GHAPP
Gastroenterology & Hepatology Advanced Practice Providers

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H. Pylori Diagnosis and Therapies
What’s New?

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Disclosures

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No financial relationships to disclose.
Objectives

• Epidemiology of *H. pylori*
• Bacteriology
• Clinical presentation
• Indication for testing
• Diagnosis
• Treatments
Epidemiology

- *H. pylori* colonizes the gastric mucosa of ~50% of the World’s population
- 70-80% in developing countries
- Estimated to colonize 30-40% of the U.S. population
Bacteriology

- Gram negative bacillus
- Urease-producing
- Humans are the only known host
- Person-to-person transmission
Virology

• The bacteria has flagella which allows mobility in the viscous mucus
• Secretion of urease enzyme converts urea into ammonia and carbon dioxide
• Damage is caused by toxins secreted
Clinical Presentation

Asymptomatic

Peptic ulcer disease (gastric and duodenal)

Gastric carcinoma

Gastric mucosa-associated Lymphoid tissue lymphoma (MALT)
Conditions Arising From *H. pylori*
How Common Is Gastric Cancer?

- Gastric carcinoma is, worldwide the second leading cause of cancer related mortality
- May present as abdominal pain, weight loss, early satiety and anemia
- Upon diagnosis most patients have advanced, incurable disease
- 95% of gastric cancer is adenocarcinoma
- Screening is only performed in countries with high incidence (Japan, Chile, Venezuela)
Gastric Cancer

• 1 in 12 of all oncological deaths are attributable to gastric cancer

• Gastric cancer has the fifth highest incidence among cancers, with 5.7% of all new cases attributable to the disease

• The 5-year survival rate for gastric cancer is 31% in the United States
Indications for Testing

- Active peptic ulcer disease or history of peptic ulcer disease
- Long-term NSAID use
- Unexplained iron deficiency anemia
- Dyspepsia
H. pylori-Associated Gastritis

Duodenal ulcer: No increased cancer risk; usually associated with antral-predominant gastritis

Antral predominant gastritis: Intact acid secretion; colonization largely in antrum; No increased risk of cancer

Pangastritis: Even distribution of H. pylori; atrophy leading to hypochlorhydria; increased risk of both adenocarcinoma and MALT lymphoma

Corpus predominant: Similar to pangastritis

Gastric ulcer: More often associated with corpus-predominant or pangastritis; increased cancer risk
**H. pylori Testing**

### Noninvasive Testing
- Stool PCR – predicts *H. pylori* Clarithromycin susceptibility or resistance
- Stool antigen
- Urea breath test

### Invasive testing
- Gastric biopsy (Antrum preferred)
- Rapid urease test
- Culture
H. *pylori* Stool PCR

- Stool PCR
  - Predicts *H. pylori* clarithromycin susceptibility or resistance
Advantage

- Tests for active infection only
- Sensitivity and specificity near 100%
- Must stop PPIs 14 days prior to testing
- Cheaper and requires less equipment than breath test

Disadvantages

- Stool collection may be distasteful for patient
Urea Breath Test

• Advantages
  – Only detects active infection
  – Sensitivity and specificity near 100%
  – Must stop PPIs 14 days prior to testing
  – More expensive than stool testing

• Disadvantages
  – False negative results can occur with use of PPI or recent antibiotic use
  – Resources and personnel required to perform testing
  – C¹⁴ radiation exposure
Serology Testing (IgG Antibody)

- Cannot detect active vs. past infection
- No longer used
- Can be useful in research
Gastric Biopsy

- **Advantages**
  - Sensitivity and specificity 95-99%
  - Provides additional information about gastric mucosa

- **Disadvantages**
  - Expensive
  - Requires endoscopy and sedation
  - May be less accurate with use of PPI
Rapid Urease Test

• Advantages
  – Rapid results
  – Sensitivity and specificity 93%
  – Accurate in patients off PPIs or antibiotics

• Disadvantages
  – Requires a high density of bacteria in the specimen
  – Requires endoscopy
Cultures

• Advantages
  – Provides *H. pylori* isolate which is subjected to amoxicillin, levofloxacin, clarithromycin, metronidazole, and tetracycline susceptibility testing
  – Sensitivity and specificity 100%

• Disadvantages
  – Requires trained staff and properly equipped facilities
  – Expensive
  – Requires endoscopy
  – Not done at all facilities
When Is Endoscopy Indicated

- Age 60 or older
- Under age 60 with high risk of gastric cancer (eg, Southeast Asian descent)
- Under age 60 with more than one alarm feature
Alarm Features

- New onset of symptoms age 60+
- Unexplained weight loss
- Progressive dysphagia
- Odynophagia
- Persistent vomiting
- Overt GI bleeding
- Palpable mass
- Iron deficiency anemia
- Jaundice
- Fam history of GI cancer
## Treatment regimens:
**First-line therapies**

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Drugs (doses)</th>
<th>Dosing Frequency</th>
<th>Duration (days)</th>
<th>FDA Approval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clarithromycin triple*</td>
<td>PPI (standard or double the standard dose)</td>
<td>BID</td>
<td>14</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>Clarithromycin 500mg</td>
<td>BID</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Amoxicillin 1 gram or metronidazole 500 mg</td>
<td>BID or TID</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bismuth quadruple</td>
<td>PPI (standard dose)</td>
<td>BID</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>BSS 120 to 300 mg&lt;sup&gt;a&lt;/sup&gt; or 420 mg&lt;sup&gt;b&lt;/sup&gt; or BSS 300 or 524 mg</td>
<td>QID</td>
<td>10 to 14&lt;sup&gt;o&lt;/sup&gt;</td>
<td>No</td>
</tr>
<tr>
<td></td>
<td>Tetracycline 500 mg</td>
<td>TID to QID</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Metronidazole 250 to 500 mg</td>
<td>TID to QID</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clarithromycin -based concomitant*</td>
<td>PPI (standard dose)</td>
<td>BID</td>
<td>10 to 14</td>
<td>No</td>
</tr>
<tr>
<td></td>
<td>Clarithromycin 500 mg</td>
<td>BID</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Amoxicillin 1 gram</td>
<td>BID</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Metronidazole or tinidazole 500 mg</td>
<td>BID</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clarithromycin -based sequential*</td>
<td>PPI (standard dose) plus amoxicillin 1 gram for 5 days followed by PPI,</td>
<td>BID</td>
<td>10 to 14</td>
<td>No</td>
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<tr>
<td></td>
<td>clarithromycin 500 mg plus either metronidazole or tinidazole 500 mg</td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

BSS, bismuth subsalicylate; PPI, proton pump inhibitor.

<sup>a</sup>Not available in US;

<sup>b</sup>available in North American and elsewhere as part of Pylera® combination pill.
Initial approach to antibiotic treatment for *Helicobacter pylori* infection

**Active infection with *H. pylori***
Are ANY of the following present?
- Prior exposure to macrolides for any reason
- Local clarithromycin resistance rates ≥15% or eradication rates with clarithromycin based triple therapy ≤85%*

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**Yes**

Pencillin allergy present?

**Yes**

*Metronidazole use within the past few years?*
- Yes
  - Bismuth quadruple therapy
- No
  - Clarithromycin based triple therapy with amoxicillin

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**No**

Treat with any one of the following regimens:
- Clarithromycin based triple therapy with metronidazole
- Bismuth quadruple therapy
Clarithromycin Based Therapy

- Amoxicillin 1 Gram BID
- Clarithromycin 500 mg BID
- Omeprazole 20 mg BID
- Treatment duration 14 days
- Penicillin allergy:
  - Metronidazole 500 mg BID
- Eradication rates with clarithromycin-based therapy are below 80%
- Therapy should be reserved for geographic areas where resistance to clarithromycin is less than 15% and for patients without previous macrolide exposure
- FDA-approved treatment regimen
Bismuth Quadruple Therapy

- Tetracycline 500 mg QID
- Metronidazole 250-500 mg QID
- Bismuth QID
- Omeprazole 20 mg
- Treatment duration 10-14 days

- Eradication rates with Quadruple therapy average 91%
Levofloxacin Based Therapy

- Levofloxacin 500 mg QD
- Amoxicillin 1 Gram BID
- Omeprazole 20 mg BID
- Eradication rate of 81%
- Can also be used with Quadruple therapy
Sequential Therapy

- Amoxicillin 1 Gram BID + omeprazole 20mg BID for 5-7 days
- Clarithromycin 500mg BID + metronidazole 500 mg BID + omeprazole 20 mg BID for 5-7 days
- Not endorsed by guidelines as first line therapy due to its complexity
Salvage Therapy

- Amoxicillin 1 Gram BID
- Rifabutin 300 mg QD
- Omeprazole 20 mg BID
  - Moxifloxacin 400 mg QD can be used for PCN allergy

- 20% of patients fail initial attempt at *H. pylori* eradication
Predictor of Treatment Success

Factors affecting eradication

- Poor patient compliance
- Resistance to antibiotics prescribed
- Resistance rates for amoxicillin, tetracycline and rifabutin are low
- Clarithromycin resistance can be greater than 15% in some areas
Test for Eradication

• Urea breath test
• Fecal Antigen testing
• Must wait at least 4 weeks after completing treatment
• Stop PPI 14 days prior to testing for eradication
Key Points

- Emerging evidence suggests an association between *H. pylori* and unexplained iron deficiency anemia.

- In populations with a low pretest probability of *H. pylori* infection, non-endoscopic tests such as the urea breath test and fecal antigen test offer superior positive predictive value compared with antibody tests.

- Eradication rates with a PPI, clarithromycin, and amoxicillin are decreasing worldwide.
Key Points

• Fourteen-day courses of therapy are more effective than 7-days treatment regimens

• Newer treatments such as sequential therapy require validation in the United States before they can be recommended as a standard first-line therapy (not FDA approved)

• A PPI, levofloxacin, and amoxicillin for 10 days appear to be more effective and better tolerated than a PPI, bismuth, tetracycline, and metronidazole in patients with persistent *H. pylori* infection but require validation in North America
Questions and Comments