The important difference between these two studies is that Gaslander 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). 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 hypergastrinemia may be at least as relevant as the more transient hypercholecystokininaemia. That cholecystokinin alone could play a part in the 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, an operation that lowers serum gastrin.

Using a different surgical model, massive enterectomy, we found two candidate hormones for the role of pancreatotropin: enteroegglucagon and cholecystokinin. Cholecystokinin may be the more important in this setting 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. The strongest stimulus to pancreatic growth and carcinogenesis in our experience has been pancreato- biliary diversion; here again cholecystokinin seems to be the key intermediary, and lorglumide prevents the response.4,5

Letters

T E ADRIAN
Cancer Center,
Creighton University School of Medicine,
Omaha, USA

GASSLANDER
Department of Surgery,
University Hospital,
Linköping, Sweden

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) on the surface of human small intestinal Peyer's patches, in particular the combinations interferon γ (IFN-γ)/tumour necrosis factor α, and IFN γinterleukin 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 find ICAM-1 beneath the villus epithelium. They therefore speculated that the massive lymphocytic 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.7,8 In humans the diffusely scattered intraepithelial lymphocytes are mainly CD8+ T cells7 of the T cell receptor αβ variety with a small (4–5%) admixture of γδ T cells.5,9 The natural killer cells of such aggregated lymphocytes consist of B cells—apparently representing topical extensions of the underlying follicles—together with a comparatively high proportion of CD8+CD45R0+ T cells (memory-helper phenotype),10 but without admixture of the T cell receptor γδ subset.7 It is indeed different
ICAM-1 below the follicle associated epithelium, as reported by Fujimura and Kihara, should have anything to do with the numerically and phenotypically heterogeneous distribution of lymphocytes in this epithelium. The authors further discuss extensively the nature of membrane cells; without reservation it is claimed that these cells express MHC class II molecules and therefore may be present luminal antigens to MHC class II cells. This area is quite controversial, and, however, the first study on class II expression in rat Peyer's patches reported that the complete follicle associated epithelium is negative. This has been contradicted subsequently but we found human membrane cells to be negative for HLA-DR compared with the strongly positive remaining follicle associated epithelium. The antigen presenting capacity of these membrane cells is therefore questionable although they are probably to some extent able to degrade foreign material as suggested by their lysosome like structures and cathepsin E expression. We have recently proposed that membrane cells might provide an opportunity for juxtaposed B cells to present partially processed luminal antigens to CD4+ memory T cells, thereby promoting diversification of mucosal immune responses.

In view of this immunobiological complexity of gut associated lymphoid tissue we feel it is too speculative when Fujimura and Kihara on the basis of their findings in rat Peyer's patches for blocking of ICAM-1 as a potential treatment for inflammatory bowel disease in the future.

P BRANDTZÆG
T N FARSTAD
Laberatory for Immunohistochimistry, Institute of Pathology (LIHIPAT), The National Hospital, Rikshospitalet, N-0027 Oslo, Norway


Kvale D, Brandtzæg P, Constitutive and cytokine-induced expression of HLA molecules, secretory component (SC), and ICAM-1 are modulated by butyrate in the colonic cell line epithelial cell line HT-29. Gut 1995; 37: 132-43.


Ménétrier's disease

EDITOR.—We read with interest the case report by Bayerdorff et al showing that Helicobacter pylori is a potential cause of Ménétrier's disease (Gut 1994; 35: 701-4). The findings in their patient showed clearly that H pylori gastritis can present as hypertrophic gastritis combined with protein loss and that eradication of the H pylori infection can lead to rapid disappearance of the hypertrophic lesion and restoration of normal gastric mucosa. We disagree, however, with the authors' presumption that Ménétrier's disease and hyper- trophic gastropathy are synonymous. There are many reasons for believing that equating the two terms is ill advised. (1) A variety of conditions can cause enlarged gastric folds. In addition to the true 'hyperplastic gastropathies' Ménétrier's disease and Zollinger-Ellison syndrome are both characterized by the development of gastric folds are seen in hypertrophic gastritis associated with various infections, including H pylori, cytomegalovirus, histoplasmosis, and syphilis, and in miscellaneous other diseases such as sarcoidosis, allergic (eosinophilic) gastritis, and Cronkhite-Canada syndrome. (2) While increased gastric protein loss can be found occasionally in many disorders that are associ- ated with increased gastric folds, increased protein loss is not a universal feature of any of these disorders. It is typically lacking in Zollinger-Ellison syndrome, and its reported occurrence in Ménétrier's disease is variable and depends on the dietary conditions that may occur in the aetiologies of Menetrier's disease. (3) The cases described in 1888 by Ménetrier as 'polyadeno- noma en nappe' had as their cardinal feature exuberant proliferation of gastric mucous cells. This is a distinct entity that has been appropriately termed 'massive foveolar hyperplasia'. Furthermore, Ménetrier's description and illustrations do not suggest that chronic gastritis, the hallmark of H pylori gastritis, is a condition that should be considered as a criterion for this gastropathy. (4) The concept that massive foveolar hyperplasia is a definitive feature of true Ménetrier's disease is greatly strengthened by studies showing that there is an accompanying change in the distribution and activity of transforming growth factor alpha in the gastric mucosa in Ménetrier's disease. In addition, the experimental induction of an excess of gastric transforming growth factor alpha in transgenic mice results in similar mucus cell hyperplasia. It is highly probable that 'hypertrophic hypersecretory gastropathy' (Schindler's disease), another distinctive entity that has sometimes been mistaken for Menetrier's disease, is probably a manifestation of H pylori gastritis with large folds. We urge authors and editors not to use the term Ménetrier's disease as a generic designation for conditions associated with gastric mucosal expansion.