In 1995, Verdu et al published in Gut the interesting finding that the 24 hour intragastric pH during omeprazole therapy was about 5.5 in Helicobacter pylori infected volunteers compared with about 3.5 in uninfected controls, whereas the intragastric pH was similar in these groups without treatment. Later in 1995 they reported in Gut that this effect of H pylori disappears six weeks after its eradication (their reference 2). In 1996 a further paper in the Scandinavian Journal of Gastroenterology showed that this correction is not transient but persists one year after eradication. Later in 1996 a paper in Gastroenterology from the same group showed that the same effect occurs in patients with duodenal ulcer disease (their reference 1). Interestingly, in relation to the present report, they noted that during treatment with omeprazole 20 mg at 09.15 hours, H pylori infection had more effect on night time pH (6.4 in infected v 2.1 in uninfected subjects) than on overall 24 hour pH (5.5 v 3.0 respectively). The study by Labenz et al in this issue asked whether H pylori infection similarly increases the effect of the histamine H2-receptor antagonist ranitidine (see page 33). Eighteen patients with duodenal ulcer were studied during administration of ranitidine 300 mg at night before and after eradication of H pylori. Night time pH was again significantly higher in infected subjects (6.8 v 5.4 in uninfected subjects) but daytime pH was not affected. The authors point out that this difference can be explained by the lower potency and shorter duration of action of ranitidine compared with omeprazole. In short, therefore, these papers show that H pylori infection exaggerates the effect of acid suppressing drugs on intragastric pH, and this occurs whether acid is suppressed using either the proton pump inhibitor omeprazole or the H2-receptor antagonist ranitidine.

The authors discuss some of the putative mechanisms which might be responsible for this effect. Several products of H pylori are known to inhibit secretion of acid by parietal cells. These include a protein described by Cave and Vargas, some unusual fatty acids produced by this bacterium and the vacuolating toxin. In addition, parietal cells can be inhibited by factors released in H pylori gastritis. These include the cytokines tumour necrosis factor-α and interleukin-1β (their reference 19) and inhibitory autoantibodies directed against the proton pump itself. In an abstract, the authors provide data to support the idea that ammonia generated by the H pylori enzyme urease causes the effects simply by neutralising gastric acid (their reference 10). Of course, the effect might be owing to a hitherto unrecognised factor and in this context it is important to note that intragastric pH is not only determined by parietal cell function. For example, the effect could be explained by changes in motility. H pylori apparently increases the rate of emptying of gastric acid into the duodenum, which might be expected to raise the intragastric pH. Increased duodenogastric reflux in H pylori infection could also contribute.

Whatever the mechanism, the results of this series of studies bear on the important and unresolved question of whether acid suppression alters the natural history of H pylori gastritis. According to one view, the finding that acid suppression exaggerates the acid lowering effects of H pylori supports other evidence that such treatment exacerbates H pylori gastritis in the acid secreting corpus of the stomach. The authors cite the reports that proton pump inhibitors increase the number of bacteria and the degree of gastritis in this region (their references 5 and 6). In addition a report by Kuipers et al suggested that prolonged treatment with proton pump inhibitors exacerbates the tendency of H pylori to promote gastric atrophy. However, this area remains contentious and more well designed studies are needed. The authors propose an alternative mechanism. H pylori might increase parietal cell activity by producing N^9-methylhistamine (their reference 15), increasing gastrin and decreasing somatostatin concentrations, thus increasing the conversion of omeprazole to the active sulphinamide which depends on a low pH in the parietal cell canaliculus. However, this seems incompatible with their finding that intraluminal pH is raised. Finally, it should be borne in mind that the interaction could simply reflect the fact that pH is an inverse log10 scale, which means that minor changes in proton concentration have a much greater effect on pH at higher pH. The number of protons required to change the pH by 1 point decreases by a tenth every time the pH is increased by 1 point.

The effect that the authors report may prove to be clinically important. The effect of H pylori on the response to acid suppressing agents goes some way to explain variations in the response of different patients to these agents. A greater effect of acid suppressants in infected subjects may improve their contribution to H pylori eradication regimens. Conversely, a fall in gastric pH following eradication of H pylori might contribute to the frequent persistence of dyspeptic symptoms, such as acid reflux, the appearance of oesophagitis, and the frequent failure of those with non-ulcer dyspepsia to improve after eradication therapy. The finding also bears on the question of whether to eradicate H pylori, if it is present, before beginning long term acid suppression in patients with oesophagitis. This was recommended at a recent consensus meeting in Maastricht. Undoubtedly, the stomach will be histologically healthier if this is done, although there is currently no evidence that this will be of clinical benefit to the patient. However, by increasing the effect of acid suppressing therapy, persisting H pylori infection might lead to a healthier oesophagus and lower doses of medication. More research please!

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