Helicobacter spp. infection in cats: evaluation of the humoral immune response and prevalence of gastric Helicobacter spp.

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Abstract

The principal aims of this study were to evaluate the humoral immune response (IgG) of cats with gastric Helicobacter spp. infection, and to determine the prevalence of different types of Helicobacter spp. in the stomachs of cats. The Helicobacter infection status of 45 cats (12 healthy spay/neuter cats, 9 sick cats, 24 colony cats) was determined by evaluating endoscopic gastric biopsies for urease activity, presence of Helicobacter-like organisms (HLO) on histopathology, and genus and species-specific PCR. Serum samples were evaluated with a kinetic enzyme linked immunosorbent assay (ELISA) utilizing the high molecular cell-associated protein (HM-CAP) fraction of \textit{H. felis} ATCC 49179.

Seventeen of 45 cats were infected with Helicobacter spp.: “\textit{H. heilmannii}” 9/17, \textit{H. felis} 4/17, mixed “\textit{H. heilmannii}” and \textit{H. felis} 3/17, unclassified-Helicobacter spp. 7/17. \textit{H. pylori} was not detected in any cat. Kinetic ELISA results were significantly higher for infected cats, than for uninfected cats. Cats infected with different Helicobacter spp. showed similar distribution of OD/min values. There were no effects of age or clinical signs on the results of kinetic ELISA. No correlation between colonization density and seroconversion was observed. There were statistically significant, but weak correlations between the degree of seroconversion and the degree of inflammation, and the number of lymphoid follicles. Infected cats had more severe inflammation in the pylorus and fundus than uninfected cats. Infected sick cats had a higher degree of pyloric, but not fundic inflammation, than healthy infected cats and uninfected sick cats.
The results indicate that naturally acquired infection with gastric *Helicobacter* spp. is associated with seroconversion (IgG) in cats. The similar ELISA values in cats infected with a variety of *Helicobacter* spp. suggests substantial antigenic homology between different *Helicobacter* spp. The higher degree of inflammation in infected than uninfected cats, supports a role for *Helicobacter* as a cause of gastritis in cats. © 2001 Elsevier Science B.V. All rights reserved.

Keywords: Cat; *Helicobacter felis*; *Helicobacter heilmannii*; *Helicobacter pylori*; Serology; Prevalence; Histopathology

1. Introduction

Recent studies suggest a high prevalence of gastric *Helicobacter* infection in cats. Gastric *Helicobacter*-like organisms (HLO) have been observed in gastric biopsies from 41 to 100% of clinically healthy (Weber et al., 1958; Geyer et al., 1993; Otto et al., 1994; El Zaatari et al., 1997; Papasouliotis et al., 1997; De Majo et al., 1998; Neiger et al., 1998; Yamasaki et al., 1998), and 57 to 100% of vomiting cats (Geyer et al., 1993; Hermanns et al., 1995; Papasouliotis et al., 1997; Yamasaki et al., 1998). Diagnosis of infected individuals and determination of the prevalence of infection with gastric *Helicobacter* spp. in cats are hampered by the fact that diagnosis depends on invasive tests such as urease testing, histopathology, and cytology. The measurement of circulating antibodies (IgG) to *H. pylori* is a sensitive and specific means of diagnosing infection with *H. pylori* in humans and can easily be used to screen a large number of serum samples. ELISA has also enabled the detection of seroconversion in dogs (Strauss-Ayali et al., 1999), and cats after experimental infection with *H. felis* (Simpson et al., 2000), and *H. pylori* (Fox et al., 1995). However, the serological response of domestic cats with naturally acquired *Helicobacter* infections is unknown.

The presence of multiple *Helicobacter* spp. in cats with naturally acquired infections and co-infection in some cats present a challenge to the development of useful serological assay for the diagnosis of infections in non-experimental cats. To date, *H. felis*, *H. pametensis* and an *H. heilmannii*-like bacterium (“*H. heilmannii*”) have been identified in the stomachs of pet cats (Lee et al., 1988; Neiger et al., 1998). *H. pylori* has been cultured only from a group of laboratory cats (Handt et al., 1994). Few reports mention the prevalence of specific *Helicobacter* spp. in the stomach of cats as it requires specialized techniques. *H. felis* has been cultured from 3/21 *Helicobacter* infected cats in Finland (Jalava et al., 1998), whereas “*H. heilmannii*” was identified by PCR in 38/49 Swiss cats (Neiger et al., 1998), and *H. felis/“H. heilmannii”*-like organisms were identified by partial sequence of the 16S rRNA in 10/15 cats from the US (Norris et al., 1999).

The principal aims of this study were to evaluate the humoral immune response (IgG) of cats with gastric *Helicobacter* spp. infection, and to determine the prevalence of different types of *Helicobacter* spp. in the stomachs of cats. Subsidiary aims were to evaluate the histopathological changes in infected and uninfected cats, and to investigate the relationship of individual *Helicobacter* spp. to gastric inflammation.
2. Materials and methods

2.1. Animals

Forty-five cats were included in this study: 12 clinically healthy young-adult cats (exact age unknown, 7F, 5M) from the local Society for the Prevention of Cruelty to Animals (SPCA), presented for routine spay/neuter prior to adoption (group A). Nine cats (age \( X \pm S.D. \) 13.9 ± 2.4 years, 5FS, 4MC) presented for investigation of chronic vomiting (7/9), diarrhea (3/9), and weight loss (2/9) (group B). Twenty-four cats from a commercial colony considered to be specific pathogen free (SPF) (age \( X \pm S.D. \) 5.3 ± 1.6 months, 24M) (group C).

The presence or absence of gastric *Helicobacter* spp. was ascertained in all cats by evaluating gastric biopsies for urease activity, tissue sections for the presence of HLO, and gastric biopsies for *Helicobacter* DNA (see the next section). Serum samples were obtained prior to endoscopy.

2.2. Gastric biopsy

Biopsies of the stomach were obtained from anesthetized cats with a pediatric endoscope and biopsy forceps (Olympus, Melville, NY). Endoscopic biopsies were procured from the pyloric antrum (incisura to pyloric sphincter), the body (greater curvature) and the cardia. Three biopsies were taken from each site for light microscopy, two from each site for urease testing and one from each site for PCR. Endoscopic biopsy samples for PCR analysis were pooled and frozen at \(-80^\circ C\) pending analysis. The endoscope was thoroughly cleaned, then sterilized using an activated aldehyde solution (Metrex, Parker, CO). Biopsy forceps were sterilized in a similar fashion and the biopsy cups were immersed in Chlorox (1:10 in water) for 10 min to destroy residual DNA.

2.3. Biopsy urease

Biopsy urease production was evaluated as previously described (Radin et al., 1990). In short, gastric mucosal biopsies were placed in sterile tubes containing 200 \( \mu l \) of a solution composed of urea, sodium azide, phenol red and phosphate buffered saline (pH 6.5). Biopsies were incubated for 24 h and observed at 2, 4, 12 and 24 h for a change in the color of the indicator medium. A change from orange–red to bright pink was considered a positive result and the time of color change was recorded. Urease results were additionally scored as follows: positive at \( 2h = 4 \), positive at \( 4h = 3 \), positive at \( 12h = 2 \), positive at \( 24h = 1 \), negative at \( 24h = 0 \).

2.4. Histopathology

Samples for histopathology were fixed in 10% buffered formalin, embedded in paraffin, and sectioned at 4–6 \( \mu m \). Serial sections of each block were stained with hematoxylin and eosin (H&E) and modified Steiner’s stain (Garvey et al., 1985). Samples
were examined in a blinded fashion by one pathologist (ES), and evaluated for the number of organisms, degree of inflammation, and the presence of lymphoid follicles. The number of organisms was graded as follows: 0 = no organisms; 1 = presence of Helicobacter in <5% of gastric glands; 2 = presence of Helicobacter in 5–50% of gastric glands; 3 = presence of Helicobacter in >50% of gastric glands. The degree of inflammation was graded as follows: 1 = mild; 2 = moderate; 3 = severe. The number of lymphoid follicles was graded as follows: 1 = one lymphoid follicle; 2 = two to three lymphoid follicles; 3 = greater than three lymphoid follicles per specimen.

2.5. PCR

Gastric biopsies collected endoscopically were frozen at −80°C. DNA was extracted from biopsies with a Qiamp tissue kit (Qiagen, Santa Clarita, CA). PCR was performed using primers that amplify the urease B genes of H. felis, H. pylori, “H. heilmannii” (Neiger et al., 1998), and with Helicobacter genus-specific primers directed against 16S rRNA (Fox et al., 1998). DNA samples (2 µl) were added to a reaction mixture containing 400 µM dNTPs (Pharmacia Biotech, San Francisco, CA), PCR buffer (Gibco BRL, Grand Island, NY), 2 mM MgCl2 (Gibco BRL), 1.5 units of Taq DNA polymerase (Gibco BRL), 0.5 or 0.6 µM of each primer and distilled water in a total volume of 50 µl. H. felis PCR was performed as previously described (Simpson et al., 2000), using a Biometra personal thermocycler (Biometra, Tampa, FL). PCR cycles for the H. heilmannii and H. pylori-specific primers included heating to 95°C for 5 min once, annealing for 5 min at 57°C, followed by 35 cycles of extension at 72°C for 1 min, denaturation at 94°C for 1 min, primer annealing at 57°C for 2 min, and a final extension at 72°C for 10 min. The cycle for the Helicobacter genus-specific primers was heating to 94°C for 4 min once, followed by 35 cycles of denaturation at 94°C for 1 min, primer annealing at 55°C for 2 1/2 min, and extension at 72°C for 3 min, with a final extension at 72°C for 15 min. PCR products were subjected to electrophoresis on a 1% agarose gel and visualized with ethidium bromide.

2.6. Serology

Serum samples were evaluated for the presence of IgG against gastric Helicobacter spp. by the use of an ELISA. Checkerboard titration of two different antigens that originated from H. felis (crude detergent extract and high-molecular-mass cell-associated protein (HM-CAP)) at a concentration of 1 µg/well, serum (1:50 and 1:100), and conjugate (1:2000, 1:3000, 1:4000) was performed with sera from 2 SPF cats that were previously vaccinated subcutaneously with H. felis crude detergent extract, and 2 Helicobacter-free SPF cats. The combination of H. felis HM-CAP (1 µg/well) (Evans et al., 1989) with a serum dilution of 1:100 and a conjugate dilution of 1:3000, gave the greatest differences between uninfected vaccinated and unvaccinated sera, and was used for all samples evaluated in this study. Nineteen of 21 sera of cats from groups A and B, and 24 sera from cats of group C were evaluated by a kinetic ELISA as previously described (Simpson et al., 2000; Strauss-Ayali et al., 1999).
2.7. Statistical analysis

Differences in ELISA values, gastric bacterial colonization density, inflammation and lymphoid follicles between infected and uninfected cats were evaluated using the Mann–Whitney test. Differences in gastric bacterial colonization density, inflammation and lymphoid follicles, between different groups of cats (A: spay–neuter, B: sick cats (infected, uninfected), and C: SPF Helicobacter-free cats), were evaluated with the Kruskal–Wallis test. Differences in gastric bacterial colonization density, urease activity, inflammation and lymphoid follicles, between site (pylorus vs fundus/cardia) in each cat were evaluated using Wilcoxon signed rank test. The effects of age and the presence of clinical signs on the degree of seroconversion, pyloric and fundic inflammation and the number of lymphoid follicles were evaluated using the Kruskal–Wallis test. Correlation between bacterial colonization density, inflammation and lymphoid follicles and the degree of seroconversion was assessed using the Spearman rank correlation coefficient. Statistical significance was set at $P = 0.05$.

3. Results

3.1. Infection status

Large HLO were visualized in modified-Steiner stained sections of 17 of 21 cats (12/12 cats undergoing spay/neuter, group A; 5/9 sick cats (cats 17–21) group B; Table 1). All cats colonized with large HLO were positive on biopsy urease tests. There was no difference in urease activity (median) between the pylorus (4), fundus (4) or cardia (4) of infected cats, and between healthy and sick infected cats (groups A and B).

There was complete concordance between the results of Helicobacter genus-specific PCR, histopathology and urease tests (Table 1). Nine of 17 infected cats were positive on “H. heilmannii”-specific PCR, 4/17 were positive with H. felis-specific PCR (Table 1). Mixed infections of “H. heilmannii” and H. felis were detected in 3 cats. Seven of the 17 cats that were positive with Helicobacter-genus specific PCR were negative on species-specific PCR. A similar range of Helicobacter spp. was observed in healthy and sick cats (groups A and B). None of the 17 Helicobacter spp. infected cats was infected with HLO resembling H. pylori or had positive results with H. pylori-specific primers on PCR (Table 1).

All cats from group C and 4/9 sick cats (cats 13–16 from group B; Table 1) had no HLO on histopathology, and were negative for urease activity and Helicobacter-genus specific PCR.

3.2. Serology

Kinetic ELISA results were significantly higher for infected cats (median = 0.14 OD/min, interquartile range = 0.079–0.21), than for uninfected cats (median = 0.035 OD/min, interquartile range = 0.025–0.056) ($P < 0.0001$) (Fig. 1). Only 1 uninfected cat had an ELISA OD $> 0.07$ OD/min. Choosing a cutoff value for this assay of 0.07 OD/min
Table 1
*Helicobacter* infection status

<table>
<thead>
<tr>
<th>Groups</th>
<th>Cats No</th>
<th>Urease</th>
<th>Histology</th>
<th><em>Helicobacter</em>-genus&lt;sup&gt;a&lt;/sup&gt;</th>
<th><em>H. heilmanni</em>b</th>
<th><em>H. felis</em>c</th>
<th><em>H. pylori</em>d</th>
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</tbody>
</table>

<sup>a</sup> PCR with *Helicobacter* genus-specific primers directed against the 16S rRNA gene (Fox et al., 1998).

<sup>b</sup> PCR with *H. heilmanni*-specific primers directed against the urease B gene (Neiger et al., 1998).

<sup>c</sup> PCR with *H. felis*-specific primers directed against the urease B gene (Neiger et al., 1998).

<sup>d</sup> PCR with *H. pylori*-specific primers directed against the urease B gene (Neiger et al., 1998).

Fig. 1. ELISA values (OD/min) of infected and uninfected cats. The horizontal line represents the median of each group, and the vertical line represents the interquartile range (10–90%).
yielded a specificity of 96.4%, sensitivity of 80%, positive predictive value (PPV) of 92.28%, negative predictive value (NPV) of 89.95% and diagnostic accuracy of 90.6%. However, it is important to consider that the inclusion of a large number of uninfected cats from a commercial colony (group C) reduced the prevalence of infection to 34.8% (17/45), in comparison to 81% (17/21) in non-colony cats. While, this did not influence test sensitivity and specificity (100 and 80%, respectively, in non-colony cats) the NPV (54%), and the diagnostic accuracy (85%) would be lower at this prevalence of infection.

Cats infected with different *Helicobacter* spp. showed similar distribution of OD/min values (Fig. 2). There were no effects of age or clinical signs on the results of kinetic ELISA $(P > 0.05)$. No correlation between colonization density and seroconversion was observed $(P > 0.05; \rho = 0.297)$. They were statistically significant, but weak correlation between the degree of seroconversion and the degree of inflammation $(P < 0.05; \rho = 0.678)$, and the number of lymphoid follicles $(P < 0.05; \rho = 0.345)$.

3.3. Histopathology

3.3.1. Colonization density

The density of bacterial colonization in the pylorus and fundus/cardia was similar in healthy and sick cats (from groups A and B) $(P > 0.05)$ (Table 2). There was no difference in the density of bacterial colonization between the pylorus and the fundus/cardia within individual cats $(P > 0.05)$. The density of bacterial colonization appeared comparable in cats infected with *H. heilmannii* alone, cats infected solely with *H. felis*, cats with mixed infections, and cats infected with unclassified *Helicobacter* sp.
Table 2
Histopathological findings

<table>
<thead>
<tr>
<th>Groups</th>
<th>Infection status</th>
<th>No. of cats</th>
<th>Age (year)</th>
<th>Bacterial colonization</th>
<th>Lymphoid follicles, pylorus</th>
<th>Inflammation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Pylorus</td>
<td>Fundus/cardia</td>
<td>Pylorus</td>
</tr>
<tr>
<td>A</td>
<td>Infected healthy</td>
<td>12</td>
<td>Young</td>
<td>2&lt;sup&gt;b&lt;/sup&gt; (12/12)&lt;sup&gt;c&lt;/sup&gt;</td>
<td>3 (12/12)</td>
<td>0 (1/12)</td>
</tr>
<tr>
<td>B</td>
<td>Infected GI signs</td>
<td>5</td>
<td>13</td>
<td>2 (5/5)</td>
<td>3 (5/5)</td>
<td>0 (2/5)</td>
</tr>
<tr>
<td></td>
<td>Uninfected GI signs</td>
<td>4</td>
<td>13.75</td>
<td>0 (0/4)</td>
<td>0 (0/4)</td>
<td>0 (0/4)</td>
</tr>
<tr>
<td>C</td>
<td>Uninfected healthy</td>
<td>24</td>
<td>0.44</td>
<td>0 (0/24)</td>
<td>0 (0/24)</td>
<td>0 (1/24)</td>
</tr>
</tbody>
</table>

<sup>a</sup> Statistically significant difference between infected (groups A + B) and uninfected cats (groups B + C) (P < 0.05).

<sup>b</sup> The median score.

<sup>c</sup> The proportion of cats showing any histopathological change.

<sup>d</sup> Statistically significant difference vs infected cats with GI signs (group B) (P < 0.05).
3.3.2. Inflammation

Blinded evaluation of endoscopic biopsies revealed that infected cats had more inflammation in the pylorus \((P < 0.05)\) and fundus \((P < 0.01)\) than uninfected cats (Table 2). No difference in the degree of inflammation was apparent between the pylorus and the fundus/cardia of individual cats \((P < 0.05)\). Inflammation was generally mild and mononuclear in nature, and there was an overlap between the degree of inflammation in infected and uninfected cats. Eosinophils, neutrophils and plasma cells were rarely observed: eosinophils were present in the infiltrates of 2/12, and neutrophils in 1/12 healthy infected cats (group A). Neutrophils were also present in 1/4 uninfected sick cats from group B.

Further analysis indicated that infected sick cats (group B) had a higher degree of pyloric, but not fundic inflammation than uninfected sick cats and healthy infected cats (group A) \((P < 0.05)\) (Table 2). The inflammatory infiltrates in infected sick cats were almost exclusively mononuclear in nature, with inflammation categorized as grade 2 (moderate) in 3/5 cats. Marked differences in the degree of pyloric and fundic inflammation were not apparent in cats infected with different Helicobacter spp., except for cats infected with a non-“H. heilmannii” non-H. felis Helicobacter sp.: 6/7 of those cats had no pyloric inflammation, and none had fundic inflammation.

3.3.3. Lymphoid follicles

Lymphoid follicles were observed in the pylorus of 4/45 cats, and the fundus of 1/45 cats (from group A) (Table 2). There was no difference in the number of pyloric lymphoid follicles between infected and uninfected cats, or different groups of cats \((P > 0.05)\).

4. Discussion

The serologic diagnosis of H. pylori infection in humans is accurate and relatively simple. The human stomach is almost exclusively colonized by H. pylori, and tests based on semi-purified antigens such as the HM-CAP of H. pylori and others (Evans et al., 1989; Stacey et al., 1990), have high sensitivity and specificity.

In contrast to humans infected mostly with H. pylori, the use of serology for the detection of anti-gastric Helicobacter spp. antibodies in cats is complicated by the presence of at least three different gastric Helicobacter spp., and the possibility of co-infection with more than one species. Our findings demonstrate that an ELISA utilizing the HM-CAP fraction of H. felis ATCC 49179 was able to detect circulating anti-Helicobacter IgG in cats with naturally acquired infection with “H. heilmannii”, H. felis, and unclassified-Helicobacter sp. There was no obvious effect of the presence of individual Helicobacter spp. on the magnitude of seroconversion observed. Those observations suggest that there is antigenic homology between Helicobacter spp., and are consistent with findings in dogs, where sera from infected dogs bind in a similar way to antigen from H. felis, H. pylori and H. bizzozeronii antigen (Strauss-Ayali et al., 1999). H. felis antigen was chosen for the present study, as “H. heilmannii” is not cultivable at this stage. A previous study, which evaluated sera from 49 cats with unknown Helicobacter spp. infection status using H. felis sonicated antigen, and pre-absorbed sera found that
39% of the cats showed clear positive absorbance reading consistent with seroconversion to *Helicobacter* spp. (Seidel et al., 1999). However, it is difficult to compare the results of this study to those of the present study, as the *Helicobacter* spp. infection status of the cats in the previous study was not determined.

The specificity of the HM-CAP ELISA for cats is similar to that reported in dogs (Strauss-Ayali et al., 1999), humans and rhesus monkeys (Feldman et al., 1995; Handt et al., 1997). The sensitivity is lower than that reported for humans and monkeys, but much higher than the 52.6% reported in dogs (Strauss-Ayali et al., 1999). The prevalence of infection in the non-colony cats in this study was in agreement with previous results of 41–100% in clinically healthy cats (Weber et al., 1958; Geyer et al., 1993; Otto et al., 1994; El Zaatari et al., 1997; Papasouliotis et al., 1997; De Majo et al., 1998; Neiger et al., 1998; Yamasaki et al., 1998), and of 57–100% in vomiting cats (Geyer et al., 1993; Hermanns et al., 1995; Papasouliotis et al., 1997; Yamasaki et al., 1998). At this prevalence the NPV and diagnostic accuracy of ELISA are similar to those obtained in dogs (Strauss-Ayali et al., 1999).

The infection status of 3/15 of the cats infected with gastric *Helicobacter* spp. could not be determined by ELISA. For those cats repeated sampling to detect seroconversion or other diagnostic means, would be needed. As the exact species of *Helicobacter* infecting 38% of the infected cats in this study was not known it is possible that the use of antigen derived from *H. heilmannii*-like organisms, or other unknown *Helicobacter* spp. infecting cats, could increase the sensitivity of the ELISA. Alternatively, the significant, but weak correlation between ELISA values and gastric inflammation suggests that variation in host inflammatory response to infection may also influence detection by ELISA. The density of bacterial colonization and presence of lymphoid follicles did not appear to influence the magnitude of seroconversion.

While many studies describe the prevalence of HLO in cats, few have provided details of the prevalence of individual *Helicobacter* spp. The prevalence of infection with “*H. heilmannii*”–like organisms in the present study (38%) was lower than in Swiss cats (78%) (Neiger et al., 1998), while the prevalence of infection with *H. felis* (19%) was higher than Swiss (0%) (Neiger et al., 1998), and Finnish (14%) (Jalava et al., 1998) cats. Interestingly, mixed infections with “*H. heilmannii*” and *H. felis* infections were detected in 14% of the cats in the present study. To our knowledge, this is the first time that a mixed infection of *Helicobacter* spp. has been described in cats, whereas mixed infections have been previously described in dogs (Lockard and Boler, 1970; Happonen et al., 1996; Fox and Lee, 1997). Our observation that 38% of cats were heavily colonized with large urease producing *Helicobacter* spp. that were positive on genus-specific, but negative on species-specific PCR, suggests that these cats were infected with non-“*H. heilmannii*”, non-*H. felis*, and non-*H. pylori*, *Helicobacter* sp. This resembles the situation in dogs where unclassified large gastric HLO have been further categorized as *H. bizzozeronii* and *H. salomonis* (Lockard and Boler, 1970; Lee et al., 1988; Eaton et al., 1996; Haninnen et al., 1996; Jalava et al., 1997). Further investigation is required to rule out the possibility that a mutation in known *Helicobacter* sp. caused the negative PCR results and to determine the precise species infecting these cats.

Histological findings in infected and uninfected cats in the present study ranged from “normal” gastric mucosa to mild or moderate chronic gastritis, and were similar to
previous studies (Geyer et al., 1993; Otto et al., 1994; Hermanns et al., 1995; Happonen et al., 1996; Papasouliotis et al., 1997; De Majo et al., 1998; Neiger et al., 1998; Yamasaki et al., 1998; Norris et al., 1999). In the present study the degree of pyloric and fundic inflammation was significantly higher in infected than uninfected cats, findings similar to those of Hermanns et al. (1995), and Happonen et al. (1996). The degree of inflammation was highest in the pylorus of infected sick cats and mirrors observations in *Helicobacter* infected dogs, where dogs with signs of gastritis had more severe gastritis than healthy dogs (Happonen et al., 1998). The higher degree of inflammation in *Helicobacter* infected sick cats in the present study compared to uninfected sick cats of similar age suggests that gastritis is *Helicobacter* related. However, the evaluation of larger numbers of sick cats, possibly before and after eradication of *Helicobacter*, in a study specifically designed to control for factors such as clinical signs and age differences, is required to substantiate this finding.

Our observation that pyloric and fundic inflammation tended to be particularly mild in cats infected with unclassified *Helicobacter* sp. also merits further investigation.

Few lymphoid follicles were observed in gastric biopsies from the pylorus of infected and uninfected cats in the present study. This probably reflects the small size of endoscopic biopsies, as previous studies that have evaluated full thickness biopsies (Otto et al., 1994; Hermanns et al., 1995; Happonen et al., 1996; Serna et al., 1997; Simpson et al., 2000), rather than endoscopic biopsies (Papasouliotis et al., 1997; Neiger et al., 1998; Yamasaki et al., 1998; Norris et al., 1999), have found a correlation of infection to lymphoid follicle hyperplasia.

In summary, this study indicates that naturally acquired infection with gastric *Helicobacter* spp. is associated with seroconversion (IgG) in cats. The similar ELISA values in cats infected with a variety of *Helicobacter* spp. suggests substantial antigenic homology between different *Helicobacter* spp., and the higher degree of inflammation in infected than uninfected cats, supports a role for *Helicobacter* as a cause of gastritis in cats.

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References


Failure to isolate *Helicobacter pylori* from stray cats indicates that *H. pylori* in cats may be an anthroponosis — an animal infection with human pathogen. J. Med. Microbiol. 46, 372–376.


