The important difference between these two studies is that Gasslander et al found a raised plasma cholecystokinin concentration in rats with duodenogastric reflux (at two weeks and six weeks), whereas we found a normal plasma cholecystokinin concentration (at six months). Cholecystokinin receptor antagonist dazevapide did not completely inhibit the tropic effect of the operation, they suggest that gastrin may also be important as an intermediary, our own data clearly support this interpretation. In the context of promoting neoplasia, the longer term hypergastrinemia may be at least as relevant as the more transient hypercholecystokininaemia. That cholecystokinin alone could play a part in the induction of pancreatic cancer in patients with previous gastrectomy is confirmed by another study (again not cited) showing enhanced pancreatic carcinogenesis in rats with distal gastrectomy, an operation that lowers serum gastrin.

Using a different surgical model, massive enterectomy, we found two candidate hormones for the role of pancreaticotropin: enteroglucagon and cholecystokinin.1,4 Cholecystokinin may be the more important because the cholecystokinin receptor antagonist lorglumide completely abolished the effect of this operation on pancreatic growth. We have previously speculated on the relation between these two hormones.2 The strongest stimulus to pancreatic growth and carcinogenesis in our experience has been pancreatico-biliary diversion; here again cholecystokinin seems to be the key intermediary, and lorglumide prevents the response.6

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Reply

EDITOR.—We appreciate the interest that Professors Williamson and Watanapa have shown in our paper and apologise for failing to reference the important contributions they have made in the field of pancreatic growth and carcinogenesis. These authors suggest that an important difference between their study and ours is that we saw an increase in circulating cholecystokinin concentrations and they did not. In fact basal cholecystokinin concentrations in their study were 59% higher in animals with split gastrojejunostomy than controls, although this did not reach statistical significance. Further, in a larger series it is probable that this would have reached statistical significance. Furthermore, in their study of partial gastrectomy, basal cholecystokinin concentrations were only 46% above control and lower than those seen in their split gastrojejunostomy group, but here they concluded that partial gastrectomy increases plasma cholecystokinin.2 It is interesting to note that humans with long-standing pancreatic hyperplasia and pancreatic cancer had increased concentrations of cholecystokinin postprandially, although their gastrin concentrations are quite normal.3 Although gastrin concentrations were increased after gastrojejunostomy, we do not feel that this hormone alone is responsible for the pancreatic growth as the tropic effect is not mimicked by omeprazole treatment even though gastrin concentrations are higher than after split gastrojejunostomy.

We do not fully agree with the conclusion drawn that the study of distal gastrectomy in rats confirms that cholecystokinin may play a part in the increased incidence of pancreatic cancer, by way of the tumour suppressor gene because in their study no trophic effect on the pancreas was seen. Furthermore, while we agree that these hormones are of importance for pancreatic growth and neoplasia in the rat, their role in human ductal adenocarcinoma, the common tumour type in humans, is controversial.4,5 The authors go on to state that they found two candidate hormones, enteroglucagon and cholecystokinin, for the pancreaticotropic effect associated with the massive small bowel resection and pancreatico-biliary diversion. However, the increase of cholecystokinin and enteroglucagon and pancreatic growth associated with these surgical procedures had been described earlier.6,7

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Expression of adhesion molecules in human Peyer’s patches

EDITOR.—We became aware of a publication in Gut by Fujimura and Kihara on human Peyer’s patches while reviewing published works (Gut 1994; 35: 46–50); the title of this paper was exciting because our laboratory has not without success tried to show expression of intercellular adhesion molecule-1 (ICAM-1) in human lymphoid follicles.5,6 Particularly, we were interested in the particular combinations interferon gamma (IFN-gamma), tumour necrosis factor alpha, and IFN y and interleukin 1 in the presence of butyrate.6 It was therefore quite intriguing when the title of the article by Fujimura and Kihara suggested that the follicle associated epithelium of Peyer’s patches expresses ICAM-1. Unfortunately, the study had been performed in rats rather than humans and the title was further misleading because the localization described for ICAM-1 was restricted to a subepithelial layer of fibroblasts. Contrasting this finding, which was claimed to be related to the unique immunobiology of follicle associated epithelium, was the authors that the follicle associated epithelium of ICAM-1 beneath the villus epithelium. They therefore speculated that the massive lymphocyte traffic between follicle associated epithelium and the lymphoid follicles of Peyer’s patches might be explained by the topical ICAM-1 expression.

In our opinion this hypothesis is not plausible. Lymphocytes in follicle associated epithelium are unevenly dispersed, being particularly concentrated in small aggregates related to the ‘membrane’ cells; outside these foci the intraepithelial occurrence of lymphocytes is more similar to that seen in the villus epithelium in terms of numerical as well as phenotypic distribution.4,5 In humans the diffusely scattered intraepithelial lymphocytes are mainly CD8+ T cells7 of the T cell receptor a/b variety with a small (4–5%) amount of T cell receptor a/a cells.8 Further, the only adhesion molecule suggested to be important for their homing to the epithelium is the integrin aE87 (detected by monoclonal antibody HML-1),10 which apparently binds to E-cadherin on follicle associated epithelium. It is therefore difficult to speculate whether such aggregated lymphocytes consist of B cells—apparently representing topical extensions of the underlying follicles—together with a comparatively high proportion of CD4+ CD43R0+ T cells (memory-helper phenotype),12 but without admixture of the T cell receptor y/s subset.9 It is indeed