Spiral bacteria were identified in the stomachs of humans and animals in the late 1800s. However, it was not until the early 1980s that Warren and Marshall proposed a relationship between *Helicobacter pylori* and gastric disease in humans. Soon after, studies in dogs and cats clearly demonstrated that spiral bacteria were commonly found in the stomachs of clinically normal dogs and cats as well as dogs and cats with signs of gastrointestinal disease. However, a direct causal relationship between spiral bacteria and gastric disease has not been established in dogs or cats. Although the potential pathogenic role of *Helicobacter* spp in dogs and cats is being investigated, we routinely determine whether the organisms are present in all dogs and cats with signs of chronic vomiting. A percentage of these patients have been treated for *Helicobacter* spp, and some have responded favorably. We want to emphasize that a thorough diagnostic evaluation to search for other potential causes of vomiting should always be conducted before considering *Helicobacter* spp to be etiologic agents.

This article describes the common methods of identifying spiral bacteria in the stomachs of dogs and cats. *Helicobacter* spp are gram-negative, microaerophilic, motile, and curved or spiral bacteria with multiple terminal flagella. They contain large quantities of the enzyme urease, which results in production of ammonia and bicarbonate from urea. This alters the pH surrounding the bacteria and helps them colonize the acidic environment of the stomach.

More than 30 *Helicobacter* spp have been identified in humans and animals. In addition to the species found in the stomach, others have been identified in the intestine and liver. *H. pylori* is the most common gastric species in humans. It has been shown to be a major cause of gastritis and peptic ulcers as well as to increase the risk of gastric cancer. Infection rates in humans can approach 100% in developing countries and 25% to 60% in developed countries. Infection is usually acquired in childhood and most often persists for life. Most infected humans remain asymptomatic. However, peptic ulcers may develop in 10% and gastric cancer in 1% to 2% of those infected.
Although *H. pylori* has been identified in research colony cats,21–23 infection of pet dogs and cats with other species occurs most commonly. Most *Helicobacter* spp commonly found in the stomachs of dogs and cats are larger than *H. pylori* (1.5 to 3 µm).13 Large spiral bacteria (4 to 10 µm) identified in the stomachs of dogs were initially called *Gastrospirillum hominis*. They were later reclassified as *Helicobacter heilmannii*.10,12 Other large gastric spiral bacteria such as *Helicobacter felis*, *Helicobacter bizzozeronii*, and *Helicobacter salomonis* have been identified and are indistinguishable from *H. heilmannii* using routine light microscopy.24–26 Multiple species can be present in an individual animal.27

Besides the potential role of *Helicobacter* spp in the pathogenesis of gastritis and chronic vomiting, zoonotic potential is another reason to identify these species in dogs and cats. Although most evidence suggests that the zoonotic potential is very low, some evidence supports potential zoonotic transmission. *H. heilmannii* is a rare cause of gastritis in humans, accounting for approximately 0.1% of cases.28 An epidemiologic survey of humans with *H. heilmannii* gastritis showed that contact with dogs and cats was a significant risk of infection.28 In addition, there was an association between *H. Heilmannii* gastritis and gastric lymphoma, although this could be coincidental.29 *H. pylori* has been identified in research colony cats, demonstrating that cats could serve as a reservoir.21,22 Several studies have identified cat ownership as a risk factor for *H. pylori* infection in humans.30,31 However, other studies have shown that contact with dogs or cats is not a risk factor for *H. pylori* infection.12–17 Although the potential for zoonotic transmission appears slight, until this issue is conclusively resolved, it seems prudent to determine whether *Helicobacter* spp are present in dogs and cats during diagnostic evaluation of gastric disorders.

Invasive methods of diagnosing *Helicobacter* infection in humans include bacterial culture, routine microscopic or ultrastructural examination, polymerase chain reaction testing, and rapid urease testing of gastric mucosal biopsy specimens, which are usually obtained via endoscopy.14,38–40 Noninvasive methods of diagnosis include urea breath testing, fecal antigen determination, and serology.14,38–45 Although noninvasive methods as well as polymerase chain reaction testing, scanning electron microscopy, and culture of gastric biopsy specimens have been investigated in dogs and cats,8,9,21,23,27,44–50 they are not routinely available to practitioners. Presently, clinical diagnosis of *Helicobacter* infection in dogs and cats requires endoscopic examination or exploratory celiotomy. Spiral bacteria can be identified in gastric biopsy or brush cytology specimens or indirectly by rapid urease testing of gastric mucosal samples.5–9

Results of histologic evaluation of biopsy samples require 24 to 72 hours. Results of gastric brush cytology and rapid urease testing are available much sooner.

**BRUSH CYTOLOGY**

Gastric brush cytology is the least expensive and most practical diagnostic method and has the quickest turnaround time. After an endoscopic examination has been completed and biopsy samples from the duodenum and stomach have been collected, a brush cytologic specimen can be collected. A guarded cytology brush should be passed through the biopsy channel of the endoscope into the gastric body along the greater curvature. The cytology brush should be extended from the sheath and gently rubbed along the mucosa from the antrum toward the fundus along the greater curvature. Hemorrhagic areas associated with previous biopsy sites should be avoided. The brush should be retracted into the protective sheath and withdrawn from the endoscope. The brush should be extended from the sheath and gently rubbed across several glass microscope slides, which are air-dried and stained with a rapid Wright’s stain. The slide should be magnified ×100, immersed in oil, and examined. Areas with numerous epithelial cells and large amounts of mucus should initially be viewed. If present, spiral bacteria should be easily seen. They are usually at least as long as the diameter of an erythrocyte, and their classic spiral shape is obvious (Figure 1). The number of spiral bacteria can be highly variable (i.e., from one in every several fields to massive numbers in most fields). We examine at least 10 oil-immersion fields on two slides before the specimen is considered negative. Unlike diagnostic tests

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**Helicobacter spp may cause or contribute to gastritis and vomiting in dogs and cats.**

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that involve using a single (or several) small biopsy sample(s), brush cytology gathers surface mucus and epithelial cells from a much larger area, increasing the chance of identifying bacteria. Brush cytology was found to be more sensitive than urease testing or histopathologic examination of gastric tissue in identifying *Helicobacter* organisms in dogs and cats.\(^6,51,52\)

**RAPID UREASE TEST**

The rapid urease test detects the presence of bacterial urease produced by *Helicobacter* spp in a biopsy sample.\(^13,14\) We use the CLOtest (Ballard Medical Products, Draper, UT; Figure 2), which is commercially available. Individual tests cost approximately $6. The test consists of agar gel with urea and a pH indicator (i.e., phenol red) in a small, plastic well. Tests should be kept refrigerated before use. To conduct the test, a biopsy sample obtained from the angularis incisura of the stomach should be pushed into the gel. The test should be maintained at room temperature and examined frequently for 24 hours. If bacterial urease is present, urea will be hydrolyzed to ammonia, changing the pH of the gel. The gel should turn from yellow to magenta. The rate at which the gel changes color is proportional to the number of *Helicobacter* organisms present. When large numbers of bacteria are present in the biopsy sample, the rapid urease test quickly changes color, often within 15 to 30 minutes.\(^7\) If the color of the gel has not changed within 24 hours, the result should be interpreted as negative. A CLOtest with negative results can be reused within a short period if it is kept at room temperature.\(^53\) Urease tests can also be made by placing 10% unbuffered urea in distilled water and 1% phenol red into a tube, but most practitioners prefer the convenience of commercially available tests.\(^6,11,46\)
We have occasionally observed false-positive test results perhaps because of urease-producing pharyngeal or intestinal bacteria and false-negative results because of the patchy distribution of bacteria within the stomach or administration of drugs that decrease acid secretion (increases in pH alter the activity of urease).\textsuperscript{13,14,54} False-negative results should be suspected when spiral bacteria are observed in brush cytology specimens or during histopathologic assessment of biopsy samples. Including biopsy samples from multiple areas of the stomach can help reduce false-negative results in rapid urease testing.\textsuperscript{55} Contamination of biopsy specimens with blood does not seem to alter test results.\textsuperscript{56} False-positive results should be suspected when spiral bacteria are not observed in brush cytology specimens or during histopathologic assessment of multiple biopsy samples with routine and silver stains. We feel that, of the common diagnostic methods, rapid urease testing is the least valuable because of false-positive and negative results, cost, and turnaround time for test results (especially if negative).

**HISTOPATHOLOGIC IDENTIFICATION**

Histopathologic identification of *Helicobacter* spp within gastric biopsy samples using hematoxylin and eosin (H & E) or special stains has a specificity of 100% and a sensitivity of greater than 90% in human studies.\textsuperscript{14,38,39} Because of the patchy distribution of organisms within the stomach,\textsuperscript{12} examination of samples from multiple gastric locations can increase sensitivity. In our clinic, samples from the pylorus, angularis incisura, gastric body along the greater curvature, and cardia are routinely examined. In humans, the best site to detect *H. pylori* is the antrum.\textsuperscript{40} In some studies in dogs and cats, organisms have been identified with a higher frequency in the body and fundus than in the antrum and pylorus.\textsuperscript{6,7,10,21,22,48,49,59} Spiral bacteria can be seen within mucus covering the surface epithelium as well as within the gastric pits, glandular lumen, and parietal cells\textsuperscript{5–7,10,21,22,48,49,59} (Figure 3). In cats, bacteria have been identified submucosally within gastric lymphoid follicles.\textsuperscript{60} Spiral bacteria associated with the mucosal surface or within gastric pits are relatively easy to detect with routine H & E staining of tissue. However, if the distribution of bacteria favors gastric glands and glandular epithelial cells, bacteria are much more readily detected with the silver technique. Therefore, if bacteria cannot be identified with H & E staining, a modified Steiner’s silver stain should be used (Figure 4). Because of similarities in morphologic characteristics, it is not possible to identify specific species using routine histologic staining techniques. Besides identifying *Helicobacter* spp, histopathologic evaluation of biopsy samples allows assessment of underlying inflammation (Figure 5) and neoplasia\textsuperscript{6,7,10,21,22,58,61} which may be the cause of a patient’s clinical signs.

**BACTERIAL CULTURE**

Although bacterial culture of gastric biopsy specimens is commonly used to detect *H. pylori* in humans, culture is far less useful in dogs and cats.\textsuperscript{8,62} *H. heilmannii* has not been successfully cultured.\textsuperscript{57} *H. bizzozeronii, H. felis,*
and *H. salomonis* have been cultured from dogs with and without clinical signs. Even in humans, *H. pylori* is considered difficult to culture because of demanding transport and handling requirements. Culture of gastric biopsy specimens from dogs and cats in clinical practice is not routinely conducted.

**UREA BREATH TESTING**

Urea breath testing is commonly used to assess the effectiveness of treatment in humans and diagnose infection in children. Urea breath testing has been used experimentally in dogs and cats, but because of equipment limitations, radiation regulations, and difficulty collecting breath samples from patients, this testing is not routinely available to veterinary practitioners. To conduct the test, radioactive carbon $^{14}$C- or heavy $^{13}$C-labeled urea should be placed within the stomach via intubation in animals or ingestion in humans. If *Helicobacter* spp are present, urease will hydrolyze the urea and release the $^{13}$C or $^{14}$C, which diffuses into blood and is expired as carbon dioxide ($CO_2$). Breath samples should be collected for up to 60 minutes and analyzed for abnormal $CO_2$ ($^{14}$C requires a scintillation counter and $^{13}$C a mass spectrometer). Tests with positive results contain a large amount of abnormal $CO_2$ liberated by the urease produced by gastric *Helicobacter* spp.

**CONCLUSION**

The role of *Helicobacter* spp in gastritis and chronic vomiting in dogs and cats remains unknown. However, it seems prudent to determine whether spiral bacteria are present in the stomachs of dogs and cats evaluated for chronic vomiting. A diagnosis of spiral bacteria is best made by examining gastric cytology samples and confirmed by histologic evaluation of gastric biopsy samples. Rapid urease tests can also be used to indirectly identify the organism. Specific treatments cannot be recommended until the potential role of *Helicobacter* spp in dogs and cats with chronic vomiting has been studied further.

**REFERENCES**


3. Which *Helicobacter* sp has not been identified in the stomachs of dogs?
   a. *H. heilmannii*  
   b. *H. pylori*  
   c. *H. felis*  
   d. *H. bizzozeronii*

4. Which of the following is considered a noninvasive test to detect *Helicobacter* spp?
   a. histologic examination of gastric mucosal biopsies  
   b. rapid urease test  
   c. electron microscopic examination of gastric mucosal biopsies  
   d. urea breath testing

5. Which statement regarding evaluation of gastric brush cytology specimens is incorrect?
   a. They are insensitive in identifying spiral bacteria.  
   b. Evaluation is inexpensive.  
   c. There is a rapid turnaround time for results.  
   d. Identification of spiral bacteria requires simple staining methods available in all practices.

6. The rapid urease test
   a. is expensive (approximately $25 per test).  
   b. detects the presence of bacterial urease from *Helicobacter* organisms.  
   c. needs to be incubated at 98.6˚F (37˚C) for 2 to 3 days.  
   d. can have false-negative results if a large number of *Helicobacter* spp are present within the biopsy sample.

7. Which of the following is not a potential advantage of identifying spiral bacteria by histologic evaluation of gastric mucosal samples?
   a. Spiral bacteria are usually clearly visible with H & E staining if present on the mucosal surface or within gastric pits.  
   b. Underlying inflammatory or neoplastic conditions can be identified.  
   c. The turnaround time for results is rapid (i.e., usually less than 12 to 24 hours).  
   d. It is easy to increase diagnostic sensitivity by evaluating samples from multiple regions of the stomach.

8. Bacterial culture of *Helicobacter* spp in dogs and cats is
   a. not commonly conducted because *H. heilmannii* has not been successfully cultured.  
   b. the diagnostic test of choice because of high sensitivity and specificity.  
   c. very convenient because it can be conducted with fresh feces.
d. not commonly conducted because of the long period necessary to grow the organisms, resulting in very long turnaround times (7 to 10 days).

9. Which statement regarding the urea breath test is incorrect?
   a. It is considered a noninvasive test.
   b. It can easily be conducted in small animal practices.
   c. $^{14}$C- or $^{13}$C-labeled urea is hydrolyzed by bacterial urease in the stomachs of animals with gastric Helicobacter spp and can be measured as CO$_2$ in expired air.
   d. It has been used in adult humans to monitor treatment efficacy and in children to make a diagnosis.

10. Based on cost, ease of performance, sensitivity, specificity, turnaround time, and practicality, which test is best in diagnosing gastric Helicobacter infection in dogs and cats?
   a. histologic assessment of gastric biopsy samples
   b. rapid urease testing of gastric biopsy samples
   c. assessment of gastric brush cytologic specimens
   d. bacterial culture of gastric biopsy samples