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 pancreatectomy diversion to mid small bowel. These new Scandinavian data complement or confirm a number of our own published findings.3,4 ACFs were available to the authors at the time of submission4 but none of which were cited.

Dr Chu and his colleagues carried out gastric fundectomy alone, restoring continuity by direct anastomosis.3 In our experiment, this operation increased circulating gastrin concentrations but not cholecystokinin concentrations. We carried out a 60 per cent distal gastrectomy and 77 per cent truncal vagotomy. en Y anastomosis 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 with considerable effects to both cholecystokinin concentrations, both fasting and postprandial.5 When split gastrojejunostomy was done to provide complete duodenogastric reflux, the same hyperplastic/neoplastic effect was encountered in the pancreas, but on this occasion plasma gastrin was raised instead of cholecystokinin. This 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 pancreatectomy diversion has a more pronounced effect on the development of gastric carcinogenesis than that matter, massive enterectomy.6 Although 90 per cent proximal small bowel resection increases circulating concentrations of enteroglucagon as well as cholecystokinin,7 the cholecystokinin receptor antagonist CR-1409 (longlumide) inhibits the associated pancreatic hyperplasia.8 The primacy of cholecystokinin is further shown by experiments using the pancreatectomy diversion model to stimulate pancreatic carcinogenesis.9,10 In 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 metaphase arrest after vincristine.11 It also abolished the effect of pancreatectomy diversion in enhancing pancreatic carcinogenesis among animals exposed to azaserine.12 Thus cholecystokinin emerges as the dominant candidate for the role for pancreatotropin, but certain other gastrointestinal peptides probably play a subsidiary part.13 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 pancreatectomy diversion.14 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 research by Dr Chu and 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 the role of longstanding hypergastrinaemia after fundectomy, using pancreatectomy diverted animals with hypercholecystokininemia as positive controls. In some aspects, fundectomy simulates severe atrophic gastric epithelial damage which is not the case with distal gastric resection or split gastrojejunostomy. In another study in rats focusing on the effects of pancreatobiliary diversion and fundectomy after azaserine exposure (Perez-Perez 1993; 8: 330–7), the studies of Professor Williamson et al are cited.

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