LETTERS TO THE EDITOR

Lymphocytic gastritis and coeliac disease

EDITOR,—We would like to comment on the paper by Miettinen *et al* on lymphocytic gastritis in patients with gastric lymphoma (*Gut* 1995; **37:** 471–6). They found lymphocytic gastritis in about a third of patients with gastric lymphoma, and they looked for the relation between lymphocytis gastritis and *Helicobacter pylori* infection. They were surprised to find that lymphocytic gastritis occurred more frequently in patients without *H pylori* infection, and they were not able to explain the mechanism of the gastritis in patients with gastric lymphoma without *H pylori* infection. The authors, however, were aware that lymphocytic gastritis may occur in coeliac disease, but they did not discuss this possibility for their patients. We are convinced that coeliac disease may indeed explain the occurrence of lymphocytic gastritis in those patients with gastric lymphoma and without *H pylori* infection. In fact, as previously reported,[1] we have found the presence of lymphocytic gastritis in nine of 25 children with coeliac disease and in none of 36 children with *H pylori* infection. These nine coeliac patients represent all the cases of lymphocytic gastritis we found in 245 consecutive children who had upper gastrointestinal endoscopy. This strongly suggests that this peculiar form of chronic gastritis is, in children, almost exclusively related to gluten intolerance.

Taking into account that gastrointestinal lymphomata may be related to untreated coeliac disease,[2] there is one further reason to think that the patients reported by Miettinen *et al* with gastric lymphoma and without *H pylori* infection, could be affected by silent coeliac disease and could benefit from a gluten free diet.

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Reply

EDITOR,—We appreciate the interest Dr Maggiore and colleagues have shown in our article. We agree that lymphocytic gastritis may indeed be a manifestation of sensitivity to gluten.[1 2]

We have evaluated all available duodenal biopsy specimens from our gastric lymphoma patients with lymphocytic gastritis to investigate possible association with coeliac disease (*Gut* 1995; **37:** 471–6). Duodenal specimens were available in six cases among seven lymphoma patients with lymphocytic gastritis (three, duodenal bulbus; three, descending part of duodenum). No duodenal specimens had been taken in one *H pylori* negative patient. In five cases there was no villous atrophy; three of the patients were *H pylori* negative by histology, while two were positive. In one case a specimen from duodenal bulbous showed severe villous atrophy and an increase of intraepithelial lymphocytes. The gastric lymphoma in this patient was of B cell lineage (L26-positive and UCHL1 negative); no *H pylori* organisms were found in the gastric mucosa. No information about the use of gluten free diet is available.

Because of the retrospective nature of our study, we are not able to exclude duodenal villous abnormalities in all patients. In most of our patients, however, coeliac disease does not seem to explain the occurrence of lymphocytic gastritis.

The mechanisms of lymphocytic gastritis in most of our patients remain speculative. *H pylori* infection is closely associated with gastric lymphoma and has been suspected to be a cause of lymphocytic gastritis.[3 4] As we have discussed in our paper, the absence of *H pylori* in some patients with lymphocytic gastritis and gastric lymphoma might be connected with atrophic changes in the body mucosa.

Most of the lymphomas complicating coeliac disease are located in the small intestine,[5 6] and gastric lymphoma is rare.[6] We agree with Maggiore *et al*, however, that the exclusion of coeliac disease is probably useful in patients with gastric lymphoma and lymphocytic gastritis.

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1 Karttunen T, Niemelä S. Lymphocytic gastritis and coeliac disease. *J Clin Pathol* 1990; **43:** 436–7.
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Concentrations of epidermal growth factor in human saliva and gastric juice

EDITOR,—We read with interest the article by Tunio and Hobsley (*Gut* 1995; **37:** 335–9) examining the concentrations of EGF in gastric juice and saliva. We are somewhat surprised by their findings that the concentration of EGF in basal gastric juice exceeds that found in saliva. On the basis of these findings, they go on to conclude that much of the EGF in gastric juice is probably secreted by the stomach. Many groups have measured EGF concentrations in saliva and gastric juice using radioimmunoassay and agree with the salivary concentrations quoted in Tunio's and Hobsley's paper (about 3 ng/ml).[1–3] However, the concentrations of EGF found in gastric juice in this paper (about 4 ng/ml) are about 10 times higher than found by other groups,[1–4] including the paper by Konturek quoted by the authors themselves.[3] The major concern over the validity of this work is therefore not related to the salivary sample collection method, which is discussed in the paper, but over the concentration of EGF in basal gastric juice. Some explanation for this order of magnitude discrepancy between their results and other groups' findings needs to be given. This paper will therefore stand as a beacon to highlight the dangers of accepting 'established facts' such as the statement that 'it is well established that gastric juice EGF is mainly of salivary origin', which is often quoted in studies examining the importance of EGF; alternatively, it will crash on the rocks of methodological inaccuracy.

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1 Maccini DM, Veit BC. Salivary epidermal growth factor in patients with and without acid peptic disease. *Am J Gastroenterology* 1990; **85:** 1102–4.
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4 Playford RJ, Marchbank T, Calam J, Hansen FH. EGF is digested to smaller, less active, forms in acidic gastric juice. *Gastroenterology* 1995; **108:** 92–101.

Reply

EDITOR,—We thank Dr Playford, Professor Wright, and Dr Goodlad for their comments. The first of these is that they are surprised that the concentration of EGF in basal gastric juice in our study exceeded that in the contemporaneous saliva. However, we did not report that fact. Reference to our summary shows that 'There was no difference between basal salivary and gastric EGF concentrations ($p>>0{\cdot}05$)'. We certainly therefore did not suggest that, to quote their letter, 'On the basis of these findings, they go on to conclude that much of the EGF in gastric juice is probably secreted by the stomach'. What we did conclude was that, after stimulation with histamine, the output of EGF was so greatly increased (compared with any changes in the saliva) that in those circumstances much of the EGF in the gastric juice was probably secreted in the stomach. The third comment is that, while our results for EGF concentration in resting saliva agree with those of other workers, our concentrations in the gastric juice were much larger than those workers (including themselves) have found. They conclude that our methods of measurement must have been in error, but fail to explain how the methodological rocks on which they believe our research vessel will founder were only present in the gastric and not the salivary samples.

There are considerable differences between the way we collected and stored the gastric juice samples and the methods used by other workers. The articles need to be read in detail to determine all of these, but we mention the

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following: in our subjects, a period of 30 minutes was permitted after passage of the nasogastric tube before sampling started, there was no balloon impacted in the pylorus, we deliberately did not instruct the patient to spit out rather than swallow his saliva (because in our experience this factor encourages salivation and the swallowing of saliva), and we did not incubate the gastric juice samples with trasylol.

On the basis of three of the four studies they quote (reference 4 is irrelevant to this subject), they assume that their techniques are right and that ours are wrong. Three against one is hardly statistical significance. Is it possible that the rocks are in their court?

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Helicobacter pylori infection density and gastric inflammation in duodenal ulcer and non-ulcer subjects

EDITOR,—Without an explicit quantification of the sensitivity of bacterial culture, and prevalence of *H pylori* infection in the population from which their subjects were derived, Khulusi *et al* would not be justified in utilising culture positivity as a criterion either for 'ruling in', or for 'ruling our' *H pylori* related gastritis (*Gut* 1995; **37:** 319–24). Although the 100% specificity of bacterial culture confers a 100% positive predictive value for the diagnosis of *H pylori* related gastritis, sensitivity can vary from 70–95%,[1] and the resulting reduction in negative predictive value would, in turn, be correlated with the prevalence of *H pylori* infection in the community. Only the absence of histological stigmata of type B gastritis yields a 100% negative predictive value for the diagnosis of *H pylori* related gastritis.[2]

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1 Fennerty MB. Helicobacter pylori. *Arch Intern Med* 1994; **154:** 721–7.
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BOOK REVIEW

Clinician's Guide to *Helicobacter pylori*. By J Calam. (Pp 182; illustrated; £39.50.) London: Chapman & Hall, 1996. ISBN 0-412-74000-1.

By any standard, the English language is a pretty remarkable implement, yet it is not without its limitations. There are certain words in other tongues (such as *schadenfreude, chutzpah*) that are without an English counterpart so that they have entered our common usage – and now even feature in the Oxford English Dictionary. Undoubtedly, Dr Johnson had other ideas about what sort of words might find themselves in an English dictionary. Perhaps we urgently need an Anglo-Saxon equivalent of the Academie Francaise to protect the language.

Another limitation to our native tongue is its fairly limited range of superlatives. I suspect this is a reflection of the traditional British tendency of understatement (which clearly has not been exported across the Atlantic). So limited is the conventional language in this respect that phrases of generous appreciation can seem so restrained that even a very positive critique may seem to be damning with faint praise.

Both these problems came to my mind in composing this review. Surely, *chutzpah* is just about the only word that gets anywhere near describing the manner in which Barry Marshall persisted in convincing the largely sceptical world of his ideas. The man seemed almost unbearable at times yet he has been proved right and only the most curmudgeonly would deny him his rewards (be they in this world or the next). The problem of finding appropriate words of praise confronts the reader of John Calam's book. Quite simply, it is the finest monograph in gastroenterology that I have encountered.

The evolving story of *Helicobacter pylori* must be familiar to most of this journal's readers. In a specialty that has changed much more dramatically in 30 years than any other within medicine, the *H pylori* tale is about as dramatic as medical sagas get. Perhaps it is a good 'acid test' of Calam's book that he unravels the mysteries of the organism with a freshness and clarity that, as near as it is possible to be for a medical text, this book is 'unputdownable'. Aside from his clarity of prose, the book is interlaced with sparkling good humour. We all knew that being a gastroenterologist is a risk factor for carrying *H pylori*. Maybe you were unaware that being a submariner also carries a risk. However, you will have to buy the book to learn about the putative mechanism (suffice it to say, it has something to do with flushing toilets and barometric pressure).

In the best traditions of medical teaching in the UK, the book is stuffed full of anecdotes, which makes it end to end readable. However, it is also very academic in the truest sense of the term. Competing hypotheses are discussed intelligently, areas of uncertainty are allowed to remain uncertain, and the book is massively referenced. If the Grand Inquisition were to return to Europe, I feel its most effective weapon of torture against a gastroenterologist would be not the rack but a cell furnished just with a chair (or, especially for us, a stool) in which the only reading matter would be all the abstracts ever written on *H pylori*. Many of us would willingly confess to virtually any crime within a few hours. No one should ever be asked to write a comprehensive systematic review on *H pylori*. Yet, Calam works from an extensive reference base and is always clear and never didactic except at the end where, sadly, he has failed to resist the temptation to provide algorithms for clinical management. Let's be fair and place the blame on his publishers for this error of judgement.

There are so many vested interests in the wonderful world of *H pylori*. The pharmaceutical industry is fighting for its particular drug combination to be the numero uno in eradication. The epidemiologists have had their say but just what is to be done about the *H pylori* carrier who carries a cancer risk – we will need the answer well before we get results from prospective studies. There is much important work to be done in the laboratory particularly to explain causation of *H pylori*-linked disease ... and so forth. The clinician would also like some guidance from the great and good as to management guidelines. There have been helpful *ex cathedra* consensus statements from the USA. Yet there have not been clear guidelines from the United Kingdom, which many gastroenterologists would dearly welcome, particularly in their negotiations with the authorities that purchase health care for British citizens. Surely, we should be offering patients with such an incredibly common condition as dyspepsia a comparable standard of clinical service throughout this country. It is otherwise difficult to understand the meaning of the term 'National Health Service'.

Calam says everything a clinician should know about the most interesting bacterium to have turned up for many years. Several small books on *H pylori* have appeared in the recent past. This is a veritable giant among them.

IAN FORGACS

NOTES

Crohn's disease

The Colitis and Crohn's Week will be held on 15–22 June 1996. The aims for the week are to increase awareness of colitis and Crohn's disease and their effects on people's lives. Further information from Richard Driscoll, Director of National Association for Colitis and Crohn's Disease, PO Box 205, St Albans, Herts AL1 1AB. Tel: 01727 844296.

Liver disease

The XXIst International update on Liver Disease will be held at the Royal Free Hospital School of Medicine, London on 4–6 July 1996. For further details and information: Professor Neil McIntyre, University Department of Medicine, Royal Free Hospital, Pond Street, London NW3 2QG. Tel: 0171-794 0500 Ext: 3969; Fax: 0171 830 2321.

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