Helicobacter Pylori Revisited

Clarisa E. Cuevas M.D.

The more I read and study this organism, the more I marvel about its role in gastric pathology. Since 1982, when it was successfully cultured by Marshall and Warren, there have been multiple evolving studies about its pathogenesis, diagnostic tests and treatment.

Helicobacter pylori colonize the stomach of over half the world's population. In developing countries, the infectious process occurs during childhood by intrafamilial transmission with a prevalence later on of greater than 60% in the adult population. In developed countries, the acquisition of this organism is felt to be around 1%. Eventually, more than 30% of the adult population will be colonized. Prolonged infection and inflammation leads to ultimate chronic gastritis. This chronic inflammation can lead to severe gastric pathologies such as peptic ulcer, gastric adenocarcinoma and gastric mucosa associated tissue lymphoma. In addition to its role in gastroduodenal disease, H. pylori has been implicated in the development of ITP, iron deficiency anemia and appetite suppression.

The World Health Organization has classified H. pylori as a class 1 carcinogen in humans. The chronic atrophic gastritis caused by these organisms is considered the major precursor of gastric cancer. Eradication of H. pylori can result in complete lymphoma remission in 75% of patients. The challenge is to try to identify those patients that will have intestinal metaplasia and neoplasia at an early stage where eradication of the organism will result in cancer cure. Major stumbling blocks to eradication include patient compliance; H. pylori strain resistance to antibiotics and asymptomatic patients that remain at risk of developing atrophic gastritis and eventual cancer.

In 2005, Shiotani et al. published an article implicating H. pylori infection with decreased levels of plasma ghrelin. This in turn resulted in adverse appetite symptoms such as nausea and lack of appetite. They theorized that the suppression of ghrelin by this bacterium resulted in growth failure in infected children. Both ghrelin and leptin are present in the gastric mucosae and play an important role in appetite regulation.

The current first line of treatment therapy recommended in the United States and in the Western world is clarithromycin, amoxicillin or metronidazole plus a PPI twice a day. The more effective duration is 14 days. Treatment regimens of seven, ten or fourteen days will likely depend on the population and resistance pattern in the specific area. More critical than the duration of therapy is the resistant of H. pylori to a specific antibiotic. Most treatment failures occur when the organism is resistant to clarithromycin. In that case, metronidazole, amoxicillin and bismuth base therapy along with a twice a day PPI becomes the treatment of choice. In the review article "Bismuth- based therapy for Helicobacter pylori eradication in children," an attempt was made to see the evidence of this last treatment regimen. The Bismuth compounds felt to be appropriate for medical use were colloidal bismuth subcitrate, bismuth subsalicylate and ranitidine bismuth citrate. Bismuth monotherapy showed very low efficacy. When combined with antibiotics eradication rate was 60-76% depending on the center studied and their specific antibiotic resistance. Side effects when Bismuth salts were used included dark stool, urine discoloration, black tongue, burning tongue and marked darkness of the gums.

The major challenge pertaining to Helicobacter pylori infection is that of identifying the mechanisms leading to ulcer formation and gastric malignancies. Available studies seem to suggest that gastric immune and inflammatory responses depend on the host genetics and its response to the infectious organism. Thus we can have three responses: (1) mild pangastritis without significant disease, (2) antral predominant gastritis with high gastric acid secretion and increased risk for duodenal disease, and (3) fundus predominant with gastric atrophy, hypochlorhydria and increased risk of gastric cancer. The combination of new technologies with information on clinical phenotypes and genotypes will enhance our knowledge of this disease and help in the development of biomarkers for diagnosis, treatment and prevention of H. Pylori infection.

Because H. Pylori infection affects half of the human population and because of issues of compliance and tolerance of pharmacologic therapy, vaccine production is felt to be beneficial and cost effective. At present there are several animal studies but no human vaccines are yet available. The consensus is that the vaccine should be given to children at the time of other pediatric vaccinations so as to prevent the disease.

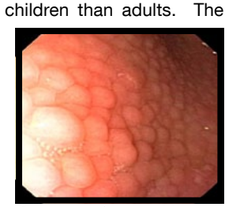
Diagnosis for Helicobacter pylori

Youhanna S. Al-Tawil, M.D.

H. pylori can be found in a normal stomach and be asymptomatic. When there is a strong suspicion that H. pylori are causing clinical symptoms, testing can not only detect the presence of H. pylori but also confirm a diagnosis.

Endoscopic Tests

Upper gastrointestinal endoscopy and biopsy remains the 'gold standard' in the diagnosis and identification of H. pylori infection and its consequences in childhood. It allows visualization of the upper gastrointestinal tract. Nodularity within the stomach is seen more frequently in children than adults. The mucosa is irregular in appearance, resembling a cobblestone pavement. Seen most often within the gastric antrum, it is frequently referred to as antral nodular gastritis.



Endoscopic view of H. pylori gastritis in a child

Endoscopy facilitates the collection of mucosal biopsies, which include a variety of direct tests:

Histopathology – On H&E staining of gastric mucosal biopsies obtained from H. pylori-infected patients, a superficial infiltrate is usually seen with substantial numbers of plasma cells and lymphocytes within the mucosa. Detection of the H. pylori bacterium can be done using a variety of different stains.

Rapid Urease Test (RUT) – Urease catalyzes the hydrolysis of urea into ammonia and carbon dioxide. The production of ammonia leads to an increase in the local pH. Samples are placed within a gel containing urea and a pH indicator. A color change occurs as urea is broken down by the bacteria. Use of RUTs in pediatrics is limited by a significantly lower sensitivity compared to histology.

Culture – a potential 'gold standard' for the diagnosis of suspected H. pylori infection. Its sensitivity has been reported to vary greatly between laboratories.

Nonendoscopic Tests

Serologic – H. pylori infection induces both cellular and humoral immune responses, resulting in an early increase in specific IgM, and a later and persistent increase in specific IgA and IgG. In children, IgA-based tests detects only 20-50% of H. pylori infected patients. Serologic tests based on the detection of specific anti-H. pylori IgG antibodies in the serum offer a better sensitivity than IgA-based tests. Their most important limitation is the inability to distinguish active from past infection.

Urea Breath Test (UBT) – Urea is labeled with either 13 C (non-radioactive) or 14 C (radioactive) isotopes, and then ingested. 13 C is a naturally occurring non-radioactive isotope. It can be safely used in even very young infants, and can be repeated without risk to the child. Labeled urea comes into contact with the mucosa and diffuses through the mucus. Urea hydrolysis by H. pylori produces ammonia and labeled carbon dioxide. Urea rapidly passes down its concentration gradient into the epithelial blood supply, and within minutes appears in the breath. Breath samples are collected at variable times postingestion.

Stool antigen – H. pylori antigen can be detected in the stool. Stool testing is a potentially inexpensive, non-invasive method for determining H. pylori infection. Overall sensitivity and specificity of the stool test are comparable to the UBT (94% and 97% respectively). A rapid H. pylori stool antigen test is available that permits testing during a clinic visit but is slightly less accurate than a traditional laboratory based stool test. The sensitivity of stool testing is negatively affected by PPIs, bismuth, and antibodies, which can decrease bacterial load.

Ref: Pacifico, L., Osborn, J.F., Anania, C., Vaira, D., Olivero, E., and Chiesa, C. Review article: bismuth-based therapy for Helicobacter pylori eradication in children. Alimentary Pharmacology & Therapeutics 2012; 35:1010-1026.

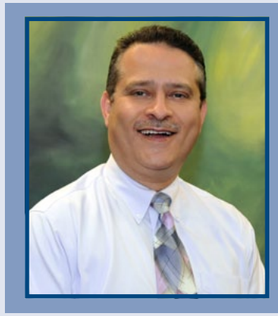
Nutrition and H. Pylori

Ashley Rogers, MS,RD,LDN

Helicobacter pylori (H. pylori) is a major cause of certain diseases of the upper gastrointestinal tract. A number of foods may be useful to prevent colonization with H. pylori, including: green tea, red wine, broccoli sprouts, garlic, probiotics and flavonoids (1). Probiotics present a low-cost, large scale alternative solution to prevent or decrease colonization. Probiotic intake, although not a cure in themselves, has been shown to strengthen the mucosal barrier by stimulating local IgA responses, thus leading to a stabilizing effect of the mucosa. Supplementing the diet with yogurt containing lactobacillus and bifidobacterium has been shown to help improve the rates of eradicating H. pylori (2). Flavonoids are water soluble plant pigments that are beneficial to our health. They offer antioxidant, anti-inflammatory, and anti-viral properties. Good sources of flavonoids include: citrus fruits, berries, apples, cabbage, onions, parsley, tea, and dark chocolate. The following foods could make symptoms worse or cause the bacteria in the gut to grow: fried/greasy foods, spicy, tomato-rich foods, caffeinated beverages and refined flours. The following are steps that can be taken to help prevent the infection of H. pylori: 1) Wash hands with soap and water frequently; 2) Drink water from clean and safe source; 3) Eat foods that have been washed and cooked properly; and 4) Do not eat food that has been sitting out all day.

Resources used:
1. Wikipedia, The Free Encyclopedia. Heliocobacter pylori. Available at: http://en.wikipedia.org/wiki/Helicobacter_pylori. Accessed on July 16, 2012.
2. Draholava Lesbros-P. Helicobacter pylori and Probiotics. J. Nutr. March 2007; 37:812-818. Available at: http://jn.nutrition.org/content/137/3/812S.full . Accessed on July 16, 2012.

GI for Kids — Meet our New Providers



M. Samer Ammar, MD, FAAP, FAGA

Education:
Pediatric Gastroenterology, Hepatology & Nutrition Fellowship, 2002 –
Div. of Pediatric Gastroenterology, Hepatology & Nutrition,
James Whitcomb Riley Hospital for Children,
Indiana University School of Medicine,
Indianapolis, IN.

Pediatric Residency –
Dept. of Pediatrics, Louisiana State University of Medical Center, Shreveport, LA, 1999.

Medical School –
Damascus University School of Medicine,
Damascus, Syria

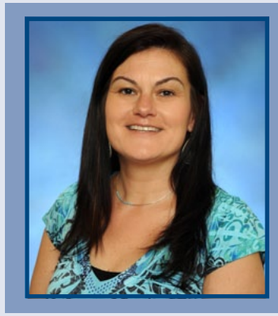
Professional/Board Certifications:
General Practice, Pediatric Gastroenterology

Callie McCamy, RD, LDN

Education:
Bachelor of Science in Food and Nutrition –
University of Alabama, Tuscaloosa, AL, 2010

Registered Dietitian (RD) – 2011
Licensed Dietitian Nutritionist (LDN) – State of Tennessee

Professional Affiliations:
Knoxville District Dietetic Association
Tennessee Dietetic Association
American Dietetic Association
Birmingham District Dietetic Association
Alabama Dietetic Association



Tamila Mayberry, P.A.-C

Education:
Master of Science, Advanced Physician Assistant Studies, 2007
A.C. Still University of Health Sciences, Mesa, AZ
Bachelor of Science, Physician Assistant, 2003
Kettering College of Medical Arts, Kettering, Ohio

Professional Certifications
- Physician Assistant Licensure, Tennessee and Ohio
- National Commission on Certification of Physician Assistants (NCCPA)
- Advanced Cardiac Life Support
- Pediatric Advanced Life Support
- Basic Life Support
- School Health Clinic Training, American Red Cross

Professional Affiliations
- Member, Society of Emergency Medicine Physician Assistants (SEMPA)
- Member, American Academy of Physician Assistants (AAPA).

Our behavior health clinicians can help your pediatric patients with:

- **GI-related disorders** including recurrent abdominal pain, food allergies, celiac disease, irritable bowel syndrome & inflammatory bowel disease, constipation & encopresis
- **Other disorders** including adjustment to illness, family dysfunction, sleep difficulties, conduct disorder, depression, generalized anxiety, panic attacks, eating disorders, non-compliance to medical regimens, and more…

Visit our website for more details: www.GIforKids.com

Call for an appointment today!
865.546.3998

transitions
BEHAVIORAL HEALTH CLINIC

BEE FIT 4 KIDS

- ✔ A one-on-one pediatric weight management program administered by a multi-disciplinary team.
- ✔ The format allows Registered Dietitians to identify nutrition and fitness trouble areas immediately. This helps the staff make appropriate changes so weight management success is maximized.

Visit our website, www.BeeFit4Kids.com, for more details, or call 865.546.3998.

Now accepting insurance!

East Tennessee Children's Hospital
Gastroenterology and Nutritional Services
Medical Office Building
2100 Clinch Avenue, #510
Knoxville, TN 37916

GI for Kids PLLC

East Tennessee Children's Hospital
Gastroenterology and Nutrition Services

Fall 2012 | www.giforkids.com | Volume 5 Issue 4

Friends and Colleagues,

This summer we welcomed an addition to our practice, M. Samer Ammar, MD, a highly trained Pediatric Gastroenterologist, Heptology and Nutrition physician. He will be a valuable asset to our practice as we offer our services to help you and our patients.

Summer has been a time to relax and enjoy the warm weather. In a few short weeks it will be back to school for our children. Our thoughts have been on relaxing and having fun and not on the many infections that can cause illness.

In the past few months our practice has seen an increase in the number of children diagnosed with infection from H. pylori. It is believed that half of the world's population has this infection, and is especially common in developing countries. Poor sanitation, contaminated water, and transmission through fecal and oral exposure all serve as sources for these bacteria. Proper diagnosis and treatment is essential to eradicating H. pylori. In this issue we will review some of the evolving studies discussing its pathogenesis, diagnostic testing and treatment.

Please visit our website at www.giforkids.com for more information on all of the pediatric services our practice provides.

Regards,

Youhanna S. Al-Tawil, MD
Medical Director

Allergy 4 Food is an online company that assists people who are having difficulty obtaining nutritional supplements from outside resources at a lower cost. Many of these specialized formulas, for children and adults, are not sold in stores and can be time-consuming trying to obtain them through the local pharmacy. We offer brand named products ranging from calorie supplements to the most restricted diet supplements needed to treat food allergies and other medical conditions. Products sold at Allergy 4 Food are appropriate for infants, children and adults, and are manufactured by the world's leading producers of nutritional supplements. Major credit cards are accepted.

To place an order: www.allergy4food.com