Treating *H. pylori* in 2016

The Case:

- A 38 yo Russian man presents with recurrent epigastric pain which occurs after meals and sometimes awakens him at night. He was born in Moscow but moved to the U.S. in his 20s. His symptoms have been escalating for the past 12 months. He reports mild nausea but no vomiting. He has lost 6 pounds over the past 6 months related to his symptoms. His mother has a history of “ulcers”. PE is otherwise normal.
• EGD reveals a 1.2 cm duodenal bulb ulcer
  – Gastric histology is positive for H. pylori

• The patient is treated with triple therapy (OAC) for 14 days

• He feels better for “a couple of weeks” but then his dyspeptic symptoms recur

• A urea breath test 4 weeks after completion of triple therapy is positive for persistent H. pylori

• What should you do???
Current US Treatment Paradigm for *H. pylori*

First Line
- **Triple Therapy**

Salvage
- **Quadruple Therapy**

Salvage
- **Levo Triple Therapy**

*Vakil & Vaira, J Clin Gastroenterol 2013;47:383–388*
# First-line *H. pylori* 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</td>
<td>PPI (standard or double dose)</td>
<td>BID</td>
<td>14</td>
<td>Yes*</td>
</tr>
<tr>
<td>Triple</td>
<td>Clarithromycin (500 mg)</td>
<td></td>
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<td></td>
<td>Amoxicillin (1 gm) or Metronidazole (500 mg TID)</td>
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<td></td>
</tr>
<tr>
<td>Bismuth Quadruple</td>
<td>PPI (standard dose)</td>
<td>TID or QID</td>
<td>10-14</td>
<td>No**</td>
</tr>
<tr>
<td></td>
<td>Bismuth subsalicylate (300 mg)</td>
<td></td>
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<tr>
<td></td>
<td>Tetraacycline (500 mg)</td>
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<td></td>
<td>Metronidazole (250-500 mg)</td>
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<tr>
<td>Concomitant</td>
<td>PPI (standard dose)</td>
<td>BID</td>
<td>10-14</td>
<td>No</td>
</tr>
<tr>
<td></td>
<td>Clarithromycin (500 mg)</td>
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<tr>
<td></td>
<td>Amoxicillin (1 gm)</td>
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<tr>
<td></td>
<td>Nitroimidazole (500 mg)*</td>
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</tbody>
</table>

*Chey et al, Am J Gastroenterol, in press*
First-line Therapies for *H. pylori*

**Recommended First-Line Therapies for *H pylori* Infection**

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Drugs (doses)</th>
<th>Dosing Frequency</th>
<th>Duration (Days)</th>
<th>FDA approval</th>
</tr>
</thead>
</table>
| **Clarithromycin Triple** | PPI (standard or double dose)  
  Clarithromycin (500 mg)  
  Amoxicillin (1 grm) or Metronidazole (500 mg TID) | BID              | 14              | Yes*         |
| **Bismuth Quadruple** | PPI (standard dose)  
  Bismuth subcitrate (120-300 mg) or subsalicylate (300 mg)  
  Tetracycline (500 mg)  
  Metronidazole (250-500 mg) | TID or QID       | 10-14           | No**         |
| **Concomitant** | PPI (standard dose)  
  Clarithromycin (500 mg)  
  Amoxicillin (1 grm)  
  Nitroimidazole (500 mg)* | BID              | 10-14           | No           |

*Chey et al. Am J Gastroenterol, in press*

**Other First-line Therapies**

| Sequential       | PPI (standard dose) + Amoxicillin (1 grm)  
  PPI, Clarithromycin (500 mg) + Nitroimidazole (500 mg)* | BID       | 5-7              | No           |
| Hybrid           | PPI (standard dose) + Amox (1 grm)  
  PPI, Amox, Clarithromycin (500 mg), Nitroimidazole (500 mg)* | BID       | 7               | No           |
| Levofoxacin Triple | PPI (standard dose)  
  Levofoxacin (500 mg)  
  Amox (1 grm) | BID       | 10-14           | No           |
| Levofoxacin Sequential | PPI (standard or double dose) + Amox (1 grm)  
  PPI, Amox, Levofoxacin (500 mg QD), Nitroimidazole (500 mg)* | BID       | 5-7              | No           |
| LOAD             | Levofoxacin (250 mg)  
  PPI (double dose)  
  Nitazoxanide (500 mg)  
  Doxycycline (100 mg) | QD       | 7-10             | No           |

*Chey et al. Am J Gastroenterol, in press*
Antibiotic Resistance of *H. pylori*:  
*Single Center Data from the Houston VAMC*

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Resistance Rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metronidazole</td>
<td>20</td>
</tr>
<tr>
<td>Clarithromycin</td>
<td>16</td>
</tr>
<tr>
<td>Levofloxacin</td>
<td>31</td>
</tr>
<tr>
<td>Tetracycline</td>
<td>&lt;2</td>
</tr>
<tr>
<td>Amoxicillin</td>
<td>&lt;2</td>
</tr>
</tbody>
</table>

Antibiotic resistance rates of *H. pylori* strains in the US, 2009-2011
Data based on *single center* study of 128 strains of *H. pylori* obtained from US veterans

Clarithromycin and Metronidazole:  
*Any previous exposure increases resistance*

- 125 pts infected with *Hp* from Alaska
  - 30% Clari-R, 66% Metro-R, 29% Dual-R
  - Clarithromycin resistance
    - Previous macrolide 92% in those with Clari-R vs. 57% in those with Clari-S (p<0.001)
    - Likelihood of resistance related to number of courses of macrolide
    - Rx failed in 77% with Clari-R vs 13% with Clari-S strains
  - Metronidazole resistance
    - Previous Rx 60% vs. no previous Rx 10% (p<0.001)
    - Rx failed in 11% with Met-R vs 38% with Met-S strains

**Effect of Previous Antibiotic Use on H. pylori Resistance**

<table>
<thead>
<tr>
<th>Antibiotic course</th>
<th>Antibiotic sensitivity tested</th>
<th>0 courses</th>
<th>1 course</th>
<th>2+courses</th>
<th>RR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quinolone</td>
<td>Levofloxacin</td>
<td>114 (4%)</td>
<td>7 (14%)</td>
<td>11 (27%)</td>
<td>1.8</td>
<td>1.24-2.49</td>
</tr>
<tr>
<td>Metronidazole</td>
<td>Metronidazole</td>
<td>114 (28%)</td>
<td>13 (38%)</td>
<td>5 (100%)</td>
<td>1.6</td>
<td>1.46-1.75</td>
</tr>
<tr>
<td>Clarithromycin</td>
<td>Clarithromycin</td>
<td>103 (7%)</td>
<td>21 (19%)</td>
<td>8 (25%)</td>
<td>1.5</td>
<td>0.92-2.41</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>Clarithromycin</td>
<td>104 (8%)</td>
<td>15 (20%)</td>
<td>13 (15%)</td>
<td>1.1</td>
<td>0.82-1.59</td>
</tr>
</tbody>
</table>

*This is the ratio of the risk of being resistant per unit increase in number of courses*


**First Line H. pylori Therapy**

Key Questions:
1. Is there a penicillin allergy?
2. Has a macrolide antibiotic been taken in the past (for any reason)?

(-) Penicillin (-) Macrolide
- Treatments: Bismuth quadruple therapy
- Concomitant therapy
- Triple therapy
- Levofloxacin based therapies

(-) Penicillin (+) Macrolide
- Treatments: Bismuth quadruple therapy
- Levofloxacin based therapies
- Concomitant therapy

(+) Penicillin (-) Macrolide
- Treatments: Bismuth quadruple therapy
- PCM

(+) Penicillin (+) Macrolide
- Treatment: Bismuth quadruple therapy

Modified from Saad & Chey, Gastro & Endo News, June 2015

ACG 2016 Annual Postgraduate Course
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Post-Treatment

*H. pylori* Testing

- Whenever *H. pylori* infection is identified and treated, testing to prove eradication should be performed using a urea breath test, fecal antigen test or biopsy based testing at least 4 weeks after the completion of antibiotic therapy and after PPI therapy has been withheld for 1-2 weeks.

- There may be infrequent situations which make eradication testing impractical or unnecessary.

*Chey, et al. Am J Gastroenterol, in press*
**Post-Therapy *H. pylori* Testing**

- **Urea breath test**
  - Perform >4 wks after completion of therapy
  - May be accurate when done 2 weeks after therapy

- **Fecal antigen test**
  - Perform >4 wks after completion of therapy
  - Monoclonal test preferred

- **Biopsy-based testing**
  - Histology ± RUT
  - Requires multiple biopsies

*Chey et al. Am J Gastroenterol, in press*

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**Salvage Therapy for Persistent or Recurrent *H. pylori* Infection**
Salvage Therapy for *H. pylori*

- Do not use the same antibiotics
- Stress the importance of compliance and review possible side effects
- Treat for 10-14 days
- Use high dose PPI BID
- Consider culture and sensitivity testing after 2 failed attempts at empiric treatment

Chey, et al. Am J Gastroenterol, in press

Song M, Ang TL World J Gastroenterol 2014;20(6): 1517

## Salvage Regimens for Persistent *H. pylori*

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Drugs (doses)</th>
<th>Dosing Frequency</th>
<th>Duration (Days)</th>
<th>FDA approval</th>
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</thead>
<tbody>
<tr>
<td>Bismuth Quadruple</td>
<td>PPI (standard dose)</td>
<td>BID QID QID</td>
<td>14</td>
<td>No**</td>
</tr>
<tr>
<td></td>
<td>Bismuth subcitrate (120-300 mg) or subsalicylate (300 mg)</td>
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<tr>
<td></td>
<td>Tetracycline (500 mg)</td>
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<td>TID or QID</td>
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<tr>
<td>Levofloxacin Triple</td>
<td>PPI (standard dose)</td>
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<td>Levofloxacin (500 mg)</td>
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<td>Rifabutin triple</td>
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<td>Rifabutin (300 mg)</td>
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<td></td>
<td>Amoxicillin (1 gm)</td>
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<tr>
<td>High-dose dual</td>
<td>PPI (standard to double dose)</td>
<td>TID or QID</td>
<td>14</td>
<td>No</td>
</tr>
<tr>
<td></td>
<td>Amoxicillin (1 gm TID or 750 mg QID)</td>
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</table>

Chey et al. Am J Gastroenterol, in press
ACG Guideline Recommendations

- **Bismuth quadruple or levofloxacin salvage regimens** are the preferred treatment options if a patient received a first-line treatment containing clarithromycin.

- **Clarithromycin- or levofloxacin salvage regimens** are the preferred treatment options if a patient received first-line bismuth quadruple therapy.

- Selection of the best salvage regimen should be directed by local antimicrobial resistance data and the patient’s previous exposure to antibiotics.

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**Salve Therapy for Persistent H. pylori**

Chey et al. Am J Gastroenterol, in press
Take Home Points:

- Key factors to consider when choosing primary therapy for Hp:
  - PCN allergy?
  - Local antimicrobial resistance data?
  - Previous macrolide exposure?
  - Quadruple therapies are replacing traditional triple therapy

- Key Factors to consider when choosing salvage therapy:
  - Avoid drugs used previously
  - Treat for 14 days
  - Quadruple therapies and Levofloxacin therapies are preferred
  - HD PPI & Amoxicillin and Rifabutin Triple therapies are other considerations