STOMACH

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INFLAMMATORY DISEASE OF THE STOMACH

- The gastric lumen is strongly acidic, with a pH close to one more than a million times more acidic than the blood.
- Multiple mechanisms have evolved to protect the gastric mucosa and disruption of any of these protective mechanisms will lead to Acute or chronic gastritis

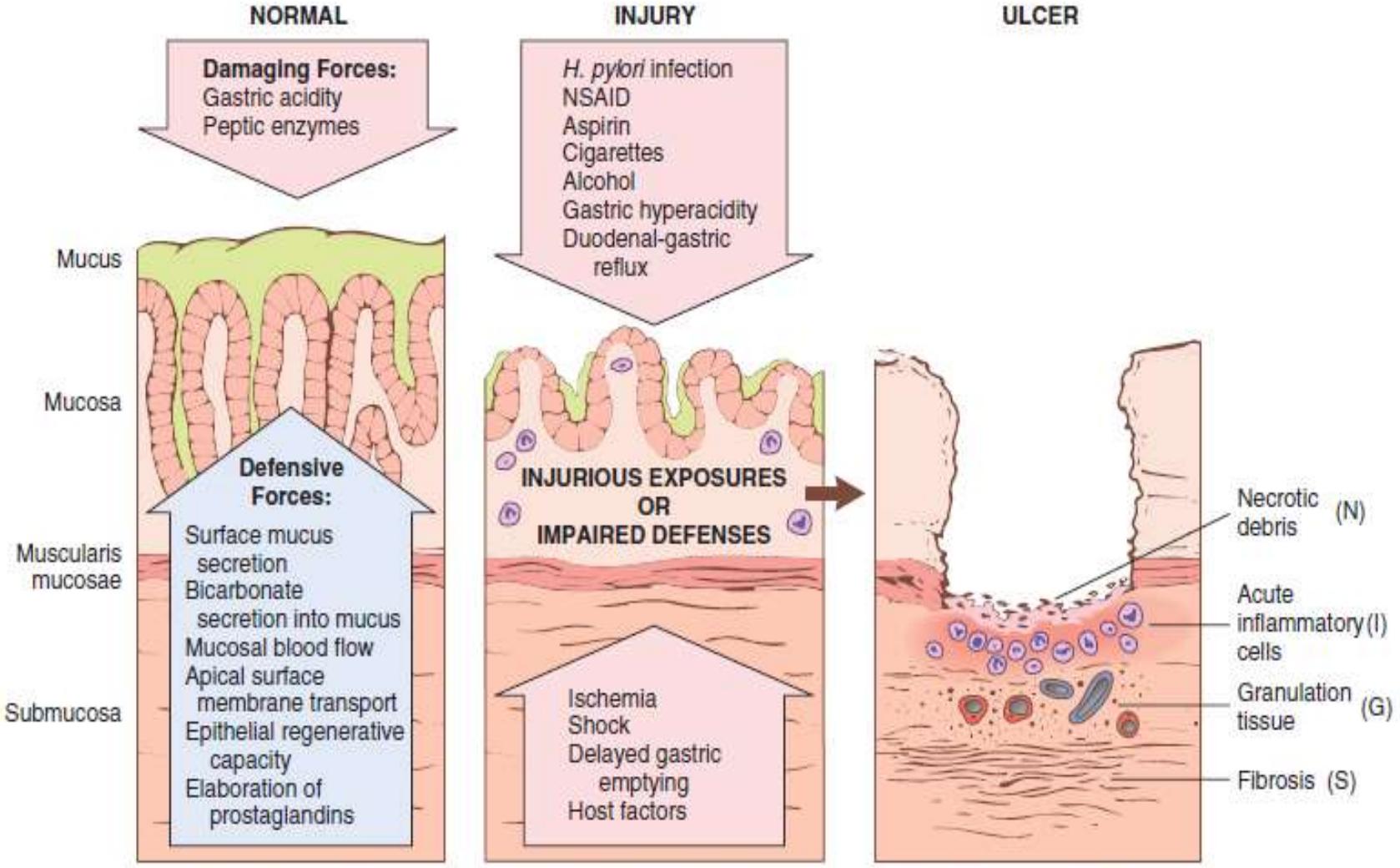


Figure 14–13 Mechanisms of gastric injury and protection. This diagram illustrates the progression from more mild forms of injury to ulceration that may occur with acute or chronic gastritis. Ulcers include layers of necrotic debris *(N)*, inflammation *(I)*, and granulation tissue *(G)*; a fibrotic scar *(S)*, which develops over time, is present only in chronic lesions.

Acute Gastritis

- On histologic examination,. Lamina propria lymphocytes and plasma cells are prominent. The presence of neutrophils above the basement membrane—specifically, in direct contact with epithelial cells—is abnormal in all parts of the gastrointestinal tract and signifies **active inflammation.**

Acute Peptic Ulceration

- *Stress ulcers*, most commonly affecting critically ill patients with shock, sepsis, or severe trauma.
- *Curling ulcers,* occurring in the proximal duodenum and associated with severe burns or trauma
- *Cushing ulcers,* arising in the stomach, duodenum, or esophagus of persons with intracranial disease, have a high incidence of perforation.

- Symptoms of gastric ulcers include nausea, vomiting, and coffee-ground hematemesis.

Chronic Gastritis

Helicobacter pylori *Gastritis*

- These spiral-shaped or curved bacilli are presentin gastric biopsy specimens .
- *H. pylori* organisms are present in 90% of patients with chronic gastritis affecting the antrum.
- In addition, the increased acid secretion that occurs in *H. pylori* gastritis may result in peptic ulcer disease of the stomach or duodenum; *H. pylori* infection also confers increased risk of gastric cancer.
- The incidence of *H. pylori* infection correlates most closely with sanitation and hygiene during an individual's childhood

MORPHOLOGY

- MORPHOLOGY
- Gastric biopsy specimens generally demonstrate :

*1- H. pylori*organism is concentrated within the superficial mucus overlying - epithelial cells inthe surface and neck regions.

2- The superficial lamina propria includes large numbers of plasma cells, neutrophils and lymphocytes.

3- Lymphoid aggregates with germinal centers and represent an induced form of **mucosa-associated lymphoid tissue** (MALT) that has the potential to transform into lymphoma.

4- Intestinal metaplasia, characterized by the presence of goblet cells and columnar absorptive cells.

- A noninvasive serologic test for anti–*H. pylori* antibodies includes:

1- Fecal bacterial detection.

2- urea breath test based on the generation of ammonia by bacterial urease.

3- Polymerase chain reaction (PCR)assay for bacterial DNA.

- Effective treatments include combinations of antibiotics and proton pump inhibitors.

Autoimmune Gastritis

- *Autoimmune gastritis* accounts for less than 10% of cases of chronic gastritis.
- In contrast with that caused by *H. pylori,* Autoimmune gastritis typically spares the antrum and induces *hypergastrinemia* .
- Autoimmune gastritis is characterized byAntibodies to parietal cells and intrinsic factor are present early in disease, but pernicious anemia develops in only a minority of patients.
- The median age at diagnosis is 60 years, and there is a slight female predominance.
- Autoimmune gastritis often is associated with other autoimmune diseases.

PATHOGENESIS

- Autoimmune gastritis is associated with loss of parietal cells, which secrete acid and intrinsic factor. Deficient acid production stimulates gastrin release, resulting in hypergastrinemia and hyperplasia of antral gastrin-producing G cells.
- Lack of intrinsic factor disables ileal vitamin B12 absorption,

leading to B12 deficiency and megaloblastic anemia **(pernicious anemia);** reduced serum concentration of pepsinogen I reflects chief cell loss.

- Although *H. pylori* can cause hypochlorhydria, it is not associated with achlorhydria or pernicious anemia, because the parietal and chief cell damage is not as severe as in autoimmune gastritis.

MORPHOLOGY

- Autoimmune gastritis is characterized by diffuse **damage of the oxyntic** (acid-producing) **mucosa** within the body and fundus.
- With **diffuse atrophy,** the oxyntic mucosa of the body and fundus appears markedly thinned, and rugal folds are lost.
- The inflammatory infiltrate more commonly is composed of lymphocytes, macrophages, and plasma cells;
- In contrast with ***H. pylori* gastritis,** the inflammatory reaction most often is deep and centered on the gastric glands.
- **Parietal and chief cell loss** can be extensive, and **intestinal metaplasia** may develop.

Table 14–2 Characteristics of *Helicobacter pylori*–Associated and Autoimmune Gastritis

Feature	Location	
	H. pylori–Associated: Antrum	Autoimmune: Body
Inflammatory infiltrate	Neutrophils, subepithelial plasma cells	Lymphocytes, macrophages
Acid production	Increased to slightly decreased	Decreased
Gastrin	Normal to decreased	Increased
Other lesions	Hyperplastic/inflammatory polyps	Neuroendocrine hyperplasia
Serology	Antibodies to *H. pylori*	Antibodies to parietal cells (H^+,K^+-ATPase, intrinsic factor)
Sequelae	Peptic ulcer, adenocarcinoma, lymphoma	Atrophy, pernicious anemia, adenocarcinoma, carcinoid tumor
Associations	Low socioeconomic status, poverty, residence in rural areas	Autoimmune disease; thyroiditis, diabetes mellitus, Graves disease

Gastric adenomas

- Gastric adenomas are most commonly located in the antrum.
- By definition, all gastrointestinal adenomas exhibit

epithelial dysplasia, which can be classified as low- or highgrade.

- Both grades may include enlargement, elongation, and hyperchromasia of epithelial cell nuclei, epithelial crowding, and pseudostratification.
- High-grade dysplasia is characterized by more severe cytologic atypia and irregular architecture, including glandular budding and gland-within-gland, or

cribriform, structures.

Gastric cancer

- Gastric cancer is more common in lower socioeconomic groups and in persons with *multifocal mucosal atrophy and intestinal metaplasia*. PUD does not impart an increased risk of gastric cancer.

- Gastric adenocarcinomas are classified according to their location in the stomach as well as gross and histologic morphology.

- The **Lauren classification** that separates gastric cancers into **intestinal** and **diffuse** types

- Intestinal-type cancers tend to be bulky and are composed of glandular structures similar to esophageal and colonic adenocarcinoma.

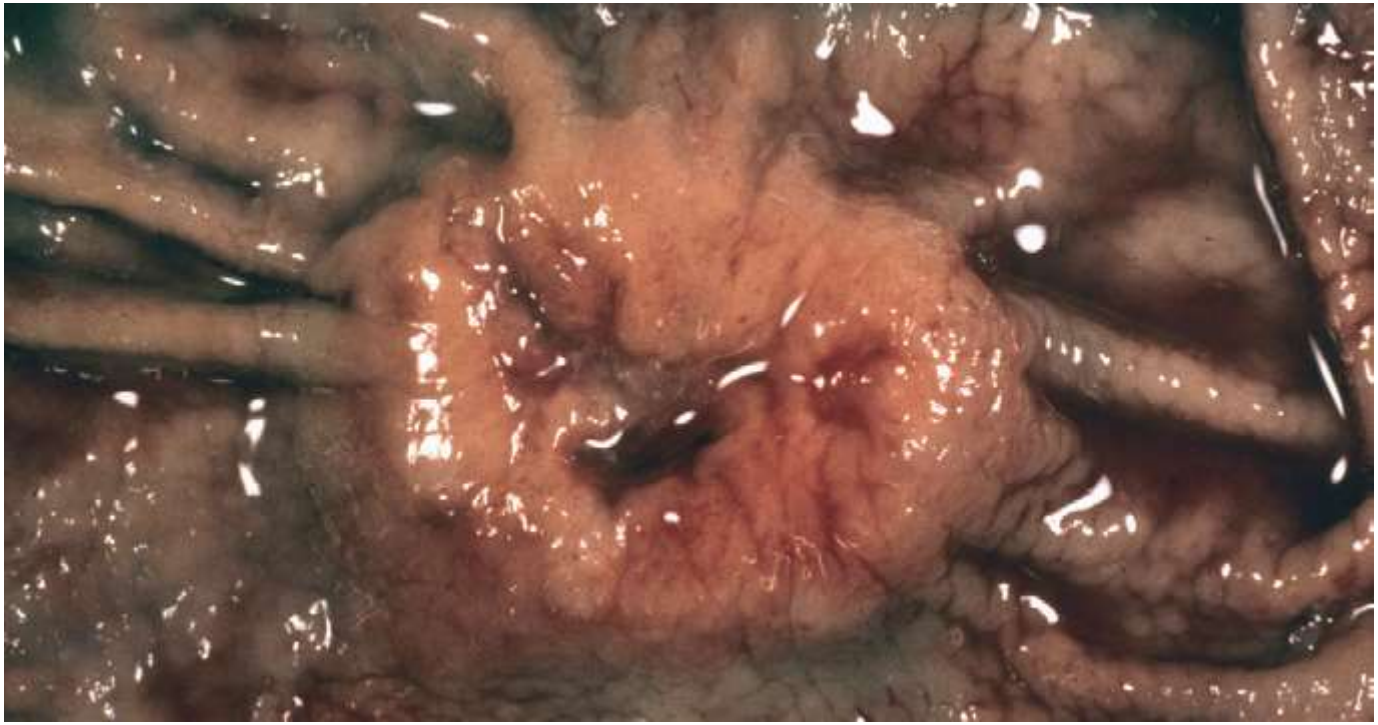
- They typically grow along broad cohesive fronts to form either an exophytic mass or an ulcerated tumor.

- The neoplastic cells often contain apical mucin vacuoles, and abundant mucin may be present in gland lumina.

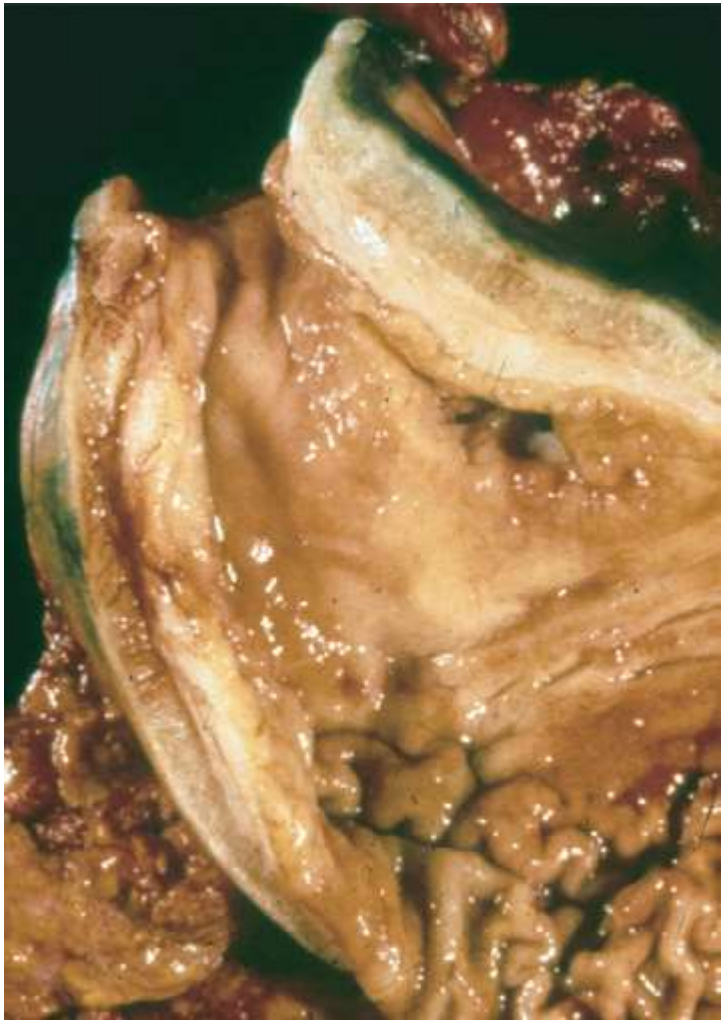
- Diffuse gastric cancers display an infiltrative growth pattern and are composed of discohesive cells with large mucin vacuoles that expand the cytoplasm and push the nucleus to the periphery, creating a **signet ring cell** morphology.

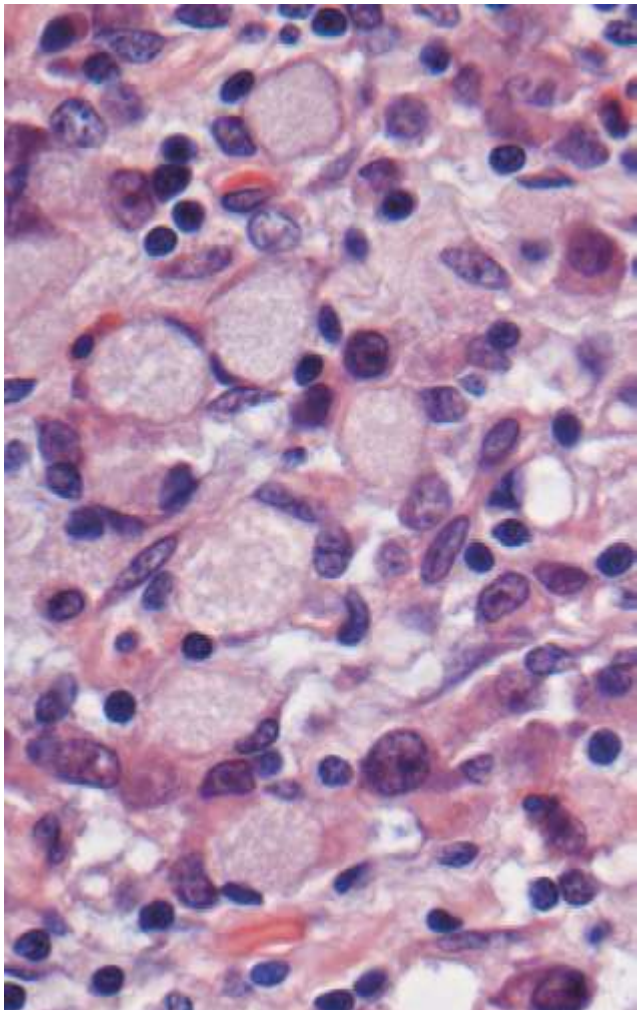
- These infiltrative tumors often evoke a **desmoplastic** reaction that stiffens the gastric wall and may cause diffuse rugal flattening and a rigid, thickened wall that imparts a “leather bottle” appearance termed **linitis plastica.**

Intestinal-type adenocarcinoma consisting of an elevated mass with heaped-up borders and central ulceration



A, Linitis plastica. The gastric wall is markedly thickened, and rugal folds are partially lost. B, Signet ring cells with large cytoplasmic mucin vacuoles and peripherally displaced, crescent-shaped nuclei.





- Clinical Features
- The mean age at presentation of Intestinal-type gastric cancer :

is 55 years, and the male-to-female ratio is 2 : 1.

- By contrast, the incidence of diffuse gastric cancer is occurs at similar frequencies in males and females.

- *The depth of invasion and the extent of nodal and distant metastasis at the time of diagnosis remain the most powerful prognostic indicators for gastric cancer.*

Lymphoma

- Although extranodal lymphomas can arise in virtually any tissue, they do so most commonly in the gastrointestinal tract, particularly the stomach.

- Nearly 5% of all gastric malignancies are primary lymphomas, the most common of which are indolent lymphomas of *mucosa-associated lymphoid tissue* (MALT), or *MALTomas*.

Carcinoid Tumor

- Carcinoid tumors arise from neuroendocrine organs (e.g., the endocrine pancreas) and neuroendocrine-differentiated gastrointestinal epithelia (e.g., G-cells).

- A majority are found in the gastrointestinal tract, and more than 40% occur in the small intestine.

- Gastric carcinoids may be associated with endocrine cell hyperplasia, chronic atrophic gastritis, and Zollinger-Ellison syndrome.
- The most current WHO classification describes these as low- or intermediate grade neuroendocrine tumors.

- It is important to recognize that site within the GI tract and extent of local invasion are also important prognostic indicators .

- High-grade neuroendocrine tumors, termed *neuroendocrine carcinoma*, frequently display necrosis and, in the GI tract, are most common in the jejunum.

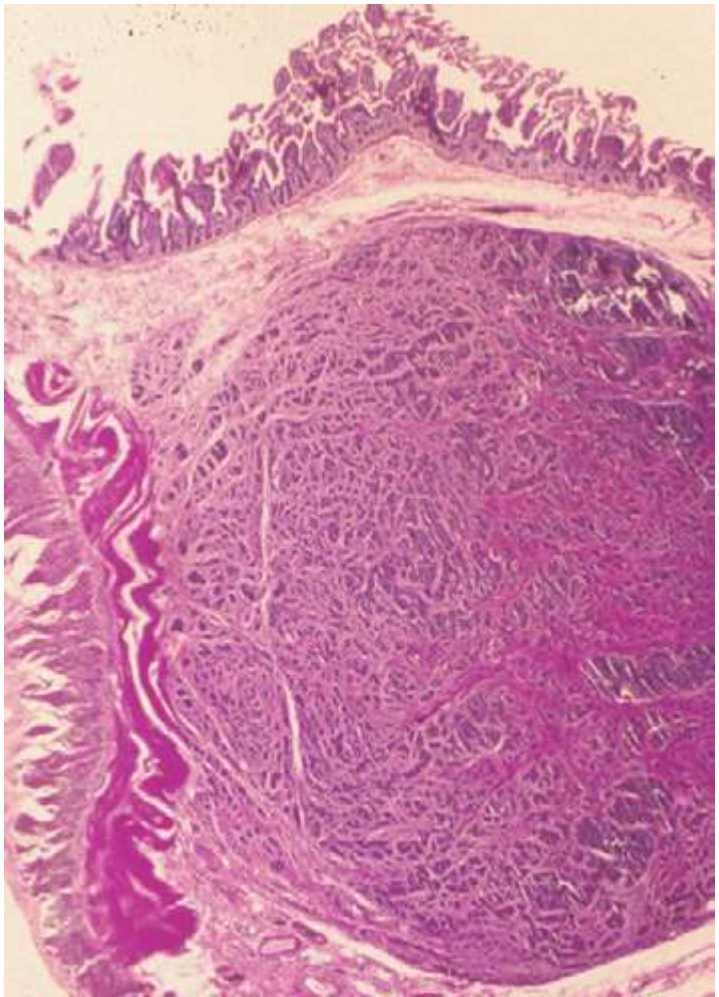
- MORPHOLOGY
- Carcinoid tumors are intramural or submucosal masses that create small polypoid lesions .
- On histologic examination, carcinoid tumors are composed

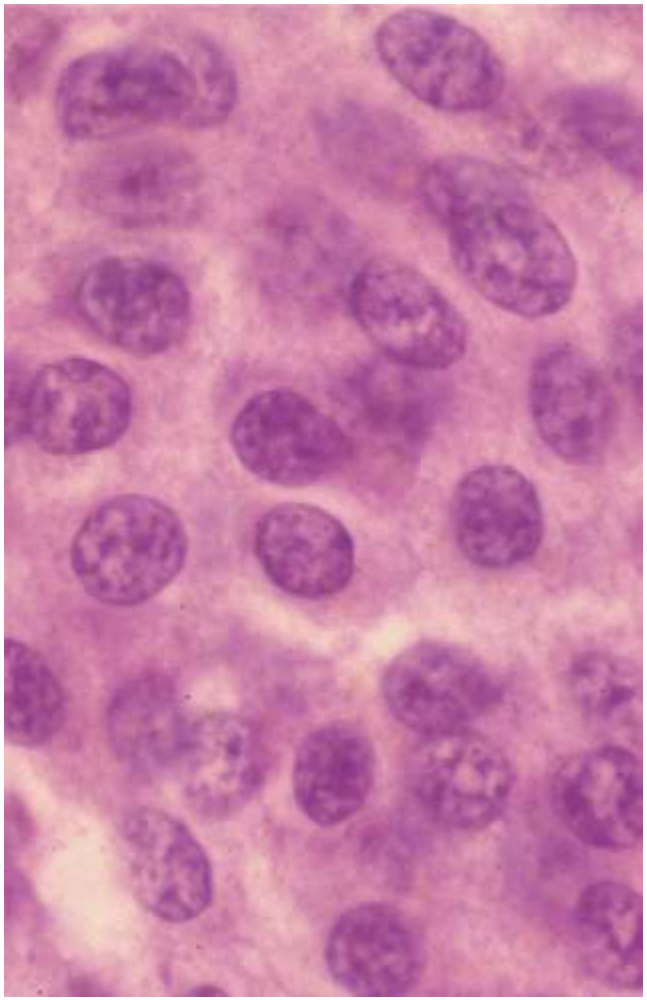
of islands, trabeculae, strands, glands, or sheets of uniform cells with scant, pink granular cytoplasm and a round to oval stippled nucleus.

Clinical Features

- The peak incidence of carcinoid tumors is in the sixth decade.. Symptoms are determined by the hormones produced. For example, the *carcinoid syndrome* is caused by vasoactive substances secreted by the tumor that cause cutaneous flushing, sweating, bronchospasm, colicky abdominal pain, diarrhea, and right-sided cardiac valvular fibrosis.

Gastrointestinal carcinoid tumor (neuroendocrine tumor). **A,** Carcinoid tumors often form a submucosal. B. Shows the bland cytology that typifies carcinoid tumors. The chromatin texture, with fine and coarse clumps, frequently assumes a **"salt and pepper" pattern**.
aggressive.





The most important prognostic factor for gastrointestinal carcinoid tumors is location:

. *Foregut carcinoid tumors,* those found within the stomach, duodenum proximal to the ligament of Treitz, and esophagus, rarely metastasize and generally are cured

by resection.

• *Midgut carcinoid tumors* that arise in the jejunum and ileum often are multiple and tend to be aggressive. In these tumors, greater depth of local invasion, increased size, and presence of necrosis and mitosis are associated with poor outcome.

• *Hindgut carcinoids* arising in the appendix and colorectum typically are discovered incidentally. Those in the appendix occur at any age and are almost uniformly benign.

Gastrointestinal Stromal Tumor

- The most common mesenchymal tumor of in the stomach.

- Overall, GISTs are slightly more common in males. The peak incidence of gastric GIST is around 60 years of age,with less than 10% occurring in persons younger than 40 years of age.

- Approximately **75% to 80% of all GISTs have oncogenic, gain-of-function mutations of the gene encoding the tyrosine kinase c-KIT,**

Clinical Features

- Symptoms of GISTs at presentation may be related to mass effects or mucosal ulceration.
- Complete surgical resection is the primary treatment for localized gastric GIST.
- The prognosis correlates with tumor size, mitotic index, and location,
- Patients with unresectable, recurrent, or metastatic disease often respond to *imatinib*, an inhibitor of the tyrosine kinase activity of c-KIT and PDGFRA.

- MORPHOLOGY
- Primary gastric GISTs usually form a solitary, wellcircumscribed, fleshy, submucosal mass.
- In GISTs can be composed of thin, elongated **spindle cells** or plumper **epithelioid cells.**
- The most useful diagnostic marker is c-KIT, consistent with the relationship between
- GISTs and interstitial cells of Cajal, which is immunohistochemically detectable in 95% of these tumors.