Review of the Diseases of the Upper GI Tract

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Disclosure Statement

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Learning Objectives

1. Determine the approach to the patient with dyspepsia.
2. Discuss the common disorders of the esophagus: motility and GERD.
3. Describe the diagnosis and treatment of PUD and *Helicobacter pylori*. 
Esophageal Disorders

- Disorders of motility
  - Gastro-esophageal Reflux Disease
  - Inflammatory Diseases
  - Tumors of the Esophagus

Esophageal Disorders
Symptoms From the Esophagus

*History*

- Swallowing difficulties – dysphagia
- Pain – heartburn, odynophagia, chest pain
- Regurgitation – effortless appearance of gastric or esophageal contents in the oral cavity
Esophageal Motility Disorders

• Achalasia
• Spasm
  – Diffuse
  – Localized – “nutcracker” esophagus
• Scleroderma
1. Which of the following is an indicated treatment for achalasia?

A. Beta blockers
B. Alpha blockers
C. Calcium channel blockers
D. H2 blockers
1. Which of the following is an indicated treatment for achalasia?

A. Beta blockers 3%
B. Alpha blockers 7%
C. Calcium channel blockers 78% ✓
D. H2 blockers 12%
## Motility Disorders

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Clinical</th>
<th>Diagnosis</th>
<th>Treatment</th>
</tr>
</thead>
</table>
| **Achalasia**
(Absence of peristaltic progression) | Dysphagia – solids and liquids, increased risk of SCC | Barium swallow, manometry | Long-acting nitrates, Ca channel blockers, pneumatic dilatation of LES |
| **Diffuse Esophageal Spasm**
(Spastic Motor Disorder) | Heartburn, chest pain, or dysphagia; often swallow-induced – always exclude CAD. | Barium swallow | Long-acting nitrates, Ca channel blockers |
| **Scleroderma Esophagus**
(90% of patients with scleroderma have esophagus involved.) | None to severe reflux; often with strictures, motility abnormalities | Barium swallow, manometry | Manage reflux; treat esophagitis with H2 blockers, PPIs, prokinetic drugs. |
GERD

Symptoms

• Typical Symptoms: heartburn, acid regurgitation
• **Atypical Symptoms:** wheezing, hoarseness, atypical chest pain
• Diagnosis usually based on history and physical, and trial of empiric therapy
2. Which of the following diagnostic tests is recommended in the patient with GERD refractory to maximum PPI therapy?

A. Esophageal manometry
B. 24 hour pH monitoring
C. Barium radiology
D. Urea Breath Test
2. Which of the following diagnostic tests is recommended in the patient with GERD refractory to maximum PPI therapy?

A. Esophageal manometry

B. 24 hour pH monitoring

C. Barium radiology

D. Urea Breath Test

42% B. 24 hour pH monitoring
GERD

**Diagnosis**

- No *gold* standard; EGD is to assess complications (*SOR: A*).
  - Erosive esophagitis
  - Stricture
  - Barrett’s esophagus
  - Cancer
- EGD lacks adequate sensitivity in determining pathologic reflux (*SOR B*)
Diagnostic Testing

- Esophageal manometry is recommended in the pre-operative evaluation, e.g. Nissen fundoplication (SOR: C)
- Esophageal manometry is NOT recommended in the diagnosis of GERD
- **24-hour pH monitoring is recommended in patients refractory to PPI therapy or when the diagnosis is in question (SOR: C)**
- 24-hour pH monitoring is NOT recommended in the routine diagnosis of GERD and is NOT required in the presence of Barrett’s esophagus (SOR: B)
- Barium radiology: Limited usefulness; not recommended (SOR: A)
Diagnostic Testing

- Screening for *Helicobacter pylori* infection is NOT recommended *(SOR: C)*
- Eradication of *H. pylori* is not routinely required as part of antireflux therapy
- FDA concluded that there was insufficient evidence to recommend testing of all patients on long-term PPI therapy
- Controversial: European recommendation in favor of screening all patients for *H. pylori*

GERD Diagnosis

• An empiric trial of acid suppression therapy for 4-8 weeks can identify patients with GERD who do not have alarm symptoms (SOR: A)

• Obtain upper endoscopy in patients with alarm symptoms or those at high risk for complications (SOR: B)

• Alarm symptoms
  – Black or bloody stools
  – Choking
  – Chronic cough
  – Dysphagia
  – Early satiety
  – Hematemesis
  – Hoarseness
  – Iron deficiency anemia
  – Odynophagia
  – Weight loss
## Summary of Diagnostic Testing for GERD

<table>
<thead>
<tr>
<th>Diagnostic test</th>
<th>Indication</th>
<th>Highest level of evidence</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>PPI trial</td>
<td>Classic symptoms and no red flags</td>
<td>Meta-analysis</td>
<td>Negative trial does not rule out GERD</td>
</tr>
<tr>
<td>Barium swallow</td>
<td>Not for GERD, use for dysphagia</td>
<td>Case-control</td>
<td>Not recommended for GERD diagnosis</td>
</tr>
<tr>
<td>Upper endoscopy</td>
<td>Alarm symptoms or screening of high-risk patients</td>
<td>RCT</td>
<td>Those at risk for Barrett's, non-cardiac CP, unresponsive to PPI</td>
</tr>
<tr>
<td>Esophageal manometry</td>
<td>Pre-operative evaluation</td>
<td>Observational</td>
<td>Not recommended for GERD diagnosis</td>
</tr>
<tr>
<td>24-hour pH monitoring</td>
<td>Refractory symptoms or question GERD diagnosis</td>
<td>Observational</td>
<td>Not recommended for GERD diagnosis</td>
</tr>
</tbody>
</table>

Slide courtesy of Thad Wilkins, MD, *with permission*
Treatment

• $H_2$RA less effective than PPIs (less expensive than PPIs)
• PPIs are more effective for relieving heartburn than $H_2$RA or prokinetic agents (SOR: A)
• Different PPIs have similar efficacy at standard doses (SOR: A)
• Long-term PPI use may increase fracture risk, but inconsistent evidence regarding hip fracture (SOR: C)
On-demand Maintenance Therapy Versus Continuous PPI Therapy for GERD

Systematic review
16 studies
n = 14,142

<table>
<thead>
<tr>
<th>Comparisons</th>
<th>Severity of GERD</th>
<th>Number of trials (n)</th>
<th>Willingness to continue with treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>On-demand PPI vs continuous PPI</td>
<td>Nonerosive</td>
<td>1 (622)</td>
<td>93% vs 88%*</td>
</tr>
<tr>
<td></td>
<td>Nonerosive or mildly erosive</td>
<td>1 (176)</td>
<td>75% vs 86%†</td>
</tr>
<tr>
<td></td>
<td>Uninvestigated</td>
<td>1 (1292)</td>
<td>52% vs 83%‡</td>
</tr>
<tr>
<td></td>
<td>Erosive</td>
<td>1 (477)</td>
<td>58% vs 81%‡§</td>
</tr>
</tbody>
</table>

*Statistically significant difference in favor of on-demand PPI.
†Outcome is symptom relief.
‡Statistically significant difference in favor of continuous PPI.
§Outcome is endoscopic remission.

Slide courtesy of Thad Wilkins, MD, with permission

3. In discussing the initiation of a patient on a proton pump inhibitor (PPI), which of the following is a potential risk of therapy that should be reviewed with the patient?

A. Long-term PPI use may increase risk for community acquired pneumonia
B. Increased risk of hypermagnesemia
C. Increased risk of Vitamin B$_{12}$ deficiency
D. Increased risk of iron deficiency anemia
3. In discussing the initiation of a patient on a proton pump inhibitor (PPI), which of the following is a potential risk of therapy that should be reviewed with the patient?

A. Long-term PPI use may increase risk for community acquired pneumonia  
35%

B. Increased risk of hypermagnesemia  
4%

C. Increased risk of Vitamin $\text{B}_{12}$ deficiency  
47%

D. Increased risk of iron deficiency anemia  
14%
Potential Risks Associated with PPIs

Patients with known osteoporosis can remain on PPI therapy (SOR: C)

- Increased risk of hypomagnesemia
- Increased risk of vitamin $B_{12}$ deficiency
- Increased risk for *Clostridium difficile* infection

Short-term PPI use may increase risk for community acquired pneumonia (risk is not elevated in long-term PPI users)

PPI therapy does not need to be altered in concomitant clopidogrel (Plavix) users

Am J Gastroenterol 2013; 108:308 – 328
Treatment

• Limited evidence regarding lifestyle measures for GERD
• Weight loss if overweight or obese (SOR: C)
• Elevate head of bed if regurgitation or heartburn when lying down (SOR: C)
• Long-term acid suppression therapy for GERD should be titrated to the lowest effective dose (AGA; Choosing Wisely Campaign)

Gastroenterology 2008 Oct;135(4):1383
Am J Gastroenterol  2013; 108:308–328
Treatment Guidelines

**American College of Gastroenterology – 2005 Volume 135, Issue 4; 1383-1391.e5, October 2008**

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**Step 1**  
*Mild symptoms*  
- Dietary modifications  
- Lifestyle modification (SOR C)  
- Trial of patient-directed therapy with antacids or OTC H2 antagonists

**Step 2**  
*Non-responders*  
*Non-erosive disease*  
- Continue lifestyle/dietary modification.  
- H2 antagonists (SOR A)  
- Proton pump inhibitor (PPI)* (SOR A)  
- Pro-motility agent (SOR A)  
- 8-12 weeks of therapy

**Step 3**  
*Severe symptoms*  
*Erosive disease*  
- Continue with measures.  
- GI workup (+/-) endoscopy  
- High-dose H2 antagonists  
- Higher dose PPI

*PPI should be taken 30-60 minutes prior to a meal (the first meal of the day) to optimize effectiveness (SOR: B).*
4. Risk factors for esophageal intestinal metaplasia (Barrett’s Esophagus) include which one of the following characteristics?

A. Female sex
B. African American race
C. Tobacco
D. Hiatal hernia
4. Risk factors for esophageal intestinal metaplasia (Barrett’s Esophagus) include which one of the following characteristics?

A. Female sex
B. African American race
C. Tobacco
D. Hiatal hernia

- D. Hiatal hernia

15%
Barrett’s Esophagus

- Risk of intestinal metaplasia (Barrett’s) and adenocarcinoma increases with GERD symptom severity, duration, and frequency.
- Endoscopic surveillance for dysplasia is indicated in Barrett’s esophagus – ???
  - Surveillance of known Barrett’s esophagus is controversial, because adenocarcinoma of the esophagus is rare in the US (6000-7000 cases/yr) and GERD/Barrett’s occurs in 0.4%-0.8% of the population
  - Risk of developing esophageal adenocarcinoma in patients with Barrett’s esophagus is less than 1%
AGA Position Statement on Screening for Barrett’s Esophagus 2011

• Whom to screen?
  – Long-standing (> 5 years) heartburn symptoms
  – Long-standing (> 5 years) need for medication
• Recommend against screening the general population
• Support is stronger for screening those patients with multiple risk factors.
Risk Factors for Barrett’s Esophagus

- Men
  - Screening women for Barrett’s is like screening men for breast cancer.
- Caucasian
- Age > 50 years
- Hiatal hernia
- Increasing BMI
- Abdominal fat distribution (abdominal obesity)
2008 ACG Guidelines for Surveillance of Barrett’s Esophagus

EGD

Barrett’s Esophagus

No dysplasia
- Second EGD with biopsies within year to confirm there is no dysplasia
- If both EGDs with biopsies (−) for dysplasia, repeat EGD with biopsy q 3 years.

Low-grade dysplasia (LGD)
- Review by expert pathologist to rule out HGD.
- Repeat EGD with biopsies within 6 months to reassess for dysplasia.
- If (−) for dysplasia on repeat EGD, yearly EGD with biopsy recommended until 2 years with EGDs showing no dysplasia.

High-grade dysplasia (HGD)
- Expert pathologist confirm HGD.
- Mucosal irregularity – remove with endoscopic mucosal resection (EMR).
- EGD with biopsies repeated in 3 months to look for HGD and small cancers.
- Possible interventions for HGD: esophagectomy, EMR, photodynamic therapy, radiofrequency ablation, ablation using cryotherapy.

At the present time, only specialized intestinal metaplasia of the esophagus is classified as Barrett’s esophagus. Currently, it is recommended that only patients with this diagnosis undergo periodic cancer surveillance.
Medical Versus Surgical Treatment

• Medical treatment as effective as surgery (SOR:B)

• Surgery
  • Laparoscopic fundoplication increases quality of life in patients with GERD but many patients still require medication after surgery (SOR: B)

• Endoscopic Procedures
  • May reduce symptoms in patients with GERD
## Summary of GERD Treatment Recommendations

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>SOR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Obtain upper endoscopy in patients with alarm symptoms or those at high risk for complications</td>
<td>B</td>
</tr>
<tr>
<td>Strong evidence supports association of GERD and esophageal adenocarcinoma with Barrett esophagus as precursor lesion</td>
<td>A</td>
</tr>
<tr>
<td>Chronic reflux has been suspected to play a major role in the development of Barrett’s esophagus, yet it is unknown if outcomes can be improved through surveillance and medical treatment</td>
<td>C</td>
</tr>
<tr>
<td>PPIs are more effective for relieving heartburn in short term than H₂RA or prokinetic agents</td>
<td>A</td>
</tr>
<tr>
<td>Different PPIs have similar efficacy at standard doses</td>
<td>A</td>
</tr>
<tr>
<td>Patients with known osteoporosis can remain on PPI therapy</td>
<td>C</td>
</tr>
<tr>
<td><strong>Concomitant use of PPIs and clopidogrel appears safe</strong></td>
<td>B</td>
</tr>
<tr>
<td>If symptoms remain unchanged in a patient with a prior normal EGD, repeating EGD is <strong>not</strong> recommended</td>
<td>C</td>
</tr>
<tr>
<td>Anti-secretory therapy has <strong>not</strong> been shown to reduce the need for recurrent dilation from esophageal stricture formation</td>
<td>A</td>
</tr>
</tbody>
</table>
## Summary of GERD Treatment Recommendations

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>SOR</th>
</tr>
</thead>
<tbody>
<tr>
<td>There are no significant differences among equivalent doses of PPIs for the treatment of nonerosive GERD</td>
<td>A</td>
</tr>
<tr>
<td>Anti-reflux surgery should generally be reserved for patients with contraindications to PPI therapy or when PPI therapy alone is insufficient to control symptoms</td>
<td>C</td>
</tr>
<tr>
<td>Screening for Barrett esophagus is NOT routinely recommended in patients with GERD, but it may be considered in white men 50 years or older who have had GERD symptoms for at least five years</td>
<td>C</td>
</tr>
<tr>
<td>Endoscopy should be limited to patients who have alarm symptoms or persistent GERD symptoms after an adequate trial of PPI therapy</td>
<td>C</td>
</tr>
<tr>
<td>Testing for Helicobacter pylori in patients with GERD is NOT recommended</td>
<td>A</td>
</tr>
</tbody>
</table>

Anderson et. al., Am Fam Physician. 2015;91(10):692-697
## Inflammatory Disorders

### Esophagitis

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Offending “Agents”</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pill-induced</td>
<td>Doxycycline, NSAIDs, steroids</td>
</tr>
<tr>
<td>Infective*</td>
<td>HSV, CMV</td>
</tr>
<tr>
<td>• Viral</td>
<td></td>
</tr>
<tr>
<td>• Fungal</td>
<td>Candida</td>
</tr>
<tr>
<td>Corrosive</td>
<td>Alkalis or acids</td>
</tr>
<tr>
<td>Eosinophilic: <em>pronounced eosinophilic infiltration</em></td>
<td>Allergic or idiopathic; Tx – steroids, diet, anti-allergy medications</td>
</tr>
</tbody>
</table>

*Mostly in immunosuppressed patients*
Esophageal Tumors

• 90% are cancer
  – Much more common in males; 10% 5-yr survival rate overall (treatment improving)
  – Dx – endoscopy and radiography

• Squamous cell carcinoma
  – Most common, declining incidence
  – Predominant esophageal cancer in African Americans
  – More common with heavy alcohol and tobacco use

• Adenocarcinomas
  – Arise from columnar epithelium in cardia or from Barrett’s
  – Recall that the lower esophagus is lined by specialized intestinal epithelium.
  – GERD is a risk factor
Diseases of the Stomach

- Acid Peptic Disorders of the Stomach and Duodenum
  - Infections
  - Motor Disorders
  - Cancer

Diseases of the Stomach
5. A 49 yo female presents with a 4-week history of epigastric pain. She reports the pain gets a bit better when she eats but worse within an hour of eating. She has been using an over-the-counter liquid antacid that she reports decreases her symptoms. She denies weight loss, hematemesis, melena, or hematochezia. With the exception of midepigastric tenderness, her exam is unremarkable. Her only medication is periodic acetaminophen, which she uses for headaches. Which of the following diagnostic tests would you recommend in your evaluation?

A. Serum gastrin
B. *Helicobacter pylori* serology
C. Esophagagogastroduodenoscopy
D. Urea Breath Test
5. A 49 yo female presents with a 4-week history of epigastric pain. She reports the pain gets a bit better when she eats but worse within an hour of eating. She has been using an over-the-counter liquid antacid that she reports decreases her symptoms. She denies weight loss, hematemesis, melena, or hematochezia. With the exception of midepigastric tenderness, her exam is unremarkable. Her only medication is periodic acetaminophen, which she uses for headaches. Which of the following diagnostic tests would you recommend in your evaluation?

A. Serum gastrin
B. Helicobacter pylori serology
C. Esophagogastroduodenoscopy
D. Urea Breath Test

36% ✓ D. Urea Breath Test
Acid Peptic Disorders

Stomach and Duodenum

- Common Problem
  - 5%-10% of population will have PUD in their lifetimes; 50% recurrence in 5 years
  - DU/GU 4:1
    - 90% DU in duodenal bulb
    - GU most common on lesser curve

<table>
<thead>
<tr>
<th>Ulcer Type</th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duodenal Ulcer</td>
<td>1/100,000</td>
<td>0.5/100,000</td>
</tr>
<tr>
<td>Gastric Ulcer</td>
<td>1.5/100,000</td>
<td>1.2/100,000</td>
</tr>
</tbody>
</table>

Mortality Rates
Why Do Acid Peptic Disorders Develop?

• Current theory
  – PUD is an imbalance between protective and aggressive factors.

<table>
<thead>
<tr>
<th>Protective factors</th>
<th>Aggressive factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Surface epithelial cells with mucus and bicarbonate</td>
<td>• Production of gastric acid</td>
</tr>
<tr>
<td>secretions</td>
<td>• NSAIDs</td>
</tr>
<tr>
<td>• Apical surface membrane of gastric mucosal cells</td>
<td>• Corticosteroids</td>
</tr>
<tr>
<td>• Prostaglandins E1 and E2</td>
<td>• Smoking</td>
</tr>
<tr>
<td></td>
<td>• Alcohol consumption</td>
</tr>
<tr>
<td></td>
<td>• ? Psychological stress</td>
</tr>
<tr>
<td></td>
<td>• Probably <em>not</em> diet</td>
</tr>
</tbody>
</table>
Predisposing Factors

- **H. pylori** infection
- NSAIDs
  - Double the annual chance of complicated PUD from 1-2 to 3-4%
  - Worse with alcohol
  - Longer-acting NSAIDs are worse
  - Dose, duration important variables
- Milk: May slow healing of DU
- Caffeine: No clear evidence of worsening
- Peppers: No slowing of DU healing
- Alcohol: Worse with NSAIDs; unclear otherwise
- Tobacco: *Much* higher rates of ulcer *and* slower healing
- Stress: Remains controversial
# PUD and *H. pylori*

<table>
<thead>
<tr>
<th>Disorder</th>
<th><em>H. pylori</em> (+)</th>
<th>Associated <em>H. pylori</em> gastritis</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duodenal ulcer</td>
<td>90%</td>
<td>70%</td>
<td>▪ Eradication of infection markedly decreases recurrences of DU.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>▪ A 1-2 week course of <em>H. pylori</em> eradication therapy is an effective treatment for <em>H. pylori</em> (+) PUD.</td>
</tr>
<tr>
<td>Gastric ulcer</td>
<td>70%</td>
<td>60%-80%</td>
<td></td>
</tr>
</tbody>
</table>
Peptic Ulcer Disease

Diagnosis

• History
  – Persistent pain relieved by food and antacids
    • Pain in upper abdomen or back
    • Hematemesis, melena, or hematochezia
    • Cannot usually separate GU from DU by history

• On exam
  – Mid-epigastric tenderness

• Laboratory
  – Limited usefulness, except *H. pylori* tests
  – Consider serum gastrin (gastrinoma, Zollinger-Ellison; especially if recurrent ulcer disease, multiple ulcers)
  – Hematocrit
  – Stool guaiac

• Endoscopy (SOR: A)
  – 90% sensitivity and specificity
# Diagnostic Tests for *Helicobacter pylori*

<table>
<thead>
<tr>
<th>Test</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Noninvasive</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Urea Breath Test</em></td>
<td>97%</td>
<td>100%</td>
<td>Used for initial diagnosis AND test of cure (4-6 weeks post treatment)</td>
<td>Expensive and inconvenient; 6 hour fast required</td>
</tr>
<tr>
<td><strong>Stool monoclonal antigen tests</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Enzyme immunoassay</td>
<td>92%</td>
<td>94%</td>
<td>Detect active infection; use for test of cure</td>
<td>Expensive</td>
</tr>
<tr>
<td>• Immuno-chromatography</td>
<td>69-87%</td>
<td>87-93%</td>
<td>May be used in office</td>
<td>Varying reliability</td>
</tr>
<tr>
<td><strong>Antibody tests</strong></td>
<td>76-84%</td>
<td>79-80%</td>
<td>Lower cost; easily available</td>
<td>Not useful as test of cure</td>
</tr>
</tbody>
</table>
## Diagnostic Tests for *Helicobacter pylori*

<table>
<thead>
<tr>
<th>Test</th>
<th>Usefulness</th>
<th>Sens (%)</th>
<th>Specif (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Invasive</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Endoscopy with biopsy</td>
<td>Diagnostic strategy of choice in children with persistent or severe upper abdominal symptoms</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Histology</td>
<td>Sensitivity reduced by PPIs, antibiotics, bismuth-containing compounds.</td>
<td>&gt; 95</td>
<td>100</td>
</tr>
<tr>
<td>Urease activity</td>
<td>Test of choice when endoscopy indicated; rapid results (20 min); (−) results <em>may</em> need confirmation by histology or other test; sensitivity reduced by PPIs, antibiotics, bismuth-containing compounds, and active bleeding.</td>
<td>93-97</td>
<td>&gt; 95</td>
</tr>
<tr>
<td>Culture</td>
<td>Technically demanding; only use for resistant organism or refractory disease.</td>
<td>70-80</td>
<td>100</td>
</tr>
</tbody>
</table>
Summary

Diagnostic H. pylori Testing

• In patients who do not require endoscopic evaluation for evaluation of new onset dyspepsia (< age 55 and no alarm symptoms), initial diagnosis of *H. pylori* should be made with a test for active infection (stool antigen or urea breath test).
  o Serology, as it cannot differentiate between past or current infection and has a low positive predictive value in much of the United States, is not recommended in patients with a low pretest probability.

• Endoscopic biopsy reserved for patients who are undergoing a diagnostic endoscopy and are found to have an ulcer and for those who require endoscopy to follow up a gastric ulcer or for the diagnosis or follow-up of suspected MALT lymphoma.
  o Biopsy urease testing can be performed in patients not taking antibiotics or a proton pump inhibitor when histopathology is not required.

• Confirmation of eradication [because of the availability of accurate, relatively inexpensive, noninvasive tests (stool and breath tests) and because of increased resistance to antibiotic therapy,] at least **four weeks after treatment** (Grade 2B)
## Treatment Regimens for *H. pylori* Infection

<table>
<thead>
<tr>
<th>Type</th>
<th>Regimen</th>
<th>Duration</th>
<th>Eradication rate</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>First line</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Standard triple therapy</td>
<td>PPI, amoxicillin 1 g, and clarithromycin 500 mg (Biaxin) twice daily</td>
<td>7-10 days (up to 14 days)</td>
<td>70-85%</td>
</tr>
<tr>
<td></td>
<td>PPI, clarithromycin 500 mg, and metronidazole 500 mg (Flagyl) twice daily</td>
<td>10-14 days</td>
<td>70-85%</td>
</tr>
<tr>
<td>Sequential therapy</td>
<td>PPI and amoxicillin 1 g twice daily, followed by PPI, clarithromycin 500 mg, and tinidazole 500 mg (Tindamax) or metronidazole 500 mg twice daily</td>
<td>10 days (5 days for each regimen)</td>
<td>&gt;84%</td>
</tr>
</tbody>
</table>

## Treatment Regimens for *H. pylori* Infection

<table>
<thead>
<tr>
<th>Type</th>
<th>Regimen</th>
<th>Duration</th>
<th>Eradication rate</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Second line</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-bismuth-based quadruple therapy (concomitant therapy)</td>
<td>PPI, amoxicillin 1 g, clarithromycin 500 mg, and tinidazole 500 mg or metronidazole 500 mg twice daily</td>
<td>10 days</td>
<td>90%</td>
</tr>
<tr>
<td>Bismuth-based quadruple therapy</td>
<td>Bismuth subsalicylate 525 mg or subcitrate 300 mg, metronidazole 250 mg, and tetracycline 500 mg, four times daily; and PPI twice daily</td>
<td>10-14 days</td>
<td>75-90%</td>
</tr>
<tr>
<td>Levofloxacin-based triple therapy</td>
<td>PPI and amoxicillin 1 g twice daily, and levofloxacin 500 mg (Levaquin) once daily</td>
<td>10 days</td>
<td>-----</td>
</tr>
</tbody>
</table>

Specific Ulcer Treatment

**Anti-secretory**

- Anti-secretory therapy
  - Mainstay of therapy in uninfected patients
    - PPI, H$_2$ blocker
  - Appropriate for maintenance therapy in selected cases
  - Usually 4-6 weeks for DU
  - Generally longer for GU – 12 weeks
  - PPIs lead to faster healing than H$_2$ blockers.
Treatment for *H. pylori* Infection

**Summary**

- Most important therapy in affected individuals
- No therapy 100% effective
- Triple or quadruple therapy most effective
- Use of anti-secretory agents with antimicrobials increases eradication rate.
  - Increased gastric pH *increases* efficacy of some antibiotics.
  - PPIs have intrinsic *in vivo* activity against *H. pylori*.
  - Anti-secretory therapy hastens relief of ulcer symptoms.
- Compliance is essential for eradication.
6. In considering NSAID-induced ulcers, which of the following statements is true?

A. Peptic ulcers are less common in patients taking NSAIDs who are *H. pylori* (+) compared with those who are (-)

B. Eradicating *H. pylori* in NSAID users reduces the likelihood of peptic ulcer by about one-half

C. The use of a maintenance PPI is less effective than *H. pylori* eradication therapy for preventing NSAID-related ulcers

D. Patients who will be on long-term NSAID therapy should be empirically treated for *H. pylori*
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D. Patients who will be on long-term NSAID therapy should be empirically treated for *H. pylori*
NSAID Ulcers

- Risk factors
  - Prior adverse GI event (ulcer, hemorrhage)
  - Age > 60 (Older age)
  - High-dose NSAID (> twice normal)
  - Use of
    - Glucocorticoid use
    - Anticoagulant use
    - Aspirin

- Risk for NSAID-induced GI toxicity 9% at 6 months with multiple risk factors present

- In naïve NSAID users, \textit{H. pylori} is significant risk factor for complicated ulcer disease – screening may be indicated.
# Recommendations for Prevention of NSAID-Related Ulcer Complications

<table>
<thead>
<tr>
<th>Cardiovascular Risk</th>
<th>Gastrointestinal Risk</th>
<th>ACG Recommendation (2009)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>Low (No risk factors)</td>
<td>NSAID</td>
</tr>
<tr>
<td></td>
<td>Moderate (1 or 2 risk factors)</td>
<td>NSAID plus PPI or misoprostol</td>
</tr>
<tr>
<td></td>
<td>High (&gt; 2 risk factors)</td>
<td>Alternative therapy IF POSSOBLE, or COX-2 inhibitor plus PPI or misoprostol</td>
</tr>
<tr>
<td>High</td>
<td>Low</td>
<td>Naproxen plus PPI or misoprostol</td>
</tr>
<tr>
<td></td>
<td>Moderate</td>
<td>Naproxen plus PPI or misoprostol</td>
</tr>
<tr>
<td></td>
<td>High</td>
<td>Avoid NSAID and COX-2 inhibitor; alternative therapy</td>
</tr>
</tbody>
</table>

NSAID Users: *Medical Treatment of Peptic Ulcer Practice Guidelines*

- Treatment of NSAID ulcers
  - D/C NSAIDs
  - PPIs superior to H₂ receptor antagonists
- The ACG guideline recommends that patients who will be on long-term NSAID therapy be tested for *H. pylori* infection and eradication therapy given if (+)

*NEJM.* 1998;338:727.


Conclusion

- For patients who have multiple risk factors for NSAID-related gastroduodenal toxicity – FDA approved options include:
  - COX-2 selective inhibitor or
  - Nonselective NSAID in combination with a proton pump inhibitor (PPI) or misoprostol. High dose H$_2$ receptor antagonists are a reasonable alternative to a PPI or misoprostol
    - Approved doses of these drugs: Misoprostol (200 mcg QID), Lansoprazole (15 or 30 mg daily), and esomeprazole (20 or 40 mg daily).
Treatment
Non-\textit{H. pylori} PUD

- Withdrawal of potential offending or contributing agents
  - NSAIDs, cigarettes, excess ETOH
- No firm dietary recommendations – avoid foods that precipitate dyspepsia.
- Address psychosocial issues and comorbidities – no firm evidence, but \textit{may} have deleterious health consequences.
Controversy: *Treatment of H. pylori in Non-ulcer Dyspepsia*

- Efficacy of treatment is controversial.
- Recent review of RCTs: Eradication provides small but significant benefit for dyspeptic symptoms.*
- Eradication may be cost-effective intervention for non-ulcer dyspepsia.
- *And … H. pylori* appears to have a net suppressive effect on acid production, so treating may make GERD worse.

An Approach to Dyspepsia

55 years old
No alarm features

H. Pylori prevalence < 10%

Trial of PPI

Fails

Test and treat for H. pylori.

Fails

Consider upper endoscopy.

H. pylori prevalence ≥ 10%

Test and treat for H. pylori.

Fails

Trial of PPI

Fails

Consider upper Endoscopy.

> 55 years old or presence of alarm symptoms, family or personal Hx GI CA or PUD, wt. loss, GI bleeding, anemia, or dysphagia

Upper endoscopy
Risk Factors for Ulcer Complications

• Previous history of complications
• Prior refractory or protracted course
• Big ulcers (> 2 cm)
• Deformed ulcer bed or dense fibrosis
Complications of PUD

• **Bleeding**
  – Most common complication and leading cause of death (4%-9% mortality rate)
  – Occurs in 10%-20%
  – Patients with 1 episode of bleeding more likely to re-bleed
  – 90% stop without specific treatment.
  – Increased morbidity with associated portal hypertension*

* Am J Gastro 1998;93:336
Complications of PUD

- **Gastric outlet obstruction**
  - Usually mechanical obstruction due to edema or scar
  - Most due to DU
  - Rare: 2% of ulcer patients

- **Perforation and penetration**
  - 2% of ulcers perforate.
  - Average duration of Sx prior to perforation: 5 years

- **NOTE:** Complicated ulcer disease less likely to involve *H. pylori*
PUD

*Surgical Treatment/Management*

- Dramatically declined over past two decades
- Indications
  - Hemorrhage not responsive to medical therapy
  - Gastric outlet obstruction not reversed by medical treatment
  - Perforation
  - Malignancy
### Clinical Recommendation

<table>
<thead>
<tr>
<th>Clinical Recommendation</th>
<th>Evidence Rating</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>A “test-and-treat” strategy is recommended in patients with symptoms of dyspepsia.</td>
<td>A</td>
<td>Test-and-treat strategy reduces endoscopies and use of anti-secretory medications.</td>
</tr>
<tr>
<td><em>Helicobacter pylori</em> eradication therapy is recommended to prevent recurrence and re-bleeding in patients with peptic ulcer.</td>
<td>A</td>
<td>It is unnecessary to continue anti-secretory maintenance therapy in patients after <em>H. pylori</em> eradication.</td>
</tr>
<tr>
<td>Short-course drug therapy is an option for <em>H. pylori</em> eradication in adult patients.</td>
<td>C</td>
<td>Eradication rates using short-course therapy are similar to those of traditional treatment with the potential for greater compliance.</td>
</tr>
<tr>
<td>The urea breath test is the most reliable noninvasive diagnostic test in children with suspected <em>H. pylori</em> infection.</td>
<td>C</td>
<td>Urea breath test is more reliable in children older than six years; monoclonal antibody–based stool antigen is an alternative.</td>
</tr>
<tr>
<td>Clinical Recommendation</td>
<td>Evidence Rating</td>
<td></td>
</tr>
<tr>
<td>--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
<td>-----------------</td>
<td></td>
</tr>
<tr>
<td>Use the test-and-treat strategy for patients with dyspepsia who are &lt;55 years and have no alarm symptoms for gastric cancer. Use endoscopy for all other patients.</td>
<td>A</td>
<td></td>
</tr>
<tr>
<td>Confirm eradication of <em>H. pylori</em> after therapy in patients with <em>H. pylori</em>-associated ulcer, continued dyspeptic symptoms, mucosa-associated lymphoid tissue lymphoma, and resection of gastric cancer.</td>
<td>C</td>
<td></td>
</tr>
<tr>
<td>Non–bismuth-based quadruple therapy (10 days of a proton pump inhibitor, amoxicillin 1 g, clarithromycin 500 mg [Biaxin], and metronidazole 500 mg [Flagyl] or tinidazole 500 mg [Tindamax] twice daily) has the highest success rate in eradicating <em>H. pylori</em>, although other regimens may also be used.</td>
<td>A</td>
<td></td>
</tr>
<tr>
<td>For patients at low risk of gastrointestinal complications, nonsteroidal anti-inflammatory drugs may be used, whereas cotherapy with a proton pump inhibitor or misoprostol (Cytotec) is recommended for patients with moderate risk of ulcer, and they should be avoided in those with a high risk of ulcer.</td>
<td>C</td>
<td></td>
</tr>
</tbody>
</table>
Gastric Dysmotility
Gastric Dysmotility
Slow or Delayed Emptying

• Etiology
  – Mechanical or outlet obstruction
    • PUD, bezoar, etc.
  – Functional obstruction (gastroparesis)
    • Drugs – opiates, anticholinergics, beta and Ca channel blockers
    • Diabetes, Parkinson’s, hypothyroidism, hypoparathyroidism
    • Pregnancy
    • Post-vagotomy

Trichobezoar being extracted through a gastrotomy
Gastric Dysmotility

Slow or Delayed Emptying

• Diagnosis
  – Nausea, vomiting, dysphagia, post-prandial abdominal pain, GERD
  – Tests: Scintigraphy, electrogastrogram (evaluate gastric myoelectrical utility), ultrasonography

• Treatment
  – Remove causes
  – Low-fat diet; avoid large meals
  – Metoclopramide, erythromycin, prokinetics
Gastric Dysmotility

Rapid Gastric Emptying

• Dumping Syndrome
  – Most commonly seen post-operatively from gastric surgery or a truncal vagotomy

• Symptoms
  – 15-30 minutes after eating – nausea, non-productive vomiting, sweating, flushing, abdominal cramping, diarrhea

• Treatment
  – 6-8 small, low-CHO meals/day; avoid excessive liquids; use of opiates and anticholinergic drugs; fiber products; possibly surgery
7. A 65-yr male smoker complains of dyspepsia, weight loss, early satiety, and occasional nausea and vomiting. *Which one of the following would be the initial diagnostic method of choice?*

A. Upper GI endoscopy  
B. CT of the upper abdomen  
C. Single-contrast upper GI barium swallow  
D. Endoscopic ultrasonography
7. A 65-yo male smoker complains of dyspepsia, weight loss, early satiety, and occasional nausea and vomiting. Which one of the following would be the initial diagnostic method of choice?

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B. CT of the upper abdomen  
C. Single-contrast upper GI barium swallow  
D. Endoscopic ultrasonography

71% ✓ A. Upper GI endoscopy  
14% B. CT of the upper abdomen  
12% C. Single-contrast upper GI barium swallow  
3% D. Endoscopic ultrasonography
Cancer of the Stomach

• One of the most common internal malignancies in the world
  – 95% are adenocarcinomas.
    • Chronic GERD is the leading cause of esophageal adenocarcinoma (68%-90%).
  – Only 10%-20% of US GI tumors – probably because of lower rates of *H. pylori* in US, due to cleaner food and water
    • *H. pylori* can cause chronic active gastritis and atrophic gastritis, early steps in the carcinogenesis sequence
    • 2x as common in ♂ as in ♀
    • 2x as common in African Americans and Hispanics as in Caucasians
• Dx: Endoscopic biopsy in patients with upper GI symptoms or high-risk or double-contrast barium swallow
• Tx: Surgical excision; 5-yr survival rate ≤ 10%
Pancreatic Cancer

• Fourth leading cause of cancer-related death; second only to CRC as cause of GI cancer-related death
  – Higher incidence: ♂ and African Americans
  – Risk factors: Smoking, chronic pancreatitis, diabetes, hereditary predisposition

• History/PE
  – Abd pain, weight loss, jaundice, pancreatitis
  – Jaundice, abdominal mass, ascites
Pancreatic Cancer

• Diagnosis
  – U/S, EUS CT, MRI ERCP, FNA, CA19-9
  – All sensitive and specific

• Treatment
  – Surgical resection only potential curable treatment

• Prognosis – 5-year survival
  – Node (−) 25%-30%
  – Node (+) 10%
Thank you!
Answers

1. C
2. B
3. C
4. D
5. D
6. B
7. A
Supplementary Slides
GERD: Incidence and Prevalence

- Peak prevalence at ages 30-60 years, more common in women
- Prevalence 10-20% in the Western world (lower prevalence in Asia)
- Most common GI-related diagnosis in the U.S.
- 14% of U.S. population has frequent GERD symptoms

Arch Intern Med 2001 Jan 8;161(1):45
Am J Gastroenterol 2006 Sep;101(9):2128
Am J Gastroenterol 2013; 108:308 – 328
*H. pylori* Resistance

- Metronidazole: 22%-39%
- Clarithromycin: 11%
- Amoxicillin, tetracycline: Rare
- Bismuth: None