A Guide to *Helicobacter pylori* Disease, Diagnostics, and Treatment

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Parasitology & Fecal Testing
Infectious Disease Rapid Testing

June 4, 2012
Objectives

1. Explore the pathogenesis, epidemiology, and diseases associated with *H. pylori*

2. Review the available and recommended testing strategies for diagnosing disease

3. Gain an appreciation for the challenges regarding: proper ordering practices, treatment failure, and retreatment
UNIDENTIFIED CURVED BACILLI ON GASTRIC EPITHELIUM IN ACTIVE CHRONIC GASTRITIS

J. Robin Warren

UNIDENTIFIED CURVED BACILLI IN THE STOMACH OF PATIENTS WITH GASTRITIS AND PEPTIC ULCERATION

Barry J. Marshall
J. Robin Warren

Departments of Gastroenterology and Pathology,
Royal Perth Hospital, Perth, Western Australia

The Lancet · Saturday 16 June 1984

B.J. Marshall
“I preferred to believe my eyes, not the medical textbooks of the medical fraternity.”

Dr. Robin Warren
Excerpt from Barry Marshall’s Nobel Lecture

- Koch’s 3rd Postulate
- Koch’s 4th Postulate

"Barry J. Marshall - Nobel Lecture". Nobelprix.org. 5 Mar 2012
Helicobacter pylori

- Gram negative microaerophile
- Lophotrichous flagella
- Human 1º host
- Gastric pathogen
**H. pylori** Disease Associations

- **Established:**
  - Peptic Ulcer Disease (PUD)
  - Dyspepsia
  - Non-ulcer dyspepsia (NUD)
  - Gastric adenocarcinoma
  - MALT lymphoma

- **Possible:**
  - Iron deficiency

- **Not associated:**
  - Gastroesophageal reflux disease (GERD)
  - Coronary artery disease (CAD)
Disease progression


WHO classifies *H. pylori* as the only bacterial Class 1 Carcinogen
Virulence factors

- Urease and Flagella
- Multiple adhesins
- **NAP** (Neutrophil Activating Protein)
- **VacA** (Vacuolating Cytotoxin)
- **CagA** (Cytotoxin associated gene) & Cag T4SS

Adapted from Amieva and El-Omar, *Gastroenterology*, 2008
Flagella

- Provide motility through harsh stomach environment

- Corkscrew shape of *H. pylori* + flagella allows for penetration of mucus in stomach

- Possess a sheath that masks the flagellin subunit normally recognized by Toll-like receptor 5 (TLR5)\(^1\)
  - Paddle-like structure\(^2\)

\(^1\) Andersen-Nissen *et al.* *PNAS*, 2005

\(^2\) O’Toole *et al.* *Microbed Infect*, 2000
Urease

- Highly expressed by all known gastric *Helicobacter* spp.\(^1\)
- Indirectly neutralizes the HCl in the stomach
- Breakdown of urea into CO\(_2\) and ammonia\(^2\)
  - Urea breath test exploits CO\(_2\) production
  - Ammonia neutralizes HCl
- Localized neutralization of the stomach allows for colonization\(^2\)

\(^1\) Solnick, J. *Clinical Infectious Diseases*, 2003
\(^2\) Kusters *et al.* *Clin Microbiol Rev*, 2006
Adhesins

- Surface exposed molecules
  - Haemagglutinin
  - Blood antigen binding protein
  - Lewis antigens

- Initial attachment to the host gastric epithelium

- Facilitate intimate contact

Adapted from Amieva and El-Omar, Gastroenterology, 2008
Lewis Antigens

- *H. pylori* Lewis antigens are analogous to Human Lewis blood group antigens

- Bind cell surface and reduce localized inflammation\(^1\)
  - Temporarily inactivates T and B cells
  - Temporary anti-inflammatory effect

\(^1\)Kusters et al. *Clin Microbiol Rev*, 2006

Adapted from Amieva and El-Omar, *Gastroenterology*, 2008
HP-NAP: Neutrophil Activating Protein

- Attracts/activates neutrophils, monocytes, & dendritic cells
- Leads to a proinflammatory Th1 polarized response
- MAJOR inflammatory modulator
  - Compounded by host polymorphisms & bacterial factors

Adapted from Amieva and El-Omar, Gastroenterology, 2008

VacA: Vacuolating Cytotoxin A

• Gene present in nearly all cultured strains\textsuperscript{1}
  • Protein expressed in almost all isolates
  • Active protein produced by 40% of isolates

• Implicated in peptic ulceration\textsuperscript{2}

• Forms channels that allow release of nutrients to extracellular space

• Pro-apoptotic & initiates proinflammatory response in conjunction with HP-NAP

\textsuperscript{1} Atherton & Blaser, \textit{Journal of Clinical Investigation}, 2009
\textsuperscript{2} Atherton \textit{et al. J Biol Chem}, 1995
CagA: Cytotoxicity Associated Gene

- Associated with severe disease state
  - "Oncoprotein"
- Injected into gastric cell by a Type 4 Secretion System
- Tyrosine phosphorylated on multiple repetitive conserved motifs
  - Degree of phosphorylation predicts disease severity
CagA (unphosphorylated)

- CagA targets to host membrane
  - Interrupts gastric cellular junctions
  - Disrupts the integrity of cell layers
- Alters cell cycle progression\(^1\)
  - Prolongs cell life
- Upregulates mitogenic genes implicated in carcinogenesis\(^2\)

\(^1\) Chang et al. Cell Microbiol, 2006  \(^2\) Franco et al. PNAS, 2005
CagA<sup>PY</sup> (phosphorylated)

- Interacts with phosphotyrosine binding proteins involved in:
  - cytoskeletal rearrangement
  - cell scattering
  - cell elongation

- Cell morphology termed “hummingbird phenotype”

- Triggered by interaction with a cellular oncogene<sup>1</sup>

<sup>1</sup>Rieder et al. Current Opinion in Microbiology, 2005
Couturier et al. Infect & Immun, 2006
Summary of Virulence

- Motility
- Colonization
- Immune evasion
- Immune stimulation
- Cellular damage

Adapted from Amieva and El-Omar, Gastroenterology, 2008
Global epidemiology

Why are we concerned about *H. pylori*?
Worldwide epidemiology

- ~50% of the world infected
  - Developing world/impoverished areas primarily
  - Transmission mode still unclear (familial, fecal/oral?)

Couturier, Clin Microbiol News, 2012
Epidemiological Trends

• Male skew in *H. pylori* infections (adulthood not childhood)
  – Males have higher PUD & gastric cancer rates
    (1.5 - 3.0 times more common)\(^1\)

• Infected mothers typically have infected children\(^2\)

• People of low socioeconomic standing are more likely to be infected\(^3\)

• In developed countries infection rates are higher in non-Caucasian individuals\(^3\)

• Occupational exposure to feces linked to increased infection rates\(^2\)

\(^1\)Replogle *et al.* *Am J Epidemiol.* 1995
\(^2\)Covacci *et al.* 1999 *Science*
\(^3\)Azevedo *et al.* 2009 *Helicobacter*
**H. pylori** in Northern-California

IgG based study of Northern California adults age 20-39

- Ethnic groups chosen based on different gastric cancer risks
- Confirmed sex skew in males for seropositivity
- Strong disparity between Caucasian-Americans and African & Hispanic Americans
- Increasing age also identified as a risk factor

<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td><strong>Sex</strong></td>
</tr>
<tr>
<td>Female</td>
</tr>
<tr>
<td>Male</td>
</tr>
<tr>
<td><strong>Race/ethnicity†</strong></td>
</tr>
<tr>
<td>White</td>
</tr>
<tr>
<td>African-American</td>
</tr>
<tr>
<td>Hispanic</td>
</tr>
<tr>
<td>Japanese</td>
</tr>
<tr>
<td><strong>Age (years)</strong></td>
</tr>
<tr>
<td>20–24</td>
</tr>
<tr>
<td>25–29</td>
</tr>
<tr>
<td>30–34</td>
</tr>
<tr>
<td>35–39</td>
</tr>
</tbody>
</table>

**H. pylori** seroprevalence in US Army recruits

- Male & Female recruits age 17-26 (Ft. Jackson, SC)
  - No geographic or ethnic restrictions

- Age and race were strongest predictors of “infection”

- Median income is predictive for seropositivity (↓ = ↑)

*H. pylori* in low income African Americans from 13 southern states

- Patients self-identified as “white” or “African American”
  - Degree of African ancestry determined by genetic markers as “low, medium, and high”

- Seropositivity of low-income African-Americans and Caucasian:
  - 89% African Americans
  - 69% Caucasians

- African American race 2- to 6-fold increase odds of seropositivity for VacA+/CagA+ *H. pylori*

- ↑ odds of *H. pylori*-positivity with increased African ancestry
  - Medium and high ancestry carries 2.5- and 3.4-fold increase in *H. pylori* seropositivity
  - 3.5- and 4.9-fold increase in CagA seropositivity

Arctic Epidemiology

Chesterfield Inlet/Repulse Bay

- Arctic towns share risk factors for *H. pylori* prevalence
  - Overcrowding
  - Inadequate drinking water
  - Poor sewage disposal

- 130 of 256 adults from communities tested

- 51 % *H. pylori* IgG seropositive
  - 62 % CagA seropositive
  - 35 % of *H. pylori* ELISA negative patients were CagA seropositive

McKeown et al. 1999 Am J Gastro.
Aklavik, Northwest Territory

CANHelp project: Aklavik

- Population of 600
  - 60% Inuit, 25% Dene, 15% Alaskan

- Prevalence unknown

- 313 patients screened by UBT
  - 58% positive

- Old Crow, Yukon Ter. project now underway

Cheung et al. Can J Gastroenterol, 2008
Cancer in Arctic First Nations

- Gastric cancer is 10\textsuperscript{th} most common cancer in Canadian men\textsuperscript{1,2}
  - 5\textsuperscript{th} most common cancer in NWT men\textsuperscript{1}
  - 2 X more gastric cancer in NWT\textsuperscript{1}
  - 3\textsuperscript{rd} leading cause of cancer-related death in NWT vs 9\textsuperscript{th} for all of Canada\textsuperscript{2}

<table>
<thead>
<tr>
<th>Rank</th>
<th>Male</th>
<th>Dene (n=109)</th>
<th>Inuit (n=32)</th>
<th>Other (n=193)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Colorectal (35%)</td>
<td>Trachea, Bronchus and Lung (25%)</td>
<td>Trachea, Bronchus and Lung (19%)</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Trachea, Bronchus and Lung (19%)</td>
<td>Stomach (16%)</td>
<td>Colorectal (17%)</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Prostate (7%)</td>
<td>x</td>
<td>Prostate (14%)</td>
<td></td>
</tr>
</tbody>
</table>

"Other" includes Non-Aboriginals and Métis. X = cells with less than five cases are suppressed. N values represent the number and \% values represent the proportion of cases in each gender-specific ethnic group. Source: NWT Cancer Registry (1992-2000)

- Alaska natives have 3X more gastric cancer than Caucasian Americans\textsuperscript{2}

\textsuperscript{2}Goodman et al. . Can J Gastroenterol, 2008
$H. pylori$ antibiotic resistance in Canada

- Canada-wide resistance rates for $H. pylori$ (ca. 2000)
  - Clarithromycin ~4%
  - Metronidazole 18-22%

- Unknown in first nations people of Canada

CBC

Aklavik residents, scientists hopeful antibiotics curb cancer-causing bacteria
Tuesday, May 26, 2009 | 3:10 PM ET

Fallone CA. Can J Gastroenterol 2000
A prediction of antibiotic resistance

2003 study of Alaska Natives in Anchorage

- 30% of *H. pylori* isolates resistant to clarithromycin
  - 13% w/ clari\(^S\) *H. pylori* failed clari-based treatment

- 66% resistant to metronidazole
  - 50% w/ metro\(^S\) *H. pylori* failed therapy

- Resistance linked to previous macrolide or metronidazole use

- Reinfection rates\(^2\)
  - 7% at six months
  - 10% at one year
  - 15% at two years

\(^2\)McMahon BJ et al. *Aliment Pharmacol Ther*, 2006
Impact of Therapy

Hospitalization rates between 1998 and 2005 for PUD & related complications w/ special focus on *H. pylori* diagnosis in the USA

• 21% Decrease (Age adjusted)

• Decline in most ethnic groups
  – Lowest rates in whites & decrease in African Americans
  – No decline in Hispanics
  – Many native American tribes declined, others increased dramatically

• Hospitalization for PUD highest for ≥65 years old
  – Higher for men than women

• Age adjusted *H. pylori* hospitalization rates also declined overall

What effect will treatment have?

<table>
<thead>
<tr>
<th>Condition</th>
<th>H. pylori causation</th>
<th>Effect of H. pylori eradication</th>
</tr>
</thead>
<tbody>
<tr>
<td>PUD</td>
<td>Yes</td>
<td>Reduces recurrence</td>
</tr>
<tr>
<td>Dyspepsia</td>
<td>Yes in some</td>
<td>Symptom improvement in some</td>
</tr>
<tr>
<td>NUD</td>
<td>Possibly in few</td>
<td>Improvement in some</td>
</tr>
<tr>
<td>Gastric Cancer</td>
<td>Yes</td>
<td>Little effect if any</td>
</tr>
<tr>
<td>MALT lymphoma</td>
<td>Yes</td>
<td>Remission in $\geq 50%$</td>
</tr>
<tr>
<td>Iron Deficiency</td>
<td>Likely in some</td>
<td>Improvement in some</td>
</tr>
<tr>
<td>NSAID ulcers</td>
<td>Naïve users?</td>
<td>May reduce incidence</td>
</tr>
<tr>
<td>GERD</td>
<td>No</td>
<td>None</td>
</tr>
<tr>
<td>CAD</td>
<td>No</td>
<td>None</td>
</tr>
</tbody>
</table>

To Treat or Not to Treat

...and how to treat

First we must decide whether to test
New Dyspepsia Guidelines

• “Chronic or recurrent pain or discomfort centered in the upper abdomen”

• The AGA recommends that:

  “Patients 55 years of age or younger without alarm features should receive *H. pylori* test and treat followed by acid suppression if symptoms remain.”

• Despite this clear mandate…
  this is not happening!

Talley et al. *Gastroenterology*, 2005
New AGA Dyspepsia Guidelines

Dyspepsia without GERD or NSAIDs

Age > 55 or alarm symptoms* present
- EGD

Age < 55
- No alarm symptoms
- Test for H. pylori
  - Negative
    - PPI trial 4-6 weeks
    - Fails
    - Reassurance, Reassess diagnosis
    - Fails
    - Consider EGD
  - Positive
    - Treat for H. pylori
    - Fails
    - PPI trial 4 weeks

*Alarm features include:
- Age >55 w/ new onset dyspepsia
- Family h/o gastric cancer
- Unintended weight loss
- GI bleeding
- Persistent dysphagia
- Unexplained iron-deficiency anemia
- Persistent vomiting
- Palpable mass or lymphadenopathy
- Jaundice

EGD: esophagastroduodenoscopy

Not only the AGA…
New ACG Dyspepsia Guidelines

Dyspepsia (uninvestigated)

- Age > 55 or alarm features*
  - EGD

- Age < 55
  - No alarm features

*Alarm features include:
  - Age > 55 w/new onset dyspepsia
  - Family h/o gastric cancer
  - Unintended weight loss
  - GI bleeding
  - Persistent dysphagia
  - Unexplained iron-deficiency anemia
  - Persistent vomiting
  - Palpable mass or lymphadenopathy
  - Jaundice

H. pylori prevalence <10%
  - PPI trial
    - Fails
    - Test and treat for H. pylori
      - Fails
      - Consider EGD

H. pylori prevalence >10%
  - Test and treat for H. pylori
  - Fails
  - PPI trial
  - Fails
  - Consider EGD

EGD: esophagogastrroduodenoscopy

Testing Methods

Laboratory testing

Endoscopy-based (Invasive)
- Culture from biopsy & susceptibility
- Rapid urease from biopsy (CLO)
- Immunohistochemistry

Non-endoscopy (Non-invasive)
- Serology (IgA, IgM, IgG)
  - No longer recommended!
- $^{13}$C or $^{14}$C-urea breath test
- Stool antigen test
Endoscopy-based: Culture

Advantages:
- Provides clinical isolate for susceptibility testing
- Direct evidence of infection

Disadvantages:
- Limited sensitivity
- Demands highly experienced microbiologists
- Invasive procedure
Endoscopy-based: Rapid Urease (CLO)

Advantages:
- Direct evidence of infection with CLO
- Rapid turn around time
- Limited technical expertise required

Disadvantages:
- Non-specific
- Invasive procedure
Non-Endoscopy: Urea Breath Test

$^{13}\text{C}$ or $^{14}\text{C}$-urea ingested by patient; test for isotopic $\text{CO}_2$ in patient breath

Advantages:

- Rapid result: can be performed in the doctors office (if available)
- Direct measure of CLO infection
- Test post treatment (confirm eradication)
- High sensitivity
- FDA approved for pediatric use

Disadvantages:

- $^{14}\text{C}$ involves exposure to radiation
- PPIs & antibiotics must be stopped 2 weeks prior
- Requires technical demands from physician office
- Not specific for $H.\ pylori$
- Limited availability & expensive
Non-Endoscopy: Stool Antigen Test

Immunoassay detection of *H. pylori* antigen in the stool

**Advantages:**
- Detect active infection/monitor therapy
- Least invasive
- Excellent for pre- and post-treatment
- Readily available
- High specificity and sensitivity
- FDA approved for pediatric use

**Disadvantages:**
- Stigma in sample type
- PPIs & antibiotics should be stopped
- Variable performance across vendors
  - Poly vs monoclonal

Vaira and Vakil, Gut 2001
Non-Endoscopy: Serology

Includes IgA, IgM, and IgG testing

Advantages:
- Easily establish prevalence in research studies
- Non-invasive and inexpensive
- Not directly affected by antibiotic or PPI use

Disadvantages:
- Does NOT diagnose an active infection
- CANNOT be used as test-of-cure
- Limited sensitivity; negative result does not rule out
- Can lead to clinical confusion
- May NOT reimburse in some states/insurance carriers
# Test Performance of Non-Invasive Testing

<table>
<thead>
<tr>
<th>Test</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stool antigen test</td>
<td>90-95%</td>
<td>90-95%</td>
</tr>
<tr>
<td>Urea breath test</td>
<td>95-100%</td>
<td>90-95% ??</td>
</tr>
<tr>
<td>Serum IgG antibody*</td>
<td>80-85%</td>
<td>75-80%</td>
</tr>
</tbody>
</table>

*Does NOT test for active infection*
“We must to it right at UUHC”

January 2011 – December 2011

<table>
<thead>
<tr>
<th></th>
<th>UBT</th>
<th>SAT</th>
<th>IgG</th>
<th>IgG &amp; IgA</th>
<th>IgA</th>
<th>IgM</th>
</tr>
</thead>
<tbody>
<tr>
<td>UU Hospital</td>
<td>104</td>
<td>319</td>
<td>290</td>
<td>384</td>
<td>12</td>
<td>360</td>
</tr>
</tbody>
</table>

- UUH – 423 active tests / 1046 serology

~1 active : 3 passive
**Helicobacter pylori Testing**

**Indications for Testing**
- Persistent dyspepsia, abdominal pain
- Obvious cause
  - Nonsteroidal anti-inflammatory drug (NSAID) use
  - Known gastroesophageal reflux disease (GERD)
- >55 years
- OR
- Alarm symptoms
  - Gastrointestinal bleeding
  - Unexplained iron deficiency anemia
  - Early satiety
  - Unexplained weight loss
  - Progressive dysphagia
  - Odynophagia
  - Recurrent vomiting
  - Family history of upper gastrointestinal cancer
  - Previous esophagastroduodenal malignancy

Remove cause if possible
OR
Treat based on etiology

**Order**
- Helicobacter pylori Breath Test
- Helicobacter pylori Antigen, Fecal by EIA

**Negative**
- Empiric trial of proton pump inhibitor for 4-6 weeks

**Positive**
- Treat with triple therapy (amoxicillin or metronidazole, clarithromycin, and proton pump inhibitor) to eradicate H. pylori

Reevaluate after completion of therapy

**Symptoms still present**
- Consider EGD
- Consider repeat H. pylori testing during EGD

**No symptoms present**
- No further therapy required
| Helicobacter pylori Antigen, Fecal by EIA 0065147 Method: Qualitative Enzyme Immunoassay | Determine if H. pylori has been eradicated or just temporarily suppressed, especially in adult patients with complicated, recurrent or refractory peptic ulcers Antigen testing should be performed no sooner than 1 month after therapy concluded. | Less accurate in pediatric patients (low sensitivity) |
| Helicobacter pylori Antibodies, IgG & IgA 0050964 Method: Semi-Quantitative Enzyme Immunoassay | Determine if H. pylori is causing active infection Not recommended for primary diagnosis | May require repeat testing if results are equivocal and clinical suspicion present |
| Helicobacter pylori by Immunohistochemistry 2003941 Method: Immunohistochemistry | Aid in histologic diagnosis of H. pylori Stained and returned to client pathologist; consultation available if needed | |

Additional Tests Available

- Click the plus sign to expand the table of additional tests.
ORDERING RULES FOR CPOE

- **WARNING FLAG** for IgG, IgA, IgM:

- “Do not use to diagnose *H. pylori*; order *H. pylori* urea breath test or fecal antigen by EIA”

- Active in March, will re-evaluate efficacy at 6 months.
Evolving Issues with *H. pylori* testing

- Many major insurance carriers no longer reimbursing for certain *H. pylori* testing

- Serology rapidly viewed as "medically unnecessary testing"

- SAT & UBT on a single patient in non-reimbursable
Serology non-reimbursement

• Major insurance plans NOT reimbursing for serology
  – Aetna, Cigna, BC/BS, & Geisinger
    • Likely many others

• States affected:
  – NY, CA, PA, FL, WV, KY, IN, MO, OH, WI, others?

• Specific CPT codes defined as:
  “medically unnecessary”
So we’ve correctly diagnosed

Now how do we treat???
**Helicobacter pylori treatment**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Regimen</th>
<th>Duration (Days)</th>
<th>Cure Rate</th>
<th>Indications</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Triple (clarithromycin)</strong></td>
<td>PPI, clarithromycin, amoxicillin</td>
<td>10-14</td>
<td>70-85%</td>
<td>Primary therapy for patients with no macrolide exposure or penicillin allergies</td>
</tr>
<tr>
<td></td>
<td>PPI or H$_2$RA, clarithromycin, metronidazole</td>
<td>10-14</td>
<td>70-85%</td>
<td>Primary therapy for penicillin allergic patients with no macrolide exposure or patients unable to tolerate bismuth quadruple therapy</td>
</tr>
<tr>
<td><strong>Quadruple</strong></td>
<td>Bismuth subsalicylate, metronidazole, tetracycline, PPI</td>
<td>10-14</td>
<td>75-90%</td>
<td>Primary therapy for patients with macrolide exposure or patients with penicillin allergies</td>
</tr>
<tr>
<td><strong>Sequential</strong></td>
<td>PPI, amoxicillin</td>
<td>5</td>
<td>&gt;90%</td>
<td>Consider as alternative primary therapy to triple therapy (not validated in USA). May be effective in patients with macrolide resistant strains</td>
</tr>
<tr>
<td></td>
<td>PPI, clarithromycin, tinidazole</td>
<td>5</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
H. pylori re-treatment

**Salvage therapy indicated on treatment failures**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Regimen</th>
<th>Duration (Days)</th>
<th>Cure Rate</th>
<th>Indications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quadruple</td>
<td>Bismuth subsalicylate, metronidazole, tetracycline, PPI</td>
<td>7</td>
<td>68%</td>
<td>Salvage therapy after triple therapy failure</td>
</tr>
<tr>
<td>Triple (levofloxacin)</td>
<td>PPI, amoxicillin, levofloxacin</td>
<td>10</td>
<td>87%</td>
<td>Patients who failed triple and/or quadruple therapy. May not be effective in patients with prior quinolone exposure</td>
</tr>
</tbody>
</table>

**Alternative salvage therapies include:**

- Fluoroquinolones
- Rifabutin (TB drug) 40-90% effective
**Helicobacter pylori** treatment

- Recommended to **not** repeat the same therapy after initial failure
  - Avoid using therapy consisting of previously used antibiotics

- Re-infection:
  - 5% in developed countries\(^1\)
  - Re-infection may be a result of incomplete clearance *i.e.* relapse

---
\(^1\) Azevado et al. 2009 *Helicobacter*
Possible “reinfection” scenarios

\[ \$ = \text{Hp (clarithro}^R\text{)} \]
\[ \$ = \text{Hp (clarithro}^S\text{)} \]

Incomplete clearance

Second Exposure

Resistance to treatment, reestablished infection
Summary

- *H. pylori* infections remain a global health issue

- Pathogenesis is complex and involves multiple unique virulence factors

- Genetic/ethnic/geographic/socioeconomic disparities exist

- Proper patient management: testing for active infection and appropriate antimicrobial therapy

- Antibiotic resistance and treatment failures are an ongoing challenge
Questions?