LETTERS TO THE EDITOR

Gastric acid secretion

EDITOR,—The study by Harris *et al* (*Gut* 1996; 38: 663–7) demonstrating that gastric acid secretion in the basal state, as well as gastrin releasing peptide and pentagastrin stimulated states, decreases after *H. pylori* eradication in duodenal ulcer patients is interesting and adds further weight to the hypothesis that *H. pylori* is responsible for driving the acid secretory abnormalities in duodenal ulcer disease. The significant fall in pentagastrin stimulated output, seen in their eight patients, is particularly interesting in the light of the inability of most previous studies to show such an effect. However from the data and methods presented, an alternative explanation for this result might be possible. That is that *H. pylori* eradication reduces gastrin stimulated acid output if patients have previously been primed with an infusion of gastrin releasing peptide (GRP), rather than a specific change in parietal cell mass. There may be several explanations for such an effect related to *H. pylori* pathophysiology. Functional and absolute deficiency of somatostatin has been clearly documented in *H. pylori* infection.^{1,2} In addition to being a potent gastrin secretagogue GRP increases release of both antral and fundic somatostatin³ and in animal experiments increases somatostatin gene expression.⁴ This ability to stimulate both inhibitory and stimulatory pathways may explain why GRP stimulated acid secretion is the most impressive of the changes in *H. pylori* infection. Somatostatin has a variety of inhibitory actions against parietal cells and ECL cells and it has clearly been shown that somatostatin can inhibit gene transcription and transcription factor function.⁵ It is unclear for how long such inhibitory influences would act after stimulation of somatostatin release by any agent and whether they have returned to normal after the wash out period. In addition to local mechanisms leading to somatostatin release, GRP also stimulates the release of a variety of small intestinal hormones including the enteroglucagons, cholecystokinin and gastric inhibitory polypeptide, which all probably inhibit gastric acid secretion by the intermediary of gastric somatostatin release. The half lives of oxyntomodulin and glucagon-like peptide-1 (up to 17 minutes) appear to be significantly longer than that of gastrin-17 (five minutes) and it is possible that significant functional acid inhibitory concentrations of these peptides were still circulating after the wash out period. Because of the relative somatostatin deficiency, the potent acid inhibitory effects of these peptides would be diminished in *H. pylori* positive patients and then restored with eradication. Thus somatostatin deficiency could explain the changes in pentagastrin stimulated acid output after the priming with GRP.

An alternative explanation may reside in the biological activities of pro-gastrin processing products. Classically the carboxy terminus non-amidated gastrins have been regarded as biologically inactive, but it is now clear that non-amidated glycine extended gastrin-17 (G-Gly) has actions on the parietal cell and as a growth factor. Glycine extended gastrin is

stored within antral G-cells and circulating values approximate to those of amidated gastrin.⁶ It has been shown that *H. pylori* associated hypergastrinaemia is associated specifically with an increase in these non-amidated gastrins.⁷ Although G-Gly is ineffective as an acid secretagogue alone, in experimental models it potentiated the stimulatory effect of gastrin⁸ and pre-incubation of cultured parietal cells with G-Gly increases their acid secretory capacity.⁹ Thus the previous GRP infusion might have increased parietal cell function in *H. pylori* positive subjects by the increased secretion of non-amidated gastrins, which increased acid secretory activity during the subsequent pentagastrin challenge. Thus it is possible to explain the fall in pentagastrin stimulated acid secretion during these studies when GRP and pentagastrin were given sequentially, by these changes in physiology without any change in parietal cell mass as the authors suggest.

The authors have clearly taken some care over choosing their 30 minute GRP wash out period; however, the previous studies with acid output have shown that studies in small groups may not always be reproducible in others and the different forms of GRP and bombesin may not always produce comparable responses.¹⁰

While these hypotheses to explain the results remain speculative and there may indeed be a significant fall in parietal cell mass, it is unfortunate that the data do not fully support this rather than suggest that the fall in pentagastrin stimulated acid output is a phenomenon related to the specific method used.

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Reply

EDITOR,—We thank Dr Beales for his comments on our paper on the effect of *H. pylori* eradication on acid output in patients with duodenal ulcer disease (DU). Dr Beales suggests that the significant decrease in pentagastrin stimulated peak acid output (PAOP_g) six months after eradication of *H. pylori* in patients with DU may be related to the methods used in the study and not as a result of an actual decrease in parietal cell mass. In our study PAOP_g was measured 30 minutes after the end of gastrin releasing peptide (GRP) infusion. Dr Beales suggests that because GRP stimulates the release of somatostatin and non-amidated gastrins, both of which affect parietal cell function, the subsequent measurement of PAOP_g may not be an accurate reflection of parietal cell mass. Furthermore Dr Beales draws attention to the 'inability of most previous studies to show such an effect'.

Since the original presentation of our findings,¹ two independent groups have reported a significant decrease in PAOP_g after eradication of *H. pylori* in patients with DU; neither of these studies used GRP infusions before pentagastrin.^{2,3} These corroboratory findings suggest that the significant decrease in PAOP_g is related to either a decrease in parietal cell mass, or possibly decreased sensitivity of the parietal cells to gastrin⁴ after *H. pylori* eradication, and not caused by a methodological epiphenomenon.

Dr Beales states that 'GRP stimulated acid secretion is the most impressive of the changes in *H. pylori* infection'. However our results suggest that both for the acid hypersecretion of *H. pylori* positive patients with DU when compared with *H. pylori* negative controls, and for the normalisation of this hypersecretion after eradication of *H. pylori* in patients with DU, there were no significant differences between these comparisons for the three types of measurements – basal, after GRP, and after pentagastrin.

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- 2 Jacobson K, Chiba N, James C, Armstrong D, Barrientos M, Hunt RH. Protracted gastric acid secretion in *H. pylori* positive DU patients following eradication. *Gastroenterology* 1995; 108: A122.
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Helicobacter pylori and duodenal ulcers

EDITOR,—We read with interest the article by A W Harris *et al* (*Gut* 1996; 38: 663–7). They measured basal, pentagastrin stimulated, and gastrin releasing peptide (GRP) stimulated acid output in 10 normal *Helicobacter pylori* negative and 10 duodenal ulcer (DU) *H. pylori* positive patients. After eradication of *H. pylori*, technically satisfactory secretion studies

became available in seven of the DU patients. No specific mention was made of corrections for pyloric losses or duodenal reflux. Their chief findings were statistically significant falls in basal, maximal, and GRP stimulated secretion in the seven patients with dual tests. They suggest that *H pylori*, by increasing sensitivity to gastrin, increases parietal cell mass and that this is the cause of the well known increased maximal acid output in DU patients compared with controls.

This suggestion is at odds with the paper¹ from this department that demonstrated that *H pylori* positive subjects, both patients with non-ulcer dyspepsia and patients with DU, had lower maximal gastric secretion (in response to continuous intravenous histamine) than *H pylori* negative patients of the corresponding diagnostic groups. Our study was performed in 64 subjects. Corrections were made for pyloric losses and duodenogastric reflux (both especially important when low secretion rates or small differences in secretion rates are being measured).

The GRP stimulated responses seen by Harris *et al* were clearly submaximal, because they were only 40–70% of the pentagastrin responses. The latter were also possibly submaximal (intramuscular route, one shot injection). Therefore it is possible that the phenomenon they have described (if it is confirmed in a larger number of patients with correction of collection errors) represents an effect of *H pylori* that primarily reduces parietal cell mass, and thereby increases sensitivity to gastrin (GRP or pentagastrin). This alternative hypothesis was discussed and referenced in our article.¹ The important point is that the findings described by Harris *et al* do not necessarily indicate that *H pylori* increases the parietal cell mass.

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Reply

EDITOR,—We thank Dr Oshowo and Professor Hobsley for their interesting comments.

We fully accept that *H pylori* may produce gastric hyposecretion from atrophic changes in body mucosa with loss of parietal cells. We believe that *H pylori* can also produce gastric hypersecretion leading to duodenal ulcer disease, but it is unclear which host or microbial factor is responsible for the one or other pathology.

Six months after eradication of *H pylori*, pentagastrin-stimulated peak acid output (PAO_{PG}) significantly decreased in all our eight patients, and not in seven as stated in the letter. It was the basal (BAO) and gastrin releasing peptide-stimulated (PAO_{GRP}) acid outputs that were available in only seven of eight patients. We did not make Hobsley's corrections for pyloric losses or duodenogastric reflux, but such corrections would probably have been slight at the high rates of secretion in patients with duodenal ulcer.¹ There are reasonable data that measurement of PAO after one injection of 6 µg/kg of pentagastrin is comparable with intravenous infusion.¹

Oshowo and Hobsley state that we 'suggest that *H pylori*, by increasing sensitivity to gastrin, increases parietal cell mass'. We actually suggested that 'the increased PAO_{PG} (an indirect measure of the parietal cell mass) in *H pylori* positive patients with duodenal ulcer may be caused by a combination of exaggerated gastrin release and acid response to gastrin' and not purely as a result of a change in sensitivity to gastrin.

Our finding of reduction of PAO_{PG} after eradication of *H pylori* has since been confirmed^{2,3} and we look forward to Professor Hobsley's study of his patients with duodenal ulcer after eradication of *H pylori* with 'a large number of patients with correction of collection errors'.

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- 1 Baron JH. *Clinical tests of gastric secretion*. London: Macmillan Press, 1978.
- 2 Jacobson K, Chiba N, James C, Armstrong D, Barrientos M, Hunt RH. Protracted gastric acid secretion in *H pylori* positive DU patients following eradication. *Gastroenterology* 1995; 108: A122.
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Ultrasound for gastroenterologists

EDITOR,—I read with interest the leading article by Dr Derrick Martin (*Gut* 1996; 38: 479–80) in which I believe he makes a very good case for not training gastroenterologists in ultrasound.

The argument in favour of training gastroenterologists is, I believe, a weak one, based on an increasing waiting time for ultrasound in radiology departments, the requirement of the European Union of Medical Specialities, and the perceived attractiveness of an 'instant' diagnosis at the first outpatient clinic attendance.

These arguments are far outweighed by many reasons in favour of maintaining and constantly improving radiology services. As a radiologist, Dr Martin concedes that ultrasound is 'a difficult technique, technical artefacts in the image abound and can create diagnostic confusion'. What defence is there when a renal tumour is missed, an aortic aneurysm unrecognised, an ovarian cyst undetected or pleural effusions not looked for? The high level of training of the radiologist enables him or her to search routinely for all of these potential pitfalls. Dr Martin states that many radiologists are keen to train others. This is certainly true but there is scant evidence that they are keen to train gastroenterologists. Without doubt, training would require to be thorough and systematic.

The leading article also deals with equipment and with the need to make efficient use of expensive resources. 'You get what you pay for' is certainly true and high quality ultrasound requires the appropriate level of investment in equipment. How is it possible therefore to justify the purchase of expensive ultrasound equipment for the gastroenterology clinic based on a throughput of perhaps 20 cases per week (or less!), which is equivalent to two radiology ultrasound sessions per

week. Dr Martin readily acknowledges the unpredictable nature of the gastroenterology workload and the variable commitments of those intending to use ultrasound. This is a further good reason for focusing ultrasound in the radiology department with its dedicated centralised staff and resources. There have been obvious precedents in which hospitals have accumulated expensive ultrasound equipment outwith the radiology department in renal units, urology departments, cardiology units and stroke units, which stands unused for most of each week. Furthermore equipment located outwith the radiology department runs the risk of infrequent or inadequate maintenance. Excellent hard copy facilities are a key factor in image quality and it is unlikely that the high cost of expensive laser printers could be justified outwith the radiology department.

Formal reporting of ultrasound images has many pitfalls and the gastroenterologist would be at particular risk of meeting one or more of these.

The issue of waiting lists in radiology departments is an important one. Whenever a Trust makes a clinical appointment, it needs to ask a question "What service department (including radiology) consequences will this appointment inevitably bring with it?"

There is an increasing tendency within radiology departments towards subspecialisation, particularly in teaching hospitals. Properly controlled, this is a beneficial development, because it encourages improved skills and concentrates experience in a focused way, which benefits patient care, education and research, for example in interventional radiology, magnetic resonance, computed tomography, and not least ultrasound where biopsy techniques, power Doppler, and tissue characterisation are most likely to flourish in the hands of dedicated radiologists. It would be completely inappropriate for me to have any involvement in breast screening mammography without extensive training in it and a major ongoing commitment to it. Training physicians and surgeons in ultrasound operates in the opposite direction to this focused specialised approach. It is not sufficient to simply say 'there will be some enthusiasts with sufficient workload to support this service and they will need guidance and training'.

The decree of the European Board of Gastroenterology that training in ultrasound should be included is not necessarily a wise one and in any case is probably relevant to comparatively few UK gastroenterologists.

Elsewhere¹ Dr Martin highlights the benefits of the patient focused approach to diagnosis and therapy, but surely the way forward is to focus ultrasound services within the imaging department ensuring that the highest possible standard is established and maintained with respect to rapid, accurate and complete diagnosis, instant reporting, education, and research.

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- 1 Martin DF. Ultrasound training for non-radiologists. *Clin Radiol* 1995; 50: 589–92.

Reply

EDITOR,—I am grateful to Dr Vallance for his comments, as this is clearly a topic where debate is essential if we are to reach a logical conclusion that allows the fulfilment of ambi-