Experimental induction of bacterial gastritis and gastric ulcer disease in gnotobiotic swine inoculated with porcine Helicobacter-like species

Steven Krakowka, DVM, PhD; D. Michael Rings, DVM, MS; John A. Ellis, DVM, PhD

Objective—To determine whether 2 isolates of recently isolated swine-origin Helicobacter pylori-like bacteria are pathogenic in pigs and compare the signs of gastric disease induced by these isolates with those detected in H pylori- and Helicobacter heilmannii-infected pigs.

Animals—36 neonatal gnotobiotic pigs.

Procedure—Groups of separately housed pigs were inoculated orally with swine-origin Helicobacter-like isolates 2662 or 1268, H pylori (human gastric pathogen), or a gastric homogenate from gnotobiotic swine containing H heilmannii. Noninoculated pigs were used as control animals. Clinical signs and development of homologous and heterologous antibodies against Helicobacter organisms were assessed. After euthanasia, gastric tissues were examined grossly and microscopically; Helicobacter organisms were detected by use of Warthin-Starry and immunohistochemical stains.

Results—Both porcine Helicobacter-like isolates colonized the stomachs of swine. Isolate 2662 was highly pathogenic; in 13 isolate 2662-inoculated pigs, gastroesophageal ulcerations developed in 9 and ulceration of the gastric glandular mucosa was detected in 5. Histologically, inflammatory gastritis consisting of multifocal to diffuse lymphohytic and plasmacytic cellular infiltrates and lymphoid follicle formation in the gastric lamina propria accompanied bacterial colonization of the gastric compartment. In contrast, H heilmannii was minimally pathogenic in that only modest inflammatory cell infiltrates were seen. Gastroesophageal or mucosal ulcers were not evident in pigs inoculated with H heilmannii.

Conclusions and Clinical Relevance—These data indicate that swine-origin H pylori-like bacteria can be pathogenic in pigs and suggest that porcine gastric disease may be mediated, in part, by colonization of the stomach by swine-origin H pylori-like bacteria. (Am J Vet Res 2005;66:945–952)
ulcers.30-31 That *Helicobacter*-like bacterial infections are contributors to gastric disease in pigs, including ulceration of the gastric pars esophagae (or *gastro-esophageal ulceration* [GEU]), is an attractive hypothesis and is plausible given the known effects of *H pylori* infection in humans and the gastric similarities between these 2 species. In modern intensive production systems, the development of ulcers and erosions of the nonglandular esophagae (cardiac) gastric lining and antral gastric mucosa is a common and serious disease problem in pigs.30 The reported prevalence of GEU in pigs is 5% to 100%, and death losses from gastric hemorrhages may be as high as 3% or more.30,31 Sublethal economic losses are also substantial. In pigs, ulceration of the gastric pars esophagae and mucosa is attributed to reflux of acidic gastric contents onto the unprotected pars esophagae.32-33 Development of exces-sive gastric acid content is multifactorial and thought to be largely due to a combination of an excess production of hydrochloric acid by parietal cells and luminal hydrolysis of luminal carbohydrate, both coupled with a loss of pH gradient in the stomachs of swine fed a finely ground, low-roughage, high-carbohydrate diet. There is the widespread, albeit undocumented, belief that social stress associated with close confinement and exposure to other infectious diseases and airborne pollutants (eg, dust and ammonia), particularly when combined with genetic selection for pigs with accelerated body growth and lean body phenotypes, promotes ulcerogenesis in pigs.34 Objective proof for this belief has been difficult to obtain. Under current intensive swine production operations, any or all of these mechanisms of stress and gastric hyperacidity may be contribut-ing factors.

An infective bacterial component to porcine ulcer disease and GEU was first suggested in reports46-37 that associated *gas trospirillum* (*Helicobacter*)-like organisms, initially named *Gastrospirillum suis* and subsequently renamed *H heilmannii*, with a high inci-dence of ulcer disease in swine in slaughterhouses. Similar or identical microbes are commonly found in other carnivores such as dogs,46-49 cats,50-52 and cheetahs.44-46 Experimental pathogenesis studies46-47 involving *H heilmannii* in target species are hampered by the fact that this agent is not ordinarily amenable to culture in artificial media. Results of recent work have confirmed the high incidence of *H heilmannii* in swine,37 and some investigators have associated *H heilmannii* colonization with development of porcine GEU.35,37-39 However, attempts to reproduce porcine GEU and mucosal ulcer disease with murine-passaged *H heilmannii* were unsuccessful.40 Furthermore, the gastric niche for *H heilmannii* appears to be predominately the gastric pits and pari etal cells of the acid-secreting gastric f undus, both un common sites of ulceration in swine. Moreover, most swine that are colonized by *H heilmannii* are ulcer-free, suggesting that the contribution of *H heilmannii* to the development of porcine gastric ulcer disease is indirect at best.

Previously, we reported30 the recovery of 2 isolates of *Helicobacter*-like bacteria that were morphologically and antigenically distinct from *H heilmannii* from the gastric mucosa of swine. The purposes of the present study were to determine whether these 2 isolates of *Helicobacter*-like bacteria are pathogenic in pigs and compare the signs of gastric disease induced by these isolates with signs that develop in *H pylori* - and *H heilmannii*-infected pigs.

### Materials and Methods

**Gnotobiotic swine**—Thirty-six gnotobiotic neonatal pigs from portions of 7 litters were used in this study.37 In brief, pigs were derived from 7 sows purchased from a local pork producer. After epidural administration of lidocaine (20 mL of a 2% solution), a Cesarean section was performed on each sow and the gravid uterus was exteriorized, severed from its abdominal attachments, and placed into a transfer tank filled with chlorine disinfectant. The sows were imme-diately euthanatized via electrical stunning (transcranial route) and exsanguination. Piglets were removed from each uterus and stimulated to breathe; after resection of the umbilici, the neonates were transferred into sterile pen-tub isolation units containing 6 separate partitions. The pigs were fed a sow’s milk replacement diet and infant formula fortified with iron 3 to 4 times daily until they were euthana-tized by use of an IV injection of sodium barbital solution at 35 days of age. Animals were maintained in accordance with The Ohio State University Institutional Animal Care and Use Committee approval of the specific protocol for this study.

**Bacterial inocula**—Pure cultures of *H heilmannii* were obtained from parietal cell suspensions initially obtained from *H heilmannii*-infected nude mice, as described.33 In brief, *H heilmannii* was separated from other bacterial species and microbial contaminants through exploitation of the affinity of this bacterium for the canalicular system of parietal cells. Isolated parietal cells were frozen in aliquots as starting material. The *H heilmannii* isolate was passaged twice in gnotobiotic mice by use of *H heilmannii*-laden gastric homogenates (con-firmed by examination of Warthin-Starry–stained cytospin preparations of the homogenates). A single passage of *H heil manii* was performed in 2 gnotobiotic pigs, and the infective inoculum was maintained by further passages of infected porcine gastric homogenates (10% [wt/vol]) in 2 gnotobiotic pigs. The infective homogenate was divided into 2-mL volumes and frozen (–70°C) until used for in vivo studies.

Pure cultures (fourth passage and beyond) of porcine *Helicobacter*-like isolates 1268 and 2662 were recovered from 2 young conventionally raised swine, as described.36 For in vivo inoculations, isolates were expanded in *Brucella* broth. At 3 days of age, 106 organisms (2-mL volume) recovered during log-phase growth were orally administered to each pig. As infection controls, 9 gnotobiotic pigs were each orally administered 2 mL of *Brucella* broth containing *H pylori* strain 26695 adapted for optimal growth in swine and similarly prepared. Uninfected control pigs received either *Brucella* broth alone or were not inoculated. To exclude inadvertent contamination among inoculation groups, each group was separately housed in gnotobiotic isolation units. The distribution of pigs by bacterial inoculation group was as follows: 13 pigs from 4 different litters were orally inoculat-ed with isolate 2662 at 3 days of age, 3 pigs from 1 litter were inoculated orally with isolate 1268 at 3 days of age, 6 pigs from 1 litter were inoculated orally with *H heilmannii*-containing gastric homogenates at 5 (n = 3) or 21 days of age (3), 9 pigs from 4 litters were inoculated orally with *H pylori* strain 26695 at 3 days of age, and 3 pigs from 2 litters were used as uninfected controls.

**Assessment of pathologic changes**—After euthanasia, a standardized procedure for collection and evaluation of gas-
tric tissues from pigs was used. Food was withheld from pigs for 12 hours and they were heavily sedated by use of ketamine HCl (1.0 mL [20 mg/kg], 1M) prior to removal from the isolation units. After collection of a blood sample to provide serum, the pigs were euthanatized by use of an IV injection of 2.0 mL of sodium barbital (100 mg/kg). The stomach of each pig was exteriorized; after ligation of the esophagus and proximal portion of the duodenum, the stomach and its contents were removed. The stomachs were aseptically opened by dissection along the greater and lesser curvatures, and half of each stomach was excised for quantitative microbial culture of the gastric mucosa. Pertinent gross findings in the remaining half of the stomach (ie, subjective assessments of submucosal edema, amount of luminal mucus, presence and extent of lymphoid follicles, and erosions or ulcers if present) were recorded by one of the investigators (SK), and photographs of ulcerative lesions, if present, were obtained (SK). In the absence of ulcers, sections of the cardiac portion of the stomach (including the pars esophagea), fundus, antrum, and the region of the pylorus and proximal portion of the duodenum were collected for microscopic evaluation. Suspected ulcerative areas or lesions in the pars esophagea and glandular mucosa were transected such that the surface containing the ulcers or erosions was available for microtome sectioning from the face of the paraffin section blocks. Gastric samples were immersed in 10 volumes of 10% phosphate-buffered formalin for at least 24 hours prior to further processing. Formalin-fixed gastric mucosa samples were dehydrated in graded alcohols, processed for histologic evaluation, and embedded in paraffin blocks by standard methods. Five-micrometer section replicates were stained with H&E for morphologic evaluation, Warthin-Starry stains to detect microbial contaminants were not identified. For preparation of swabs from feed pans, feces, and isolation units. euthanatized, isolation units were screened for extraneous microbial contaminants via aerobic and anaerobic microbial culture of swabs from feed pans, feces, and isolation units. Biological contaminants were not identified. For preparation of inocula, organisms were cultured in Brucella broth (2.8% [wt/vol] with fetal calf serum [10% [vol/vol]]) and harvested in the log-phase growth. Bacterial enumeration was accomplished by use of a hemocytometer, and counts were adjusted to 10^6 microbes/2 mL/pig. Assays for bacterial urease, catalase, and oxidase activities and motility were performed as described.23 For quantitative determination of the number of bacterial CFUs per gram of gastric mucosa in inoculated pigs, the mucosa was separated from the underlying tunica muscularis in tissue samples, weighed, and homogenized in 10% [wt/vol] Brucella broth; 10-fold dilutions were plated in duplicate onto blood agar plates, which were examined after 4 days incubation at 37°C, and 95% humidity in an atmosphere of 10% carbon dioxide, 5% oxygen, and 85% nitrogen. In addition to stomach mucosa, multiple areas of the gastrointestinal tract were also cultured for organisms in 5 of the piglets inoculated with isolate 2662. Porcine reisolates were identified as Helicobacter spp on the basis of gram-staining properties, morphologic features of colonies, urease and catalase enzyme activities, and immunoreactivity with both monospecific antisera against H pylori collected from infected gnotobiotic swine and commercially available H pylori-specific rabbit antisera.

Assessment of serum antibody responses by ELISA—Microtiter plate ELISAs were constructed by use of H pylori sonicates and Helicobacter-like isolates 1268 and 2662 (100 to 500 μg of bacterial sonicates in basic bicarbonate coating buffer [pH, 9.0]) as antigen, essentially as described.34

Results

Clinical signs—An occasional transient (24-hour) episode of anorexia has been detected in some H pylori-infected gnotobiotic swine,18,27 and there were similar findings in 2 of 13 pigs inoculated with isolate 2662 in the present study. This was determined chiefly through the presence or absence of a liquid diet in the feeding pans at the time of subsequent feedings; the residual amount of feed never exceeded 20% of the original volume. Among the pigs that became transiently anorexic, there was no apparent relationship between this clinical sign and the experimental group or day after inoculation. Uninfected control pigs maintained a normal appetite throughout the study. Aside from this transient anorexia, inoculation of gnotobiotic swine with porcine Helicobacter spp was clinically inapparent and no overt differences in size, weight, or demeanor were noted among inoculated pigs and uninfected control animals.

Gross findings—Gross lesions of gastric disease (GEU, glandular mucosal ulcers, lymphoid follicles [particularly along the lesser curvature of the stomach], excess luminal mucus, and mucosal edema) typical of infection with Helicobacter organisms in gnotobiotic pigs27,30,64 were detected in most of the isolate 2662-inoculated and H pylori-inoculated gnotobiotics (Table 1). Ulceration of the pars esophagea was identified in 9 of 13 pigs inoculated with isolate 2662 (Figure 1); similar ulceration was identified in 5 of 9 piglets inoculated with H pylori and 2 of 5 piglets inoculated with isolate 1268. None of the 6 Helimannii-inoculated or the 3 uninfected control pigs developed GEU. In addition, small ulcers of the glandular gastric mucosa were detected in 1 of 5 isolate 1268-inoculated and 4 of 13 isolate 2662-inoculated pigs (Figure 2). No ulcers of the glandular gastric mucosa were detected in the control, H pylori-inoculated, and H Helimannii-inoculated pigs. Ulcers varied in size from microscopic to approximately 0.5 cm and involved from 10% to 50% of the pars esophagea. Enlargement of gastric lymph nodes was detected in many of the Helicobacter spp-inoculated pigs as well.

Histologic findings—Histologic findings confirmed that the GEU detected in the isolate 2662- and H pylori-inoculated pigs was erosive and ulcerative in nature (Figure 3). With the exception of 1 isolate 1268-inoculated pig, penetrating ulcers of the gastric glandular mucosa were histologically only in pigs that had been orally inoculated with isolate 2662. In addition to gastric mucosal ulcers, microulceration of the proximal portion of the duodenum was detected in 1 isolate 2662-inoculated pig (Figure 4). Signs of gastric inflammation (eg, presence of lymphocytic and plasmacytic inflammatory cell infiltrates and mucosal lymphoid follicle formation) were most prominent in isolate 2662-inoculated pigs. These inflammatory
lesions were most noticeable in the lesser curvature of the stomach near the nonglandular cardiac portion of the stomach, in the antral mucosa, anterior to the gastric pylorus, and distal to the fundus (Figure 5). Pigs inoculated with either isolate 1268 or Helicobacter heilmannii had minimal evidence of inflammation in the gastric mucosa; only 2 of 5 isolate 1268-inoculated pigs had any inflammatory cell infiltrates, and none of these pigs had lymphoid follicles. Gastric lymph nodes from many of the isolate 2662- and Helicobacter pylori-inoculated pigs were highly cellular and had developing lymphoid follicles suggestive of an induced local immune or inflammatory response in the stomachs of these animals.

Microbiologic and immunologic assessments—All 13 pigs inoculated with isolate 2662 and 3 of 9 pigs inoculated with Helicobacter pylori were used for quantitative recovery of bacteria. In the isolate 2662-inoculated pigs, the level of infection varied from recovery after restreaking (approx equivalent to $10^3$ bacterial CFUs/g) to $>6 \times 10^6$ bacterial CFUs/g. There was no apparent association between the amount of bacteria isolated and either the size or number of ulcers.

Table 1—Pathologic and microbiologic findings (number of pigs with finding/number of pigs examined) in 36 young gnotobiotic pigs inoculated with swine-origin Helicobacter-like gastric isolates 2662 or 1268, Helicobacter heilmannii, or Helicobacter pylori strain 26695, compared with findings in uninfected control pigs.

<table>
<thead>
<tr>
<th>Inoculation group</th>
<th>Uninfected control pigs(3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grossly evident mucosal ulcers</td>
<td>4/13</td>
</tr>
<tr>
<td>Grossly or histologically evident gastroesophageal ulceration*</td>
<td>9/13</td>
</tr>
<tr>
<td>Histologically evident mucosal microulcer</td>
<td>5/13</td>
</tr>
<tr>
<td>Lymphocytic-plasmacytic mucosal inflammation</td>
<td>13/13</td>
</tr>
<tr>
<td>Lymphoid follicles in the antrum and lesser curvature of the stomach</td>
<td>13/13</td>
</tr>
<tr>
<td>Helicobacter organisms obtained via culture and isolation (No. or range of bacterial CFUs/g of gastric mucosa)</td>
<td>13/13</td>
</tr>
<tr>
<td>Helicobacter organisms detected in gastric tissues by use of Warthin-Starry stain</td>
<td>12/13</td>
</tr>
<tr>
<td>Helicobacter organisms detected immunohistochemically in gastric tissues</td>
<td>9/9</td>
</tr>
<tr>
<td>Seroconversion against Helicobacter pylori detected via ELISA</td>
<td>13/13</td>
</tr>
<tr>
<td>Detectable response to Helicobacter pylori in an ID skin test</td>
<td>4/5</td>
</tr>
<tr>
<td>Detectable response to isolate 2662 in an ID skin test</td>
<td>4/5</td>
</tr>
<tr>
<td>Seropositive for Helicobacter pylori by ELISA</td>
<td>13/13</td>
</tr>
<tr>
<td>Detectable response to Helicobacter pylori in an ID skin test</td>
<td>4/5</td>
</tr>
<tr>
<td>Positive response to isolate 2662 in an ID skin test</td>
<td>4/5</td>
</tr>
</tbody>
</table>

*Specifically, ulceration of the pars esophagea.†Focal lymphocytic inflammatory cell infiltrates were detected in the cardiac portion of the stomach of 1 piglet in this group. ND = Not done.

Examination of the remaining tissues revealed no remarkable findings.
like bacteria were recovered from 1 of 5 pigs inoculated with isolate 1268 and from none of the control pigs. No attempt was made to recover *H heilmannii* from the *H heilmannii*-inoculated swine.

Use of the Warthin-Starry stain on tissue sections confirmed gastric infection with *Helicobacter* organisms in the *Helicobacter*-inoculated pigs. Organisms that had morphologic features consistent with those of *H pylori* (ie, small curved rods with occasional gull-wing replicative forms) were identified extracellularly in gastric tissues from 12 of 13 pigs inoculated with isolate 2662 but not in tissues from isolate 1268-inoculated pigs (Figure 6). In the former, bacteria were most abundant in the cardiac portion of the stomach (adjacent to the pars esophagea), the lesser curvature of the stomach, and the gastric antrum; organisms were scarce or nonexistent in the fundus. Tissues from all 6 pigs inoculated with *H heilmannii* contained Warthin-Starry–stained microbes. *Helicobacter heilmannii* were easily distinguished from *H pylori* or isolate 2662 by their size (3-fold longer) and unique spiral appearance.

Although some *H heilmannii* microbes were located in the cardiac portion of the stomach, most were in the gastric pits of the fundus. Immunostaining for *Helicobacter* organisms yielded positive results when replicate sections of gastric tissues from isolate 2662-inoculated pigs were stained with rabbit anti-*H pylori* antiserum in an immunohistochemical assay (Figure 7). Bacteria that reacted with this reagent were identified in gastric sections from 9 of 9 pigs inoculated with isolate 2662, 2 of 5 pigs inoculated with isolate 1268, and 3 of 3 from pigs inoculated with *H heilmannii*. These reagents reacted weakly with isolate 1268 and strongly with the other microbes. Compared with results of microbial culture and reisolation, both the Warthin-Starry staining method and immunohistochemical assay were insensitive techniques for identification of *Helicobacter*-like bacteria in porcine tissues; gastric tissues from stomachs that contained < 10⁶ recoverable bacterial CFUs/g were frequently identified as negative for the bacteria by use of those techniques.²⁷
In 5 of the isolate 2662-inoculated gnotobiotes, microbial culture and reisolation of the organisms were also performed in tissue samples collected from throughout the gastrointestinal tract (esophagus to rectum). Trace amounts of isolate 2662 were recovered in the proximal portion of the duodenum of 2 of these 5 pigs and in the ileum and jejunum of 1 of the 5 pigs; there were no histologic lesions in these tissues (data not shown). Trace amounts of Helicobacter-like organisms were recovered via microbial culture from only 1 of 5 isolate 1268-inoculated pigs; this pig had GEU but no gastric mucosal ulcers. Because *H. heilmannii* is not amenable to culture on artificial media, we relied on examination of tissue sections stained with Warthin-Starry stain to confirm gastric colonization with this agent.

Sera obtained from all pigs immediately prior to euthanasia were evaluated for homologous and heterologous antibodies against the *Helicobacter* spp via ELISAs. All serum samples from the 13 isolate 2668-inoculated pigs reacted to both *H. pylori* and isolate 2668 antigens, whereas none of the serum samples from *H. heilmannii*- and isolate 1268-inoculated pigs reacted with these same antigens. Convalescent sera from isolate 1268-inoculated pigs reacted only with isolate 1268-origin ELISA antigen.

A subset of pigs from each inoculation group was evaluated via ID skin tests involving ID inoculation of 10 mg of either *H. pylori* or isolate 2662 sonicates into the external aspect of the ear, 24 or 48 hours prior to euthanasia. In ID skin tests involving *H. pylori* sonicates, histologic evaluation of skin test sites revealed dermal delayed-type hypersensitivity responses to skin test antigens in 4 of 5 pigs inoculated with isolate 2662, 4 of 5 pigs inoculated with isolate 1268, and 7 of 9 pigs inoculated with *H. pylori*. The dermis and subcutaneous tissues contained mononuclear cell infiltrates with a scattering of neutrophils and eosinophils typical of delayed-type hypersensitivity responses to bacterial proteins (Figure 6). The same 4 pigs inoculated with isolate 2662 also responded to isolate 2662 sonicates, as did 5 of 6 pigs inoculated with *H. heilmannii* (Table 1). There was no observable histologic difference between ID skin test sites when either source of bacterial sonicate was used.

**Discussion**

The objective of the present study was to assess the pathogenic potential of swine-origin *Helicobacter*-like isolates in gnotobiotic pigs and compare the signs of gastric disease induced by these isolates with clinical signs that develop in *H. pylori* - and *H. heilmannii*-inoculated gnotobiotes. Of the 2 isolates, our data indicate that isolate 2662 is more pathogenic. As described,40 isolate 2662 is similar to human-origin *H. pylori*. Compared with the other inoculation groups, a greater proportion of pigs inoculated with isolate 2662 had erosions and ulcers of the gastric pars esophagea; in this group, 9 of 13 pigs had GEU, compared with 5 of 9 pigs inoculated with *H. pylori*, 2 of 5 pigs inoculated with isolate 1268, and 0 of 3 pigs inoculated with *H. heilmannii*. However, the incidence of ulceration in the glandular mucosa was more important. Although *H. pylori* will cause mucosal ulcers on occasion,41 mucosal ulcers were detected in 5 of 13 pigs inoculated with isolate 2662 in the present study. In addition, an ulcer in the proximal portion of the duodenum was detected in one of the pigs in this inoculation group. This incidence of true gastric mucosal ulceration was unexpected and exceeds that associated with *H. pylori* (a known human and porcine gastric ulcerogen) in either humans' or swine.42 It is noteworthy that *H. heilmannii*, a microbe associated with the development of GEU and ulcer disease in pigs by other investigators,35,37,45,46 induced neither GEU nor gastric mucosal ulceration in pigs inoculated with this agent in the present study.

In *H. pylori* infection in both humans and gnotobiotic swine,8,10,18,27,35,36 the developing inflammatory response in the gastric mucosa to gastric bacterial colonization is predominately lymphocytic with well-developed lymphoid follicles in the antral and cardiac portions of the stomach. These gastric inflammatory lesions are distinct from the porcine Peyer's patchlike structures previously identified in porcine gastric cardiac mucosa.53 Gastric mucosal neutrophilic infiltrates, either in the mucosa or within the gastric pits, were not seen in isolate 2662-inoculated piglets. Although it was not quantitated in the present study, the intensity of the inflammation in the cardiac and antral portions of the stomach was most evident in pigs inoculated with isolate 2662 and least evident in the pigs inoculated with isolate 1268. As reported previously,47 *H. heilmannii*-associated nonsuppurative inflammation is modest in gnotobiotes infected with that agent alone. Also, as detected in *H. pylori* infection in humans and in infected gnotobiotic pigs transferred from isolation units into a conventional environment,47,48 gastric infection with *Helicobacter* organisms appears to be persistent despite the development of vigorous antibody and T-cell-mediated responses to bacterial antigens.

The role of the *Helicobacter*-like isolates in the pathogenesis of GEU in conventionally reared pigs has not yet been defined. Our data suggest that gastric col-
onization with Helicobacter-like gastric microbes may be a critical factor in the initiation of gastric ulcer disease in pigs. From this assumption, it follows that GEU in pigs may actually be an infectious bacterial disease, rather than a disease caused by consumption of high-carbohydrate diets or modern swine production methods. An unpublished ELISA serologic survey performed by our group, in which >1,000 serum samples from conventionally reared pigs (weaning to adult stages) were evaluated, revealed that pigs begin the process of seroconversion against isolate 2662 antigens at 5 to 6 weeks of age; by adulthood, >80% of the pigs have IgG-isotype antibodies against H pylori and isolate 2662, as determined via an ELISA. Although it is possible that this high incidence of infection could be due, in part, to colonization and subsequent cross-reactivity with H helmanii, it is noteworthy that no sera from the gnotobiotic pigs inoculated with H helmanii in the present study reacted in ELISAs to H pylori and isolate 2662 antigens, even when these sera were tested for activity by use of IgM isotype-specific secondary reagents. In that study, 2 faint bands were distinguished via western blot immunassays when convalescent sera from H helmanii-inoculated pigs were tested against H pylori and isolate 2662.

The contributions of diet to the pathogenesis of GEU in pigs are undeniable. The evidence for gastric luminal acid–mediated damage of the pars esophagea is strong, and the fact that the diet can be specifically manipulated to decrease the incidence of GEU in pigs argues strongly for the role that diet plays in promoting gastric ulcerogenesis. In pigs, the general strategy for management of GEU and gastric mucosal ulceration is centered around prevention of acidic reflux into the pars esophagea by provision of diets that are coarsely ground and limiting the consumption of fermentable carbohydrates. This approach represents a compromise between providing a diet that promotes optimal growth and weight gain among pigs during the fattening period of production and the prevention of GEU. The interactions of diet formulation, dietary carbohydrate content (chiefly as corn, cornstarch, and corn byproducts), and certain species of gastric microbes (eg, the Helicobacter organisms and the carbohydrate-fermenting commensals such as Bacillus and Lactobacillus spp) with the development of GEU in pigs maintained under conventional management conditions remain to be determined. If an infectious component of gastric ulcer disease in pigs is established, then specific measures such as specific antimicrobial treatments, targeted probiotics, and vaccines containing H pylori-like or other relevant bacterial antigens could be developed to prevent or control bacterial gastritis. In this manner, producers would be provided with additional methods for the control of GEU and mucosal ulcer disease in pigs.

References