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 results in reduced gastrin secreted 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, gastrin releases both antral and fundic somatostatin3 and in animal experiments somatostatin has plasma.4 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 glugan-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 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.5 It has been shown that H pylori associated hypergastrinaemia is associated specifically with an increase in these non-amidated gastrins.6 Although G-Gly is ineffective as an acid secretagogue alone, in experimental models it potentiated the stimulatory effect of gastrin7 and pre- incubation of cultured parietal cells with G-Gly increased their acid secretory capacity.8 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 increase acid secretion during the second pentagastrin challenge. This 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 might well produce comparable responses.9 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.


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 gastric juices, increases pyloric cell mass and that this is the cause of the well known increased maximal acid output in DU patients compared with controls.

This finding is at odds with the papers 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 duodenogastro-intestinal reflex (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 phenomena 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 pyloric cell mass, and thereby increases sensitivity to gastrin (GRP or pentagastrin). This alternative hypothesis was discussed and referred to 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 pyloric cell mass.

Oshowo and Hobsey state that ‘we suggest that H pylori, by increasing sensitivity to gastrin, increases pyloric cell mass’. We actually suggested that ‘the increased PAO₂ (an indirect measure of the pyloric cell mass) in H pylori positive patients with duodenal ulcer may be caused by a combination of exaggerated gastrin response to gastrin’ and not purely as a result of a change in sensitivity to gastrin.

Our finding of reduction of PAO₂ after eradication of H pylori has since been confirmed2 and we look forward to Professor Hobsey’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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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. This is just as true for 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 cause diagnostic confusion’. What defence is there when a renal tumour is missed, an aortic aneurysm recognised, 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 some evidence that they are keen to train gastroenterologists. Without doubt, training would require to be thorough and systematic. The leading article decries the lack of 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 commitment 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 previous 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 facsimile is one area where 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 is not at particular risk of meeting one or more of these.

‘The issue of waiting lists in radiology departments is an important one. Whenever a service is under pressure, there is a 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 specialise, 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 which is not only outwith my main speciality but also an area in which patients develop acute anxiety due to fear of the ‘possibility of cancer’. I believe the specific training and skills that I have developed are of key importance to the patients and satisfying the information needs of patients. I believe that such training and skills are best provided within the traditional and well established department of radiology.

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Reply

EDITOR—I am grateful to Dr Vallance for his comments, as this is clearly a topic where debate will take place in the interests of patients and the radiology service. It is important to appreciate that the issues of cost and time are critically important for ultrasound and that this must be balanced against the expert and comprehensive service that radiologists provide in a number of areas, including mammography and ultrasound of the abdomen.

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