Helicobacter pylori Diagnosis

Presenter:
Robin Patel, M.D.
Consultant, Division of Clinical Microbiology
Elizabeth P. and Robert E. Allen Professor of Individualized Medicine
Professor of Medicine and Microbiology

Department of Laboratory Medicine and Pathology
at Mayo Clinic, Rochester, Minnesota
Disclosures

Dr. Patel reports grants from CD Diagnostics, Merck, Hutchison Biofilm Medical Solutions, Accelerate Diagnostics, ContraFect, TenNor Therapeutics Limited and Shionogi. Dr. Patel is a consultant to Curetis, Specific Technologies, Next Gen Diagnostics, PathoQuest, Selux Diagnostics, 1928 Diagnostics and Qvella; monies are paid to Mayo Clinic. In addition, Dr. Patel has a patent on Bordetella pertussis/parapertussis PCR issued, a patent on a device/method for sonication with royalties paid by Samsung to Mayo Clinic, and a patent on an anti-biofilm substance issued. Dr. Patel receives travel reimbursement from ASM and IDSA, an editor’s stipend from IDSA, and honoraria from the NBME, Up-to-Date and the Infectious Diseases Board Review Course.

Helicobacter pylori: Bacteriology

- Slender, curved Gram-negative bacillus
- Urease-producer
- Mucosa stomach
- Growth
  - Microaerophilic atmosphere, slow
- World Health Organization
  - Group 1 carcinogen (gastric carcinoma)
**Helicobacter pylori: Clinical Presentation**

- Asymptomatic
- Peptic ulcer disease (gastric, duodenal)
- Nonulcer dyspepsia
- Gastric carcinoma
- Gastric mucosa-associated lymphoid tissue lymphoma
  - MALT lymphoma, MALToma, marginal zone B-cell lymphoma of MALT type

**Helicobacter pylori: Indications for Testing**

- Active peptic ulcer disease or history of peptic ulcer disease (unless *H. pylori* eradicated)
- Low-grade gastric mucosa–associated lymphoid tissue lymphoma or history of endoscopic resection of early gastric cancer
- Uninvestigated dyspepsia
- Long-term NSAID or aspirin use
- Unexplained iron-deficiency anemia (after evaluation for other causes)
- Immune thrombocytopenia in adults

**Helicobacter pylori: Treatment**

- Typically treated with combinations of antibiotics along with a PPI
  - “…initial course of eradication therapy…generally offers the greatest likelihood of treatment success. Thus, careful attention to the selection of the most appropriate first-line eradication therapy for an individual patient is essential.”
  - “The main determinants of successful *H. pylori* eradication are the choice of regimen, the patient’s adherence to a multi-drug regimen with frequent side-effects, and the [susceptibility] of the *H. pylori* strain to the combination of antibiotics administered.”

---

**Susceptibility of 413 Helicobacter pylori Isolates, Mayo Clinic Laboratories**

<table>
<thead>
<tr>
<th>Amoxicillin (n = 410)</th>
<th>Ciprofloxacin (n = 409)</th>
<th>Clarithromycin (n = 412)</th>
<th>Metronidazole (n = 330)</th>
<th>Tetracycline (n = 409)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MIC n %</td>
<td>MIC n %</td>
<td>MIC %</td>
<td>MIC n</td>
<td>MIC n %</td>
</tr>
<tr>
<td>≤2 405 98.8</td>
<td>≤1 190 46.5</td>
<td>≤0.25 27.7 114</td>
<td>S</td>
<td>≤2 61 41.3</td>
</tr>
<tr>
<td>4 1 0.2 R</td>
<td>2 8 2.0</td>
<td>0.06 8 1.9</td>
<td>R</td>
<td>16 24 7.3</td>
</tr>
<tr>
<td>8 2 0.5 R</td>
<td>&gt;2 211 51.6</td>
<td>&gt;0.5 70.4 290</td>
<td>R</td>
<td>&gt;8 64 16</td>
</tr>
<tr>
<td>&gt;8 2 0.5 R</td>
<td>128 63 19.1 R</td>
<td>256 2 0.6 R</td>
<td>&gt;256 1 0.3 R</td>
<td></td>
</tr>
</tbody>
</table>

MIC, minimum inhibitory concentration (in μg/ml); *EUCAST; **CLSI; S, susceptible; I, intermediate; R, resistant.
Genetic Mechanisms of Clarithromycin Resistance, 111 Helicobacter pylori Isolates, Mayo Clinic Laboratories

- 23S ribosomal RNA gene sequencing → Assess clarithromycin resistance-associated mutations
- Overall concordance phenotypic & genotypic results - 106 (95%) isolates
  - Resistant isolates - 88
    - A2143G - 70
    - A2142G - 12
    - A2142C - 3
    - Wild type - 3
  - Susceptible isolates – 23
    - A2143G – 2
    - Wild type - 21

Helicobacter pylori: Diagnosis

- Non-invasive tests
  - Stool PCR
    - Predicts H. pylori clarithromycin susceptibility or resistance
  - Stool antigen
  - Helicobacter pylori (urea) breath test
    - C\textsuperscript{13} or C\textsuperscript{14}-labeled urea ingested → C\textsuperscript{13} or C\textsuperscript{14}-labeled CO\textsubscript{2} detected

- Invasive tests - gastric biopsy
  - Rapid urease test
  - Stain of tissue
  - Culture
    - Provides H. pylori isolate which is subjected to amoxicillin, levofloxacin, clarithromycin, metronidazole and tetracycline susceptibility testing
**Immunostaining**

**H&E**

Photos by Tsung-The Wu MD, PhD

---

**Helicobacter pylori on HP agar**

**Susceptibility control plate**

0.25 μg/ml clarithromycin

Photos by Jamie Elvert
Summary

- Antimicrobial resistance in *Helicobacter pylori* is rising
- Consideration should be given to assessing for *H. pylori* antimicrobial susceptibility in patients testing positive for *H. pylori*
- Stool PCR with prediction of clarithromycin susceptibility provides an option in this regard, as does endoscopy with biopsy for culture and susceptibility testing
References


Thank You