LETTERS TO THE EDITOR

Gastric acid secretion

Editor,-The study by Harris et al (Gut 1996; 38: 665–7) 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 In addition to being a potent gastrin secretagogue GRP increases release of both antral and fundic somatostatin1 and in animal experiments increases somatostatin gene expression.2 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.3 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 acid stimulating factors including the enteroglucagon, cholecystokinin and gastrin inhibitory polypeptide, all which 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 inhibition 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 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 inert. 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.4 It has been shown that *H pylori* associated hypergastrinaemia is associated specifically with an increase in these non-amidated gastrins.5 Although G-Gly is ineffective as an acid secretagogue alone, in experimental models it potentiated the stimulatory effect of gastrin6 and pre-incubation of cultured parietal cells with G-Gly increased their acid secretory capacity.7 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 still produce comparable responses.8 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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3 Schubert ML, Jong MJ, Makkhold GM. Bombesin/GRF related peptides inhibit gastrin secretion mediated by gastrin in the antrum and intrin-


7 Graham DY, Go MF, Lew GM, Genta RM, Rehfeld JF. Helicobacter pylori infection and exaggerated acid secretory effects of inflamma-


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 (PAO3) six months after eradication of *H pylori* in patients with DU may be related to the eradication methods used in the study and not as a result of an actual decrease in parietal cell mass. In our study PAO3 was measured 30 minutes after the end of gastrin releasing peptide (GRP) infusion. Dr Beales suggests that the stimulus which releases somatostatin stimulates the release of somatostatin and non-amidated gastrins, both of which affect parietal cell function, the subsequent measurement of acid output in DU, there were no significant differences on 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 patients with DU had a significant decrease in PAO3 after eradica-

1 tion of *H pylori* in patients with DU; neither of these studies used GRP infusions before pentagastrin. These corroboration findings suggest that the decrease in acid output in patients with DU is related to either a decrease in parietal cell mass, or possibly decreased sensitivity of the parietal cells to gastrin1 after *H pylori* eradica-

1 tion, and not caused by a methodological explanation.

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 in *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, GRP, and after pentagastrin.

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1 Harris AW, Gummett PA, Phuell PS, Jacya MR, Misiewicz JJ, Raper JH. Proton pump inhibitors in duodenal ulcer after Helicobacter pylori eradication is related to high acid output. Gut 1995; 36 (suppl 1): A50.


3 Parente F, Maconi G, Sangalenti O, Minguzzi M, Vago L, Bianchi Porro G. Behaviour of acid secretion, gastric release, serum pepsin-


Helicobacter pylori and duodenal ulcers

Editor,—We read with interest the article by A W Harris et al (Gut 1996; 38: 665–7). They measured basal, pentagastrin stimulated, and gastrin releasing peptide (GRP) stimulated acid outputs, but it is clear that *H pylori* infected DU is a negative and 10 duodenal ulcer (DU) *H pylori* positive patients. After eradication of *H pylori*, technically satisfactory secretion studies

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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 throughout Europe. This is not surprising given the struggles 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 such 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 gastroenterologists deal with endoscopy 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. 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 commitment of those intending to use ultrasound. This is a further good reason for focusing ultrasound in the radiology department with its dedicated staff and resources. There has been no previous precedent 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 facsimile is an important feature 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 should 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 and E makes a clinical diagnosis, it requires the need 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 to market ultrasound equipment, particularly in teaching hospitals. Properly controlled, this is a beneficial development, because it encourages improved skills and concentrates on a technology which benefits patient care, education and research, for example in interventional radiology, magnetic resonance, computed tomography, and least ultrasound where biopsy techniques, power Doppler imaging, 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 and ultrasound for A and E patients. A further requirement towards the recognition of Gastroenterologists, particularly in teaching hospitals. Properly controlled, this is a beneficial development, because it encourages improved skills and concentrates on a technology which benefits patient care, education and research, for example in interventional radiology, magnetic resonance, computed tomography, and least ultrasound where biopsy techniques, power Doppler imaging, 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 and ultrasound for A and E patients.

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

Elsewhere 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.