LETTERS TO THE EDITOR

Effect of *Helicobacter pylori* on the gastric mucus gel

EDITOR,—In their paper on the basis of viscosimetric studies performed on human gastric mucus Markesich *et al* challenge the concept that *Helicobacter pylori* exerts unfavourable effects on the mucous layer coating the gastric mucosa (*Gut* 1995; 36: 327–9).

Their results are clearly at variance with the bulk of the experiments carried out in this area¹ and Markesich and colleagues try to show the reasons for this discrepancy by pointing out the potential drawbacks of the previous studies.

Even if we accept Markesich's concept, however, that the results of some experiments on *H. pylori* have to be discarded because they are not performed on human mucus, other data are consistent with a mucus damaging effect of the micro-organism in humans. Assessing the quality of gastric soluble mucus in humans we found that, although on the whole mucus is normal both in chronic gastritis and in duodenal ulcer,² the lowest values are detectable in subjects with *H. pylori* infection.³

Sidebotham *et al* also observed a breakdown of gastric mucus in patients infected with *H. pylori*, although they ascribed this phenomenon to a carbonate-bicarbonate buffer at the mucosal surface due to the urease activity of the germ, rather than to a direct mucolytic activity.⁴ Measurements of the gastric mucus gel thickness in vivo showed that the mucous coating is significantly thinner in *H. pylori* infected patients,⁵ possibly resulting from increased erosion.

In keeping with the above results *H. pylori* infection seems to reduce mucosal hydrophobicity of human gastric mucus, which returns to normal after successful eradication.⁶

The reason for the discrepancy of Markesich's results is probably the method used to examine mucus. Reference is made to a study⁷ to justify the use of viscosity analysis for assessing the characteristics of mucus, but it is well recognised that viscosimetry is an unreliable technique for evaluating mucus properties.⁸ The finding that gastric mucus viscosity is increased in duodenal ulcer patients⁷ is only a further demonstration of how misleading the method can be.

As only luminal mucus was examined in Markesich's study, it must be also considered that proteolytic enzymes produced by *H. pylori* could promote a greater peptic erosion of the adherent mucus gel with consequent increase in the mucoprotein content of gastric juice influencing viscosity measurements. Eradication of *H. pylori* would clearly reduce mucus shedding and thus apparently decrease the viscosity of intraluminal mucus.

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Reply

EDITOR,—Guslandi takes issue with our finding that gastric mucus gel in *H. pylori* patients has a higher viscosity than in the unaffected. We simply gathered and tested the clear mucus gel that is normally present in the stomach. We used standard methodology for evaluating the viscosity of a gel. Our data were both consistent and reproducible.

There are many possible reasons why the gastric mucus gel in patients with *H. pylori* infection may be more viscous than those without. As the mucus cells seem to be under pressure to actively secrete, the gel may be younger than in uninfected subjects. It may also contain many more cells and cellular debris including DNA, which will in itself enhance viscosity. We make no apologies for the fact that Dr Guslandi studied soluble mucus and obtained different results.¹ This should not be a surprise as soluble mucus is 'used' mucus that has completed its function and is probably best considered a waste product. The fact that the mucus gel coat might be thinner in *H. pylori* infected patients, tells us nothing about the rate of synthesis, erosion, effectiveness or viscosity. We have previously shown that changes in mucosal hydrophobicity can be separated from the *H. pylori* infection.² The changes in hydrophobicity seem more likely to be due to the inflammatory infiltrate (as has been previously shown in the colon) than for any factor made by the bacteria.³ More than 40 years ago, Hollander described increased viscosity in response to damage and other workers in gastric physiology who previously published on breakdown of gastric mucus have had no difficulty incorporating our findings.^{4,5}

The history of peptic ulcer disease has been one of exploring what turned out to be blind alleys. Researchers have seen their cherished beliefs destroyed and discovered that their lifelong work has not been in the main stream, but has been in investigating only a minor tributary.⁶ The truth will be discovered over time and only by additional experimentation.

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Audit of percutaneous liver biopsy

EDITOR,—The 50% liver biopsy rate cited by Gilmore *et al* (*Gut* 1995; 36: 437–41) for patients aged >65 with suspected malignancy would only be justified if concurrent clinical, biochemical, and ultrasonographic stigmata were equivocal. Given the fact that the diagnostic specificity of ultrasonography can be as high as 96.2%, with corresponding likelihood ratio=18 (depending on subtype of ultrasonographic stigmata),¹ you can utilise the principles of Bayes' theorem² to predict the post-test probability of hepatic metastases in a subgroup of patients who already have clinical and biochemical stigmata of this diagnosis. Under such circumstances the minimal increment in post-test probability, generated by the adjunctive use of needle biopsy, might well be largely offset by the risk of procedure related morbidity and mortality.

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EDITOR,—One of the benefits of this audit is that it has supported the widely held belief that coagulopathy predisposes to haemorrhagic complications following liver biopsy. It is surprising that previous large reviews have, in contrast, failed to support this belief, with the exception of haemophilic patients undergoing biopsy.^{1–4}

It would have been interesting to know in the audit what measures, if any, were taken to correct the coagulation abnormalities before biopsy; practice probably varied between different units. Therein may lie the reason for the different incidence of haemorrhagic complications between this and other audits.

There are few data on which to base decisions on when and how to correct coagulopathy before liver biopsy. Parenteral vitamin K should be given at least six hours beforehand, but if coagulopathy persists then fresh frozen plasma is the agent of choice for correction.⁵ The level of prolongation of the prothrombin time at which fresh frozen plasma should be given has not been defined but a prolongation of three seconds or more is generally accepted to require correction.⁶ If fresh frozen plasma is given then the dose should follow published guidelines – that is, 12–15 ml/kg body weight,⁷ given immediately before the biopsy.

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1 Guslandi M, Ballarin E. Assessment of mucus-bicarbonate barrier in the stomach of patients with chronic gastric disorders. *Clin Chim Acta* 1994; 114: 133–6.

The level of prolongation of the prothrombin time at which a contemplated percutaneous biopsy should be abandoned in favour of a transjugular or plugged procedure has likewise not been defined. It would be helpful if future audits or reviews aimed to clarify this point. A prospective study of the efficacy and duration of action of fresh frozen plasma is underway at the Queen Elizabeth Hospital.

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Reply

EDITOR,—As Dr Jolobe will be aware from the design of the study, we are reporting on current practice over a wide range of hospitals in England and Wales, and, as he points out, suspected malignancy was the indication in about half of those patients over 65 years of age who had a percutaneous liver biopsy. As the data were drawn from the last 10 biopsies done in each hospital, they do not tell us how many patients with suspected hepatic malignancy were treated without histological confirmation, but it is likely that there were many. The frequency with which clinicians found the result helpful, however, emphasises that they found the confirmation useful in discussions with the patient and relatives and in establishing a management plan in a condition that has such a poor prognosis. Clinicians will be only too aware of the harm that can be done by the occasional mistaken diagnosis of a terminal condition. The relative roles of biochemistry, imaging, and liver biopsy in the diagnosis of hepatic malignancy in this study is the subject of a separate communication,¹ but in this study the specificity of ultrasonography was only 86% and sensitivity 82%. Furthermore, in a small number of cases a non-malignant diagnosis was positively established at liver biopsy when malignancy had been suspected on ultrasound examination.

Like Dr Fisher, we believe the data supporting the relation between coagulopathy and haemorrhagic complications are important in view of previous negative reports. Bleeding can occur, however, with normal clotting. The precise indications for alternative techniques such as plugged or transjugular biopsy techniques (used very rarely in this study) remain empirical, but they are an attractive alternative to the expensive and precious resource of human fresh frozen plasma.

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- 1 Jenkins D, Gilmore IT, Doel C, Gallivan S. The use of liver biopsy in the diagnosis of malignancy. *Q J Med* (in press).

Increased CA 125 in tuberculous peritonitis

EDITOR,—O'Riordan *et al* reported the case of a patient with tuberculous peritonitis, ascites, and pleural effusion who also had a remarkably increased concentration of serum CA 125 (*Gut* 1995; **36**: 303–5). Because of the increase in this tumour marker an ovarian cancer was suspected and a laparotomy was performed with negative results for cancer. The authors consider the increased values of CA 125 the most interesting aspect of the case, and review other published reports on increased CA 125 values in patients with tuberculous ascites.

I believe, however, that the only interesting and noticeable aspect of the case would have been if the patient had had a normal value of CA 125. This tumour marker, commonly used in the diagnosis and follow up of ovarian cancer, increases in a variety of processes involving pleura, pericardium, and peritoneum including endometriosis, peritonitis, pelvic inflammatory disease, and surgical trauma.^{1–3} The increase in CA 125 is not unexpected because this antigen has been detected on mesothelial cells in pleura, pericardium, and peritoneum, particularly in areas of inflammation.⁴

Benign serous effusions, particularly ascites, are associated with increased serum concentrations of CA 125 with values up to 100 times the upper normal limit in some cases.^{1–6} CA 125 has proved to be an excellent marker for ascites in patients with benign liver diseases (sensitivity 98.4%, specificity 95.9%, efficiency 96.9%).⁶ This marker is also very sensitive to minimal amounts of ascites and correlates very well with the amount of ascitic fluid.⁶ Thus, the specificity of CA 125 for ovarian cancer is very low in the presence of ascites of whatever origin.

In addition, the return of CA 125 to normal after anti-tuberculous treatment in the patient of O'Riordan *et al* is not unexpected. CA 125 decreases to normal values when the ascites is removed in cirrhotic patients and increases again when ascites recur.^{6–7}

The authors conclude that 'tuberculosis needs to be considered in the differential diagnosis of ascites with increased tumour markers'. It is well known, however, that CA 125 is an unspecific marker of ascites of whatever aetiology, and tuberculosis, a disease that only uncommonly produces peritoneal effusions, represents only one of the many aetiologies of ascites. Finally, I believe that a laparotomy should not have been performed in this case because both computed tomography and cytological study of ascitic fluid were negative for ovarian cancer and the very high concentration of CA 125 could have been easily explained by the existence of both ascites and pleural fluid.

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Reply

EDITOR,—Dr Collazos' points concerning CA 125 are valid. He is, however, an expert in the area and has published widely on CA 125. We felt this case to be of interest to a general audience because they might not have been familiar with the wide range of differentials for increased serum CA 125. The concentrations of CA 125 are high in many conditions as outlined in Dr Collazos's letter. We mentioned all of these and more in our discussion. Dr Collazos does not mention how he would have made the diagnosis. He might have legitimately requested laparoscopy in place of laparotomy. He suggests neither. We believe he overstates the value of negative computed tomography and non-diagnostic ascitic fluid cytology in excluding intra-abdominal tumour, however. Such measures can only reduce the relative risk that a tumour is present.

One additional point of some interest is that despite our considerable experience with immunocytochemistry and CA 125 in cytological preparations, we were unable to identify positive staining in the mesothelial cell population in the ascitic fluid specimen in retrospect. Had the immuno-panel been performed during the case this too would have urged us towards more invasive investigations.

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Adenomas and a family history of colorectal cancer

EDITOR,—The data presented by Gaglia *et al* (*Gut* 1995; **36**: 385–90) imply that adenomas in hereditary non-polyposis colorectal cancer (HNPCC) occur with increased frequency, show a predilection for the proximal bowel but are not especially large, dysplastic or likely to show villous change. It is interesting to note that these data are at complete variance with our own.¹ We have suggested that the high risk of colorectal cancer in HNPCC is explained not by increased initiation of