ASSOCIATION OF HELICOBACTER PYLORI INFECTION, LYMPHOID FOLLICLES, AND LYMPHOCYTIC GASTRITIS: A RISK FACTOR FOR THE DEVELOPMENT OF PRIMARY GASTRIC MALT-LYMPHOMA?

EDITOR.—A Miettinen et al have published (Gut 1995; 37: 471–6) an interesting article on the prevalence of lymphocytic gastritis in primary gastric lymphoma (32% of the cases studied). The authors ended by suggesting that the lymphocytic gastritis is a possible precursor state of gastric lymphoma.

This hypothesis can be proposed because the intraepithelial lymphocytes could represent an overflow of tumour associated T lymphocytes, necessary for the growth of the lymphoma. Alternatively, they might play a part in negative regulation of the immune response.

In the light of this and other findings, we suggest that the ‘tried’ formed by lymphocytic gastritis, lymphoid follicles, and H pylori infection, could represent a potential risk factor for the development of primary gastric lymphoma. On the other hand, in such cases the sensitive polymerase chain reaction method for immunoglobulin heavy chain rearrangement could be useful to detect a possible monoclonal cell population (histologically undetectable) among reactive inflammatory cells.

Furthermore, it is possible to obtain the disappearance of lymphoid follicles after anti-H pylori treatment, the behaviour of H pylori positive lymphocytic gastritis after antimicrobial treatment should be further investigated. This is important to establish whether an anti-H pylori vaccination is more than just a trident to eliminate the risk factor represented by the ‘tried’, to prevent the development of primary gastric MALT-lymphoma.

G CAMMAROTA A TURSI G FEDELI G GABARRINI, Department of Internal Medicine, Catholic University, Rome


COLONOCYTE METABOLISM

EDITOR.—It was a great pleasure to read Drs Clausen and Mortensen’s paper (Gut 1995; 37: 684–9) on colonocyte metabolism. Particularly as Dr Clausen spent some time in our laboratory working with colonocytes. Careful reading of Dr Clausen’s results makes it difficult to conclude that butyrate oxidation is not defective in ulcerative colitis (UC).

Their results of butyrate oxidation in UC (at 2 mmol/l butyrate) indicate a mean rate of about 190 nmol/min/g (dry weight) of 14CO2 formation, which is similar to values originally reported in UC, which varied between 90 nmol/min/g (dry weight) in acute colitis to 560 nmol/min/g (dry weight) in quiescent colitis. At complete odds with our published results are Clausen’s control values of butyrate oxidation in cases unaffected by disease. Clausen’s values, again at 2 mmol/l butyrate are about 175 nmol/min/g (dry weight), whereas our original values were 1090 nmol/min/g (dry weight). Control values of similar magnitude have been consistently published from our laboratory over a number of years. Clausen’s values, which are about 6–23 times lower than ours, suggest inadequately metabolising cells, the reason for which is not immediately evident from their paper. The values of ATP produced by colonocytes are also low and parallel the low values of 14CO2 reported by Clausen and Mortensen.

A number of points are important in colonocyte preparation: (a) constituents and pH of electrolyte solutions, (b) the presence of calcium and albumin, (c) the concentration of dilithiothreitol, (d) the warm ischaemia time of collected tissue, (e) the extent of trauma in disaggregating cells, (f) a critical weight±10–15 mg (dry weight) of colonocytes in each experiment, and (g) the specific activity of substrate, which must not be too high. If these factors were observed, we are at a loss to understand the poor oxidative metabolic performance now reported by Clausen and Mortensen. Under optimal conditions, no defect in butyrate metabolism is detectable in UC. To date, two reports1 2 indicate a metabolic defect of butyrate oxidation in UC and two (ref 3 and Clausen’s paper) fail to show such a change. Metabolic experimentation requires rigorous attention to detail and familiarisation with general biochemical methodology. We have repeatedly checked for failure of butyrate oxidation in UC and have been able to show such a deficit in all colon tissue obtained at operation.

W E W ROEDIGER M MILLARD Cell Physiology Laboratory, Department of Surgery, University of Adelaide at The Queen Elizabeth Hospital, Adelaide, SA 5011, Australia


LETTERS TO THE EDITOR

REPLY

EDITOR.—We thank Dr Roediger for his comments on our publication on human colonocyte metabolism of short chain fatty acids (SCFAs) in which we were unable to confirm a defective oxidation of butyrate in ulcerative colitis (UC). Dr Roediger has previously shown that butyrate oxidation to CO2 is decreased in colonocytes obtained from patients with acute and quiescent UC, and that this impairment correlates with the state of the disease.1 In reference to luminal concentrations of butyrate these data observed by Dr Roediger were all performed in the presence of 10 mmol/l butyrate whereas our experiments were carried out in the presence of concentrations ranging from 0.125 to 2 mmol/l. The resultant curves obeyed Michaelis-Menten kinetics, and the kinetic parameters, Vmax (maximum rate of metabolism), and Km (the substrate concentration at which the reaction has half its maximum value) were calculated by computer fitting of the data to a Michaelis-Menten plot. As pointed out by Dr Roediger our maximum rates (Vmax) of CO2 production from butyrate in controls (187 [24] mmol/min/dry weight; mean SEM) are approximately similar in quiescent UC to those reported in his original study,1 and Dr Roediger speculates that this may be due to inadequately metabolising cells.

In 1990, Dr Roediger generously invited us to work with colonocytes in his laboratory, and we have used the same method of preparing isolated colon epithelial cells from resected bowel specimens as originally described by Drs Roediger and Truelove2 with the exception that hydroethidine was omitted. Our values of CO2 production from butyrate in controls ranged from 114 to 333 nmol/min/dry weight in controls and from 90 to 400 nmol/min/dry weight in patients with UC. If the lower value of epithelial cells, our cell preparations contained 9:1 (9-0 mg/ml (mean SEM), and no significant correlation between Vmax values of CO2 production from butyrate and dry weight of epithelial cells was found (p=0.19; Spearman’s rank correlation test). The warm ischaemia time of collected tissue is difficult to determine exactly, especially in UC patients undergoing colectomy where preselection of a specific specimen is required. Consequently, we have evaluated the time of ischaemia on colonocyte metabolism by removing the colon for 30 minutes before cell preparation and found no effect on CO2 production from butyrate (unpublished data). Further experimental work in this area seems to be required to evaluate the role of colonocyte metabolism of SCFAs in the pathogenesis of UC.

M R CLAUSEN P B MORTENSEN Danish Medical Research National Association of Digestive Diseases, Rigshospitalet, University of Copenhagen, Blegdamsvej 9, DK-2100 Copenhagen, Denmark
