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 may regulate the expression of 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 peptides including the enteroglucagon, 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 (5 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 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. It is now clear that the 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 potentiates the stimulatory effect of gastrin8 and pre-incubation of cultured parietal cells with G-Gly can increase 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 output 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 washout 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 bombein may all 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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Helicobacter pylori and duodenal ulcers

EDITOR,—We thank Dr Beales for his comments on our paper on the effect of H pylori infection on gastric acid output in patients with duodenal ulcer disease (DU). Dr Beales suggests that the significant decrease in pentagastrin stimulated peak acid output (PAOpg) six months after eradication of H pylori in patients with DU may be related to the eradication used in the study and not as a result of an actual decrease in parietal cell mass. In our study PAOpg was measured 30 minutes after the end of gastric releasing peptide (GRP) infusion. Dr Beales suggests that the acid output increases which eventually stimulates the release of somatostatin and non-amidated gastrins, both of which affect parie- tal cell function, the subsequent measurement of gastrin output in patients with DU, there were no significant differences in 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 further studies have been published.2 3 One of these2 shows a significant decrease in PAOpg after eradica- tion of H pylori in patients with DU; neither of these studies used GRP infusions before pentagastrin. These corroboration findings suggest that the significant decrease in PAOpg is related to either a decrease in parietal cell mass, or possibly decreased sensitivity of the parietal cells to gastrin3 after H pylori eradica- tion, 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 in PAOpg 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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1 Harris AW, Gummett PA, Phull PS, Jasyn MR, Misiewicz JJ, Raftery PJ. Helicobacter pylori infection and duodenal ulcer after Helicobacter pylori eradication is related to high acid output. Gut 1995; 36 (suppl 1): A50.


5 Harris AW, Gummett PA, Phull PS, Jasyn MR, Misiewicz JJ, Raftery PJ. Helicobacter pylori infection and duodenal ulcer after Helicobacter pylori eradication is related to high acid output. Gut 1995; 36 (suppl 1): A50.

6 Harris AW, Gummett PA, Phull PS, Jasyn MR, Misiewicz JJ, Raftery PJ. Helicobacter pylori infection and duodenal ulcer after Helicobacter pylori eradication is related to high acid output. Gut 1995; 36 (suppl 1): A50.