Learning Objectives

• Identify general causes of upper abdominal pain
• Describe common presenting symptoms of pyloric stenosis
• Differentiate between causes of acute and chronic gastritis
• Identify the causes of peptic ulcer disease
• Describe H pylori and its mechanisms of virulence and the treatment
• Categorize the different gastric neoplasms
Pyloric Stenosis

- Congenital hypertrophy of smooth muscle of pylorus
- More common in males
- Causes projectile vomiting in first 2-6 weeks of life
- Visible peristalsis
- Olive-like mass in abdomen

Anatomy of the Stomach

- pH is 1.0
- Acidity aids in digestion
- Protection of itself
  - Mucin secretion by foveolar cells
  - Bicarbonate secretion by surface epithelium
  - Vascular supply

Upper Abdominal Pain

- Gastritis
- Peptic Ulcer Disease
- Gastroesophageal reflux disease (GERD)
- Biliary colic
- Irritable bowel syndrome
- Pancreatitis
Upper Abdominal Pain

- Gastritis
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Gastritis

- Nausea
- Epigastric pain
- Vomiting
- Hematemesis

Pathophysiology of Gastritis
Stress Related Gastric Injury

Predominantly due to local ischemia in patients with critical illness/injury

Three examples include

Stress ulcers in patients with shock, sepsis or severe trauma
Curling ulcers located in proximal duodenum, seen in patients with severe burns or trauma
Cushing ulcers located in stomach, duodenum or esophagus, seen in patients with intracranial disease

Gastritis

Acute Gastritis
• Transient process
• Nausea, vomiting, epigastric pain
• Superficial, erosive, ulcerative
• Severe cases may have hemorrhage
• Impairment of protective system: NSAIDs, ingestion, direct injury

Chronic Gastritis
• Similar symptoms as acute, hematemesis uncommon
• Symptoms less severe but more persistent
• Most common cause is *Helicobacter pylori* infection
• Other causes
  – Autoimmune (<10%)
  – Radiation injury
  – Chronic bile reflux

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Acute Gastritis

Ulcer on endoscopy

Histologic picture of a stomach ulcer

Treating Acute Gastritis

- Prevention by prescribing "stress ulcer prophylaxis" with PPI or H2 blockers (Stress related gastric injury)
- Targeted patients
  - Mechanical ventilation
  - Severe burns
  - Trauma
  - Severe sepsis
  - Intracranial injury
  - Coagulopathy
- Treatment with acid blocking agents
- Treating underlying condition
Gastritis

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  – Radiation injury
  – Chronic bile reflux
  – Mechanical injury

Chronic Gastritis: *H pylori*

*Helicobacter pylori*

• Increased risk of infection/colonization
  – Poverty
  – Living in rural areas
  – Household crowding
  – Limited education
  – African American or Mexican American
  – Poor sanitation
  – Birth outside of US

• Four modes of virulence
  – Flagella
  – Secretion of urease
  – Adhesins
  – Toxins

• Antrum most common
• Increased risk of gastric adenocarcinoma due to intestinal metaplasia (see slide 21 for picture)

MALT (mucosa-associated lymphoid tissue)

Lymphoid aggregates seen in field
Bluestain subepithelial plasma cells
Pathogenesis of H pylori Infection

Helicobacter pylori

**Diagnosis**
- Biopsy
- Serologic testing for H pylori antibodies
- Fecal detection
- Urea breath test

**Treatment**
- Proton pump inhibitors + antibiotics
- Triple therapy 10-14 days
  - PPI BID
  - Amoxicillin 1gm BID
  - Clarithromycin 500mg BID
- Quadruiple therapy 10-14 days
  - PPI BID
  - Bismuth preparation 4 x daily
  - Tetracycline 500mg 4 x daily
  - Metronidazole 250mg 4 x daily
- Sequential therapy
- Second line therapy if fail first course

Chronic Gastritis: Autoimmune

- SPARES the antrum
- Antibodies to parietal cells and intrinsic factor (IF)
- Vitamin B12 deficiency due to loss of IF→pernicious anemia
- Pepsinogen I levels due to loss of chief cells
- Impaired gastric acid secretion
  (achlorhydria)
- Median age 60 years
- Slight female > male
- Can be associated with other autoimmune diseases
- Risk gastric adenocarcinoma due to intestinal metaplasia
Review of IF and Parietal Cells

Question

- 63-year-old female with anemia and peripheral neuropathy undergoes upper endoscopy. Biopsy shows chronic gastritis of the fundus with flattened mucosa and no ulceration. Which of the following is most likely to be associated with this finding?
  A. Hyperchlorhydria
  B. Infection with H. pylori
  C. Diet high in nitrates
  D. Low gastrin levels
  E. Antibodies to parietal cells
Question

- 65-year-old female with anemia and peripheral neuropathy undergoes upper endoscopy. Biopsy shows chronic gastritis of the fundus with atrophied mucosa and no ulceration. Which of the following is most likely to be associated with this finding?
  A. Hyperchlorhydria
  B. Infection with H. pylori
  C. Diet high in nitrates
  D. Low gastrin levels
  E. Antibodies to parietal cells

Peptic Ulcer Disease

A Case

- 52y male with history of HTN, HL
- Reports burning epigastric pain
- Occurs 1-3 hours after meals
- Worse at night
- Improves with calcium carbonate
Epidemiologic Data

8.4% subjects in National Health Interview Survey reported history PUD (1997-2003)

Annual incidence 0.10% to 0.19%

Risk Factors for PUD

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Factors predicting risk for peptic ulcer disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Factors</td>
<td>Odds ratio</td>
</tr>
<tr>
<td>Peptic ulcer disease</td>
<td>3.1</td>
</tr>
<tr>
<td>Nonsteroidal anti-inflammatory drugs</td>
<td>2.2</td>
</tr>
<tr>
<td>H. pylori infection</td>
<td>2.0</td>
</tr>
<tr>
<td>Stress and neuroticism</td>
<td>1.7</td>
</tr>
<tr>
<td>Surgery and trauma</td>
<td>1.5</td>
</tr>
<tr>
<td>Hormone replacement therapy</td>
<td>1.4</td>
</tr>
<tr>
<td>Female gender</td>
<td>1.3</td>
</tr>
<tr>
<td>Alcohol intake</td>
<td>1.1</td>
</tr>
<tr>
<td>Smoking</td>
<td>1.1</td>
</tr>
</tbody>
</table>

Peptic Ulcer Disease

- Epigastric burning or aching pain occurring 1-3 hours after eating, worse at night, relieved by alkali or food
- May also having nausea, bloating, belching
- Most often due to H pylori or NSAIDs
- Most common in proximal duodenum and antrum (4:1)
- Solitary in 80% of cases
- Ulcer is a sharply punched out defect, clean base
- Perforation is severe complication
Symptoms of PUD by Anatomic Location

- Food decreases pain with Duodenal ulcers
- Pain becomes greater with Gastric ulcers

Peptic Ulcer Disease: Treatment

- Eradication of *H pylori* if present
- Removal of offending agent
- Surgery may be needed for bleeding or perforation

Question

- 40-year-old female with obesity and diabetes mellitus presents to her doctor with 2 months of intermittent RUQ abdominal pain associated with food, most notably after eating fatty foods. What is the most likely diagnosis?
  A. Biliary colic from gallstones
  B. Acute gastritis
  C. Gastroesophageal reflux disease (GERD)
  D. Autoimmune gastritis
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Let’s take a break...
Neoplasms

Gastric polyps

- Nodule or mass that projects above the level of the surrounding mucosa
- Due to hyperplasia, inflammation, ectopia, neoplasia

Gastric adenocarcinoma

Lymphoma

Carcinoid tumor

GIST

Polyp

• Nodule or mass that projects above the level of the surrounding mucosa

<table>
<thead>
<tr>
<th>Type of Polyp</th>
<th>Inflammatory and hyperplastic</th>
<th>Fundic gland polyp</th>
<th>Gastric adenoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Percentage of polyps</td>
<td>75%</td>
<td>Portion of remainder</td>
<td>50%</td>
</tr>
<tr>
<td>Peak age range</td>
<td>50-60 years</td>
<td>Any age</td>
<td>50-60 years</td>
</tr>
<tr>
<td>Gender distribution</td>
<td>Male:female</td>
<td>Male:female</td>
<td>Male:female 3:1</td>
</tr>
<tr>
<td>Neoplastic potential</td>
<td>Risk higher when &gt;1.5 cm</td>
<td>Not neoplastic</td>
<td>Risk higher when &gt;2cm</td>
</tr>
<tr>
<td>Related to chronic gastritis</td>
<td>Yes</td>
<td>Not necessarily</td>
<td>Yes</td>
</tr>
<tr>
<td>Location in stomach</td>
<td>Any</td>
<td>Body and fundus</td>
<td>Antrum</td>
</tr>
<tr>
<td>Gross pathology</td>
<td>Multiple, ovoid in shape, &lt;1cm</td>
<td>Well-circumscribed and multiple</td>
<td>Not noted</td>
</tr>
<tr>
<td>Histology</td>
<td>Irregular, cystically dilated and elongated tubular glands; lamina propria edematous</td>
<td>Cystically dilated, irregular glands lined by flattened parietal and chief cells</td>
<td>Intestinal-type epithelium with variable degrees of dysplasia</td>
</tr>
<tr>
<td>Other facts</td>
<td>If due to H pylori can regress after tx</td>
<td>Sporadic or associated with familial adenomatous polyposis (FAP)</td>
<td>Carcinoma can be present in up to 30% of adenomas</td>
</tr>
</tbody>
</table>
Lymphoma

- Extranodal lymphomas occur most commonly in GI tract, especially stomach
- Mucosa-associated lymphoid tissue (MALT)
  - Marginal zone B cell lymphomas

Carcinoid Tumor

- Arise from neuroendocrine organs
  - GI cells in stomach
- 40% occur in small intestine
- Intramural or submucosal masses, yellow or tan color
- Location determines prognosis: foregut, midgut (most aggressive), hindgut
- Peak incidence 6th decade
- Symptoms determined by hormones produced

GIST: Gastrointestinal stromal tumor

- Mesenchymal neoplasm of interstitial cells of Cajal
- Pancreatic cells of gut peristalsis
- Arises in stomach
- Solitary, well-circumscribed, flushy submucosal mass
- Males > females
- Peak incidence age 60
- 75-80% have gain-of-function mutation of tyrosine kinase c-KIT
- Symptoms related to mass effect or mucosal ulceration
Treatment of GIST

- Surgical resection if possible
- Imatinib is a drug that inhibits tyrosine kinase activity of 
  KIT and PDGFRα
- Resistance to imatinib is an issue

Gastric Adenocarcinoma: Worldwide

Gastric Adenocarcinoma: U.S.
Gastric Adenocarcinoma

**Early symptoms:** nausea, dyspepsia, dysphagia

**Diagnosed at later stages in US:** weight loss, anorexia, changes in bowel habits, anemia, hemorrhage

**Diagnosis:**
- Endoscopic ultrasound
- CT scan, MRI, and PET scan
- Biopsy

**Risk factors:**
- Low socioeconomic status
- Diet high in smoked or salted foods and low in fruits and vegetables
- H. pylori infection
- Gastric atrophy
- Blood type A
Gastric Adenocarcinoma

- *H. pylori* infection
- Epstein Barr Virus
- Chronic gastritis, proinflammatory proteins
- 10% of cases; unclear mechanism
- Proximal stomach, marked lymphocytic infiltrate
- Germline mutations of CDH1 causing loss of E-cadherin function (diffuse-type)
- Familial adenomatous polyposis coli, mutations in APC gene (intestinal-type)

Lauren classification
- Intestinal: bulky, have glandular structures, exophytic mass or ulcerated tumor
  - Mean age 55, Male:Female 2:1
  - Incidence higher in high-risk areas
- Diffuse: infiltrative growth, discohesive cells with large mucin vacuoles\*Signet ring cells
  - Linitis plastica caused by desmoplastic reaction
  - Incidence the same regardless of geography
  - Male:Female
- Prognosis based on extent of nodal involvement and whether metastases present at diagnosis
- Tx: surgical resection when possible; chemo minimally effective

Linitis plastica
Signet ring cells

*\*Signet ring cell
Metastatic Gastric Adenocarcinoma

- Left supraclavicular node: Virchow node
- Distant metastases often liver
- Periumbilical region: Sister Mary Joseph nodule (intestinal type)
- Bilateral ovaries: Krukenberg tumor (diffuse type)

www.clinicalcorrelations.org
NEJM 2013;368:e7
Arch Pathol Lab Med. 2006;130:1725–1730.

A Case

- 52y male with history of HTN, HL
- Reports burning epigastric pain
- Occurs 1-3 hours after meals
- Worse at night
- Improves with calcium carbonate

www.surgicaldiary.com

Alarm symptoms:
- Blood in stool
- Vomiting
- Anorexia
- Weight loss
- Signs of perforation

Question

- 56y female presents with abdominal fullness, nausea and weight loss worsening over 2 months. CT abdomen/pelvis shows thickening of her stomach and bilateral ovarian masses.
- What would be expected on the ovarian biopsies?
  A. Squamous cell cancer
  B. Mucinous adenocarcinoma
  C. Signet ring cells
  D. Leiomyosarcoma
19

**Question**

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**Take Home Points**

- Gastritis is the result of impaired host defenses against acid exposure or direct injury
- Most common cause of peptic ulcer disease is *H pylori* infection
- Autoimmune gastritis is due to antibodies to parietal cells and intrinsic factor, causes pernicious anemia
- Gastric adenocarcinoma is usually diagnosed at later stages and is caused by mutations, *H pylori* infection and less commonly EBV
Thank you
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