ULCER DISEASE

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OUTLINE

- Epidemiology
- Risk factors
- Pathogenesis
- Other causes
- Clinical features
- Diagnosis
- Complications
- Treatment
INTRODUCTION - DEFINITIONS

- Ulcer
  - A break in the lining of the mucosa
  - Appreciable depth at endoscopy
  - Involvement of the submucosa by histology

- Erosions
  - Breaks in the surface epithelium w/o depth

- Peptic ulcer disease
  - Erosions and ulcers in the stomach & duodenum
EPIDEMIOLOGY

- In 2004, 700,000 ambulatory care visits
- Total cost $3.1 billion
  - Direct, $2.6 billion
  - Indirect, $0.5 billion
- 9th most costly GI disease/condition

Peptic Ulcer Disease: Age-Adjusted Rates of Ambulatory Care Visits and Hospital Discharges With All-Listed Diagnoses in the US, 1979–2004

RISK FACTORS

None known

ZES, other

NSAID use

H. pylori infection

Duodenal

None known

ZES, other

NSAID use

H. pylori infection

Gastric

**RISK FACTORS – *H. pylori***

- *Helicobacter pylori* (*H. pylori*)
  - Gram-negative bacillus
  - Resides in the stomach
  - Usually acquired in childhood
  - Oral-oral transmission
  - Associated with lower socioeconomic status and crowding
DIAGNOSIS OF *H. pylori*

- Non-invasive
  - Serology
  - Stool antigen
  - Urea breath test
- Invasive
  - Rapid urease test
  - Histology
  - Culture
RISK FACTORS – ASA AND NSAIDS

- Aspirin (ASA)
  - increasingly used in the prevention and treatment of cardiovascular disease

- Non-steroidal anti-inflammatory drugs (NSAIDs)
  - used regularly by 11% of US population

NEJM
**Risk of Uncomplicated PUD**

H. pylori  | NSAIDs  | H. Pylori + NSAIDs
---|---|---
2.2 | 3.1 | 17.5

RISK OF NSAID INDUCED ULCERS

Low Risk
No risk factors

Moderate Risk
- Age > 65
- High dose NSAIDs
- Prior h/o uncomplicated ulcer
- Concurrent use of ASA, steroids or anticoagulants

High Risk
- History of complicated ulcer disease
- Multiple (>2) risk factors

1-2 Risk factors

**Risk Factors**

- Other ulcerogenic drugs
  - Cocaine, methamphetamine
  - Bisphosphonates
  - Glucocorticoids in combination with NSAIDs

- Other risk factors
  - Smoking
  - Alcohol – uncertain
  - Spicy foods – if there is an association, it’s weak
  - Stress – increase rates after natural calamities
**PATHOGENESIS**

**ULCEROGENIC FACTORS**
- Gastric acid
- Pepsin
- *H. pylori*
- ASA
- NSAIDs
- Smoking

**PROTECTIVE FACTORS**
- Epithelium
- Bicarbonate
- Alkaline tide
- Blood flow
- Prostaglandins
OTHER CAUSES OF ULCERS

- Gastrin-secreting tumors (Zollinger-Ellison syndrome)
  - Multiple gastroduodenal ulcers, diarrhea
  - 25% have Multiple Endocrine Neoplasia (MEN) Type 1
    - Pancreatic endocrine tumors, Hyperparathyroidism, and Pituitary adenomas
- Systemic mastocytosis
- Crohn’s disease
CLINICAL FEATURES

- Burning epigastric pain relieved by antacids
- Presence of risk factors
- Alarm features: age > 55, anemia, jaundice, lymphadenopathy, mass, vomiting and weight loss
- Physical exam is usually normal
  - Epigastric tenderness
- Laboratory studies
**DIAGNOSIS**

- History by specialist\(^1\):
  - Sensitivity 37-65%
  - Specificity 37-84%
  - Positive LR 2.9 (95% CI, 2.1-4.0)
- Contrast radiography
- Endoscopy\(^2\)
  - 5-15\% of pts with dyspepsia have PUD

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COMPLICATIONS

- Hemorrhage
- Perforation
- Penetration
- Obstruction
- Death
  - 80% occurred in pts ≥ 65 years old
Peptic Ulcer Disease: Age-Adjusted Rates of Death in the US, 1979–2004

MORTALITY

TREATMENT

- Assess for *H. pylori* infection
- Avoid ulcerogenic medications if possible
- Acid neutralizing/antisecretory therapy
  - Antacids
  - Histamine-2 receptor antagonists (H2RAs)
  - Proton pump inhibitors (PPIs)
- Mucosa-protective agents
  - Sucralfate, bismuth and misoprostol
TREATMENT – DUODENAL ULCER

- *H. pylori* associated
  - Course of anti-*H. pylori* regimen
  - Confirm eradication if complicated ulcer
- Long term PPI maintenance co-therapy in select patients
  - Dual antiplatelet therapy
  - NSAIDs
  - Anticoagulants
TREATMENT – GASTRIC ULCER

- *H. pylori* associated
  - Course of anti-*H. pylori* regimen
- For large (>1.5 cm) or complicated ulcers:
  - Additional antisecretory therapy to promote healing
  - Follow up EGD to:
    - Document ulcer healing
    - Exclude malignancy
    - Confirm *H. pylori* eradication
- Long term PPI maintenance co-therapy in select patients
# Treatment of *H. pylori*

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosing</th>
<th>Duration (d)</th>
<th>Eradication Rates</th>
</tr>
</thead>
<tbody>
<tr>
<td>PPI, Clarithromycin, Amoxicillin</td>
<td>Standard dose BID, 500 mg BID, 1000 mg BID</td>
<td>10-14</td>
<td>70-85%</td>
</tr>
<tr>
<td>PPI, Clarithromycin, Metronidazole</td>
<td>Standard dose BID, 500 mg BID, 500 mg BID</td>
<td>10-14</td>
<td>70-85%</td>
</tr>
<tr>
<td>Bismuth subsalicylate, Metronidazole, Tetracycline, AND Ranitidine OR PPI</td>
<td>525 mg QID, 250 mg QID, 500 mg QID, 150 mg BID, Standard dose, QD-BID</td>
<td>10-14</td>
<td>75-90%</td>
</tr>
<tr>
<td>PPI, Amoxicillin; THEN PPI, Clarithromycin Tinidazole</td>
<td>Standard dose BID, 1000 mg BID, Standard dose BID, 500 mg BID, 500 mg BID</td>
<td>5</td>
<td>&gt;90%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>5</td>
<td></td>
</tr>
</tbody>
</table>
# Treatment

## Peptic Ulcer Disease: Costliest Prescriptions 2008

<table>
<thead>
<tr>
<th>DRUG</th>
<th>Prescription (#)</th>
<th>Prescription</th>
<th>Retail Cost</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lansoprazole</td>
<td>1,341,444</td>
<td>26.7%</td>
<td>$177,496,893</td>
<td>34.2%</td>
</tr>
<tr>
<td>Pantoprazole</td>
<td>1,128,002</td>
<td>22.5%</td>
<td>123,697,885</td>
<td>23.9%</td>
</tr>
<tr>
<td>Esomeprazole</td>
<td>680,009</td>
<td>13.6%</td>
<td>85,753,825</td>
<td>16.5%</td>
</tr>
<tr>
<td>Lansoprazole/Amoxicillin/Clarithromycin</td>
<td>130,482</td>
<td>2.6%</td>
<td>40,749,140</td>
<td>7.9%</td>
</tr>
<tr>
<td>Omeprazole</td>
<td>333,879</td>
<td>6.7%</td>
<td>30,663,736</td>
<td>5.9%</td>
</tr>
<tr>
<td>Rabeprazole</td>
<td>204,602</td>
<td>4.1%</td>
<td>27,175,479</td>
<td>5.2%</td>
</tr>
<tr>
<td>Ranitidine</td>
<td>727,492</td>
<td>14.5%</td>
<td>13,039,236</td>
<td>2.5%</td>
</tr>
<tr>
<td>Nizatidine</td>
<td>89,340</td>
<td>1.8%</td>
<td>9,185,345</td>
<td>1.8%</td>
</tr>
<tr>
<td>Sucralfate</td>
<td>157,770</td>
<td>3.1%</td>
<td>5,342,588</td>
<td>1.0%</td>
</tr>
<tr>
<td>Famotidine</td>
<td>135,865</td>
<td>2.7%</td>
<td>3,072,170</td>
<td>0.6%</td>
</tr>
<tr>
<td>Other</td>
<td>89,023</td>
<td>1.8%</td>
<td>2,394,483</td>
<td>0.4%</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td><strong>5,017,908</strong></td>
<td><strong>100.0%</strong></td>
<td><strong>$518,570,780</strong></td>
<td><strong>100.0%</strong></td>
</tr>
</tbody>
</table>

**SOURCE:** Verispan
NON-HEALING ULCER

- Ongoing ASA/NSAID use
- Refractory *H. pylori* infection
- Smoking
- Other causes
  - Zollinger-Ellison syndrome (gastrinoma)
  - Crohn’s
  - Malignancy
CONCLUSIONS – ULCER DISEASE

- Common condition
- Significant cost
- Decline in incidence and mortality
- Etiology
  - *H. pylori*
  - ASA/NSAIDs
- Endoscopy
- PPIs and *H. pylori* eradication when present