LETTERS TO THE EDITOR

Association of Helicobacter pylori infection, lymphoid follicles, and lymphocytic gastritis: a risk factor for the development of primary gastric 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 ‘triad’ 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 obviate the appearance 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 therapy is more than an attempt to eliminate the risk factor represented by the ‘triad’, to prevent the development of primary gastric MALT-lymphoma.

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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 and 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 and 110 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 formation 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 disodium ethylenediamine tetraacetate, (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 the substrate should 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, a normal 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 defect in all colon tissue obtained at operation.

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Reply

Dr Clausen’s letter is in response to our paper on colonocyte metabolism. In the discussion of that paper, we draw attention to a number of factors thought to affect the metabolic activity of colonocytes and illustrate how these factors influence the metabolic activity of colonocytes. We have refined a number of these factors in our paper, and we were unable to confirm these findings in our present study. We have also found that the metabolic activity of colonocytes is influenced by a number of factors, including the state of the colonocytes used. In our present study, the metabolic activity of colonocytes was measured in the presence of 10 mmol/l butyrate whereas our experiments were carried out in the presence of 3 mmol/l butyrate. 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 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 Truelove.2 3 We have found that the exception that Helicobacter pylori has been 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. The lower values in our control group reflect a lower ability of colonocytes to oxidise butyrate. We have also found that the control values do not vary significantly from the values reported by Dr Roediger. We have found this difference in the values for CO2 production from SCFAs and glucose in our study was linear over 60 minutes in cell suspensions obtained from both UC patients and controls indicating efficient metabolic performance during the incubation period. In our present study, 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). Two further studies have investigated the colon epithelial metabolism of butyrate in UC. As these studies used a different technique (biopsy specimens), the numerical values cannot be directly compared with the results obtained by use of isolated colonocytes, but one study was in favour of a defective oxidation of butyrate in UC2 and was not confirmed. Further experimental work in this area seems to be required to evaluate the role of colonocyte metabolism of SCFAs in the pathogenesis of UC.

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REFERENCES


1 Clausen M, Mygind T, Mortensen PB. The effect of 4-15 nmol/min/g (dry weight) of 14CO2 formation, which is similar to values originally reported in UC, which varied between 90 and 110 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 formation 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 disodium ethylenediamine tetraacetate, (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 the substrate should 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, a normal 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 defect in all colon tissue obtained at operation.