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Xavier Calvet	
Proton pump inhibitors (PPI) are a major cause of false-negative <i>Helicobacter pylori</i> test results. Detecting PPI use and stopping it 2 weeks before testing is the preferred approach to improve the reliability of <i>H pylori</i> diagnostic tests. Immunoblot and molecular methods may be useful for the detection of <i>H pylori</i> infection in difficult cases. When conventional tests are negative and eradication is strongly indicated, empirical <i>H pylori</i> treatment should be considered. In this article, an updated critical review of the usefulness of the various invasive and noninvasive tests in the context of extensive PPI use is provided.	
Practical Aspects in Choosing a <i>Helicobacter pylori</i> Therapy	519
Javier Molina-Infante and Akiko Shiotani	
Cure rates greater than 90% to 95% should be expected with an antimicrobial therapy for <i>Helicobacter pylori</i> infection. Standard triple therapy does not guarantee these efficacy rates in most settings worldwide anymore. The choice of eradication regimen should be dictated by factors that can predict the outcome: (1) <i>H pylori</i> susceptibility; (2) patients' history of prior antibiotic therapy; and (3) local data, either resistance patterns or clinical success. Currently, the preferred first-line choices are 14-day bismuth quadruple and 14-day non-bismuth quadruple concomitant therapy. Bismuth quadruple (if not used previously), fluoroquinolone-, furazolidone- and rifabutin-containing regimens might be effective rescue treatments.	
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David Y. Graham and Sun-Young Lee	
Bismuth triple therapy was the first effective <i>Helicobacter pylori</i> eradication therapy. The addition of a proton pump inhibitor helped overcome metronidazole resistance. Its primary indication is penicillin allergy or when clarithromycin and metronidazole resistance are both common. Resistance to the primary first-line therapy have centered on complexity and difficulties with compliance. Understanding regional differences in effectiveness remains unexplained because of the lack of studies including susceptibility testing and adherence data. We discuss regimen variations including substitutions of doxycycline, amoxicillin, and twice a day therapy	

and provide suggestions regarding what is needed to rationally and effectively use bismuth quadruple therapy.

Is There a Role for Probiotics in *Helicobacter pylori* Therapy?

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Maria P. Dore, Elisabetta Goni, and Francesco Di Mario

The role of probiotics in *Helicobacter pylori* therapy remains unclear. *Lactobacilli* can be shown to inhibit *H pylori* in vitro. Some strains of *Lactobacilli* may exert specific antimicrobial effects. There is no strong evidence of a benefit on eradication rate when probiotics are added to a regimen. Despite promising results obtained using compounds of *L reuteri* and *S boulardii*, high-quality trials are needed to define the role of probiotics as adjuvant therapy. Variables that remain to be studied with *L reuteri*, currently the most promising strain, include dosage, frequency of administration, administration in relation to meals, and duration of therapy.

Molecular Approaches to Identify *Helicobacter pylori* Antimicrobial Resistance

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Francis Mégraud, Lucie Bénéjat, Esther Nina Ontsira Ngoyi, and Philippe Lehours

Antimicrobial susceptibility testing is needed to adapt *Helicobacter pylori* treatment to obtain the best results. Beside the standard phenotypic methods, molecular methods are increasingly used. The value of these molecular tests is that they are quick, independent of the transport conditions, easy to standardize, and commercial kits are available. In this article, these methods are reviewed, focusing on the determination of *H pylori* resistance to macrolides and fluoroquinolones, and mentioning also the methods used for tetracycline and rifampin.

When Is Endoscopic Follow-up Appropriate After *Helicobacter pylori* Eradication Therapy?

597

Ernst J. Kuipers

The effect of *Helicobacter pylori* eradication treatment needs confirmation in patients with persistent symptoms and in those with complicated peptic ulcer. Endoscopic surveillance after eradication is needed in patients with advanced premalignant gastric lesions, previous early gastric cancer, gastric MALT lymphoma, and in those with a hereditary gastric cancer risk.

Gastric Cancer Risk in Patients with *Helicobacter pylori* Infection and Following Its Eradication

609

Massimo Rugge

As *Helicobacter pylori* is a first-class carcinogen, eradication of the infection would be expected to be a beneficial measure for the (primary) prevention of gastric cancer. Given the natural history of gastric cancer, it is plausible that eradication before gastric atrophy sets in offers the best chance for cancer risk reduction. The beneficial effects of eradication may, nevertheless, still be achievable in more advanced disease. The reversibility of inflammatory lesions has been supported by undeniable evidence; the regression of mucosal atrophy/metaplasia has also been confirmed by several recent histologic studies.

Molecular Pathogenesis of *Helicobacter pylori*-Related Gastric Cancer 625

Takahiro Shimizu, Hiroyuki Marusawa, Norihiko Watanabe, and Tsutomu Chiba

Helicobacter pylori infection plays a crucial role in gastric carcinogenesis. *H pylori* exerts oncogenic effects on gastric mucosa through complex interaction between bacterial virulence factors and host inflammatory responses. On the other hand, gastric cancer develops via stepwise accumulation of genetic and epigenetic alterations in *H pylori*-infected gastric mucosa. Recent comprehensive analyses of gastric cancer genomes indicate a multistep process of genetic alterations as well as possible molecular mechanisms of gastric carcinogenesis. Both genetic processes of gastric cancer development and molecular oncogenic pathways related to *H pylori* infection are important to completely understand the pathogenesis of *H pylori*-related gastric cancer.

***Helicobacter pylori* Eradication to Eliminate Gastric Cancer: The Japanese Strategy** 639

Masahiro Asaka, Katsuhiko Mabe, Rumiko Matsushima, and Momoko Tsuda

Helicobacter pylori eradication therapy for chronic gastritis achieved world-first coverage by the Japanese national health insurance scheme in 2013, making a dramatic decrease of gastric cancer-related deaths more realistic. Combining *H pylori* eradication therapy with endoscopic surveillance can prevent the development of gastric cancer. Even if it develops, most patients are likely to be diagnosed at an early stage, possibly resulting in fewer gastric cancer deaths. Success with the elimination of gastric cancer in Japan could lead other countries with a high incidence to consider a similar strategy, suggesting the potential for elimination of gastric cancer around the world.

Treatment Strategy for Gastric Mucosa-Associated Lymphoid Tissue Lymphoma 649

Shotaro Nakamura and Takayuki Matsumoto

Recent trends and current knowledge on the diagnosis and treatment strategy for gastric mucosa-associated lymphoid tissue (MALT) lymphoma are reviewed. *Helicobacter pylori* infection plays the causative role in the pathogenesis, and *H pylori* eradication is the first-line treatment of this disease, which leads to complete remission in 60% to 90% of cases. A Japanese multicenter study confirmed that the long-term outcome of gastric MALT lymphoma after *H pylori* eradication is excellent. Treatment strategies for patients not responding to *H pylori* eradication including “watch and wait” strategy, radiotherapy, chemotherapy, rituximab immunotherapy, and combination of these should be tailored in consideration of the disease extent in each patient.

Rationale for a *Helicobacter pylori* Test and Treatment Strategy in Gastroesophageal Reflux Disease 661

Nimish Vakil

Conflicting data have been published on the effect of long-term proton pump inhibitor therapy on the gastric mucosa in *Helicobacter pylori*-infected subjects. In this article, the available data are reviewed and a

rationale is offered for why infected patients who are about to commence long-term proton pump inhibitor therapy should be offered eradication therapy.

Screening to Identify and Eradicate *Helicobacter pylori* Infection in Teenagers in Japan

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Taiji Akamatsu, Takuma Okamura, Yugo Iwaya, and Tomoaki Suga

The purpose of this study was to elucidate the prevalence and effect of *Helicobacter pylori* infection in Japanese teenagers. The study subjects were students ages 16 to 17 from one high school studied between 2007 and 2013. Students who tested positive on this screening examination underwent esophagogastroduodenoscopy and biopsy samples to determine their *H pylori* status using culture and histology. Cure of *H pylori* infections was determined by urea breath test. The low rate of prevalence of *H pylori* infection in present Japanese teenagers makes it possible and cost effective to perform examinations and carry out treatment of this infection in nationwide health screenings of high school students.

Current Status and Prospects for a *Helicobacter pylori* Vaccine

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Thomas G. Blanchard and Steven J. Czinn

Helicobacter pylori infection contributes to a variety of gastric diseases. *H pylori*-associated gastric cancer is diagnosed in advanced stages, and a vaccine against *H pylori* is desirable in parts of the world where gastric cancer remains a common form of cancer. Some of the strategies of vaccine development used in animals have been tested in several phase 3 clinical trials; these trials have been largely unsuccessful, although *H pylori*-specific immune responses have been induced. New insights into promoting immunity and overcoming the immunosuppressive nature of *H pylori* infection are required to improve the efficacy of an *H pylori* vaccine.

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