Helicobacter Infection in Dogs and Cats: Facts and Fiction

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The discovery of the spiral bacterium Helicobacter pylori and its causative role in gastric disease in humans has brought a dramatic change to gastroenterology. Although spiral bacteria have been known for more than a century to infect the stomachs of dogs and cats, recent research has been conducted mainly in the wake of interest in H. pylori. H. pylori has not been found in dogs and only very rarely in cats and zoonotic risk is minimal. A variety of other Helicobacter spp. can infect the stomach of pets; however, their pathogenic role is far from clear, and they have a small but real zoonotic potential. The prevalence of gastric Helicobacter spp. in dogs and cats is high, irrespective of clinical signs, and as in human medicine, mode of transmission is unclear. The relationship of Helicobacter spp. to gastric inflammation in cats and dogs is unresolved, with inflammation, glandular degeneration, and lymphoid follicle hyperplasia accompanying infection in some but not all subjects. Circulating anti-Helicobacter immunoglobulin G antibodies have been detected in 80% of dogs with naturally acquired infection and most dogs and cats with experimental infection. The gastric secretory axis is similar in infected and uninfected cats and dogs and no relationship of infection to gastrointestinal ulcers has been found. Differences in the pathogenicity of Helicobacter spp. are apparent, because infection with H. pylori is associated with a more severe gastritis than infection with other Helicobacter spp. in both cats and dogs. Rapid urease test, histopathology, and touch cytology are all highly accurate invasive diagnostic tests for gastric Helicobacter-like organisms in dogs and cats, whereas culture and polymerase chain reaction are the only means to identify them to the species level. Urea breath and blood tests or serology can be used to diagnose Helicobacter spp. noninvasively in dogs and cats. Most therapeutic studies in pets have not shown long-term eradication of Helicobacter spp. Whether this is due to reinfection or recrudescence has not been established.

Key words: Canine; Epidemiology; Feline; Review; Scanning electron microscopy; Spiral organisms; Therapy.

Recognition and treatment of Helicobacter pylori has greatly simplified the management of chronic ulcer disease in humans. Since isolation of H. pylori in 1983,1 it has become clear that H. pylori infection is associated with a chronic superficial gastritis in all infected humans, can cause peptic ulcers, and is a cofactor for the development of gastric carcinoma and lymphoma.2-3 The presence of spiral bacteria in the stomachs of animals has been known for more than a century,4-6 and gastric spiral organisms have been documented in dogs, cats,7-16 ferrets, monkeys, cheetahs, pigs, cows, predatory cats, and foxes, among other species.17 To date, relatively little attention has been paid to the pathogenicity of species other than H. pylori and the consequences of a Helicobacter infection in healthy and sick animals is far from clear. Danger exists that information gathered in H. pylori-infected humans will be directly applied to veterinary patients without consideration of differences in Helicobacter spp. and the response of nonhuman hosts. This review summarizes our current knowledge of gastric Helicobacter spp. infection in dogs and cats.

Species Characteristics

Helicobacter spp. are gram-negative, microaerophilic, curved to spiral-shaped, motile bacteria that, along with Campylobacter and Arcobacter, belong to a distinct phylum within the class Proteobacteria of the eubacteria: the rRNA superfamily VI.18 In addition to the stomach, they are found in the intestine and liver of various animal species.17 To date 31 organisms with typical characteristics of Helicobacter species have been described; however, many names commonly used have not been properly validated, thus causing confusion as to the taxonomic status of these bacteria.19 Most gastric Helicobacter-like organisms (GHLO) found in dogs and cats are large spiral organisms (0.5 × 5–10 μm) and cannot be distinguished by light microscopy. Early reports describing GHLO were based on electron microscopic morphologic criteria.14 However, because bacterial morphology varies in vivo and in vitro,15,20 electron microscopic appearance is not a definitive means of distinguishing different GHLO. Taxonomic classification of Helicobacter spp. relies mainly on the determination of their 16S rRNA and 23S rRNA sequence and DNA hybridization or on culture with conventional phenotype testing.19,21

To date H. felis, H. bizzozeronii, H. salomonis, “Flexispira rappini,” H. bilis, and “H. heilmannii” have been reported from the stomach of dogs,15,20,22 whereas H. felis, H. panteensis, H. pylori, and “H. heilmannii” have been reported from the stomach of cats.12,20,23 Large tightly spiraled GHLO in the human gastric mucosa were described soon after the discovery of H. pylori and were initially named “Gastrospirillum hominis.”24 The 1st large GHLO cultured was named H. felis because of its isolation from a cat stomach,25 but it can also be found in dogs15,20,22,26,27 and human patients.28 It has sparsely distributed periplasmic fibers appearing singly or in groups of 2, 3, or 4 on the crest of the helical body (Fig 1). Two other GHLO have been cultured from the dog stomach, namely H. bizzozeronii, an organism without periplasmic fibers,16 and H. salomonis, with a shorter and thicker cell body.29 A bacterium entwined with periplasmic fibers that seem to cover the entire surface of the organisms has also been found in the stomach of dogs.15,15

It is closely related to the genus Helicobacter and is classified as “F. rappini.” Uncultured large gastric spiral or-

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ganisms that lack periplasmic fibrils or have a small fiber in the valley of the helical body (Fig 2) are perhaps the most common GHLO found in cats and dogs.\textsuperscript{12,22,30} By comparison of their 16S rRNA sequence these organisms are considered members of the genus \textit{Helicobacter} and some were subsequently named “\textit{H heilmannii}” in honor of the German pathologist Konrad Heilmann.\textsuperscript{31} Only recently “\textit{H heilmannii}” strain was isolated in Denmark and typed based on its 16S rRNA sequence.\textsuperscript{32}

\textit{H pylori}, which was isolated from laboratory cats,\textsuperscript{23} is much smaller (0.5 × 1.5–3 μm), curved or S-shaped, and easily distinguished by light microscopy (Fig 3). Unexpectedly, \textit{H pylori} strain ATCC 43504 resembles morphologically, when grown on blood agar plates, \textit{H pylori}, whereas when grown in broth media, the morphologic appearance resembles that of “\textit{H heilmannii}.”\textsuperscript{33} Other Helicobacter spp. such as \textit{H panetensis} and \textit{H bilis} have been sporadically reported in the stomach of dogs and cats.\textsuperscript{15,34} Although mixed gastric infections with 2 or more \textit{Helicobacter} spp. have been reported in dogs,\textsuperscript{11,14,20,22} others have demonstrated competitive exclusion after 1 \textit{Helicobacter} sp. has colonized the stomach.\textsuperscript{35} Similarly, \textit{H salomonis} originally present in the stomach of 6-week-old puppies were suppressed by an experimental infection with \textit{H bizzozeronii}.\textsuperscript{36}

In addition to the gastric \textit{Helicobacter} spp., an increasing number of intestinal and hepatic \textit{Helicobacter} spp. have been described. \textit{H cinaedi}, \textit{H fenneliae}, and “\textit{F rappini}” have been isolated from the feces from dogs and cats.\textsuperscript{14,17,37,38} “\textit{H colifelis}” was described in a kitten with severe diarrhea,\textsuperscript{39} and \textit{H canis} was found in dogs with and without diarrhea as well as in the liver of a dog with multifocal necrotizing hepatitis.\textsuperscript{40} The pathogenicity of these nongastric \textit{Helicobacter} spp. in dogs and cats is similarly unclear at the moment.

**Epidemiology**

Gastric \textit{Helicobacter}-like organisms are highly prevalent in cats and dogs, with 86% of random-source cats,\textsuperscript{10,41} 100% of random-source dogs,\textsuperscript{46} 90–100% of clinically healthy pet cats,\textsuperscript{23,24,30,38} 67–100% of clinically healthy pet dogs,\textsuperscript{15,20,22,44} and 100% of laboratory beagles and shelter dogs infected.\textsuperscript{13,42,43} GHLO have also been demonstrated in gastric biopsies from 57–76% of cats\textsuperscript{8,9,44} and 61–95% of dogs\textsuperscript{8,9,44} presented for the investigation of recurrent vomiting. Living conditions seem an important factor because most studies using shelter or colony dogs or cats have a higher prevalence than studies using pets.\textsuperscript{15} Age may also play a role, because young animals may be less often colonized than adults,\textsuperscript{19} although this is controversial.\textsuperscript{7,8,12} Cats as young as 6 weeks were infected based on the \textsuperscript{13}C-urea breath test (Neiger, personal communication) and 10 of 10 cats <6 months old were densely colonized with \textit{H pylori} (Simpson,
personal communication). Interestingly, Yamasaki and co-workers found a lower prevalence in sick compared to healthy pets. Possible explanations for this finding could be the recent use of antibiotics in sick animals or perhaps a protective immune response.

The prevalence of GHLO in dogs and cats also depends on the techniques employed to detect Helicobacter spp. In research studies using several diagnostic tests or including a test of high sensitivity, such as impression smears or polymerase chain reaction (PCR), a higher prevalence is noted. Few reports cited above mentioned the prevalence of specific Helicobacter spp. in the stomach of cats and dogs. Recently, in Swiss cats positive for GHLO only “H heilmannii” was identified. In a study of 95 dogs, 21 strains of H bizzozeroni, 8 strains of H felis, 8 strains of H salomonis, and 2 strains of “F rappini”-like organisms were isolated, whereas among other species, 12 strains of “H heilmannii” were found in 65 Swiss dogs by PCR.

The precise mode of transmission of Helicobacter is unclear. A fecal–oral spread is hypothesized by some, because H pylori can be cultured from human and cat feces, and suboptimal sanitary conditions in underdeveloped countries might favor such a transmission. Oral–oral spread is hypothesized by others, because H pylori can be found in the saliva of infected humans and the spouses of infected people have a higher prevalence. Although gnotobiotic dogs experimentally infected with H pylori and H felis transmitted the organism to uninfected dogs, H felis- and “H heilmannii”-positive mice did not transmit the infection to naive mice, suggesting that oral–oral transmission in vomiting puppies is more likely than fecal–oral spread in co-prophageous mice. However, the recent isolation of H pylori from surface water in the United States and Sweden suggests that water-borne infection is likely to be an important route, particularly when considering that H pylori is more resistant to chlorination than is Escherichia coli. Finally, H salomonis can be transmitted from the dam to puppies during the lactation period.

Pathogenicity

In human patients extensive evidence exists implicating H pylori in the pathogenesis of chronic superficial gastritis. Eradication of H pylori by antimicrobial therapy cures gastritis and the titer of anti-H pylori antibodies decreases with time. A plethora of reports have shown many putative mechanisms by which H pylori alters gastric physiology, including the induction of gastric inflammation, by the disruption of the gastric mucosal barrier (disrupting phospholipases, secreting vacuolating cytotoxins, inducing apoptosis, and so on), or by altering the gastric secretory axis (by decreasing somatostatin release, inducing hypergastrinemia, diminishing the responsiveness of parietal cells, and so on). H pylori infection in humans has been
associated with the production of the proinflammatory cytokines interleukin (IL)-1β, IL-6, IL-8, and tumor necrosis factor-alpha (TNF-α). The production of these proinflammatory cytokines has been linked to alterations in gastrin, somatostatin, and acid secretion, and the genesis of gastritis and ulceration.

Infection with Helicobacter spp. also predisposes humans to the development of gastric cancer. The precise mechanism of carcinogenesis is unclear, but it may involve the induction of nitric oxide synthetase by proinflammatory cytokines with subsequent NO production and nitrosamine formation. It may also involve a decrease in apoptosis relative to cell proliferation.

Disease may be defined as tissue injury or clinical manifestation. This fundamental statement is important, because the relationship of Helicobacter spp. to gastric inflammation in cats and dogs is unresolved, with inflammation or glandular degeneration accompanying infection in some but not all subjects. In dogs with naturally acquired helicobacteriasis, mild gastritis with infiltration of lymphocytes and plasma cells have been commonly observed. Enlarged canaliculi and pyknotic parietal cells have also been reported. Interestingly, in a recent study, glandular degeneration was more frequent in the fundi of dogs and cats with GHLO than without GHLO, but gastric fibrosis and lymphocytic–plasmacytic enteritis were similar.

Histologic findings in infected as well as uninfected cats vary from a normal gastric mucosa to mild or moderate chronic gastritis. A correlation between the presence of GHLO and the extent of histopathologic changes was demonstrated in 1 study. Moreover, Happonen and co-workers found lymphocyte aggregates only in GHLO-positive cats, which also had more lymphocytes in the fundus and corpus than GHLO-negative cats. A more severe gastritis characterized by marked lymphoid follicular hyperplasia and infiltration of neutrophils and eosinophils has been observed in cats with H pylori infection.

Factors that must be considered when trying to interpret the results of studies performed in dogs and cats include the source of the animals, presence or absence of clinical signs, methodologies used to confirm infection status, and the criteria used to examine histopathologic sections. In several studies dogs and cats were selected on the basis of gastrointestinal signs, whereas in others, all animals were asymptomatic. Thus, drawing a relationship between GHLO colonization and symptoms is difficult.

Multiple studies have evaluated gastric histopathology and have described the type and degree of inflammatory cells, lymphoid follicles, and glandular alterations; however, the lack of standardized criteria to define histologic changes makes comparison between different studies impossible at worst or cumbersome at best. The high prevalence of infection in dogs and cats also makes finding a suitable negative control group difficult. Furthermore, because most studies have used only limited diagnostic tests...
with limited sensitivity, comparisons of colonized to non-colonized animals may have been inaccurate. Finally, the presence of multiple species complicates the investigation of pathogenicity.20,22

In addition to determining the presence of specific Helicobacter species, it is apparent that an effective study of the pathogenicity of Helicobacter spp. in dogs and cats will require us to step beyond the assessment of mucosal pathology with a light microscope to investigate the cellular, immunologic, and functional consequences of infection. In dogs with naturally acquired Helicobacter spp. infection, a variety of secretory function tests such as unstimulated gastric pH, fasting, postprandial, and bombesin-stimulated plasma gastrin levels, as well as pentagastrin-stimulated maximal acid output and titratable acidity were similar when compared to a specific-pathogen-free (SPF), Helicobacter-free control group.65 The question of clinical manifestation still must be taken into consideration.

**Experimental Studies**

Relatively few experimental studies of Helicobacter infection have been conducted in dogs and cats. Gnotobiotic dogs have been experimentally infected with *H pylori* and *H felis*.48 SPF dogs with *H pylori* and *H felis*.63,65 and SPF cats with *H pylori* and *H felis*.63,65 Only recently conventional 4- to 6-month-old Beagle puppies were experimentally infected with a mouse-adapted *H pylori* strain.67 All gnotobiotic dogs (n = 5 in both studies) showed a chronic gastritis after 4 weeks of infection with *H pylori* and *H felis* and an increase in fasting gastric pH was reported in 4 of 10 dogs after infection.48,49 In contrast, SPF dogs showed no relationship of *H felis* infection to gastric inflammation after 6 months.65 Blinded evaluation of gastric biopsies from those dogs revealed mild gastric inflammation and lymphoid follicles in both infected and uninfected dogs. No correlation was found between the number of organisms observed and the degree of gastric inflammation or number of lymphoid follicles. The gastric secretory axis, assessed by fasting and meal-stimulated plasma gastrin, mucosal gastrin and somatostatin immunoreactivity, fasting gastric pH, and pentagastrin-stimulated gastric acid secretion was similar in both infected and uninfected dogs. This study in SPF dogs also showed that fasting gastric pH was not a reliable indicator of gastric secretory function.65 *H pylori* infection in conventional puppies resulted in vomiting and loose stool shortly after inoculation. After 1 week of infection these dogs showed a marked polymorphonuclear leukocyte infiltration in the lamina propria, which over the next few weeks changed to a chronic follicular gastritis with the presence of small lymphoplasmacytic aggregates and lymphoid follicles and only scattered neutrophilic granulocytes. Additionally, IL-8 was detected immunohistochemically after the 1st and 2nd week of infection in areas of the stomach where neutrophil transcytosis was most pronounced and became undetectable in biopsies taken from week 8 onwards, when neutrophilic infiltration was much less prominent than in the early phase of infection.67

In SPF cats infected with 2 different *H pylori* strains (cytoxin-associated protein *cagA* present or absent) chronic gastritis was observed 4 to 7 months after infection.63,66 Multifocal lymphoplasmacytic follicles were prominent in the antrum and body of infected cats. Five SPF *Helicobacter*-free cats were studied before and for 1 year after inoculation with *H felis*.68 Four SPF uninfected cats served as controls. Lymphoid follicular hyperplasia, atrophy, and fibrosis were observed primarily in the pylorus of infected cats. Mild mononuclear inflammation was detected in both infected and uninfected cats, but was more extensive in infected cats, with inflammation throughout the stomach, and cardia gastritis observed only in infected cats. Eosinophilic infiltrates were observed only in infected cats.68 No upregulation of antral mucosal IL-1α, IL-1β, or TNF-α was detected by reverse transcription-PCR in any cats. The gastric secretory axis, assessed by fasting plasma gastrin and pentagastrin-stimulated gastric acid secretion, was similar in both infected and uninfected cats.66

Seroconversion was observed in all of these studies. *H felis* and *H pylori*-infected gnotobiotic dogs had fairly rapid and uniform seroconversion 3 weeks after infection, whereas *H felis*-infected SPF dogs showed more gradual and variable seroconversion over the 6-month period of infection.48,49 The serologic responses observed in SPF dogs are similar to those in SPF cats infected with *H pylori* and *H felis*, where some cats did not seroconvert until 6 months after infection and had titers 2- to 15-fold greater than baseline.65,66,68

**Diagnosis**

Diagnostic tests consist of invasive tests (rapid urease test, histopathology, touch cytology, culture, PCR, electron microscopy), which require an endoscopically taken biopsy sample, and noninvasive tests (urea breath and blood tests, serology).12,22,69

**Invasive Tests**

The rapid urease test is based on the production of urease by almost all gastric Helicobacter spp.20 A gastric biopsy is incubated in urea broth containing phenol red as a pH indicator. As urease breaks down urea into ammonia, the pH rises and a color change occurs. Other urease-producing bacteria in the stomach (eg, *Proteus* spp. in coprophagic beagles) can give a false positive reading, whereas patchy distribution or rare urease-negative Helicobacter spp. can yield false-negative results.29,71 Diagnosis in pets is obtained normally within 1–3 hours. In humans, the rapidity of the color change is somewhat proportional to a *H pylori* colonization.72

Histopathology relies on the observation of Helicobacter organisms in gastric biopsy tissue. Special staining such as silver stains,13,15 Giemsa,69 or toluidine blue,6 will enhance the visibility of GHLO when colonization density is low. Because of the patchy distribution, several biopsies from antrum, corpus, and cardia should be evaluated. *H pylori* induces in human patients a moderate to severe chronic–active gastritis characterized by a persistent active granulocytic inflammatory response.69 Only recently has a similar visual analogue scale for canine gastric biopsy specimens been introduced, making comparison between various studies possible.45

Touch cytology with Gram or Diff Quik® staining is a
simple, rapid, and sensitive diagnostic test for diagnosing infection with GHLO. However, the extent of a concurrent gastritis or lymphoid follicular hyperplasia can not be evaluated.

Bacteriologic culture of all Helicobacter spp. is cumbersome and the designation “Helicobacter heilmannii”-like organism has been suggested for uncultured Helicobacter spp., without periplasmic fibers. Only recently, several Helicobacter spp. were isolated from 51% of GHLO-positive dogs and identification was performed by standardized conventional phenotypic tests as well as by whole-cell protein profiling. Dot-blot DNA hybridization or PCR of positive culture isolates are other means of Helicobacter species identification. Positive culture is the only possibility to determine antimicrobial sensitivity.

PCR of DNA extracted from a biopsy specimen or from gastric juice permits diagnosis as well as identification of the Helicobacter species. Primers are mostly derived from either the urease gene or from the 16S rRNA gene. PCR products can subsequently be cloned and sequenced or analyzed by restriction fragment length polymorphism to identify the species and strain.

Electron microscopy has been advocated to differentiate Helicobacter species on the basis of typical morphologic criteria. Five cultured canine Helicobacter spp. could be differentiated based on transmission and scanning electron microscopy. However, other studies showed that cultured Helicobacter spp. may lose their typical in vivo morphologic characteristics.

For the diagnosis of naturally acquired Helicobacter infection in dogs and cats, rapid urease test, histopathology, and touch cytology are highly accurate. When colonization density is low, impression smears and PCR seem more accurate than modified Steiner stain and rapid urease test. Multiple biopsies should always be acquired, not only from fundus, but also from the cardia and antrum-pylorus area, because of the patchy distribution of gastric Helicobacter spp. Because of this pattern and the requirement of a gastric biopsy, less-invasive methods of diagnosing infection are clearly needed. In humans, noninvasive diagnosis of Helicobacter pylori has been achieved using serology or the urea breath test. The former is largely used as screening test, whereas the latter test is also used to confirm eradication after treatment.

Noninvasive Tests

Serology by enzyme-linked immunosorbent assay (ELISA) or immunoblotting is used extensively as a diagnostic tool in human clinics and for epidemiologic studies. The most accurate ELISA test kits are based on a variety of semipurified antigens derived from Helicobacter pylori and measure circulating immunoglobulin G (IgG) in serum. IgG or IgA can also be measured in the gastric fluid. In addition to diagnosing an infection, immunoblotting has been used to define the immunogenic moieties of Helicobacter pylori or to investigate equivocal ELISA test results. Serodiagnosis in dogs and cats represents a challenge, because they can harbor several Helicobacter species. A recent study evaluated immunoblotting and ELISA in serum samples from naturally infected dogs and from uninfected SPF dogs. Kinetic ELISA results and number of bands per lane on an immunoblotting test were significantly higher for samples from infected dogs than in uninfected dogs. Serology has limited usefulness as an aid in demonstrating therapeutic success in human patients, because titers may not decrease for 6 months or more after the infection has been cleared, although recent studies in humans show that a drop in antibody titers is consistent with eradication.

The urea breath and blood tests use urea labeled with isotopically stable 13 C or radioactive 14 C. Urease produced by Helicobacter spp. cleaves ingested labeled urea to ammonia. The released labeled C atoms are absorbed into the circulation and exhaled. Exhaled air is collected and with 13 C-urea the ratio of 13 CO2 to 12 CO2 is measured by mass spectrometry, whereas the amount of radioactive CO2 is analyzed with 14 C-urea. The ratio of 13 CO2 to 14 CO2 can also be measured in a blood sample. The 13 C-urea breath and blood test has been evaluated in cats and dogs. Because the urea breath test demonstrates the actual Helicobacter colonization, it is the preferred noninvasive method to document a successful eradication in humans and animals. However, proton pump inhibitors and histamine H2-receptor antagonists decrease the urease activity of Helicobacter spp., so the time of testing after antibiotic and antisecretory usage is important. A gap of at least 2–5 days after cessation of therapy should be maintained. Furthermore, low levels of colonization might persist for many months and may be missed by early testing.

Therapy

Guidelines of the European Study Group of H pylori infection and the American National Institutes of Health state that all patients with peptic ulcers and a H pylori infection should be treated. No therapy is recommended for H pylori-infected asymptomatic human patients. A plethora of clinical trials using different antimicrobial treatments have been conducted to assess their ability to eradicate H pylori in humans. An acid-secretory inhibitor drug-potentiated triple-therapy for 2 weeks (eg, clarithromycin, amoxicillin, bismuth plus ranitidine) or double-therapy for 1 week (eg, metronidazole or amoxicillin, clarithromycin plus omeprazole or lansoprazole) show eradication rates of >90% in human patients.

Whether antimicrobial therapy should be instituted in domestic pets with gastritis or ulcer disease is presently unknown. In a preliminary uncontrolled treatment trial use of a combination of amoxicillin, metronidazole, and famotidine resulted in clinical improvement in >90% of 63 dogs and cats colonized with GHLO and 74% of 19 dogs and cats reexamined by gastroscopy were GHLO negative. Unfortunately, the diagnostic tests used and the time elapsed between end of therapy and control endoscopy were not reported. Only few controlled, randomized, blind therapeutic studies in dogs and cats have been published. In naturally infected dogs treatment with amoxicillin, metronidazole, and famotidine for 2 weeks was highly successful when evaluated 3 days after therapy, but 28 days later GHLO were present and the urea breath test was positive in most dogs again. Similar results were observed in naturally infected cats treated either with azithromycin, tio-
idazole, bismuth, and ranitidine or with clarithromycin, metronidazole, bismuth, and ranitidine for 4 or 7 days when evaluated by urea breath test. After 3 weeks of amoxicillin, metronidazole, and omeprazole, cats with \textit{H. pylori} infection were culture negative, but 5 out of 6 cats were positive in a species-specific PCR in dental plaque, saliva, or gastric fluid samples. All these studies indicate the difficulty of eradicating \textit{Helicobacter} spp. in dogs and cats. In most studies, whether antibiotic failure was due to reinfection or recrudescence was unclear. However, in 1 recent preliminary study in dogs infected by GHLO, a 80% eradication rate after a 1-week triple therapy was reported as controlled 30 days after therapy with urea breath test, rapid urease test, and histology.

### Public Health Implication

Because of the discovery of cats harboring \textit{H. pylori} in a research colony as well as in China and according to preliminary data also in France, cats may be a potential natural reservoir of \textit{H. pylori} and could pose a zoonotic risk. In epidemiologic studies, \textit{H. pylori}-positive farm workers showed significant more contact with cats than with other animals. However, 2 studies evaluating \textit{H. pylori} antibodies in cat owners and comparing them to humans without contact to cats showed no increased risk in the 1st population. A preliminary study in veterinarians was equally negative for an increased risk of acquiring a \textit{H. pylori} infection from pets. Finally, isolation of \textit{H. pylori} from stray and pet cats has not been possible in various studies, suggesting that \textit{H. pylori} infection in cats may be an anthropogenesis—an animal infection with a human pathogen. The discovery of \textit{H. pylori} in surface water has shifted the possibility of direct transmission from pets even further.

Several reports in human patients have assumed a possible zoonotic transmission of large GHLO from dogs or cats. Only recently, an identical "\textit{H. heilmannii}" organism identified by PCR and urease-B gene sequencing has been found in a patient and 1 of his cats. The possible risk of transmission of large GHLO to human patients is rather small, considering the greater than 90% prevalence in dogs and cats and the rare (<0.5%) occurrence in humans. Notwithstanding, proper hygienic control is necessary to keep the risk to a minimum.

### Conclusion

Prevalence of gastric \textit{Helicobacter} species in healthy or sick client-owned dogs and cats is >70%. The pathogenic role of GHLO has not been clearly established. Compared to uninfected dogs, infected dogs have increased glandular degeneration, circulating anti-\textit{Helicobacter} antibodies, and a variable increase in lymphoid follicles, but similar gastric secretory function and mononuclear inflammation. The evidence to support a role for \textit{Helicobacter} in gastritis in cats is somewhat stronger than in dogs, where a relationship of infection to glandular degeneration, lymphoid follicle hyperplasia, and mononuclear inflammation has been demonstrated. No abnormalities of gastric function have been detected in cats infected with \textit{H. felis} and \textit{H. pylori}. The species of \textit{Helicobacter} may be important in regard to pathogenicity, because cats with \textit{H. pylori} infection develop more severe gastritis than those with \textit{H. felis} or \textit{H. heilmannii}.

The clinician must carefully consider other causes of gastrointestinal signs in dogs and cats, such as dietary intolerance, parasitic or bacterial enteritis, or inflammatory bowel disease, before incriminating \textit{Helicobacter} as the cause. At the authors’ institutions treatment for GHLO is undertaken only in patients with clinical signs and biopsy-confirmed gastritis and \textit{Helicobacter} infection. Treatment is then instituted with a 2-week course of 2 antibiotics, mostly amoxicillin and metronidazole or clarithromycin, with or without an antisecretory drug, such as a proton-pump inhibitor or a H\textsubscript{2}-receptor antagonist. The authors’ opinion is that well-controlled, blinded, prospective multicenter studies are required to elucidate the pathogenic role of GHLO in cats and dogs with gastrointestinal signs and gastritis.

### Footnote

-Diff Quik, Dade, Düdingen, Switzerland

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