Helicobacter pylori infection potentiates the inhibition of gastric acid secretion by omeprazole

D Gillen, A A Wirz, W D Neithercut, J E S Ardill, K E L McColl

Abstract

Background—Omeprazole has a greater intragastric pH elevating effect in Helicobacter pylori positive than negative subjects. Ammonia production by H pylori has been suggested as a probable mechanism.

Aims—To assess the effect of H pylori status on gastric acid secretion during omeprazole treatment, and to examine the possible role of ammonia neutralisation of intragastric acid in increased omeprazole efficacy in infected subjects.

Methods—Twenty H pylori positive and 12 H pylori negative healthy volunteers were examined before and six to eight weeks after commencing omeprazole 40 mg/day. On both occasions plasma gastrin and acid output were measured basally and in response to increasing doses of gastrin 17 (G-17). Gastric juice ammonium concentrations were also measured.

Results—Prior to omeprazole, measurements were similar in the H pylori positive and negative subjects. During omeprazole, median basal intragastric pH was higher in the H pylori positive (7.95) versus negative (3.75) subjects (p<0.002). During omeprazole basal, submaximal (180 pmol/kg/h G-17), and maximal acid outputs (800 pmol/kg/h G-17) were lower in H pylori positive subjects (0.0, 3.6, 6.0 mmol/h respectively) versus negative subjects (0.3, 14.2, 18.6 mmol/h) (p<0.03 for each). This effect was not explained by neutralisation by ammonia.

Conclusion—The presence of H pylori infection leads to a more profound suppression of acid secretion during omeprazole treatment. The effect cannot be explained by neutralisation of intragastric acid by bacterial ammonia production and its precise mechanism has to be explained.

(Ost 1999;44:468–475)

Keywords: omeprazole; Helicobacter pylori; ammonia; acid secretion

After the introduction of omeprazole, H pylori was recognised as a highly prevalent infectious agent of the gastric mucosa in both dyspeptic patients and asymptomatic healthy individuals. Omeprazole has been shown to exert effects on H pylori and the associated gastritis.

The presence of H pylori infection may also exert effects on the actions of omeprazole. Four studies have shown that intragastric pH during omeprazole treatment is higher in H pylori infected subjects than in H pylori negative or eradicaded subjects. The investigators in these studies have concluded that the greater elevation of pH on omeprazole in the presence of H pylori is mainly due to production of ammonia by its urease enzyme, neutralising intragastric acid.

The aims of this study were: (1) to assess the effect of H pylori status on gastric acid secretion, as opposed to intragastric pH, during proton pump inhibitor (PPI) treatment; and (2) to assess the contribution of H pylori ammonia production to any effects observed. Our findings show that the presence of H pylori leads to notably greater suppression of basal, submaximal, and maximal acid secretion during PPI treatment. They also show that ammonia production by H pylori and, indeed, neutralisation from any other source, cannot explain these observations.

Materials and methods

SUBJECTS STUDIED

Twenty H pylori negative healthy volunteers (10 men, five smokers) and 12 H pylori positive healthy volunteers (four men, four smokers) were studied. The mean weight and age of the H pylori negative volunteers were 75.9 kg and 27.9 years; those of the H pylori positive volunteers were 71.4 kg and 29.5 years. None of these volunteers were taking any medication, other than oral contraceptives. None reported any major gastrointestinal symptoms.

H pylori status was determined using the 14C-urea breath test. This test has been validated in our unit; using a cut off value of 30 (kg % dose/mmol CO2) for the 20 minute result it has a sensitivity of 98% and a specificity of 100%.

METHODS

Basal gastrin concentration, basal intragastric pH, and basal acid output were measured in all subjects. Acid output was then measured in

Abbreviations used in this paper: BAO, basal acid output; ECL, enterochromaffin-like; G-17, gastrin 17; GORD, gastro-oesophageal reflux disease; MAO, maximal acid output; PPI, proton pump inhibitor.
and during omeprazole treatment. Medians are represented by horizontal bars.

**Figure 1** Basal fasting gastric juice pH in H pylori negative and positive subjects before and during omeprazole treatment. *H pylori* negative and positive subjects, maximal samples for six of the *H pylori* negative subjects and one of the *H pylori* positive subjects. The pH and volume of each subject were repeated 24 hours after the previous dose of omeprazole.

For the gastric secretory studies, all subjects reported at 0900 after a 12 hour fast. A 16F nasogastric tube (Andersen Inc., New York, USA) was passed and its position in the dependent part of the stomach was checked using the water recovery test. After the stomach was emptied, intermittent suction was applied using an intermittent suction unit (Ohmeda, Columbia, Maryland, USA), which applies suction for 20 seconds in each 32 second cycle. A 30 minute basal acid collection was obtained, then sequential 30 minute collections were made during infusions of G-17 at doses of 7, 20, 60, 180, and 800 pmol/kg/h. Blood samples were collected each morning for gastrin determination, both basally and at the end of each infusion period. The plasma was stored at −20°C. A gastric juice sample was taken at the end of both the basal and the peak G-17 infusion periods for later ammonium measurement. These gastric juice samples were stored at −70°C. Basal samples at both time points were unavailable for two of the *H pylori* negative subjects and one of the *H pylori* positive subjects, maximal samples for six of the *H pylori* negative subjects and three of the *H pylori* positive subjects. The pH and volume of each acid collection was noted and its hydrogen ion concentration was measured by titration with 0.1 M sodium hydroxide to pH 7.0 using an autotitrator (Radiometer ETS 822, Copenhagen, Denmark).

G-17 was purchased from Peninsula Laboratories (Belmont, California, USA) as aliquots of freeze dried lyophilised powder. Subsequent preparation was performed under sterile conditions by the Western Infirmary Pharmacy Department. Each aliquot was dissolved in a small volume of ammonium bicarbonate, then made up into a stock solution. Vials containing 100 µg of G-17 were prepared and stored at −20°C until the day of the study. For each study, the content of the vial was further diluted in 0.9% sodium chloride solution containing 1% human serum albumin (Scottish National Blood Transfusion Service, Law Hospital, Carluke, Scotland, UK).

Plasma gastrin levels were measured by radioimmunoassay using antisemur R98, which has a sensitivity of 5 ng/l and detects both sulphated and unsulphated forms of G-17 and G-34 with equal affinity.

**Results**

**Basal Intragastric pH**

Pre-omeprazole, the median basal pH in the *H pylori* negative subjects was 1.6 (range 1.2–7.2), and that in the *H pylori* positive subjects was 1.6 (1.2–2.9) (*p*<0.04; fig 1). During omeprazole, the median basal pH in the *H pylori* negative subjects was 3.75 (1.7–8.5), and that in the *H pylori* positive subjects was 7.95 (2.7–8.3) (*p*<0.002; fig 1).

**Basal Plasma Gastrin Concentrations**

Before omeprazole, the median basal gastrin in the *H pylori* negative subjects was 15 ng/l (range 5–90), which was not significantly different from that in the *H pylori* positive subjects (20 (5–75) ng/l; *p*>0.29; fig 2). Basal plasma gastrin was significantly higher on omeprazole than pre-omeprazole in both the *H pylori* negative subjects (*p*<0.001) and the *H pylori* positive subjects (*p*<0.003). However, during omeprazole, the median basal plasma gastrin concentration in the *H pylori* negative subjects (35 (5–120) ng/l), was considerably lower than that of the *H pylori* positive subjects (95 (30–400) ng/l; *p*<0.006; fig 2).
negative subjects (43.85%) was also less than that of the H pylori positive subjects (61.8%), although this did not reach classical statistical significance (p<0.13). The median degree of omeprazole induced inhibition of basal intragastric acidity of the H pylori negative subjects was 83.15% which was lower than that of the H pylori positive subjects (100%; p<0.007).

**BASEL GASTRIC JUICE AMMONIUM CONCENTRATIONS AND AMMONIA OUTPUT**

Before omeprazole, the median basal ammonium concentration in the H pylori negative subjects was 1023 (396–3210) µmol/l which was lower than that of the H pylori positive subjects (3285 (975–4900) µmol/l; p<0.002). During omeprazole, the median basal ammonium concentration of the H pylori negative subjects was 1088 (387–3465) µmol/l, which was also lower than that of the H pylori positive subjects (2220 (360–4035) µmol/l; p<0.003). This represents a difference in medians on omeprazole of 1.1 mmol/l.

From data for basal gastric juice volume and basal gastric juice ammonium concentration, the basal gastric juice ammonia output can be calculated, in a similar fashion to the calculation of gastric acid output, from the product of the basal gastric juice volume and hydrogen ion concentration. Before omeprazole, the median basal ammonia output of the H pylori negative subjects (0.08 (0.01–0.59) mmol/h), was significantly lower than that of the H pylori positive subjects (0.28 (0.04–0.56) mmol/h; p<0.03). During omeprazole, the median basal ammonia output of the H pylori negative subjects (0.07 (0.01–0.36) mmol/h), was not significantly different from that of the H pylori positive subjects (0.13 (0.02–0.31) mmol/h; p<0.15).

**MAXIMAL ACID OUTPUT**

Before omeprazole, the median maximal acid output (MAO) of the H pylori negative subjects was 32.4 (17.9–53.0) mmol/h, which was similar to that of the H pylori positive subjects (32.2 (14.5–60.3) mmol/h; p<0.50; fig 4). During omeprazole, the median MAO of the H pylori negative subjects was 18.6 (3.2–39.0) mmol/h, which was greater than that of the H pylori positive subjects (6.0 (0.2–31.7) mmol/h; p<0.009; fig 4). MAO was lower on omeprazole than pre-omeprazole in both the H pylori negative (p<0.0009) and positive subjects (p<0.003).

Before omeprazole, there was no significant difference in intragastric acidity under maximal G-17 stimulation between the two groups. However, on omeprazole, the median intragastric acidity of the H pylori negative subjects (7.4 (0.0–36.4) mmol/l), was significantly greater than that of the H pylori positive subjects (0.0 (0.0–14.8) mmol/l; p<0.006).

During omeprazole, the median degree of inhibition of BAO in the H pylori negative subjects was 93.05% (=18.2% to 100%), which was less than that of the H pylori positive subjects (100% (75% to 100%); p<0.008). The median degree of inhibition of the basal volume of gastric juice secreted by the H pylori
the *H pylori* negative subjects (33.0% (−82.6% to 81.8%)) was less than that of the *H pylori* positive subjects (50.0% (1.3% to 84.4%); p<0.04). The median degree of omeprazole induced inhibition of intragastric acidity of the *H pylori* negative subjects (29.8% (−16.6% to 59.5%)) was less than that of the *H pylori* positive subjects (61.7% (26.3% to 96.1%)); (p<0.001).

**GASTRIC JUICE AMMONIUM CONCENTRATION AND AMMONIA OUTPUT DURING MAXIMAL G-17 STIMULATION**

Before omeprazole, the median ammonium concentration in the *H pylori* negative subjects was 661.5 (276–1425) µmol/l, which was lower than that in the *H pylori* positive subjects (1958 (178–5670) µmol/l; p<0.009). During omeprazole, the median ammonium concentration in the *H pylori* negative subjects was 825 (378–1485) µmol/l, which was also lower than that in the *H pylori* positive subjects (2025 (915–8055) µmol/l; p<0.0002). This represents a difference in medians on omeprazole of only 1.2 mmol/l.

Before omeprazole, the median ammonia output of the *H pylori* negative subjects (0.16 (0.07–0.53) mmol/h), was significantly lower than that of the *H pylori* positive subjects (0.51 (0.04–1.34) mmol/h; p<0.04). During omeprazole, the median ammonia output of the *H pylori* negative subjects (0.16 (0.07–0.48) mmol/h) was not significantly different from that of the *H pylori* positive subjects (0.23 (0.10–1.07) mmol/h; p<0.16).

**SUBMAXIMAL ACID OUTPUTS DURING G-17 STIMULATION**

Table 1 shows median acid outputs at infusion rates of 7, 20, 60, and 180 pmol/kg/h of G-17. Before omeprazole there were no significant differences at any G-17 infusion rate. However, on omeprazole, the acid outputs of the *H pylori* negative subjects were significantly greater at all infusion rates (fig 5).

Table 2 shows the median intragastric acidities in both groups, at each of the submaximal doses of G-17. The *H pylori* negative subjects had a significantly lower median degree of omeprazole induced inhibition of acid secretion than the *H pylori* positive subjects at each...
Table 2  Intragastric acidity at submaximal doses of gastrin 17 in H pylori negative and positive subjects before and during omeprazole.

<table>
<thead>
<tr>
<th>Gastrin 17 infusion rate (pmol/kg/h)</th>
<th>7</th>
<th>20</th>
<th>60</th>
<th>180</th>
</tr>
</thead>
<tbody>
<tr>
<td>H pylori negative, before omeprazole</td>
<td>69.7</td>
<td>96.7</td>
<td>116.7</td>
<td>127.0</td>
</tr>
<tr>
<td>(25.9–116.0)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>H pylori positive, before omeprazole</td>
<td>71.6</td>
<td>102.4</td>
<td>117.5</td>
<td></td>
</tr>
<tr>
<td>(11–71)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>H pylori negative, during omeprazole</td>
<td>7.6</td>
<td>28.0</td>
<td>66.2</td>
<td>87.2</td>
</tr>
<tr>
<td>(0.0–57.2)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>H pylori positive, during omeprazole</td>
<td>0.0</td>
<td>2.4</td>
<td>17.4</td>
<td>30.6</td>
</tr>
<tr>
<td>(0.0–28.2)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Intragastric acidity expressed as median (range) in mmol/l.
Acidity less in H pylori positive than in H pylori negative subjects at *p<0.02, †p<0.01, ‡p<0.003, §p<0.001.

Table 3  Serum gastrin concentrations during infusions of gastrin 17 in H pylori negative and positive subjects before and during omeprazole.

<table>
<thead>
<tr>
<th>Gastrin 17 infusion rate (pmol/kg/h)</th>
<th>7</th>
<th>20</th>
<th>60</th>
<th>180</th>
</tr>
</thead>
<tbody>
<tr>
<td>H pylori negative, before omeprazole</td>
<td>25.0</td>
<td>70.0</td>
<td>205.0</td>
<td>640.0</td>
</tr>
<tr>
<td>H pylori positive, before omeprazole</td>
<td>37.5</td>
<td>95.0</td>
<td>242.5</td>
<td>680.0</td>
</tr>
<tr>
<td>H pylori negative, during omeprazole</td>
<td>35.0</td>
<td>80.0</td>
<td>200.0</td>
<td>540.0</td>
</tr>
<tr>
<td>H pylori positive, during omeprazole</td>
<td>97.5*</td>
<td>135.0*</td>
<td>265.0</td>
<td>580.0</td>
</tr>
</tbody>
</table>

Gastrin concentration expressed in ng/l.
*Significantly greater than H pylori negative subjects during omeprazole, p<0.01.

Discussion

Previous studies have shown that during omeprazole treatment, intragastric pH is more notably elevated in H pylori positive versus negative healthy subjects. In addition, intragastric pH on omeprazole is higher in H pylori infected subjects than in the same subjects after the infection has been eradicated. In these studies, the mean 24 hour pH in H pylori infected subjects on omeprazole was 5.0–5.5, compared with 3.0–3.5 in H pylori negative or eradicated subjects. This difference in pH represents a very small difference in hydrogen ion concentration of less than 1 mmol/l. This has led the groups which have documented the pH phenomenon to conclude that it may represent nothing more than neutralisation of intragastric acid by H pylori produced ammonia. Our current studies investigated whether H pylori status might be affecting the degree of suppression of gastric acid secretion produced by omeprazole, which would make the phenomenon of greater clinical significance.

Our study confirms these previous pH observations. The median fasting pH in the H pylori negative subjects on omeprazole was 3.75 versus 7.95 in the H pylori positive subjects. Only 25.0% of the H pylori negative subjects had neutral basal pH values 24 hours after the previous dose of the PPI, compared with 83.3% of the infected subjects. The previous studies reporting the influence of H pylori status on the pH raising efficacy of omeprazole had been conducted after seven days of dosing. Our present study was performed after at least six weeks of omeprazole and indicates that the phenomenon persists with longer courses of therapy.

In addition to measuring fasting intragastric pH, we performed detailed studies of basal, submaximal, and maximal acid output. Prior to commencing omeprazole, there were no differences between the H pylori positive and H pylori negative healthy subjects with respect to basal and G-17 stimulated maximal acid output. This is consistent with our previous studies showing that increased acid secretion induced by H pylori infection is mainly confined to duodenal ulcer patients. Submaximal G-17 stimulated acid output was slightly lower in the H pylori positive than in the H pylori negative subjects. This was more apparent when the acid output was assessed against the gastrin concentration than against the G-17 dose, as the latter does not take into account the higher endogenous gastrin level in the H pylori positive subjects. The reduced acid response to gastrin in the infected subjects is consistent with our recent report of reduced sensitivity to G-17 in H pylori infected healthy volunteers.
Marked differences in acid secretion were apparent between the *H pylori* positive and negative subjects on omeprazole. The median BAO in the *H pylori* positive subjects was 0.0 mmol/l, compared with 0.3 mmol/l in the uninfected subjects. This difference in BAO could not be explained by any neutralising effect of ammonia produced by *H pylori*. The median ammonia output on omeprazole was 0.13 mmol/l in the *H pylori* positive and 0.07 mmol/l in the *H pylori* negative subjects. This represents a difference in ammonia output of only 0.06 mmol/l, which is fivefold less than the difference in BAO. Furthermore, the greater degree of inhibition of BAO in the *H pylori* positive versus negative subjects on omeprazole was due to a greater degree of inhibition of both volume of gastric juice secreted and its acidity. This provides further evidence that the difference in acid measured was due to greater inhibition of acid secretion in the *H pylori* positive subjects and not merely neutralisation by either ammonia or other neutralising factors.

MAO to G-17 was also considerably lower in the *H pylori* positive versus negative subjects on omeprazole, being 6.0 mmol/l and 18.6 mmol/l respectively. As with BAO, this difference in MAO of 12.6 mmol/l could not be explained by a neutralising effect of ammonia produced by *H pylori*. The median ammonia output during maximal G-17 stimulation of omeprazole was 0.23 mmol/l in the *H pylori* positive subjects and 0.16 mmol/l in the uninfected subjects. This difference of 0.07 mmol/l between the infected and uninfected subjects could not explain the more than 180-fold greater 12.6 mmol/l difference in median MAO. Furthermore, this difference in acid output on omeprazole was also due to a greater degree of inhibition of volume, as well as acidity, and this again excludes neutralisation by ammonia, or indeed other neutralising substances, as a feasible explanation of this observation.

Acid output on omeprazole in response to submaximal stimulation with G-17 showed a very notable difference between the *H pylori* positive and negative subjects (figs 5 and 6). At a dose of 60 pmol/kg/h, the median acid output in the *H pylori* negative subjects was 7.4 mmol/l compared with 1.6 mmol/l in the *H pylori* positive subjects. At a dose of 180 pmol/kg/h, the corresponding values were 14.2 and 3.6 mmol/l respectively. Significant differences in acid output were also apparent at 7 and 20 pmol/kg/h. Furthermore, at 7 and 20 pmol/kg/h of G-17 during omeprazole, the plasma gastrin concentrations achieved during the gastrin infusion were significantly higher in the *H pylori* positive versus the *H pylori* negative subjects, to some degree masking the true magnitude of the difference of the acid response to gastrin at these doses of G-17. This difference in gastrin concentrations between the *H pylori* negative and positive subjects during the lower doses of the G-17 infusion can be explained by the contribution of the higher endogenous gastrin levels in the infected subjects.

Our studies have thus shown that omeprazole produces more notable suppression of BAO, submaximal acid output, and MAO in *H pylori* positive versus in *H pylori* negative subjects. The degree of inhibition of BAO was 100% in the *H pylori* positive versus 93.35% in the negative subjects, 93.6% versus 74.05% for submaximal (60 pmol/kg/h) acid output, and 79.8% versus 54.6% respectively for MAO.

Sensitivity to gastrin stimulation can be assessed by plotting plasma gastrin concentration against acid output at the various doses of G-17 and calculating the concentration of G-17 to produce half maximal response. However, in this present study, the degree of acid suppression, particularly in the *H pylori* positive subjects on omeprazole, made it impossible to produce a concentration/acid response curve of sufficient accuracy to calculate the sensitivity to gastrin. Despite this, the observation that the gastrin concentration/acid response curve in the *H pylori* positive subjects on omeprazole is shifted notably to the right, compared with that of the *H pylori* negative subjects on omeprazole, is consistent with the former having a lower sensitivity to gastrin on omeprazole.

All of the previously published studies of the influence of *H pylori* status on the response to omeprazole only measured intragastric pH. These studies concluded that the difference in pH could be largely explained by neutralisation of intragastric acid by *H pylori* produced ammonia. Our current study indicates that there is a notable difference in the degree of suppression of gastric acid secretion in *H pylori* positive versus negative subjects and that neutralisation by ammonia production cannot explain more than 20% of the difference in BAO or 6% of the difference in MAO. Similarly, the fact that the volume of gastric juice secreted is affected, as well as its acidity, indicates that the presence of any other neutralising substances, such as enhanced mucosal bicarbonate production or *H pylori* related duodenogastric reflux cannot explain the observation.

The previously reported studies were performed after seven days of therapy, whereas our present study examined subjects after six to eight weeks of treatment, being representative of a typical course in clinical practice. It is possible that intragastric ammonia levels and degree of inhibition of acid varies slightly with different duration of treatment.

Our findings thus indicate that some interaction is occurring between *H pylori* infection and omeprazole treatment which is potentiating the antisecretory efficacy of the drug. A plausible explanation for this is the intense inflammation of the oxyntic mucosa which develops in *H pylori* positive subjects during PPI treatment. This increased gastritis is likely to impair the function of the oxyntic mucosa and thereby supplement the pharmacological effect of the drug. Recent observations by ourselves and others that there is a negative correlation between *H pylori* associated inflammation of the oxyntic mucosa and pentagastrin stimulated peak acid output in *H pylori* infected
patients is consistent with this theory. Furthermore, eradication of the organism and the accompanying resolution of oxyntic inflammation result in prompt recovery of acid secretory function. An alternative or additional explanation for the more notable inhibition of acid secretion in *H pylori* positive subjects is that ammonia produced by the urease in *H pylori* is able to penetrate the oxyntic mucosa during omeprazole treatment due to more being in the more lipophilic unionised form at the higher intragastric pH. This could allow increased delivery of NH₄⁺ ions close to the proton pumps, where they can act as K⁺ surrogates, and lead to uncoupling of the proton pumps. We believe that the more profound inhibition of acid secretion in *H pylori* positive subjects on PPI treatment is unlikely to be due to acid inhibitory products of the bacterium, as such treatment does not increase the density of bacterial colonisation of the oxyntic mucosa. However, one cannot exclude such products being able to gain greater access to the acid secreting cells when acid secretion is inhibited or their being more active at less acidic pH.

Our observation that the influence of *H pylori* status on the pH elevating effect of omeprazole is due to a difference in the actual acidity and volume of the gastric secretion increases the clinical importance of the phenomenon. Gastric acid is an important element of the phylogenetically conserved non-specific immune system. The *H pylori* positive patients rendered profoundly hypochlorhydric by PPIs are therefore likely to be at increased risk of enteric infections, as susceptibility to such infection is known to exist in other low acid states. Certainly, increased susceptibility to enteric infection on omeprazole has been reported, but the *H pylori* status of the patients was not known. Our own group has recently reported a greater number of non-*H pylori* bacteria colonising the gastric juice of *H pylori* positive versus negative subjects during omeprazole treatment. Such bacterial colonisation may also result in the intragastric synthesis of potentially carcinogenic nitrosamines.

The findings from our present study that the degree of inhibition of both the volume and acidity of gastric secretion by omeprazole is considerably less in the *H pylori* negative than positive subjects makes it highly likely that its efficacy in controlling acid/peptic disease will also be less in *H pylori* negative subjects. All the clinical studies to date which have assessed the antisecretory efficacy of PPI treatment have involved groups which have been either predominantly (ulcer patients) or partially *H pylori* positive. The current literature on the antisecretory efficacy of PPI treatment is consistent with this finding in the *H pylori* negative population. There have been recent reports of difficulty in controlling intragastric acidity in some GORD subjects with PPI treatment. This may be due to reduced efficacy in *H pylori* negative subjects. Whether increasing the dose of the PPI will achieve increased control is at present unclear and will need to be addressed in *H pylori* negative subjects.

In summary, *H pylori* status has a major influence on the inhibition of acid secretion produced by PPI treatment. A more profound inhibition of acid secretion is seen in *H pylori* positive subjects and this cannot be explained by acid neutralisation, either by ammonia or any other substances. While this increased antisecretory effect will facilitate the control of acid/peptic disease, it will also predispose to enteric infections and gastric colonisation by nitrosating bacterial species.

We gratefully acknowledge the kindness of the Scottish National Blood Transfusion Service in their provision of serum albumin.

We are also most grateful to Dr Andrew Kelman for his kind advice on appropriate pharmacokinetic modelling.


50 Ruddell WSJ, Losowsky MS. Severe diarrhoea due to small intestinal colonisation during cimetidine treatment. *BMJ* 1980;281:73.


**Helicobacter pylori** infection potentiates the inhibition of gastric acid secretion by omeprazole

D Gillen, A A Wirz, W D Neithercut, J E S Ardill and K E L McColl

*Gut* 1999 44: 468-475
doi: 10.1136/gut.44.4.468

Updated information and services can be found at:
http://gut.bmj.com/content/44/4/468

These include:

**References**

This article cites 56 articles, 16 of which you can access for free at:
http://gut.bmj.com/content/44/4/468#BIBL

**Email alerting service**

Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

**Topic Collections**

Articles on similar topics can be found in the following collections

- Gastrointestinal hormones (848)
- Campylobacter, Salmonella, Shigella, Escherichia coli (242)
- Helicobacter pylori (218)

**Notes**

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/