Improving ordering practices for the diagnosis of *Helicobacter pylori*

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Infectious Disease Rapid Testing

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Objectives

1. Briefly outline the importance of *H. pylori*

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

3. Discuss the challenges facing ordering practices and evolving reimbursement issues
Helicobacter pylori

- Gram negative microaerophile
- Highly motile
- Gastric pathogen of humans
Worldwide epidemiology

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


**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
What effect will treatment have?

<table>
<thead>
<tr>
<th>Condition</th>
<th><em>H. pylori</em> causation</th>
<th>Effect of <em>H. pylori</em> 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

*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

Positive

Treat for H. pylori

PPI trial 4-6 weeks

Fails

Reassurance, Reassess diagnosis

Fails

Consider EGD

Negative

PPI trial 4 weeks

Fails

Reassurance, Reassess diagnosis

Consider EGD

EGD: esophagastroduodenoscopy

Not only the AGA…

New ACG Dyspepsia Guidelines

Dyspepsia (uninvestigated)

Age > 55 or alarm features*

EGD

Age < 55
No alarm features

H. pylori prevalence <10%

PPI trial

Fails

Test and treat for H. pylori

Fails

Consider EGD

H. pylori prevalence >10%

PPI trial

Fails

Consider EGD

*Alarm features include:
- Age >55 w/new onset dyspepsia
- Family h/o gastric cancer
- Unintended weight loss
- GI bleeding
- Persistent dysphagia
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EGD: esophagogastroduodenoscopy

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
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)
- Remove cause if possible or treat based on etiology
- >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 esophagogastric malignancy

**ORDER**
- Helicobacter pylori Breath Test OR 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 0550694 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”
Summary

- *H. pylori* infections remain a global health issue
- Multiple tests are available both invasive and non-invasive
- Guidelines for investigation of dyspepsia and *H. pylori* diagnosis recommend active testing:
  - UBT or SAT when EGD is not indicated
- The landscape of reimbursement is changing
Questions?