Acute perforated duodenal ulcer is not associated with *Helicobacter pylori* infection

D H Reinbach, G Cruickshank, K E L McColl

Abstract
Most patients with chronic duodenal ulcer disease have *Helicobacter pylori* infection and eradicating it considerably reduces the relapse rate. The prevalence of *H pylori* in 80 patients (mean age = 52 years, range 17–85) presenting with acute perforated duodenal ulcer was examined and compared with age and sex matched hospital control patients. *H pylori* state was assessed by serum anti-*H pylori* IgG (Helico-G, kit, Porton) using a titre of 18 or less as negative with a specificity of 89% and sensitivity of 88%. Only 47% of the perforated duodenal ulcer patients were positive for *H pylori* and this was similar to the value of 50% in the controls. In 51 of the perforated duodenal ulcer patients 14C-urea breath tests were also performed 4–10 weeks after surgery and this confirmed that only 49% were positive for *H pylori*. None of these patients had received perioperative drugs that might have eradicated the infection. The *H pylori* positive and *H pylori* negative perforated duodenal ulcer patients were similar with respect to age (53, 51), smoking (84%, 83%), and consumption of more than 15 units of alcohol per week (42%, 38%). Duodenal ulcer disease had been diagnosed before acute perforation in only 24% of those with *H pylori* and also 24% of those without the infection. Regular non-steroidal anti-inflammatory drug (NSAID) use was common in both those with (44%) and without (45%) *H pylori*. In conclusion, the lack of association of acute perforated duodenal ulcer and *H pylori* infection suggests that perforated duodenal ulcer has a different pathogenesis from chronic duodenal ulcer disease, and that the first should not be regarded simply as a complication of the second.

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*Helicobacter pylori* infection of the antral mucosa plays an important part in the pathogenesis of chronic recurrent duodenal ulceration. More than 95% of such patients have the infection and eradicating it considerably reduces the ulcer recurrence rate.** The role of *H pylori* infection in chronic duodenal ulcer disease may be explained by the fact that it causes excessive release of gastrin by the antral mucosa, which in turn stimulates excessive acid secretion.**

Although the role of *H pylori* in the pathogenesis of chronic duodenal ulcer disease is now well established, its importance in acute perforated duodenal ulcer is unknown. The aim of this study was to assess the prevalence of *H pylori* infection in patients having a laparotomy for repair of a perforated duodenal ulcer.

Patients and methods
Over a one year period, patients presenting with a perforated duodenal ulcer were recruited from seven hospitals in the Glasgow area, covering a population of approximately one million. All patients were identified by regular contact with the Emergency Theatre departments of each hospital. The patients were visited during their hospital stay, usually between days 3–5 after operation. The operation notes were examined (by DHR) and only those patients identified as having perforation of a duodenal ulcer were included. Patients with perforation of prepyloric or gastric ulcers were excluded.

After informed consent was obtained, the following details were recorded: age, sex, past medical history, past history of ulcer disease, history of dyspepsia, drug history, smoking and drinking habits, family history, and drugs given during hospital stay. A patient was only considered to have a past history of duodenal ulcer disease if an active ulcer or deformed duodenum had been shown previously by barium meal or endoscopy or at previous laparotomy. A patient was considered to have a history of dyspepsia if they had experienced intermittent upper abdominal pain with some relation to eating. Information was also obtained from the operation notes or speaking to the surgeon who performed the procedure, or both to ascertain whether the perforated ulcer had the appearance of an acute or chronic ulcer.

Within five days of the patients admission for acute perforated duodenal ulcer, 30 ml of venous blood was taken for *H pylori* serology. This was allowed to clot and then centrifuged and the serum stored at −20°C. As a further means of assessing *H pylori* state, patients were requested to attend for a 14C-urea breath test at the Western Infirmary, Glasgow. This was performed at least four weeks after both discharge and withdrawal from any drugs. On that occasion a further blood sample was obtained from these patients for repeat *H pylori* serology.

For control purposes, serum samples were obtained for *H pylori* serology from 80 age and sex matched patients admitted to one of the hospitals. This serum was again obtained within two days of admission and those patients suffered from a wide range of medical and surgical conditions.

Studies were also performed to exclude the possibility that laparotomy might interfere with the serology test for *H pylori* infection. This was
Acute perforated duodenal ulcer is not associated with Helicobacter pylori infection

TABLE I Details of the three patients who had recurrent perforations

<table>
<thead>
<tr>
<th>Sex</th>
<th>Time interval</th>
<th>Drug treatment</th>
<th>Alcohol</th>
<th>Smoker</th>
<th>H pylori state</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>39 years</td>
<td>Regular H₂</td>
<td>&lt;10 units/week</td>
<td>Yes</td>
<td>Positive</td>
</tr>
<tr>
<td></td>
<td>12 years</td>
<td>antagonists</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>61 years</td>
<td>Intermittent H₂</td>
<td>None</td>
<td>Yes</td>
<td>Positive</td>
</tr>
<tr>
<td></td>
<td>5 years</td>
<td>antagonists</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>49 months</td>
<td>Regular H₂</td>
<td>&gt;20 units/week</td>
<td>Yes</td>
<td>Positive</td>
</tr>
<tr>
<td></td>
<td>6 months</td>
<td>antagonists</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Done by obtaining serum samples from three patients obtained before and five days after surgery.

Analyses

*H pylori* serology was performed using a commercial IgG ELISA kit (Helico G serology kit, Porton, Cambridge, UK). This has been validated in our own hospital and with a titre of 18 IU/ml or less as negative, has a sensitivity of 88% and specificity of 89%.

The ¹⁴C-urea breath test was performed as previously described. This has also been validated in our own unit and using a 20 minute value of >20 (percentage ¹⁴C dose per mmol CO₂×10⁰×kg body wt) as positive has a sensitivity and specificity of >95%. The study was approved by the Western Infirmary Ethical Committee.

Results

One hundred and eleven patients were identified with acute perforated duodenal ulcer during the 12 months of the study. Thirty one of those were unsuitable for entry to the study because of early postoperative death, refusal to sign a consent form, or inability to sign it on account of mental confusion. Consequently, 80 patients were enrolled into the study. Their mean age was 52 years (range 17-85) and 59 (74%) were men. Three (4%) were taking steroids and 51 (44%) NSAIDs. Sixty seven (84%) of the patients smoked and 32 (40%) drank more than 15 units of alcohol per week. Twenty one (26%) had a family history of ulcer disease. Only 19 (24%) had a past history of ulcer disease and only 31 (39%) had a history of dyspepsia for more than three months. Eighteen (22%) had been on acid inhibitory treatment at the time of perforation and only a further 10 (13%) had previously had acid inhibitory treatment.

Two of the patients had experienced a previous perforation, which had been treated by simple closure and omental patch. A further patient who presented with his first perforation in this study was treated with simple closure and omental patch presented with a further perforation of duodenal ulcer six months later. Only his first presentation was included in the analysis. Table I gives further details of these three patients.

In 71 of 80 patients, the surgeon considered the perforation to be acute and in only nine was it considered to be a perforation against a background of chronic duodenal ulceration. All patients except three were treated surgically by simple closure and omental patch. Because of a history of chronic duodenal ulceration, one patient, a 39 year old man, had a vagotomy and pyloroplasty, and one patient, a 55 year old man, a vagotomy and gastroenterostomy. The third, a 75 year old man, had a polyvalent gastrectomy because of technical difficulties in oversewing his chronic duodenal ulcer.

Anti-*H pylori* IgG serology performed in these 80 patients during their admission for acute duodenal ulceration showed that 47% were positive and 53% negative (Fig 1). Each of the three patients with recurrent perforation were positive for *H pylori*. Fifty one patients attended for a ¹⁴C urea breath test and by this 49% were positive and 51% negative (Fig 2). The patients who attended for the breath test were representative of the entire 80 patients studied, having a mean age of 50 years (range 19-85) and 82% being men. Only five of these patients who attended for the breath test had received drugs for longer than 24 hours after their perforation and there was no association of perioperative treatment and subsequent breath test result (Table II).

The mean age of the 80 control patients was 46 years (range 19-89) and 73% were men. Fifty per cent of these control patients had positive IgG serology for *H pylori*. This rate was not significantly different from the perforated duodenal ulcer patients (Fig 1). The median anti-*H pylori* IgG titre in the control patients was 15±5 IU/ml, which was not significantly different from that of 16 IU/ml in the patients with perforated duodenal ulcers.

In the three patients whose anti-*H pylori* IgG titre was assessed before and after operation, there was no evidence of any change in the titre induced by operation. The mean titre was 25

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**Figure 1**: IgG titre to *H pylori* in 80 patients presenting with acute perforated duodenal ulcer and in 80 age and sex matched hospital controls. The median values are shown by horizontal lines and the upper limit for negative serology shown by the broken line.
and in hospital control patients. Eighty patients a-
no also 80 
By serology 
Hbreath in 
This perforated 
NSAID use. 
C. pylori 
M. pylori 
controls 
Hospital 
By serology 
Patients with perforated duodenal ulcers 

(range 22–34) before and 27 (range 13–30) five 
days after surgery. In the 51 patients who had 
their serology checked both at the time of acute 
presentation and again 6–10 weeks later, the 
proportion who were positive was similar on 
both occasions being 57% and 65%, respectively. 
A comparison was made of the M. pylori 
positive and negative perforated duodenal ulcer 
patients as assessed with IgG serology (Table 
III). This showed that they were similar with 
respect to age, sex, smoking and drinking habits, 
past history of ulcer disease, family history, and 
NSAID use. In the 38 patients presenting with 
perforated duodenal ulcer while receiving 
NSAID treatment or steroids, the prevalence of 
M. pylori was only 44%.

Discussion
This study shows that the prevalence of M. pylori 
infection in patients presenting with acute per-
oration of a duodenal ulcer is only about 50% 
and no higher than that in a control hospital 
population. This contrasts with the prevalence of 
>95% in the general duodenal ulcer patient 
population. 
The possibility that our study has under-
estimated the prevalence of the infection is 
unlikely. The serological method of determining 
the M. pylori state has been shown to be reliable 
in our own unit and in other centres. The 
possibility that the laparotomy and anasthetic 
may have adversely affected the reliability of 
the IgG ELISA test was examined and excluded. 
In addition, assessment of the M. pylori state by 
the 14C-urea breath test one month after hospital 
discharge and withdrawal of all drug treatment 
provided independent confirmation of the 
M. pylori state. Recent exposure to drugs 
can produce a negative breath test by suppressing 
the infection. Careful assessment of drugs used 
during or after surgery showed, however, that 
none of the patients had received drug regimens 
likely to have eradicated M. pylori. Our finding 
that the prevalence of M. pylori infection is not 
increased in patients presenting with perforated 
duodenal ulcer is consistent with the recent 
report by Debongie and Legros.

The previous studies that have shown a high 
prevalence of H. pylori in duodenal ulcer patients 
and have shown that eradicating the infection 
reduces the ulcer relapse rate have consisted 
almost exclusively of patients with chronic 
recurrent duodenal ulceration. The patients in 
this study who presented with perforation 
represent a different subgroup of duodenal ulcer 
disease in that only 24% had a previous history 
suggestive of duodenal ulceration and only 35% 
had ever received treatment with acid inhibitory 
agents. The appearance of the duodenum at 
surgery also showed that most of the patients had 
an acute perforation without evidence of chronic 
recurrent duodenal ulcer disease. Our patients 
therefore differed from those in whom H. pylori 
prevalence has been studied previously not only 
in presenting with a complication of duodenal 
ulceration but also by presenting with acute 
rather than chronic duodenal ulcer disease. 
Though there is convincing evidence that 
H. pylori plays a part in chronic recurrent 
duodenal ulceration, its role in acute duodenal 
ulcer disease is not supported by this study.

The possibility that acute perforated duodenal 
ulceration could be associated with the early 
phase of H. pylori infection before IgG sero-
conversion has had time to occur must be 
considered. The fact that the prevalence of the 
infection, however, was low by the urea breath 
test as well as by serology and the similar 
prevalence of seropositivity at acute presentation 
and repeat testing 6–8 weeks later exclude this 
possibility.

A recent study from Hong Kong has shown that 
patients presenting with acute bleeding 
duodenal ulceration also have a lower prev-
ience of H. pylori infection (71%) than

**TABLE II** Details of drugs given to the 25 patients with a 
positive 14C-urea breath test and 26 patients with negative 
14C-urea breath test at 4 to 10 weeks after hospital discharge

<table>
<thead>
<tr>
<th>Drug</th>
<th>H pylori positive</th>
<th>H pylori negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nil</td>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td>Cefuroxine single dose</td>
<td>3</td>
<td>Nil</td>
</tr>
<tr>
<td>Cefuroxine for 24 hours</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Cefuroxine for 3 days</td>
<td>Nil</td>
<td>1</td>
</tr>
<tr>
<td>Cefuroxine + metronidazole single dose</td>
<td>4</td>
<td>11</td>
</tr>
<tr>
<td>Cefuroxine + metronidazole for 24 hours</td>
<td>10</td>
<td>3</td>
</tr>
<tr>
<td>Cefuroxine + metronidazole + amoxycillin</td>
<td>Nil</td>
<td>1</td>
</tr>
<tr>
<td>Metronidazole single dose</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Ampicillin + gentamicin + metronidazole for 24 hours</td>
<td>Nil</td>
<td>1</td>
</tr>
</tbody>
</table>

**TABLE III** Comparison of the patients with perforated 
duodenal ulcers found to be positive and negative for H pylori 
by IgG serology

<table>
<thead>
<tr>
<th>Drug</th>
<th>H pylori positive</th>
<th>H pylori negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (y)</td>
<td>51</td>
<td>53</td>
</tr>
<tr>
<td>Range (y)</td>
<td>17–85</td>
<td>21–85</td>
</tr>
<tr>
<td>Male</td>
<td>74% (32)</td>
<td>71% (27)</td>
</tr>
<tr>
<td>Smoking</td>
<td>83% (35)</td>
<td>84% (32)</td>
</tr>
<tr>
<td>Alcohol &gt;15 units/week</td>
<td>38% (16)</td>
<td>42% (16)</td>
</tr>
<tr>
<td>Past history of duodenal ulcer</td>
<td>24% (10)</td>
<td>24% (9)</td>
</tr>
<tr>
<td>Family history of duodenal ulcer</td>
<td>29% (12)</td>
<td>24% (9)</td>
</tr>
<tr>
<td>Current steroids</td>
<td>5% (2)</td>
<td>3% (1)</td>
</tr>
<tr>
<td>Current NSAID treatment</td>
<td>45% (19)</td>
<td>44% (16)</td>
</tr>
<tr>
<td>Dyspepsia &gt;3/12</td>
<td>54% (14)</td>
<td>45% (17)</td>
</tr>
<tr>
<td>Current acid inhibitory drugs</td>
<td>14% (6)</td>
<td>32% (12)</td>
</tr>
<tr>
<td>Previous acid inhibitory drugs</td>
<td>12% (5)</td>
<td>14% (5)</td>
</tr>
</tbody>
</table>
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The authors wish to acknowledge the co-operation of the consultant surgeons in the Glasgow area who allowed their patients to be studied. We also acknowledge the secretarial assistance of Mrs Dorothy Ronney and the staff of the Department of Clinical Physics who performed the breath tests. This study was supported by a grant from the Biomedical and Clinical Research Committee of the Scottish Home and Health Department.

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