Left sided colon cancer

EDITOR,—The neurobiology of diverticular disease leading to left sided colon cancer in 7159 patients (2478 men and 4681 women (Gut 1993; 34: 499-502) is suggested by reversed cerebral asymmetry in women with left sided breast cancer.

This hypothesis is supported by the association of specific frontal asymmetries with certain immune functions, and by compulsive ruminations occurring before oculogyric crises linked to deficient cortical circuits and abnormalities of dopamine sub-serving gastrointestinal protection, immuno- cytcs, and mood.1 Therefore, we would recommend the association of severe psychiatric disorders with severe acute colitis2 and by the protective role of dopamine in preferentially maintaining splanchic blood flow.3 These findings suggest screening patients with diverticular disease for increased risk of malignancy by monitoring dopaminergic neurotransmission.

A possible result suggested by the fact that delay-dependent speeding of reaction time, reflecting motor readiness, is abolished by depletion of dopamine. Therefore, future studies may evaluate cognitive consequences of dopamine agonists and antagonists in intermediate dopamine tone in a medial-frontal striatal ‘activation’ system underlying response organisation by monitoring behavioural correlates of mood – that is, speech hesitation and speech pausing.1 We have recently developed a time base into a computer. This method is supported by participatory matching of pauses in dialogues at intermediate arousal, a joint, mutually responsive rhythm, and by the consequence of dopamine on the motor cortex.1 Therefore, it is obvious that a dopaminergic 3 system is, if effective, an amnestic and unambiguously easy to convey the conveyance of ideas, a task that is possibly of sufficient complexity 4 to assess the role of dopaminergic neurotransmission in the development and progression of diverticular disease leading to left sided colon cancer.

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Alcohol and epinephrine and polidocanol

EDITOR,—We have read with great interest the report by Rutgeerts et al (Gut 1993; 34: 348-50). The authors state that ‘absolute ethanol was superior to epinephrine-polidocanol, which was not significantly better than sham therapy’. As these results differ from other previous controlled studies even from the same group, we would like to comment on some clinical and immunological aspects that we consider of relevance.

It is worth noting that a high rebinding rate (40%) and low haemostatic efficacy (68%) in the epinephrine-polidocanol injection group compared less to the type in the sham (five patients) and alcohol groups (seven patients). It is known that shock carries a tremendous risk of rebinding2 and this could explain, at least partially, the high failure rate in the epinephrine-polidocanol group (80% and 88% respectively) was seen, but these differences were not significant.

As noted by the authors, shock was more frequently seen in the epinephrine-polidocanol group (18% of patients) than in the sham (five patients) and alcohol groups (seven patients). It is known that shock carries a tremendous risk of rebinding,2 and this could explain, at least partially, the high failure rate in the epinephrine-polidocanol group (80% and 88% respectively) was seen, but these differences were not significant.

Apart from the type of injected substance, there are probably other factors influencing the efficacy of endoscopic injection, such as the site and size of the bleeding ulcer.3 In the study by Rutgeerts et al., the authors considered the proportion of gastric and duodenal ulcers between groups but not their anatomical situation. Ulcers located high on the lesser gastric curvature or posterior in the duodenal wall are more difficult to reach and have a higher tendency to rebled.4 Furthermore, the size of the ulcer, probably one of the most important factors,3 is not mentioned in the study. In this sense, it has been shown that endoscopic injection is significantly less effective in ulcer sizes larger than 2 cm.5

Another remarkable aspect is that the study was designed specifically to compare both treatments with a combination of substances used than to other factors, such as the size and site of bleeding ulcer. These variables should be considered in studies assessing the efficacy of endoscopic injection techniques.

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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. Tumour necrosis factor generates PAF production in human monocytes. A close relation has been reported between PAF and TNF in the gastrointestinal tract where PAF mediates TNF induced damage. Platelet activating factor and TNF have been reported in the stool of patients with inflammatory bowel disease. Furthermore PAF is released in the stool of patients with bacterial (Salmonella, Clostridium difficile) but not with viral (rotavirus, adeno-virus) or parasitic (Cryptosporidium) diarrhoea. The lack of TNF in the stool of patients with Clostridium 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 of 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.

Oroesophageal transit of 5-aminosalicly 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. 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, 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. 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. Assessed 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.

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 a contribution to the understanding 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,