Study of Transmission Routes of *Helicobacter pylori* in Relation to Seroprevalence of Hepatitis A Virus

TAKAHISA FURUTA,1,2* TAKASHI KAMATA,2 MISAKO TAKASHIMA,1 HAJIME FUTAMI,1 HAJIME ARAI,1 HIROYUKI HANAI,1 AND EIZO KANEKO1

First Department of Medicine, Hamamatsu University School of Medicine, Hamamatsu 431-31,1 and Honda Motor Co., Ltd., Hamamatsu Factory, Hamamatsu Health Service Center, Hamamatsu 433,2 Japan

Received 16 December 1996/Returned for modification 3 March 1997/Accepted 18 April 1997

The seroprevalence of *Helicobacter pylori* in a group of 1,043 healthy Japanese people was compared with that of hepatitis A virus (HAV), which was used as a marker of fecal-oral exposure. No statistically significant relationship was observed between seropositivity for HAV and that for *H. pylori*. Therefore, the fecal-oral spread of *H. pylori* is of limited relevance in Japan.

*Helicobacter pylori* is now thought to be one of the most important factors in the pathogenesis of upper gastroduodenal diseases (1, 2, 6). Eradication of *H. pylori* is gaining profound significance for the treatment of many gastroduodenal diseases (14, 18, 19). Therefore, elucidation of its transmission routes is necessary to prevent patients from being infected with *H. pylori* again after successful eradication therapy. Earlier studies have indicated that person-to-person transmission is a principal mode of spread of *H. pylori* (3, 10, 13, 16, 21). However, even when *H. pylori* is transmitted from person to person, it is still controversial whether the transmission route is via an oral-oral, fecal-oral, or some other route (5, 15). In developing countries, the route is mainly fecal-oral (4, 7), but studies performed in developed countries are rare. In order to clarify whether the transmission of *H. pylori* in a developed country is related to the fecal-oral route, the seroprevalence of *H. pylori* in a group of Japanese people was compared with the seroprevalence of hepatitis A virus (HAV), which was used as a marker of fecal-oral exposure.

A total of 1,043 healthy persons who underwent medical checkups at Hamamatsu Health Service Center (Honda Motor Co., Ltd., Hamamatsu Factory, Hamamatsu, Japan) were included in the study. The group consisted of 585 males (age, 42.1 ± 11.1 years [mean ± standard deviation]) and 458 females (age, 44.7 ± 9.8 years). Blood samples obtained from subjects were centrifuged at 3,000 × g for 10 min to obtain the serum. All serum samples were stored at −20°C until measurement. The protocol was approved by the Human Institutional Review Board of Hamamatsu University School of Medicine.

Anti-HAV immunoglobulin G antibody in the serum from each subject was detected by radioimmunoassay (HAVAB RIA kit; Abbott Laboratories, Abbott Park, Ill.). Anti-*H. pylori* immunoglobulin G antibody was detected by enzyme immunoassay (HM•CAP kit; Enteric Product Inc., Stony Brook, N.Y.). All samples were measured at the laboratory center (BML Co., Tokyo, Japan).

The statistical significance of seropositivity for each pathogen was examined by the χ² test. The statistical significance of the difference in mean age between HAV-seropositive and -seronegative individuals was determined by Student’s t test. Logistic regression analysis was performed to examine the factors affecting seropositivity for *H. pylori* and for HAV. Statistical calculations were performed by using the SAS software system. Findings of *P* < 0.05 were taken to indicate statistical significance.

Of 1,043 samples, 231 (22%) were seropositive for HAV, and 416 (40%) were seropositive for *H. pylori*. Of the 231 samples seropositive for HAV, 124 (54%) were seropositive for *H. pylori*, and of the 812 samples seronegative for HAV, 292 (36%) were seropositive for *H. pylori* (*P* < 0.0001). The mean age of subjects seropositive for HAV was significantly higher than that of subjects seronegative for HAV (53.5 versus 40.4 years, *P* < 0.0001). The mean age of subjects seropositive for *H. pylori* was also higher than that of subjects seronegative for *H. pylori* (46.4 versus 41.2 years, *P* < 0.0001). Univariate analysis of the concordance between *H. pylori* and HAV statuses is shown in Table 1. The sensitivity was so low and the false-positive rate was so high that the concordance of seropositivity for *H. pylori* with that for HAV appeared to be low.

The seropositivity rates for *H. pylori* and HAV significantly increased with age (*H. pylori*, *P* = 0.0020; HAV, *P* < 0.0001) (Fig. 1). The seropositivity rate for HAV increased with age irrespective of *H. pylori* status. The seropositivity rate for HAV in the *H. pylori*-seropositive group was almost the same as that in the *H. pylori*-seronegative group in each generation (Fig. 2). As shown in Table 2, age was a significant factor which affected the seropositivity rate for *H. pylori*. HAV status did not affect the seropositivity rate for *H. pylori* in the present study.

There have been many reports concerning transmission routes of *H. pylori*. *H. pylori* was detected in human feces (20), and some reports have suggested that fecal-oral transmission might be one of the transmission routes (4, 7). Another report did not support this hypothesis (11). *H. pylori* has also been detected in human saliva and dental plaque, and some reports have suggested that oral-oral transmission was important (12, 17). But, another report did not support this hypothesis, be-

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>%</th>
<th>Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>54</td>
<td>124/231</td>
</tr>
<tr>
<td>Specificity</td>
<td>64</td>
<td>520/812</td>
</tr>
<tr>
<td>Correct</td>
<td>62</td>
<td>644/1043</td>
</tr>
<tr>
<td>False positive rate</td>
<td>70</td>
<td>292/416</td>
</tr>
<tr>
<td>False negative rate</td>
<td>17</td>
<td>107/627</td>
</tr>
</tbody>
</table>

* Corresponding author. Mailing address: The First Department of Medicine, Hamamatsu University School of Medicine, 3600 Handacho, Hamamatsu 431-31, Japan. Phone: 81-53-435-2261. Fax: 81-53-434-9447.
cause in that study live *H. pylori* was difficult to detect in such materials (9).

According to Hazell et al., who used an anti-HAV antibody as a marker of fecal-oral transmission, the fecal-oral route was important in rural areas but was of limited relevance in urban areas (8). Most of the earlier studies which had indicated a relation between the transmission routes for *H. pylori* and HAV showed that the seropositivity rates of *H. pylori* and HAV increased simultaneously with age. It was concluded that one of the transmission pathways for *H. pylori* was the same as that for HAV, which conclusion supported the fecal-oral pathway (4, 7). These investigators, however, did not examine differences in the *H. pylori* seropositivity rates between the HAV-seropositive and -seronegative groups by age. There is no doubt that the seropositivity rates for both HAV and *H. pylori* increase with age, but this does not mean that the transmission routes are simply the same. In the present study, the seropositivity rates for both HAV and *H. pylori* and HAV increased with age, and the seropositivity rate for *H. pylori* in HAV-seropositive subjects was higher than that in the HAV-seronegative subjects, but the mean age of HAV-seropositive subjects was significantly higher than that of HAV-seronegative subjects. Therefore, it was difficult to conclude that the transmission pathway of *H. pylori* coincided with that of HAV, i.e., the fecal-oral route.

As shown in Fig. 1, the seropositivity rates of HAV and *H. pylori* increased with age. As shown in Fig. 2, the seropositivity rate for HAV increased with age irrespective of *H. pylori* status, and the seropositivity rate for HAV in *H. pylori*-seropositive subjects was almost the same as that in *H. pylori*-seronegative subjects in each age group. The results obtained from the logistic multivariate analysis also revealed that there was no significant relationship between seropositivity for HAV and that for *H. pylori*. These results strongly suggest that the transmission routes of *H. pylori* and HAV are independent of each other.

In summary, our data suggest that the transmission routes of *H. pylori* are independent of those of HAV in Hamamatsu, which is an average city in Japan. Therefore, the fecal-oral route of *H. pylori* transmission appears to be of limited relevance in a developed country.

This work was supported by a grant-in-aid for Scientific Research (10010414) from the Ministry of Education of Japan.

We thank Noriya Taki (Statistical Analysis of Medicine, Fukuo, Japan) for useful advice on statistical analysis.

### REFERENCES


### TABLE 2. Logistic regression analysis of factors affecting seropositivity for *H. pylori* 

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Parameter estimate</th>
<th>SE</th>
<th>P</th>
<th>Odds ratio</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.4144</td>
<td>0.1340</td>
<td>0.0020</td>
<td>1.51</td>
<td>1.16–1.97</td>
</tr>
<tr>
<td>HAV</td>
<td>−0.1491</td>
<td>0.1777</td>
<td>0.4015</td>
<td>0.87</td>
<td>0.61–1.23</td>
</tr>
</tbody>
</table>

*SE, standard error; CI, confidence interval.*

FIG. 1. Seropositivity rates for *H. pylori* and HAV by age group. The seropositivity rate for *H. pylori* (P = 0.0002) and that for HAV (P < 0.0001) significantly increased with age.

FIG. 2. Seropositivity rate for HAV as a function of *H. pylori* status. The seropositivity rate for HAV increased with age irrespective of *H. pylori* status. The seropositivity rate for HAV in the group seropositive for *H. pylori* was almost the same as that in the group seronegative for *H. pylori* for all age groups.


