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In Brief

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Author Disclosure

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***Helicobacter pylori* Infection in Children: Recommendations for Diagnosis and Treatment**. Gold B, Colleti R, Abbott M, et al. *J Pediatr Gastroenterol Nutr.* 2000;31:490–497

***Helicobacter pylori* Diagnosis and Management**. Vilaichone R, Mahachai V, Graham D. *Gastroenterol Clin North Am.* 2006;35:229–247

New Immunoassay in Stool Provides an Accurate Noninvasive Diagnostic Method for *Helicobacter pylori* Screening in Children. Braden B, Posselt H, Ahrens P, et al. *Pediatrics.* 2000;106:115–117

Helicobacter pylori is a gram-negative microaerophilic bacillus. On microscopy it appears spiral, curved, or U-shaped and has two to six flagella at one end. Its identification is confirmed by its oxidase, catalase, and urease activity. Although most people infected with the organism (estimated to be at least 50% of the world's population) remain asymptomatic, the organism has been associated with a significant proportion of duodenal ulcers and, to a lesser extent, gastric ulcers. The development of gastric adenocarcinoma and gastric lymphomas also has been linked to chronic *H pylori* infection.

Infection is more common in developing countries, where the incidence is 3% to 10% of the population each year, compared with 0.5% in industrialized countries. Risk factors for the disease include poor socioeconomic conditions, family overcrowding, child care attendance, poor hygiene, and living with an infected family member. International adoptees and other immigrant children are at increased risk, and there may be ethnic or genetic predisposition. Asian Americans, African Americans, and Hispanic individuals living in North America have a prevalence of *H pylori* infection similar to that of residents of developing countries.

Transmission is fecal-oral, gastric-oral, or oral-oral from human-to-human contact. Thus far, no animal reservoir for human transmission has been found, but domestic cats and houseflies have been proposed as possible reservoirs. Waterborne infection also has been considered as a possibility.

As for any pathogen, a useful test for the presence of *H pylori* should be noninvasive, highly accurate, and readily available and allow the practitioner to differentiate between present and past infection. Unfortunately, the ideal test does not yet exist, but several invasive and noninvasive methods are available.

Specimens obtained directly from the prepyloric antrum by endoscopic biopsy provide the only truly reliable approach to diagnosing *H pylori* infection definitively. Once such specimens are obtained, several different methods are available to detect the organism. Histologic identification is possible employing Warthin-Starry silver stain or Steiner, Giemsa, or Genta staining. A gastric biopsy can be cultured on selective or nonselective media at 37.0°C under microaerobic conditions. Culture provides valuable information about antibiotic sensitivity, but it is expensive and success rates in many laboratories are suboptimal. Immunologic detection of *H pylori* urease activity from a gastric specimen can provide a rapid diagnosis, but despite its high negative predictive value, the test has been shown to have poor positive predictive value in children. Polymerase chain reaction performed on tissue obtained by endoscopy or from body fluids is very sensitive but is expensive and not easily available.

Invasiveness, the need for sedation or even anesthesia, and expense limit the usefulness of endoscopic biopsy as a routine diagnostic procedure. Although not as reliable as endoscopic biopsy, noninvasive testing is available. The urease breath test involves having the patient ingest urea labeled either with radioactive carbon-14 or with carbon-13. *H pylori* is rich in urease, which hydrolyzes ammonia (a primary constituent of urea) into water and carbon dioxide. With exhalation of carbon dioxide, the amount of labeled carbon atom can be measured. This test has been shown to have high sensitivity and specificity in children but requires expensive analytical equipment and is difficult to perform in small children and infants. An enzyme-linked immunosorbent assay can detect immunoglobulin G antibodies against *H pylori*, but it has poor sensitivity and specificity, and no age-related cutoff values are available. Finally, a monoclonal immunoassay to detect bacterial antigen in stool appears to have sensitivity and specificity greater than 98%. The sam-

ple is easily obtained, and the test is both less expensive than the urease breath test and technically easy to perform.

In adult patients, endoscopy is used to diagnose *H pylori* and to look for malignant gastric disease. In pediatrics, the rarity of gastric malignancy mitigates against the need for endoscopy in many circumstances, making a screen-and-treat strategy in dyspeptic children a more commonly employed option. Although noninvasive, less expensive tests such as the urease breath test and the fecal antigen test reduce the number of endoscopies, endoscopy with gastric biopsy remains the gold standard for the diagnosis of *H pylori* infection in children.

In the absence of convincing data to support routine testing of children who have recurrent abdominal pain or asymptomatic children who have a family history of peptic ulcer disease or gastric cancer, the American Academy of Pediatrics recommends testing only when treatment for *H pylori* infection would be warranted. Such candidates include patients who have either active peptic ulcer disease or a history of ulcers, or more rarely, children who have mucosa-associated lymphoid tissue-type (MALT) lymphoma or gastric cancer.

When treatment is indicated, it should be for more than 7 days (usually 14 days) and include two appropriate antimicrobials and a proton pump inhibitor (PPI). The aims of treatment are to eradicate the organism, heal the ulcer, and prevent recurrence of infection and the emergence of resistant organisms. The PPI serves to reduce gastric acidity, which may alleviate symptoms and allow acid-sensitive antimicrobials (such as amoxicillin and clarithromycin) to work more effectively.

First-line treatment regimens for children generally include clarithromycin (15 mg/kg per day divided twice a day [BID], up to 500 mg per dose) with either amoxicillin (50 mg/kg per day divided BID, up to 1 g per dose) or metronidazole (20 mg/kg per day divided BID, up to 500 mg per dose) and a PPI. For patients older than 8 years of age, a less expensive but more cumbersome regimen includes tetracycline and metronidazole along with bismuth subsalicylate and a histamine-2 blocker. These regimens have produced high cure rates ranging from 75% to more than 90% in children. To check for eradication, it is best to wait at least 6 weeks and preferably 3 months after the completion of therapy before retesting with either the urease breath test or the stool antigen test. The use of serologic tests to verify eradication is not recommended because, despite disease resolution, antibody titers can remain positive for months.

Failure to eradicate *H pylori* infection usually is related either to poor adherence to the treatment regimen or, as is becoming common with many infectious agents, antibiotic resistance, particularly to clarithromycin and metronidazole. Because of the emergence of resistance, the use of simpler single- or double-drug regimens (as opposed to the preferred three- and four-drug regimens) as initial therapy should be avoided. Retreatment regimens have included various combinations of bismuth subsalicylate, PPIs, amoxicillin, rifabutin, and when the age of the patient allows, tetracycline or a quinolone.

The long-term risks of asymptomatic *H pylori* infection are not well elucidated. Most infections are acquired during childhood, but which children are at risk for eventually developing active disease, especially gastric cancer, is not clear. No current evidence defines cost-effective criteria for screening and eradication of asymptomatic infections.

Comment: "If you build it, he will come" too often resonates in medicine: create the technology and we will use it. Now that fecal antigen testing is readily available, the ease of diagnosing *H pylori* infection in children who have epigastric pain creates the temptation to treat when the test is, indeed, positive, despite *Red Book* guidelines recommending treatment only for children who have active or past peptic ulcer disease or who have the rare MALT lymphoma. Until there is evidence that more liberal treatment really offers benefit, the risks of burgeoning resistance to available antimicrobial agents should give us pause.

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