Campylobacter pylori in the upper gastrointestinal tract of patients with HIV-1 infection

N D Francis, R P H Logan, M M Walker, R J Polson, A W Boylston, A J Pinching, J R W Harris, J H Baron

Abstract
Fifty one patients with human immunodeficiency virus (HIV-1) infection who had been consecutively endoscoped for upper gastrointestinal symptoms were biopsied (stomach or duodenum, or both) and compared with 59 age and sex matched controls for the presence of Campylobacter pylori. In 28 (47%) of the control group but in only seven (14%) of the HIV seropositive patients were C pylori seen on histological examination (p<0.001, odds ratio 3.6, 95% confidence interval 2.2-14.5). Sixteen patients who were HIV antibody positive had other index diseases for the diagnosis of AIDS in the biopsy material and, when these were excluded, comparison with the control group still showed a significant difference: p<0.01, odds ratio 3.6, 95% confidence interval 1.4-9.6. In this series, therefore, C pylori were far less common in HIV antibody positive patients than in controls. Among the HIV positive patients, a higher proportion of C pylori negative cases had AIDS but this trend was not significant.

The findings of this study indicate that whatever abnormalities of cell mediated mucosal immunoregulation are caused by HIV infection, they do not seem to be important in the response to infection by C pylori.

Considerable evidence now links the presence of Campylobacter pylori with chronic type B (non-autoimmune) gastritis and duodenal ulceration1-3; when it is present almost invariably there is histological evidence of gastritis.4 C pylori is found in the gastric mucosa of up to 90% of patients with a duodenal ulcer, in 70% with gastric ulcer, and in 60% of patients with non-ulcer dyspepsia.4 There is also serological evidence of C pylori infection in up to 20% of the adult population even when asymptomatic, a similar prevalence histologically in normal volunteers,7 and a 40-65% prevalence in unselected patients undergoing upper gastrointestinal endoscopy.6 Patients infected with human immunodeficiency virus (HIV-1), with or without AIDS, have a high incidence (50-90%) of gastrointestinal symptoms.6 This study was undertaken to assess the incidence of C pylori in histological specimens from HIV antibody positive patients and to establish what histological abnormalities were associated with the presence of these organisms. Comparison was made with an age and sex matched control group. We set out to answer the following questions: Does the incidence of C pylori differ from the normal population or from HIV antibody negative patients with upper gastrointestinal symptoms? Does HIV infection, therefore, increase susceptibility to infection by C pylori? Is there more or less tissue damage in HIV antibody positive, than in HIV antibody negative, patients with C pylori?

Methods
Fifty one HIV antibody positive patients consecutively examined by upper gastrointestinal endoscopy were studied. All had three or four gastric biopsy specimens taken from the body and antrum, and most underwent duodenal biopsy. Fifty nine age and sex matched HIV antibody negative controls were compared with the study group. The case controls were recruited from a group of 200 patients already being endoscoped for upper gastrointestinal symptoms and studied for C pylori. All of the control group also had body, antral, or duodenal biopsy specimens taken. Criteria for endoscopy were presentation with any upper gastrointestinal symptoms and were similar in study and control groups. Biopsy specimens were examined at multiple levels by light microscopy, having been stained with haematoxylin and eosin and the Gimenez9 technique to facilitate identification of C pylori. The degree of inflammation and type of gastritis were assessed—normal, chronic gastritis, active chronic gastritis, atrophic gastritis, acute gastritis—using the Whitehead classification, where the term active indicates the presence of polymorphs. Duodenitis was also assessed and the presence of gastric metaplasia noted.

Results
were analysed for confidence interval for an unmatched case control study and differences in proportions of C pylori negative cases with or without AIDS were analysed by the $\chi^2$ test.

Results
Twenty eight (47%) of the control group but only seven (14%) of the HIV patients were positive for C pylori on histological examination (p<0.001, odds ratio 5.6, 95% confidence interval 2.2-14.5). Sixteen patients in the HIV group had an AIDS index disease diagnosed on the biopsy material received, but no C pylori. These were cytomegalovirus, Kaposi's sar-
Coma, lymphoma and cryptosporidia. Two cases of giardiasis were also seen. These 16 were excluded from further study or comparison. When the remainder were compared with the controls there was still a significant difference \( p<0.01 \), odds ratio 3.6, 95\% confidence interval 1.4–9.6 (table 1).

Details of the HIV positive \( C\) \( pylori \) positive cases are shown in table 2. Two of these cases had coexistent cryptosporidia, one seen in the duodenal biopsy specimen and one in a stool sample.

Most of the patients had not received any treatment in the four weeks before investigation and none had received bismuth compounds or amoxicillin; nor had they received other drugs in doses or combinations recognised to be effective against \( C\) \( pylori \) (table 3).

In the HIV antibody positive \( C\) \( pylori \) negative patients the proportion of AIDs to non-AIDS cases was 10:18. This was not significantly different from the 1:6 ratio in the HIV antibody positive \( C\) \( pylori \) positive cases \( (p>0.05) \). Although there was a trend, there was no definite correlation with the stage of disease in HIV infection.

The histological features associated with \( C\) \( pylori \) infection in the HIV antibody positive patients were not different from those seen in either the HIV antibody negative cases or from previous reports. There was inflammation in the lamina propria in all except case 4 in whom \( C\) \( pylori \) were found in the duodenum (with inflammation) but not in the normal gastric biopsy specimens. Five of the remaining cases had active gastritis and one had chronic inflammation without polymorphs. This was similar to the findings in the control group where the presence of \( C\) \( pylori \) was associated with active inflammation in 17 and chronic inflammation in 11. None of the control group had normal gastric biopsy histology in association with \( C\) \( pylori \).

Analysis of intraepithelial lymphocyte numbers was not carried out as this is the subject of a separate study. We did not observe any subjective differences, however, between the controls and the groups with HIV with \( C\) \( pylori \) in this respect.

### Discussion

This is the first case control study of \( C\) \( pylori \) in HIV infection as far as we know and our results show that the incidence is significantly lower than in endoscopically negative patients with upper gastrointestinal symptoms and similar to that found in normal volunteers. Campylobacter jejuni and other Campylobacter-like organisms have been found in homosexual men with enterocolitis or bacteraemia \(^\text{10} \) but there has only been one case report of \( C\) \( pylori \) in a patient with AIDS. \(^\text{11} \) A study of \( C\) \( pylori \) antibody titres in homosexual men suggested that the prevalence of the organism was higher than in normal controls. \(^\text{12} \) It might therefore be expected that this infection would also be commoner in patients infected with HIV, but this is not borne out by our study.

Meiselman's case was reported as having an unusually aggressive course with histological invasion of Campylobacter into the mucosal lamina propria. \(^\text{11} \) There was evidence of mucosal erosion, however, and the invasion may therefore have been a secondary event. It was also implied that reduced mucosal immunity might explain the clinical course and florid histology and that this suggested immunological events in the control of \( C\) \( pylori \) infection.

In our positive cases neither the clinical nor histological features were unusually severe or aggressive and they were similar to those described and seen in HIV antibody negative patients infected with \( C\) \( pylori \). This suggests

### Table 1  \( C\) \( pylori \) positivity in cases and controls

<table>
<thead>
<tr>
<th>( C) ( pylori ) positive (other gastrointestinal disease excluded)</th>
<th>HIV positive</th>
<th>HIV negative controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total with</td>
<td>7</td>
<td>7</td>
</tr>
<tr>
<td>Total number</td>
<td>35</td>
<td>51</td>
</tr>
</tbody>
</table>

### Table 2  \( C\) \( pylori \) identified on biopsy

<table>
<thead>
<tr>
<th>Case No</th>
<th>HIV/AIDS</th>
<th>Gastric histology</th>
<th>( CP )</th>
<th>Duodenal histology</th>
<th>( CP )</th>
<th>Clinical details</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>HIV+</td>
<td>Active atrophic gastritis</td>
<td>+</td>
<td>Normal</td>
<td>–</td>
<td>Diarrhoea, cryptosporidia (stool)</td>
</tr>
<tr>
<td>2</td>
<td>AIDS</td>
<td>Chronic gastritis</td>
<td>+</td>
<td>Normal</td>
<td>–</td>
<td>Dyspepsia</td>
</tr>
<tr>
<td>3</td>
<td>HIV+</td>
<td>Active atrophic gastritis</td>
<td>+</td>
<td>Mild chronic duodenitis, cryptosporidia</td>
<td>–</td>
<td>Recurrent vomiting, mild gastritis</td>
</tr>
<tr>
<td>4</td>
<td>HIV+</td>
<td>Normal</td>
<td>–</td>
<td>Chronic duodenitis (gastric metaplasia)</td>
<td>+</td>
<td>Painful dysphagia</td>
</tr>
<tr>
<td>5</td>
<td>HIV+</td>
<td>Active chronic gastritis</td>
<td>+</td>
<td>Chronic duodenitis</td>
<td>–</td>
<td>Abdominal pain, atypical gastritis</td>
</tr>
<tr>
<td>6</td>
<td>HIV+</td>
<td>Acute gastritis, ulcer</td>
<td>+</td>
<td>No biopsy</td>
<td>–</td>
<td>Haematematosis, small erosion</td>
</tr>
<tr>
<td>7</td>
<td>HIV+</td>
<td>Acute gastritis</td>
<td>+</td>
<td>No biopsy</td>
<td>–</td>
<td>Dyspepsia</td>
</tr>
</tbody>
</table>

### Table 3  Treatment received by HIV positive patients during four weeks before biopsy

<table>
<thead>
<tr>
<th>No of cases</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>( C) ( pylori ) positive:</td>
<td>Nil</td>
</tr>
<tr>
<td>4</td>
<td>Ganciclovir</td>
</tr>
<tr>
<td>1</td>
<td>Didanosine, ketoconazole</td>
</tr>
<tr>
<td>1</td>
<td>Amoxicillin and fluclaxacilin</td>
</tr>
<tr>
<td>1</td>
<td>(1/52 PRIOR) fluconazole</td>
</tr>
<tr>
<td>( C) ( pylori ) negative:</td>
<td>Nil</td>
</tr>
<tr>
<td>16</td>
<td>Ganciclovir</td>
</tr>
<tr>
<td>3</td>
<td>Ketoconazole</td>
</tr>
<tr>
<td>3</td>
<td>Rifampicin, ethambutol, pyriziamide</td>
</tr>
<tr>
<td>2</td>
<td>Ganciclovir</td>
</tr>
<tr>
<td>1</td>
<td>Ganciclovir, fluconazole</td>
</tr>
<tr>
<td>1</td>
<td>Erythromycin, sulphasalazine</td>
</tr>
<tr>
<td>1</td>
<td>Cyclophosphamide, adriamycin, vincristine, prednisone, for non-Hodgkin’s lymphoma</td>
</tr>
<tr>
<td>Total 35</td>
<td></td>
</tr>
</tbody>
</table>
that the immune response and tissue damage
normally elicited by *C. pylori* infection is not
noticeably affected by HIV infection.

The role of *C. pylori* infection in causing
symptoms is unknown at present. Although this
was not a question we could specifically
answer from this retrospective study, we con-
clude that in the small number of *C. pylori*
positive patients infection with this organism
was likely to be responsible for their symptoms
and histological evidence of inflammation.
While this represents a relatively small per-
centage of gastrointestinal disease in the HIV
population, a high proportion of patients with
HIV have gastrointestinal symptoms; a diag-
nosis of *C. pylori* infection may therefore be
important in clinical management.

Intestinal mucosal immunity in HIV infec-
tion has not been studied directly, but analysis
of mucosal lymphocyte populations has shown
decreased T11 positive cells with decreased
T4, increased T8 numbers, and a reversal of the
T4:T8 ratio.\(^2\) These findings suggest that
there is impaired local cell mediated immunity
permitting infection by opportunistic and
other organisms as well as persistence of HIV.
The low incidence of *C. pylori* in our study
group does not support the view that HIV
infection or AIDS predisposes to this infection;
indeed, it suggests the opposite.

If reduced mucosal T cell dependent
immunity were a main predisposing factor in
colonisation by *C. pylori* then we would expect
to find an increased incidence of HIV antibody
positive patients and, by extension, significant-
ly fewer cases of AIDS in the *C. pylori* negative
group. Although there was a trend towards the
latter, our results showed no significant dif-
ference in *C. pylori* negativity between HIV
antibody positive patients with or without
AIDS.

Our observations and those of others show
that a large proportion of HIV antibody
positive patients have no potential secondary
pathogen or process to explain the gastrointes-
tinal symptoms after biopsy, bacteriological,
and virological investigations. This has led to
the suggestion that HIV has enteropathic
effects of its own.\(^3\)^\(^4\)^\(^5\)

The explanation for the low prevalence of
*C. pylori* in this study, compared with other
patients with upper gastrointestinal symptoms,
is not fully explained by the presence of HIV
associated diseases. An interaction with other
organisms such as cryptosporidia (as in two of
our cases) could have had an effect on *C. pylori*
colonisation. Another possibility is that
antibodies to *C. pylori* are non-specifically
raised due to the early HIV associated poly-
clonal rise in gammaglobulins and that the
bacteria are partially or completely eradicated,
or infection prevented. It is also possible that
infection of gut epithelial cells and lamina
propria monocytes and macrophages by HIV
changes the local environment and mucus,
therefore inhibiting colonisation and survival.

Some of our patients were receiving or had
recently completed treatment for other comp-
lications of HIV infection. None had received
bismuth compounds, amoxicillin, or other
drug combinations recognised to be effective
against *C. pylori* in the four weeks before
investigation. We cannot be certain, however,
that other therapeutic or prophylactic agents
received by some of the patients did not have
some activity against *C. pylori*, either directly or
indirectly. We are now conducting a prospec-
tive study of *C. pylori* infection in HIV positive
patients.

As the prevalence of *C. pylori* infection in our
study is comparable with that of normal con-
trols, HIV infection does not seem to increase
susceptibility to these organisms. The corollary
of this is that cell mediated immunity is not
involved in the control of *C. pylori* infection.

1 Warren JR, Marshall BJ. Unidentified curved bacilli on
gastric mucosa in active chronic gastritis. *Lancet* 1983;
ii:1273-5.
double-blind trial of duodenal ulcer relapse after eradi-
3 Goodwin CS. Duodenal ulcer, Campylobacter pylori and
4 Rathbone B, Wyatt JJ, Worsley BW, Trejdosiewicz LK,
Healey RV, Losowsky MS. Immune response to Cam-
5 Rathbone B, Wyatt JJ, Worsley BW, et al. Systemic and
local antibody responses to Campylobacter pylori in

6 Marshall BJ, McGechie DB, Rogers PA, Glancy RJ. Pyloric
Campylobacter infection and gastroduodenal disease.
7 Graham DY, Klein PD, Evans DJ, et al. Campylobacter
pylori detected noninvasively by the "13C-urea breath test.
8 Taylor DE, Hargreaves JA, Ng LK, Sherbaniuk RW, Jewell
LD. Isolation and characterisation of Campylobacter pylori
from gastric biopsies. *Br Med J* 1986;293:
454-50.
9 McMullen L, Walker MM, Bain IA, Karim QN, Baron JH.
Histological identification of Campylobacter using the
Gimenez technique in gastric antral biopsies. *J Clin Pathol*
1987;40:463.
10 Quinn TC, Goodell SE, Fennell C, Want SP. Infections
with Campylobacter jejuni and Campylobacter-like
11 Meiselman MS, Miller-Carchporel R, Christ M, Randall E.
Campylobacter pylori in the acquired immunodeficiency
13 Ellakany S, Whitenside TL, Shade RR, Van Thiel DH.
Analysis of intestinal lymphocyte subpopulations in
patients with acquired immunodeficiency (AIDS) and
AIDS-related complex. *Am J Clin Pathol* 1987;87:
356-64.
intrinsic autonomic nerves in human immunodeficiency
architecture and fat absorption in male homosexuals
infected with human immunodeficiency virus. *Q J Med*
Campylobacter pylori in the upper gastrointestinal tract of patients with HIV-1 infection.

N D Francis, R P Logan, M M Walker, R J Polson, A W Boylston, A J Pinching, J R Harris and J H Baron

*J Clin Pathol* 1990 43: 60-62
doi: 10.1136/jcp.43.1.60

Updated information and services can be found at:
http://jcp.bmj.com/content/43/1/60

**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.

**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/