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 ACF). 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 suggesting that such surgical procedures are associated with the development of premalignant lesions in the exocrine pancreas, in Y en Y anastomosis. Neither this paper nor any other reporting on Y anastomosis include much of the fundus and all the antrum, thereby reducing serum gastrin. We too found increased pancreatic weight and a ninefold increase in AACP (after azaserine exposure), and we noted other effects related to cholecystokinin concentrations, both fasting and postprandial. When split gastrojejunostomy was done to provide complete duodenogastric reflux, the same hyperplastic/neoplastic changes were encountered in the exocrine pancreas, but on this occasion plasma gastrin was raised instead of cholecystokinin. Thus gastrin and cholecystokinin seem to have independent tropic 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 upper gastric glands than the distal gastric glands, that matter, massive enterectomy. Although 90 per cent proximal small bowel resection increases circulating concentrations of entero-glucagon as well as cholecystokinin, the cholecystokinin receptor antagonist CR-1409 (longlumide) inhibits the associated pancreatic hyperplasia. The primacy of cholecystokinin is further shown by experiments using the pancreatobiliary diversion model to stimulate pancreatocytic hyperplasia. Two weeks after this operation serum cholecystokinin concentration was twice as high as values in sham operated rats; 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 metaplasia after vincristine. It also abolished the effect of pancreatobiliary diversion in enhancing pancreatic carcinogenesis among animals exposed to azaserine.

Thus cholecystokinin emerges as the dominant candidate for the role for pancreatotropin, but certain other gastrointestinal peptides probably play a subsidiary part. 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 pancreaticobiliary diversion. 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 these excellent studies by 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: 488-93). To keep the reference list 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 with the long-term effects of dogs suffering from gastric and duodenal ulcers. We reported that although the levels of gastrin in the blood of dogs with duodenal ulcers were usually higher than normal, they did not exceed the normal range, and that the levels of gastrin were not significantly different from those in control dogs. We also found that the levels of gastrin in the blood of dogs with duodenal ulcers were usually higher than normal, but that they did not exceed the normal range, and that the levels of gastrin were not significantly different from those in control dogs. We also found that the levels of gastrin in the blood of dogs with duodenal ulcers were usually higher than normal, but that they did not exceed the normal range, and that the levels of gastrin were not significantly different from those in control dogs.

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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 dyspepsia and abdominal pain, because these symptoms may be prominent in some patients with this condition. 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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