Overview

*Helicobacter pylori* is a Gram-negative bacteria that infects 25-50% of the world’s population, and although asymptomatic in most, it is associated with severe gastric illnesses, and causes significant morbidity in adults and children\(^1\). *H. pylori* infects the gastric mucosa causing chronic gastritis; symptoms of infection can include epigastric pain, dyspepsia, gastric bleeding, and iron deficiency anemia. It is the most important cause of primary duodenal ulcer in children. Chronic infection can lead to gastric cancer and mucosa associated lymphoid tissue (MALT) lymphoma.

The gold standard for diagnosis of *H. pylori* infection is a gastric biopsy performed using esophagogastro-duodenoscopy (EGD). However, recently the use of non-invasive tests, specifically, the urea breath test (UBT) and the stool antigen test (SAT), have been integrated into the diagnostic approach for this infection\(^1\).

**Who should be tested for *H. pylori* infection?**

- **Children** with unexplained, refractory iron deficiency anemia or first-degree relatives with gastric cancer.
- **Adults** with dyspepsia without gastroesophageal reflux disease (GERD) and who are not receiving non-steroidal anti-inflammatory drugs (NSAIDS).

The current management of dyspepsia as recommended by the American Gastroenterology Association (AGA), based on age and alarm factors, is shown in Figure 1. An alternative approach, suggested by the American College of Gastroenterology (ACG), incorporates *H. pylori* prevalence into the algorithm and recommends that in low prevalence (<10%) populations, for patients ≤ 55 years of age with no alarm features, an initial proton pump inhibitor trial be given and only if this fails is testing for *H. pylori* by either SAT or UBT done\(^1\).

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**Figure 1.** Management of dyspepsia based on age and alarm features as recommended by the AGA\(^1\)

- **Dyspepsia without GERD or NSAIDs**
  - Age >55 or alarm symptoms* present
    - EGD
  - Age ≤55 No alarm symptoms
    - Test for *H. pylori* (SAT or UBT)
      - Negative
        - PPI trial 4-6 weeks
        - Fails
          - Reassurance, Reassess diagnosis
          - Consider EGD
      - Positive
        - Treat for *H. pylori*
        - Fails
          - PPI Trial 4 weeks
          - Fails

*Alarm features include:
- age >55 with new-onset dyspepsia
- family history of gastric cancer
- unintentioned weight loss
- GI bleeding
- persistent dysphagia
- unexplained iron deficiency anemia
- persistent vomiting
- palpable mass or lymphadenopathy
- jaundice
What diagnostic testing is optimal for detection of *H. pylori* infection?

A gastric biopsy obtained by EGD is considered the gold standard for investigating dyspepsia because *H. pylori* infection as well as any cancerous changes in the mucosa can be detected. However, this is an invasive test that requires endoscopy services and for children or cognitively impaired adults can be especially challenging.

Serologic tests are no longer recommended as routine testing because ~50% of positive serology results will lead to inappropriate treatment of uninfected individuals. Kazemi et al recommends that validated IgG serology should only be used for detection of pre-malignant conditions but cautions the test has low sensitivity.

The key non-invasive diagnostic tests that are recommended include the UBT and the SAT. The UBT is not recommended for children <5 years old due to the difficulty in getting a reliable breath sample. In this age group the SAT is the recommended diagnostic test. Both SAT and UBT can be used to follow therapeutic efficiency once treatment for *H. pylori* has started. If possible, proton pump inhibitor (PPI) therapy should be stopped 2 weeks prior to any testing for *H. pylori* (i.e., biopsy for culture, rapid urease or histology, UBT or SAT).

Comparison of these testing methods (data extracted from References 1 and 3) is shown in Table 1.

### Table 1. Comparison of various methods to diagnose *H. pylori* infection

<table>
<thead>
<tr>
<th>Result</th>
<th>Gastric Biopsy</th>
<th>Nonendoscopic Testing</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Histology 1</td>
<td>RUT 1</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>89%</td>
<td>93%</td>
</tr>
<tr>
<td>Specificity</td>
<td>78%</td>
<td>75%</td>
</tr>
<tr>
<td>Accuracy</td>
<td>85%</td>
<td>86%</td>
</tr>
</tbody>
</table>

RUT: Rapid Urease Test; SAT: Stool Antigen Test; UBT: Urea Breath Test; N/A: not available

When should susceptibility testing be requested?

If repeated therapeutic failure occurs, then DSM Microbiology (SBH site) can provide culture and antibiotic susceptibility testing to help direct therapeutic choices. Macrolide resistance (specifically clarithromycin) is increasing in *H. pylori* and may contribute to treatment failure. A gastric biopsy needs to be expediently submitted (<24 hours transport; room temperature; sterile screw capped container; include 1 mL phosphate buffered saline (PBS)). The requisition should indicate there have been multiple treatment failures so susceptibility testing is needed.

### ACG treatment recommendations as summarized by Couturier 1

#### Triple therapy:

**Primary therapy for patients with no macrolide exposure or penicillin allergies:**
- PPI, clarithromycin and amoxicillin for 10-14 days (cure rate, 70-85%)

**Primary therapy for penicillin-allergic patients with no macrolide exposure or patients unable to tolerate bismuth quadruple therapy:**
- PPI, clarithromycin, metronidazole for 10-14 days (cure rate, 70-85%)

#### Quadruple therapy:

**Primary therapy for patients with macrolide exposure or patients with penicillin allergies:**
- Bismuth subsalicylate, metronidazole, tetracycline and PPI for 10-14 days (cure rate, 75-90%)

#### Salvage therapy:

**Quadruple salvage therapy after triple therapy failure:**
- Bismuth subsalicylate, metronidazole, tetracycline and PPI for 7 days (cure rate, 68%)

**Triple salvage therapy for patients who failed triple and/or quadruple therapy; may not be effective in patients with prior quinolone exposure:**
- PPI, amoxicillin and levofloxacin for 10 days (cure rate, 87%)

Consulting a DSM Microbiologist prior to submitting a gastric biopsy for culture and susceptibility testing is recommended to ensure the laboratory is adequately prepared to perform this testing.

### References:

1. Couturier MR. The evolving challenges of *Helicobacter pylori* disease, diagnostics and treatment, Part I & Part II. Clin Micro Newsletter 2013 35:3 and 4