Helicobacter pylori: From Diagnosis to Eradication

Though prevalence of *H. pylori* is decreasing in some parts of the world, it remains a common infection for many patients.\(^1,2\) *H. pylori* has been implicated in the development of certain gastrointestinal problems (e.g., ulcers, cancer, gastric mucosa associated lymphoid tissue lymphomas).\(^1,2\) Not all patients should be tested for *H. pylori*. However, testing should only be done for patients that prescribers will treat if results are positive.\(^2\)

Antibiotic resistance has reduced treatment success rates with many traditional three-drug regimens.\(^1,2\) Longer durations of therapy (e.g., 14 days) are often recommended for successful eradication.\(^1,2\) The chart below reviews common questions associated with *H. pylori* infection, including who and how to test, and recommended treatment regimens for ADULTS.

**Abbreviations:** BID = twice daily; MALT = mucosa associated lymphoid tissue; PPI = proton pump inhibitor; TID = three times daily; QD = once daily; QID = four times daily; UBT = urea breath test.

**PPI Equivalent Doses for the regimens discussed below:**\(^1,6\)
Dexlansoprazole 30 to 60 mg = Esomeprazole 20 mg\(^1\) to 40 mg\(^6\) = Omeprazole 20 mg = Lansoprazole 30 mg = Pantoprazole 40 mg = Rabeprazole 20 mg

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| Who should be tested for *H. pylori*? | • Recommend testing for *H. pylori* in patients with the following:\(^2\)  
  o Active peptic ulcer disease  
  o After resection of early gastric cancer  
  o Dyspepsia undergoing upper endoscopy  
  o Gastric MALT lymphoma  
  o History of peptic ulcer disease, unless documented cure of *H. pylori*  
• Consider testing for *H. pylori* in patients with the following:\(^2\)  
  o Idiopathic thrombocytopenic purpura (ITP)  
  o Initiating chronic nonsteroidal anti-inflammatory drugs (benefit in patients already receiving is unclear)  
  o Receiving long-term, low-dose aspirin therapy  
  o Unexplained iron deficiency anemia  
  o Uninvestigated dyspepsia without alarm features (e.g., bleeding, dysphagia, weight loss)  
• Insufficient evidence to recommend routine testing in patients with the following:\(^2\)  
  o Family history of gastric cancer  
  o Gastroesophageal reflux disease without a history of peptic ulcer disease  
  o Hyperemesis gravidarum  
  o Hyperplastic gastric polyps  
  o Lymphocytic gastritis |
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| Which tests are used with biopsy tissue obtained during endoscopy?               | • Rapid Urease Test (RUT)<sup>6</sup>  
  - Advantages: inexpensive, very good sensitivity, rapid results (usually within one to 24 hours)  
  - Disadvantages: reduced sensitivity post-treatment  
  - Recommend if no recent use of PPI (past one to two weeks) or bismuth (past four weeks).  
• Histology<sup>6</sup>  
  - Advantages: excellent sensitivity and specificity  
  - Disadvantages: expensive, requires significant personnel training  
  - Recommend if recent use of PPI, antibiotics, or bismuth.  
• Culture<sup>6</sup>  
  - Advantages: excellent specificity, provides antimicrobial sensitivities  
  - Disadvantages: expensive, difficult to perform, marginal sensitivity  
  - Avoid routinely recommending due to cost and limited availability.  
  - Recommend with endoscopies after treatment failures to assess antibiotic sensitivity.<sup>5</sup>  
• Polymerase Chain Reaction<sup>6</sup>  
  - Advantages: excellent specificity and sensitivity, provides antimicrobial sensitivities  
  - Disadvantages: lack of standardization across locations, not widely available.  
  - Avoid routinely recommending; used primarily in research.  |
| Which test should be used for patients NOT undergoing endoscopy?                | • Antibody Testing (detects IgG antibodies in serum, whole blood, or urine)<sup>6</sup>  
  - Advantages: inexpensive, rapid results  
  - Disadvantages: less accurate post-treatment; avoid in patients with previous *H. pylori* treatment  
• Urea Breath Test (UBT)<sup>6</sup>  
  - Advantages: useful before and after treatment  
  - Disadvantages: inconsistent availability and reimbursement  
  - Recommend if testing for eradication of *H. pylori*.  
• Fecal Antigen Test<sup>6</sup>  
  - Advantages: useful before and after treatment  
  - Disadvantages: requires stool collection, less validated than UBT for post-treatment  
  - Tests in the laboratory using monoclonal antibody reagents are more accurate than rapid in-office tests using polyclonal antibodies.<sup>5</sup>  |
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| **Which *H. pylori* regimens are recommended first-line?**                      | • 14 days (U.S. guidelines also offer a 10-day option) with one of the following preferred options for most patients:  
  ○ **Bismuth quadruple therapy*** (referred to as PBMT [PPI + Bismuth + Metronidazole + Tetracycline] in Canadian guidelines)  
    ▪ PPI: omeprazole 20 mg BID or an equivalent dose of an alternate PPI  
    ▪ Bismuth  
      • Bismuth subcitrate 120 mg to 300 mg QID (salt form used in *Pylera* [U.S. only])  
    OR  
      • Bismuth subsalicylate 300 mg QID (up to 524 mg per Canadian guidelines). (Note: 300 mg dose used in studies, but 262 mg tablets available in U.S./Canada.)  
    ▪ Metronidazole 250 mg QID (U.S. only) or 500 mg TID to QID  
    ▪ Tetracycline 500 mg QID  
  *Pylera* (U.S. only) contains bismuth subcitrate, metronidazole, and tetracycline which could be given with a PPI. But *Pylera* only provides ten days of treatment instead of 14 and costs a lot more than giving the drugs separately.  
  OR  
  ○ **Concomitant quadruple therapy**** (referred to as PAMC [PPI + Amoxicillin + Metronidazole + Clarithromycin] in Canadian guidelines)  
    ▪ PPI: omeprazole 20 mg BID or an equivalent dose of an alternate PPI  
    ▪ Amoxicillin 1000 mg BID  
    ▪ Metronidazole 500 mg BID  
    ▪ Clarithromycin 500 mg BID  
  **Consider using *Prevpac* (U.S.) or *Hp-PAC* (Canada), which contains a PPI (lansoprazole), amoxicillin, and clarithromycin, concomitantly with metronidazole depending on cost. |  |
| **When should clarithromycin triple therapy be considered?**                   | • Clarithromycin triple therapy can be considered in areas with documented clarithromycin-resistant rates of <15%.  
  ○ Unfortunately, these resistance rates are not always readily available and change over time.  
  ○ If resistance rates are not available, testing for proof of eradication can be considered, especially if symptoms of dyspepsia persist. |  |

*Continued...*
### Clinical Question

**Clarithromycin triple therapy, continued**

The following are the preferred clarithromycin triple therapy regimens:

- **Clarithromycin triple therapy** (referred to as **PAC** [PPI + Amoxicillin + Clarithromycin] or **PMC** [PPI + Metronidazole + Clarithromycin] in Canadian guidelines) for 14 days with one of the following regimens can be considered in patients with no history of any macrolide use (especially use for >14 days[U.S.]) or in areas with proven high local eradication rates of >85% (Canada):\(^1,2\)

  - PPI: omeprazole 20 mg to 40 mg BID or an equivalent dose of an alternate PPI
  - Amoxicillin 1000 mg BID
  - Clarithromycin 500 mg BID

  OR

  - PPI: omeprazole 20 mg to 40 mg BID or an equivalent dose of an alternate PPI
  - Metronidazole 500 mg TID
  - Clarithromycin 500 mg BID

### What additional alternative regimens can be considered first-line?

- The following are alternatives to first-line regimens:\(^1,2\)

  - **PAM** (PPI + Amoxicillin + Metronidazole) for 14 days in areas with demonstrated success rates (Canada only):
    - PPI: omeprazole 20 mg BID or an equivalent dose of an alternate PPI
    - Amoxicillin 1000 mg BID
    - Metronidazole 500 mg BID

  - **Sequential therapy** (U.S. only):
    - PPI: omeprazole 20 mg BID or an equivalent dose of an alternate PPI for five to seven days
    - Amoxicillin 1000 mg BID for five to seven days
    - Followed by **PMC** (see regimen description above) for five to seven days

  - **Hybrid therapy** (U.S. only):
    - PPI: omeprazole 20 mg BID or an equivalent dose of an alternate PPI for seven days
    - Amoxicillin 1000 mg BID for seven days
    - Followed by **PAMC** (see regimen description above) for seven days

- **Levofloxacin triple therapy** for ten to 14 days (U.S. only):
  - PPI: omeprazole 20 mg BID or an equivalent dose of an alternate PPI
  - Amoxicillin 1000 mg BID
  - Levofloxacin 500 mg QD
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| Alternatives to first-line regimens, continued                                  | - **Levofoxacin sequential therapy** (U.S. only):  
  - PPI: omeprazole 20 mg to 40 mg BID or an equivalent dose of an alternate PPI for five to seven days  
  - Amoxicillin 1000 mg BID for five to seven days  
  - Followed by five to seven days of:  
    - PPI: omeprazole 20 mg to 40 mg BID or an equivalent dose of an alternate PPI  
    - Amoxicillin 1000 mg BID  
    - Levofoxacin 500 mg QD  
    - Metronidazole 500 mg BID  
  - **LOAD therapy** (**Levofoxacin + Omeprazole + Alinia [nitazoxanide] + Doxycycline**) therapy for seven to ten days (U.S. only):  
    - Levofoxacin 250 mg QD  
    - PPI: omeprazole 40 mg once daily or an equivalent dose of an alternate PPI  
    - Nitazoxanide 500 mg BID  
    - Doxycycline 100 mg QD  
  - **LOAD therapy** (Levofoxacin + Omeprazole + Alinia [nitazoxanide] + Doxycycline) therapy for seven to ten days (U.S. only):  
  - Levofoxacin 250 mg QD  
  - PPI: omeprazole 40 mg once daily or an equivalent dose of an alternate PPI  
  - Nitazoxanide 500 mg BID  
  - Doxycycline 100 mg QD  |
| Which *H. pylori* regimens should be used after treatment failure (e.g., salvage therapy)? | - Treatment failures can be due to either antibiotic failure due to resistance and/or lack of patient adherence.  
  - Consider the following AFTER treatment failure with one of the first-line (or alternative first-line) regimens:  
    - Resistance to clarithromycin, fluoroquinolones, and rifabutin correlates strongly with their previous use.  
    - Resistance to amoxicillin and tetracycline is rare, even with previous use.  
    - Avoid retreating with clarithromycin-containing regimens after a clarithromycin failure.  
    - Referral for allergy testing can be considered with a penicillin allergy history, as many regimens contain amoxicillin.  
    - For most patients, recommend treating with 14 days with *bismuth quadruple therapy* or *levofloxacin triple therapy* (referred to as PBMT or PAL, respectively in Canadian guidelines). See regimen descriptions above.  
      - The following can be considered to possibly improve eradication:  
        - Adding bismuth to *levofloxacin triple therapy* (referred to as PAL in Canadian guidelines)  
        - Increasing the metronidazole and/or PPI dose, if retreating with *bismuth quadruple therapy* (referred to as PBMT in Canadian guidelines)  
        - Avoid *levofloxacin triple therapy* (referred to as PAL in Canadian guidelines) if associated with a prior failure or in patients with prior quinolone exposure. |

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| **Regimens after treatment failure, continued** | - For patients not appropriate for or unable to take **bismuth quadruple therapy** or **levofloxacin triple therapy** (referred to as PBMT or PAL, respectively in Canadian guidelines), the following regimens can be considered:  
  - **Concomitant quadruple therapy** for ten to 14 days (U.S. only).<sup>2</sup> See regimen description above.  
  - **High-dose dual therapy** for 14 days (U.S. only).<sup>2</sup>  
    - PPI: omeprazole 20 mg BID or an equivalent dose of an alternate PPI  
    - Amoxicillin 1000 mg TID or 750 mg QID  
  - **Rifabutin triple therapy** (referred to as PAR [PPI + Amoxicillin + Rifabutin] in Canadian guidelines) can be considered for ten days.<sup>1,2</sup>  
    - Reserve for patients with multiple (e.g., ≥3) treatment failures (Canada).<sup>1</sup>  
      - PPI: omeprazole 20 mg BID or an equivalent dose of an alternate PPI  
      - Amoxicillin 1000 mg BID  
      - Rifabutin 150 mg BID |
| **Should probiotics be recommended to improve efficacy or tolerability?** | - Avoid recommending probiotics to improve *H. pylori* eradication.<sup>1,2</sup>  
  - Data are inconsistent, ingredient combinations vary, and more trials, including use with quadruple therapy, are needed.<sup>1,3</sup>  
  - Increases cost and complexity of treatment.<sup>1</sup>  
  - Don’t routinely recommend, but don’t discourage use to improve treatment tolerability (e.g., reduce diarrhea).<sup>1,3</sup> |
| **Who should be tested to confirm eradication of *H. pylori*?** | - Patients with an *H. pylori*-associated ulcer, especially bleeding peptic ulcers.<sup>1,2</sup>  
  - Patients with persistent dyspepsia after *H. pylori* treatment.<sup>1,2</sup>  
  - Patients with *H. pylori*-associated MALT lymphoma.<sup>1</sup>  
  - Patients with a history of resection associated with gastric cancer.<sup>1</sup>  
  - Consider for patients using **Clarithromycin triple therapy** regimen if clarithromycin resistance rates are not available, especially if symptoms of dyspepsia persist.<sup>1,2</sup>  
  - For the most accurate results use the UBT or fecal antigen test, at least four weeks after treatment.<sup>2,4</sup>  
    - It is also recommended to withhold PPI therapy for one to two weeks prior to eradication testing.<sup>2</sup> |

Users of this resource are cautioned to use their own professional judgment and consult any other necessary or appropriate sources prior to making clinical judgments based on the content of this document. Our editors have researched the information with input from experts, government agencies, and national organizations. Information and internet links in this article were current as of the date of publication.
Project Leader in preparation of this clinical resource (330301): Beth Bryant, Pharm.D., BCPS, Assistant Editor

References