Diseases of stomach 1
Gastropathy and Acute Gastritis

- **Gastritis:** is a mucosal inflammatory process.
- When neutrophils are present, the lesion is referred to as **acute gastritis**.
- When inflammatory cells are rare or absent, the term **gastropathy** is applied; marked by gastric injury or dysfunction
• Pathogenesis:
- The gastric lumen has a pH of close to 1, this harsh environment contributes to digestion but also has the potential to damage the gastric mucosa.
Multiple mechanisms have evolved to protect the gastric mucosa:

- **Mucin** and **phospholipids** secreted by surface foveolar cells.
- **bicarbonate ion** secretion by surface epithelial cells.
- a continuous layer of **gastric epithelial cells** forms a physical barrier.

Complete replacement of the surface foveolar cells every **3 to 7 days** is essential for both the maintenance of the epithelial layer and the secretion of mucus and bicarbonate from these cells.
• Gastropathy, acute gastritis, and chronic gastritis can occur following disruption of any of these protective mechanisms
- **NSAIDs**: inhibit COX dependent synthesis of PG E2 and I2, Although COX-1 plays a larger role than COX-2, both isoenzymes contribute to mucosal protection.

- **uremic patients** and those infected with **urease secreting H. pylori**: may be due to inhibition of gastric bicarbonate transporters by ammonium ions.

- **older adults**: Reduced mucin and bicarbonate secretion
- high altitudes: Decreased oxygen delivery

- Ingestion of harsh chemicals (acids or bases), excessive alcohol consumption, NSAIDs, bile reflux, radiation therapy, chemotherapy: direct cellular damage.

- chemotherapy: inhibit DNA synthesis or the mitotic apparatus----- insufficient epithelial renewal.
Stress-Related Mucosal Disease

- **Stress ulcers:** are most common in individuals with shock, sepsis, or severe trauma.
- **Curling ulcers:** Ulcers occurring in the proximal duodenum and associated with severe burns or trauma.
- **Cushing ulcers:** Gastric, duodenal, and esophageal ulcers arising in persons with intracranial disease.

Pathogenesis:

*Local ischemia* due to systemic hypotension or reduced blood flow caused by **stress-induced splanchnic vasoconstriction**.

Cushing ulcers Thought to be caused by **direct stimulation of vagal nuclei**, which causes hypersecretion of gastric acid.
• Unlike peptic ulcers, which arise in the setting of chronic injury, acute stress ulcers are found anywhere in the stomach and are most often multiple.
Figure 17-11 Mechanisms of gastric injury and protection. This diagram illustrates the progression from more mild forms of injury to ulceration that may occur with acute or chronic gastritis. Ulcers include layers of necrosis (N), inflammation (I), and granulation tissue (G), but a fibrotic scar (S), which takes time to develop, is only present in chronic lesions.
• Both gastropathy and acute gastritis may be asymptomatic or cause variable degrees of epigastric pain, nausea, and vomiting.
• In more severe cases there may be mucosal erosion, ulceration, hemorrhage hematemesis, melena, or, rarely, massive blood loss.
Chronic Gastritis

• The most common cause of chronic gastritis is infection with the bacillus H. pylori.

• **Autoimmune** gastritis, the most common cause of diffuse atrophic gastritis, represents less than 10% of cases of chronic gastritis, but is the most common form of chronic gastritis in patients without H. pylori infection.

• Less common causes of chronic gastritis include:
  - radiation injury,
  - chronic bile reflux,
  - mechanical injury (e.g. an indwelling nasogastric tube),
  - involvement by systemic diseases, such as Crohn disease, amyloidosis, or graft-versus-host disease.
Helicobacter pylori Gastritis

• H. pylori present in gastric biopsy specimens of almost all patients with duodenal ulcers as well as most individuals with gastric ulcers or chronic gastritis.

• H. pylori organisms are present in 90% of individuals with chronic gastritis affecting the antrum.
Pathogenesis:

- H. pylori infection most often presents as a predominantly antral gastritis with normal or increased acid production.
- When inflammation remains limited to the antrum, increased acid production results in greater risk of duodenal peptic ulcer.

- Gastritis may progress to involve the gastric body and fundus. This multifocal atrophic gastritis is associated with patchy mucosal atrophy, reduced parietal cell mass and acid secretion, intestinal metaplasia, and increased risk of gastric adenocarcinoma.
The course of H. pylori gastritis is, the result of interplay between host factors (gastroduodenal mucosal defenses, inflammatory responses), and bacterial virulence factors.

**Host factors:**
Genetic polymorphisms that lead to increased expression of the proinflammatory cytokines (TNF, IL-1β) or decreased expression of the antiinflammatory cytokine (IL-10) are associated with development of pangastritis, atrophy, and gastric cancer.
• **bacterial virulence factors:**
  Flagella---- motile in viscous mucus
  Urease--- generates ammonia from urea, +pH, bacterial survival
  Adhesins----adherence
  Toxins/cytotoxin-associated gene A (CagA)---- disease progression

For example, CagA gene present in 90% of H. pylori isolates found in populations with elevated gastric cancer risk. This may, in part, be because CagA expressing strains can effectively colonize the gastric body and cause multifocal atrophic gastritis.
• **MORPHOLOGY:**

H. pylori display tropism for gastric epithelia and are generally not found in association with intestinal metaplasia or duodenal epithelium. Within the stomach, H. pylori are most often found in the **antrum**. Thus, an antral biopsy is preferred for evaluation of H.pylori gastritis.

Long-standing H. pylori gastritis may extend to involve the body and fundus, and the mucosa can become atrophic, with loss of parietal and chief cells. The development of atrophy is typically associated with the presence of intestinal metaplasia and increased risk of gastric adenocarcinoma.
Figure 17-12 Helicobacter pylori gastritis. A, Spiral-shaped H. pylori are highlighted in this Warthin-Starry silver stain. Organisms are abundant within surface mucus. B, Intraepithelial and lamina propria neutrophils are prominent. C, Lymphoid aggregates with germinal centers and abundant subepithelial plasma cells within the superficial lamina propria are characteristic of H. pylori gastritis.
• Lymphoid aggregates, some with germinal centers, are frequently present and represent an induced form of mucosa-associated lymphoid tissue, or MALT, that has the potential to transform into B cell lymphomas (MALTomas).
In addition to histologic identification of the organism, several diagnostic tests have been developed including:

- a noninvasive serologic test for antibodies to H. pylori
- fecal bacterial detection
- the urea breath test based on the generation of ammonia by the bacterial urease.

Gastric biopsy specimens can also be analyzed by the rapid urease test, bacterial culture, or bacterial DNA detection by PCR.
Clinical Features:
Acute H. pylori infection does not produce sufficient symptoms to come to medical attention in most cases; it is the chronic gastritis that ultimately causes the individual to seek treatment.

In contrast to acute gastritis, the symptoms associated with chronic gastritis are **typically less severe but more persistent**. Nausea and upper abdominal pain are typical, sometimes with vomiting, but **hematemesis is uncommon**.
• Effective treatments for H. pylori infection include combinations of antibiotics and proton pump inhibitors.
• Individuals with H. pylori gastritis usually improve after treatment, although relapses can occur after incomplete eradication or reinfection, which is common in regions with high endemic colonization rates.
Table 17-2 Characteristics of *Helicobacter pylori*-Associated and Autoimmune Gastritis

<table>
<thead>
<tr>
<th></th>
<th>H. pylori–Associated</th>
<th>Autoimmune</th>
</tr>
</thead>
<tbody>
<tr>
<td>Location</td>
<td>Antrum</td>
<td>Body</td>
</tr>
<tr>
<td>Inflammatory infiltrate</td>
<td>Neutrophils, subepithelial</td>
<td>Lymphocytes, macrophages</td>
</tr>
<tr>
<td></td>
<td>plasma cells</td>
<td></td>
</tr>
<tr>
<td>Acid production</td>
<td>Increased to slightly decreased</td>
<td>Decreased</td>
</tr>
<tr>
<td>Gastrin</td>
<td>Normal to decreased</td>
<td>Increased</td>
</tr>
<tr>
<td>Other lesions</td>
<td>Hyperplastic/inflammatory</td>
<td>Neuroendocrine hyperplasia</td>
</tr>
<tr>
<td></td>
<td>polyps</td>
<td></td>
</tr>
<tr>
<td>Serology</td>
<td>Antibodies to <em>H. pylori</em></td>
<td>Antibodies to parietal cells (H⁺,K⁺-ATPase, intrinsic factor)</td>
</tr>
<tr>
<td>Sequelae</td>
<td>Peptic ulcer, adenocarcinoma,</td>
<td>Atrophy, pernicious anemia, adenocarcinoma,</td>
</tr>
<tr>
<td></td>
<td>MALToma</td>
<td>carcinoid tumor</td>
</tr>
<tr>
<td>Associations</td>
<td>Low socioeconomic status,</td>
<td>Autoimmune disease; thyroiditis, diabetes</td>
</tr>
<tr>
<td></td>
<td>poverty, residence in rural</td>
<td>mellitus, Graves disease</td>
</tr>
<tr>
<td></td>
<td>areas</td>
<td></td>
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</tbody>
</table>
• Uncommon Forms of Gastritis:
  - Eosinophilic Gastritis
  - Lymphocytic Gastritis
  - Granulomatous Gastritis
Complications of Chronic Gastritis

- Peptic Ulcer Disease
- Mucosal Atrophy and Intestinal Metaplasia
- Dysplasia
- Gastritis Cystica
Peptic ulcer disease (PUD)

- PUD refers to chronic mucosal ulceration affecting the duodenum or stomach.

- Nearly all peptic ulcers are associated with *H. pylori* infection, NSAIDs, or cigarette smoking.
- The most common form of peptic ulcer disease (PUD) occurs within the **gastric antrum or duodenum** as a result of chronic, H. pylori induced antral gastritis, which is associated with increased gastric acid secretion, and decreased duodenal bicarbonate secretion.

- PUD within the **gastric fundus or body** is usually accompanied by lesser acid secretion as a result of mucosal atrophy (associated with some cases of H. pylori-induced or autoimmune chronic gastritis. And generally protected from antral and duodenal ulcers.
• PUD may also be caused by acid secreted by ectopic gastric mucosa within the duodenum or an ileal Meckel diverticulum.

• PUD may also occur in the esophagus as a result of GERD or acid secretion by esophageal ectopic gastric mucosa.
MORPHOLOGY:

Peptic ulcers most common in the **proximal duodenum**, and involve the anterior duodenal wall. Gastric peptic ulcers are predominantly located along the **lesser curvature** near the interface of the body and antrum.

Peptic ulcers are solitary in more than 80% of patients.
• Size and location do not differentiate between benign and malignant ulcers. However, the gross appearance of chronic peptic ulcers is virtually diagnostic. The classic peptic ulcer is a round to oval, sharply punched-out defect. In contrast, heaped-up margins are more characteristic of cancers.

• Malignant transformation of peptic ulcers occurs rarely, if ever, and reports of transformation probably represent cases in which a lesion thought to be a chronic peptic ulcer was actually an ulcerated carcinoma from the start.
<table>
<thead>
<tr>
<th>Complications of Peptic Ulcer Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Bleeding</strong></td>
</tr>
<tr>
<td>Occurs in 15% to 20% of patients</td>
</tr>
<tr>
<td>Most frequent complication</td>
</tr>
<tr>
<td>May be life-threatening</td>
</tr>
<tr>
<td>Accounts for 25% of ulcer deaths</td>
</tr>
<tr>
<td>May be the first indication of an ulcer</td>
</tr>
<tr>
<td><strong>Perforation</strong></td>
</tr>
<tr>
<td>Occurs in up to 5% of patients</td>
</tr>
<tr>
<td>Accounts for two thirds of ulcer deaths</td>
</tr>
<tr>
<td>Is rarely first indication of an ulcer</td>
</tr>
<tr>
<td><strong>Obstruction</strong></td>
</tr>
<tr>
<td>Mostly in chronic ulcers</td>
</tr>
<tr>
<td>Secondary to edema or scarring</td>
</tr>
<tr>
<td>Occurs in about 2% of patients</td>
</tr>
<tr>
<td>Most often associated with pyloric channel ulcers</td>
</tr>
<tr>
<td>May occur with duodenal ulcers</td>
</tr>
<tr>
<td>Causes incapacitating, crampy abdominal pain</td>
</tr>
<tr>
<td>Can rarely cause total obstruction and intractable vomiting</td>
</tr>
</tbody>
</table>
• Clinical Features:
- The majority of peptic ulcers come to clinical attention because of epigastric burning or aching pain. The pain tends to occur 1 to 3 hours after meals during the day, is worse at night (usually between 11 PM and 2 AM), and is relieved by alkali or food.
- Nausea, vomiting, bloating, belching, and significant weight loss are additional manifestations.
- Significant fraction present with complications such as iron deficiency anemia, hemorrhage, or perforation.
• the recurrence rate is now less than 20% following successful clearance of H. pylori.

• the success of proton pump inhibitors and H. pylori eradication has relegated surgical intervention to treatment of bleeding or perforated peptic ulcers.
Mucosal Atrophy and Intestinal Metaplasia

• Long-standing chronic gastritis that involves the body and fundus may ultimately lead to significant loss of parietal cell mass.

• may be associated with intestinal metaplasia, recognized by the presence of goblet cells, and is strongly associated with increased risk of gastric adenocarcinoma.

• achlorhydria of gastric mucosal atrophy permits overgrowth of bacteria that produce carcinogenic nitrosamines.

• The risk of adenocarcinoma is greatest in autoimmune gastritis.
Dysplasia

- Chronic gastritis exposes the epithelium to inflammation related free radical damage and proliferative stimuli. Over time this combination of stressors can lead to the accumulation of genetic alterations that result in carcinoma.