulation for gastric retention time.

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Comparison of computed tomography, endosonography, and intraoperative assessment in TN staging of gastric carcinoma

EDITOR.—We read the report by Ziegler *et al* (*Gut* 1993; 34: 604-10) and were impressed by the quality of the computed tomography and endogastric ultrasonograms, and by the accuracy of their endosonographic assessment of gastric tumours and node state compared with subsequent histological examination. The argument, however, which the authors use to justify their conclusion that 'endogastric ultrasonography should be introduced into the preoperative assessment of patients with gastric carcinoma' is flawed.

The authors have presented no data that support the claim of the final paragraph of their paper that 'as endogastric ultrasonography has by far the highest sensitivity and specificity for correct TN classification, the introduction of this technique in the preoperative diagnostic programme allows much better selection of inoperable patients'. They describe a comparison between computed tomography, endogastric ultrasonography, and intraoperative clinical assessment in a series of 108 patients, all of whom had total gastrectomy for their gastric tumours. They do not describe the computed tomographic findings, endogastric ultrasonographic findings or clinical assessment in any patient with inoperable tumours, and the data they present, while interesting, cannot therefore be used to support their claim relating to the selection of inoperable patients.

As clinicians, most of us would be very interested in any technique that would permit the reliable preoperative prediction of inoperability, and in some ways the paper has missed an opportunity to make an assessment of the potential clinical usefulness of endosonography. The authors must have imaging data that relate to patients who were subsequently found to be inoperable at laparotomy, and we would be very interested to see these results,

Concentration of 5-aminosalicylic acid in ileostomy fluid. FWC=faecal water concentration.