Letters to the Editor

Resection of the gastric fundus in rats

EDITOR,—We were interested to read the paper by Dr Chu et al from Sweden and Denmark (Gut 1993; 34: 988–93), which showed that resection of the gastric fundus in rats causes both pancreatic hyperplasia and the development of premalignant lesions (acidophilic atypical acinar cell foci or AACF). These changes were even more noticeable in another group of animals that had received pancreatobiliary diversion to mid small bowel. These new Scandinavian data complement or confirm a number of our own published findings. We agree that increased pancreatic weight and increased serum amylase concentrations. We carried out a 60 per cent distal pancreatectomy on 40 rats and another 40 rats on which a Roux-en Y anastomosis was performed. Ten of the rats included much of the fundus and all the antrum, thereby reducing serum gastrin. We too found increased pancreatic weight and a ninefold increase in AACF (after azaserine exposure), and we believe these effects to be related to raised cholecystokinin concentrations, both fasting and postprandial.1 When split gastrojejunostomy was done to provide complete duodenogastic reflux, the same hypergastrinaemia was encountered in the pancreas, but on this occasion plasma gastrin was raised instead of cholecystokinin.2 Thus gastrin and cholecystokinin seem to have independent trophic effects on the pancreas. We accept the additional possibility of endogenous nitration after gastric surgery with formation of a pancreatic carcinogen.

Like Dr Chu, we have shown that pancreatobiliary diversion has a more pronounced effect on the proximal stomach than on the distal stomach, for that matter, massive enterectomy. Although 90 per cent proximal small bowel resection increases circulating concentrations of entero-glucagon as well as cholecystokinin,3 the cholecystokinin receptor antagonist CR-1409 (longlumide) inhibits the associated pancreatic hyperplasia.4 The primacy of cholecystokinin is further shown by experiments using the pancreatobiliary diversion model to stimulate pancreatic growth. Two weeks after this operation serum cholecystokinin concentration was twice as high as values in sham operated rats;5 by six months there was a fourfold increase. CR-1409 completely blocked the hyperplastic response, which was manifested by increases in pancreatic RNA, bromodeoxyuridine labelling and metaphase arrest after vincristine.6 It also abolished the effect of pancreatobiliary diversion in enhancing pancreatic carcinogenesis among animals exposed to azaserine.7

Thus cholecystokinin emerges as the dominant candidate for the role for pancreatotropin, but certain other gastrointestinal peptides probably play a subsidiary part.8 In the pancreas, as in the colon, 'surgical' hyperplasia predisposes to neoplasia. The increased cell proliferation that is caused by cholecystokinin may occur partly in response to injury, because we have recently found evidence of severe ultrastructural damage to rat pancreas 14 days after pancreatobiliary diversion.9 Treatment with CR-1409 largely prevents degranulation, but vacuolation of acinar cells is still seen.

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Reply

EDITOR,—We are fully aware of and agree with the results of the excellent study of Professor Williamson et al on pancreatic changes related to surgical procedures with hormonal aberrations in the rat. We apologise for not having cited any of them in our paper (Gut 1993; 34: 988–93). To keep the reference list at a reasonable size, however, and for the sake of interpretation and debate, our choice of references was rather specific and aimed at similar studies showing diverging results. Our paper primarily concerned the role of fasting hypergastrinaemia after funectomy, with pancreatobiliary diverted animals with hypercholecystokininemia as positive controls. In some aspects, funectomy simulates severe atrophic gastritis, which is not the case with distal gastric resection or split gastrojejunoanastomosis. In another study in rats focusing on the effects of pancreatobiliary diversion and funectomy after azaserine exposure (Path Res 1993; 8: 330–7), the studies of Professor Williamson et al are cited.

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Gallstones and gall bladder motility

EDITOR,—We have read with interest the leading article Gallstones and Gall Bladder Motility (Gut 1993; 34: 440–3). We agree that vagal cholinergic and cholecystokinin mediated hormonal mechanisms are the most important factors in controlling gall bladder emptying. With regard to gall bladder emptying after truncal vagotomy, we have recently shown impaired gall bladder emptying after truncal vagotomy, with a higher fasting and residual volume and a decreased ejection fraction.1 In our subjects, we found gall bladder emptying to have a triphasic pattern with a distinct increase of filling occurring between 15 and 45 minutes, which separated two contraction phases. Minimum volume was attained between 30 and 90 minutes after the meal. It is not true that drugs having a prokinetic effect may prove valuable in preventing bile stasis and cholelithiasis in a variety of circumstances. The effect of cisapride we feel is controversial, however, as in a double blind, prospectively randomised, placebo controlled study we found no prokinetic effect of cisapride either in healthy volunteers or in vagotomised subjects.2 Another possible prokinetic modality that promises to have clinical benefit is the use of a rapid intragastric gastrointestinal transit which is believed to cause gall bladder contraction and increase cholecystokinin concentrations.3 This may be potentially important in the prevention of gall bladder sludge in patients on total parenteral nutrition.

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Iron deficiency anaemia

EDITOR,—The comment is well made that the possibility of coeliac disease should be considered in all iron deficient patients, regardless of age (Gut 1993; 34: 1102–7), and this is true also of those who present with dyspeptic and abdominal pain, because these symptoms may be prominent in some patients with this condition.1 Therefore, if endoscopy proves negative for suspected peptic ulceration or gastric cancer, the diagnostic trap to avoid is that of attributing upper gastrointestinal symptoms to colonic disease without taking the precaution to rule out coeliac disease by means of endoscopic biopsy.

Additionally, to heighten the index of suspicion, endoscopists should routinely comment on the appearance of the duodenal folds, because these may be characteristically effaced in some patients with coeliac disease.

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