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). As the cholecystokinin receptor antagonist devazepide 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 longterm hypergastrinaemia may be at least as relevant as the more transient hypercholecystokinaemia. That cholecystokinin alone could play a part in the increased incidence 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,² an operation that lowers serum gastrin.

Using a different surgical model, massive enterectomy, we found two candidate hormones for the role of pancreatotropin: enteroglucagon and cholecystokinin.^{3,4} 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.⁵ The strongest stimulus to pancreatic growth and carcinogenesis in our experience has been pancreatobiliary diversion; here again cholecystokinin seems to be the key intermediary, and lorglumide prevents the response.^{6,7}

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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 mean basal cholecystokinin concentrations in their study were 59% higher in animals with split gastrojejunostomy than controls, although this did not reach statistical significance because of data variability.¹ 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 primary duodenogastric reflux have 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 trophic 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 after gastrectomy, because in this 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 ductal adenocarcinoma, the common tumour type in humans, is controversial.⁴⁻⁸

The authors go on to state that they found two candidate hormones, enteroglucagon and cholecystokinin, for the pancreatotrophic effect associated with massive small bowel resection and pancreatobiliary diversion. However, the increase of cholecystokinin and enteroglucagon and pancreatic growth associated with these surgical procedures had been described earlier.⁹⁻¹¹

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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 without success tried to show expression of intercellular adhesion molecule-1 (ICAM-1) by human intestinal epithelium in the normal or diseased gut (unpublished findings). This is also in accordance with other reports.¹⁻⁴ We were able to upregulate ICAM-1 expression in the human adenocarcinoma cell line HT-29, however, by certain cytokines,⁵ particularly the combinations interferon γ (IFN γ)/tumour necrosis factor α , and IFN γ /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 localisation 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, the authors were unable to detect 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 distributed, 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.⁷⁻⁹ In humans the diffusely scattered intraepithelial lymphocytes are mainly CD8⁺ T cells^{7,8} of the T cell receptor $\alpha\beta$ variety with a small (4-5%) admixture of T cell receptor $\gamma\delta$ cells⁹; the only adhesion molecule suggested to be important for their homing to the epithelium is the integrin $\alpha E\beta 7$ (detected by monoclonal antibody HML-1),¹⁰ which apparently binds to epithelial E-cadherin.¹¹ The high density of lymphocytes found in relation to the membrane cells might rather be ascribed to the antigen transporting capacity of these specialised epithelial cells. In fact, about 50% of such aggregated lymphocytes consist of B cells – apparently representing topical extensions of the underlying follicles – together with a comparatively high proportion of CD4⁺CD45RO⁺ T cells ('memory-helper' phenotype),¹² but without admixture of the T cell receptor $\gamma\delta$ subset.⁹ It is indeed difficult