Helicobacter pylori Eradication in Primary Care

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What is H. pylori?
Helicobacter pylori

- Discovered in 1982 by Marshall and Warren (Royal Perth Hospital)
- Spiral, gram – rod
- Initially called Campylobacter Pyloridis

Flagellum moves bacteria to mucus layer.

Attaches to gastric epithelial cells
Urease hydrolyzes gastric urea to form ammonia – neutralize acid.
• More common in developing countries

• Infection in childhood

• Reinfection in adulthood rare <1%/year

• Transmission
  – Human-human
  – Fecal-oral route.
  – Less commonly oral-oral (H. pylori in dental plaque, saliva)

Complications of H. pylori

- Peptic ulcer
- Gastritis / Dyspepsia
- Atrophic gastritis
- Iron deficiency anemia
- Idiopathic thrombocytopenic purpura
- Gastric cancer (adenocarcinoma / lymphoma)
How to screen for H. pylori?

- **Urea breath test** (active infection)
- **Stool antigen test** (active infection)
- **Serology, H.pylori IgG** (exposure)
- **Endoscopy**
  - **Rapid urease test** (active infection)
  - **Histology** (active infection)
  - **Culture** (active infection)
H. pylori stool antigen test

- Not all stool antigen tests are the same.
- Only those validated >90% accuracy should be used.
- 198 patients with H. pylori on histology

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<thead>
<tr>
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</thead>
<tbody>
<tr>
<td>Sensitivity (%)</td>
<td>92.2&lt;sup&gt;a,b,c&lt;/sup&gt;</td>
<td>48.9&lt;sup&gt;d,e,f&lt;/sup&gt;</td>
<td>86.7&lt;sup&gt;g&lt;/sup&gt;</td>
<td>68.9</td>
</tr>
<tr>
<td>Specificity (%)</td>
<td>94.4</td>
<td>88.9</td>
<td>88.9</td>
<td>92.6</td>
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<tr>
<td>PPV (%)</td>
<td>93.3</td>
<td>78.6</td>
<td>86.7</td>
<td>88.6</td>
</tr>
<tr>
<td>NPV (%)</td>
<td>93.6</td>
<td>67.6</td>
<td>88.9</td>
<td>78.1</td>
</tr>
<tr>
<td>Accuracy (%)</td>
<td>93.4</td>
<td>71</td>
<td>88.0</td>
<td>81.8</td>
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</tbody>
</table>

Urea breath test

- Reliable non-invasive test
- Sensitivity is 88-95%, specificity 95-100%

H. pylori serology IgG

- Only test that is not affected by antibiotics, PPI, bismuth, blood, food
- Only test that cannot be used to confirm eradication
- Negative result = not infected.
- Positive result =
  - If asymptomatic – may be past exposure, rather than active infection.
  - If symptomatic – treat as active infection

Endoscopy

• Rapid urease test

<table>
<thead>
<tr>
<th>Test</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>PPV (%)</th>
<th>NPV (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HpOne</td>
<td>65.5</td>
<td>85.7</td>
<td>74.5</td>
<td>79.6</td>
</tr>
<tr>
<td>CLO test</td>
<td>63.8</td>
<td>84.6</td>
<td>72.5</td>
<td>78.6</td>
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</tbody>
</table>

PPV: positive predictive value; NPV: negative predictive value

• Histology
  – Provides other information – dysplasia, cancer, intestinal metaplasia.

• H.pylori culture
  – Performed for antibiotic sensitivity after 2 failed eradictions

H. Pylori Eradication
• First line
  – Triple therapy (Amoxicillin 1g bd + Clarithromycin 500mg bd + PPI bd)
  – 10-14 days (additional 5% success for longer duration)

• Second line therapy
  – Quadruple therapy (tetracycline, bismuth, metronidazole, PPI x 2 weeks)

• Third line (consider H.pylori culture)
  – Levofloxacin therapy (amoxicillin, levofloxacin, PPI x 10 days)
  – Sequential therapy (PPI + Amoxicillin x 5/7 -> PPI + clarithromycin + metronidazole x 5/7)

H. Pylori Eradication

- Success depends on:
  - antibiotic resistance
  - patient compliance to meds
  - gastric acidity
  - bacterial load

Different countries have different first line therapies

- Singapore, Northern Europe, Scandinavia, Netherlands
  - Triple therapy preferred

- Belgium, South Korea
  - Quadruple therapy, sequential therapy preferred.

- Italy
  - Avoid triple therapy
  - Successful in only 51%.

10d Quadruple therapy works better than 7d Triple therapy

Meta-analysis

Figure 3. Eradication rates of *Helicobacter pylori* reported with triple and quadruple therapy in a meta-analysis. Adapted from Venerito M et al. *Digestion*. 2013;88(1):33-45.29
## Singapore Eradication Rates

<table>
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<tr>
<th>Therapy Type</th>
<th>Number</th>
<th>Rate (95% CI)</th>
</tr>
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<tbody>
<tr>
<td>Triple therapy x 10/7</td>
<td>129/140</td>
<td>92.1% (86.5–95.6%)</td>
</tr>
<tr>
<td>Sequential therapy x 10/7</td>
<td>130/144</td>
<td>90.3% (84.3–94.1%)</td>
</tr>
<tr>
<td>Concomitant therapy x 10/7</td>
<td>125/132</td>
<td>94.7% (89.5–97.4%)</td>
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</table>

- Triple therapy x 10/7
- Sequential therapy x 10/7 (PPI, amoxicillin -> PPI, clarithromycin, metronidazole)
- Concomitant therapy x 10/7 (PPI, amoxicillin, clarithromycin, metronidazole)

H. pylori antibiotic resistance
Clarithromycin resistance varies between countries (triple therapy)

Levofloxacin resistance varies between countries (levofloxacin therapy)

Clarithromycin resistance and macrolide prescription

DID=Defined daily dose /1000 inhabitants

Levofloxacin resistance and quinolone prescription

Singapore data on H. pylori resistance

- Amoxicillin
  - 4.7% (2015 publication, n=106)

- Clarithromycin
  - 17.9% (2015 publication, n=106)

- Metronidazole
  - 31.7% (2003 publication, n=120)
  - 48% (2015 publication, n=106)

- Levofloxacin
  - No data

Symptoms do not predict successful eradication

N=87
Confirmation by UBT

What test to do after eradication?

• Use a test for active infection:
  – Urea breath test
  – H.pylori stool antigen test (validated lab test)
  – Endoscopy – urease test / biopsy for histology

• Serology is not useful
PPI causes false negative results

- 10 subjects (33%) false negative result

**Figure 2.** UBT results for the 10 subjects who developed transient false negative UBT results during therapy with omeprazole. All recovered by 14 days post-therapy. DOB, delta over baseline.
After treatment, when to repeat H.pylori test?

• Testing too early can cause:
  – False negative results – reduced bacterial load makes tests less sensitive.
  – False positive stool antigen results – shedding of dead organism can cause false positive result.

• Tests impaired by
  – PPI
  – Bismuth
  – Antibiotics

• Test only after stopping
  – PPI for 2 weeks
  – Antibiotics for 1 month

Summary

- H. pylori should always be eradicated.
- Triple therapy is the first line treatment.
- Quadruple therapy is the second line treatment.
- Levofloxacin triple therapy if Quadruple therapy is not available
- Confirmation of successful H. pylori eradication should be performed.
- If urea breath test is not available, stool antigen is an alternative.
- OGD only when there is a risk of cancer, ulcer, chronic dyspepsia.
Any questions?