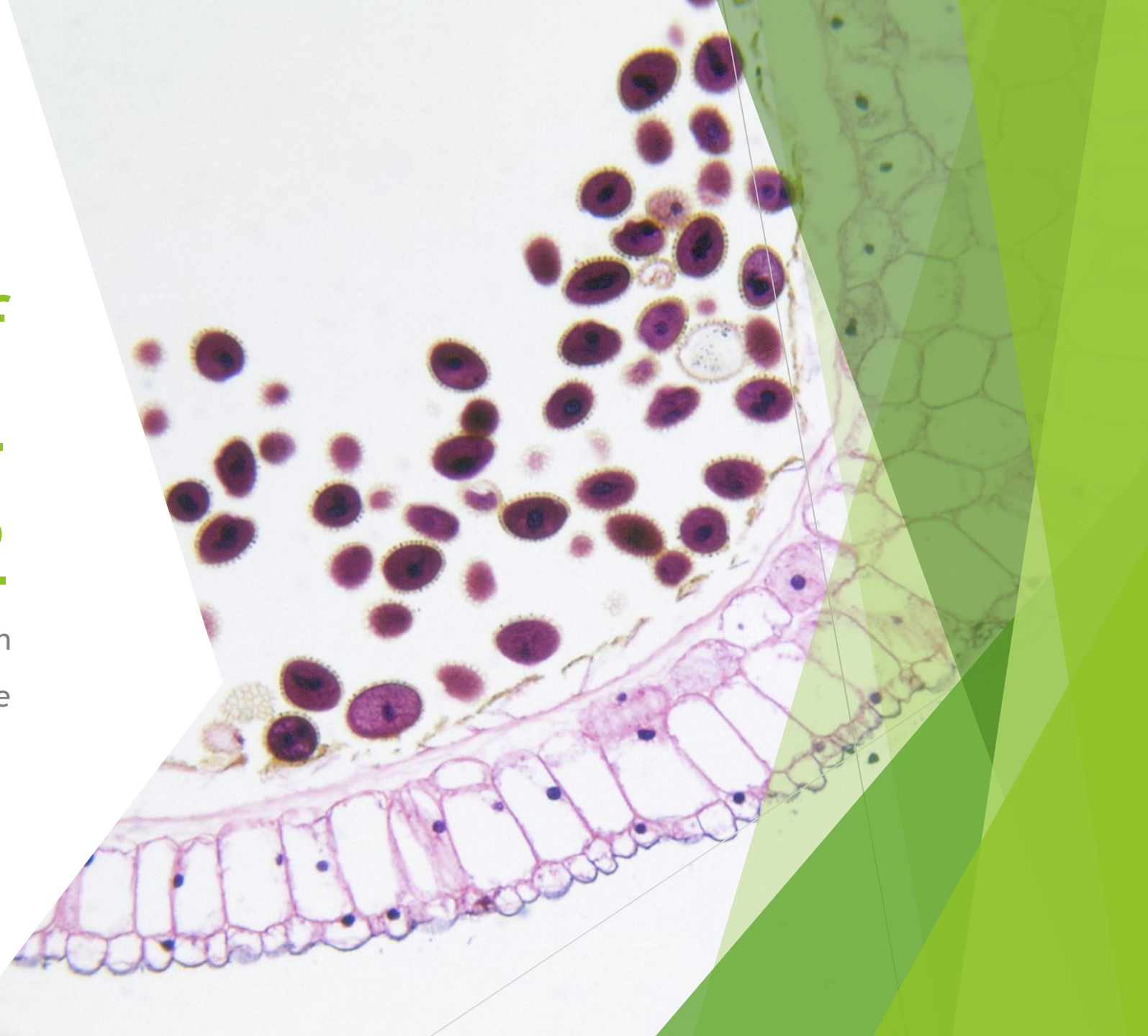
Pathology of the stomach-2

Manar Hajeer, MD, FRCPath

University of Jordan, School of medicine



Peptic Ulcer Disease

- Main factors: H. *pylori* infection or NSAID use
- **Imbalance between mucosal defenses and damaging forces.**
- USA, most cases are NSAID induced (as H. Pylori infection is falling and increased use of low-dose aspirin in aged population).
- **Any portion of the GIT exposed to acidic gastric juices**
- Most common in gastric antrum, first part of duodenum.
- Esophagus in (GERD) or ectopic gastric mucosa (Meckel diverticulum)

Pathogenesis of PUD:

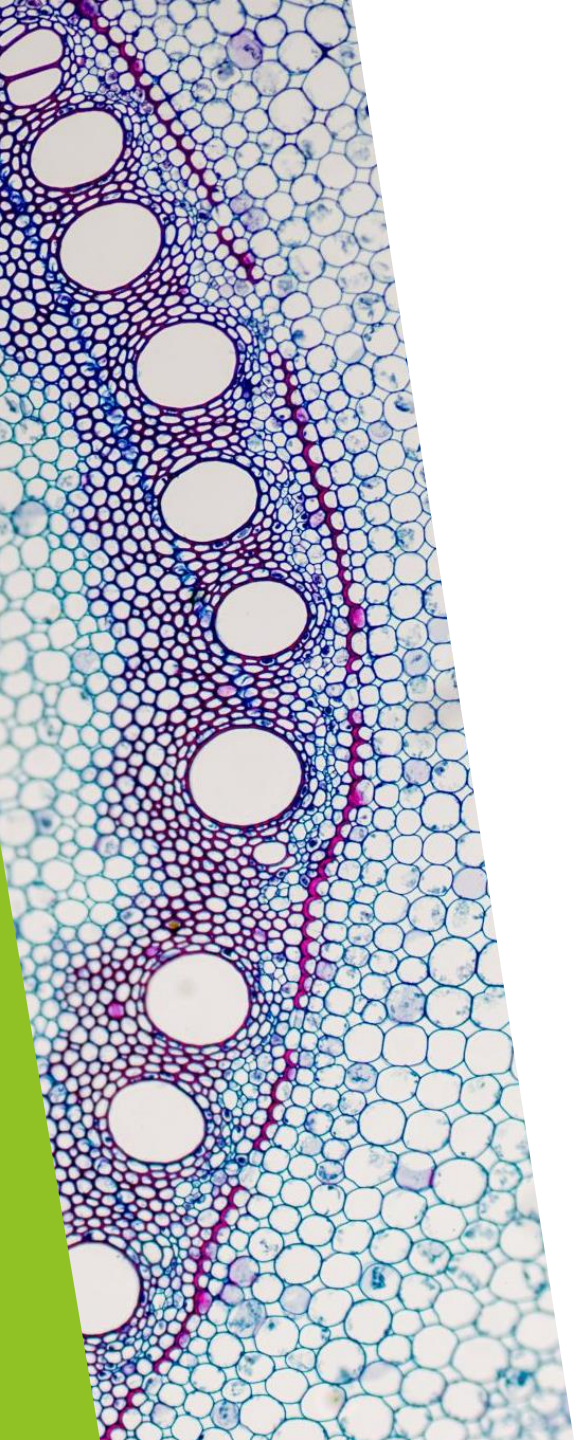
- > 70% of cases are associated with H. pylori infection worldwide.
- Only 5 -10% of H. pylori–infected persons (host factors, bacterial strains).
- Gastric acid is fundamental in pathogenesis.
- Cofactors: smoking, chronic NSAIDs, high-dose corticosteroids, alcoholic cirrhosis, COPD, CRF, hyperparathyroidism.

- **Hyperacidity is caused by**:
- H. pylori.
- Parietal cell hyperplasia.
- Excessive secretory response (vagal)
- Hypergastrinemia as in Zollinger-Ellison syndrome

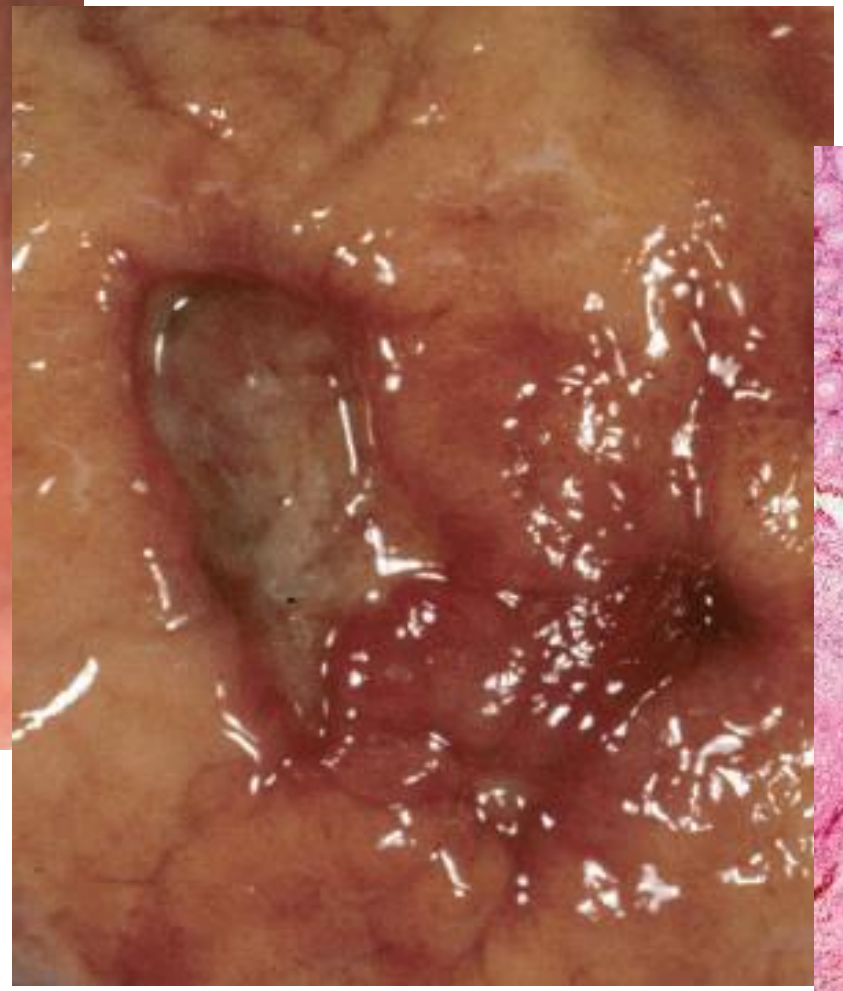
Zollinger-Ellison syndrome

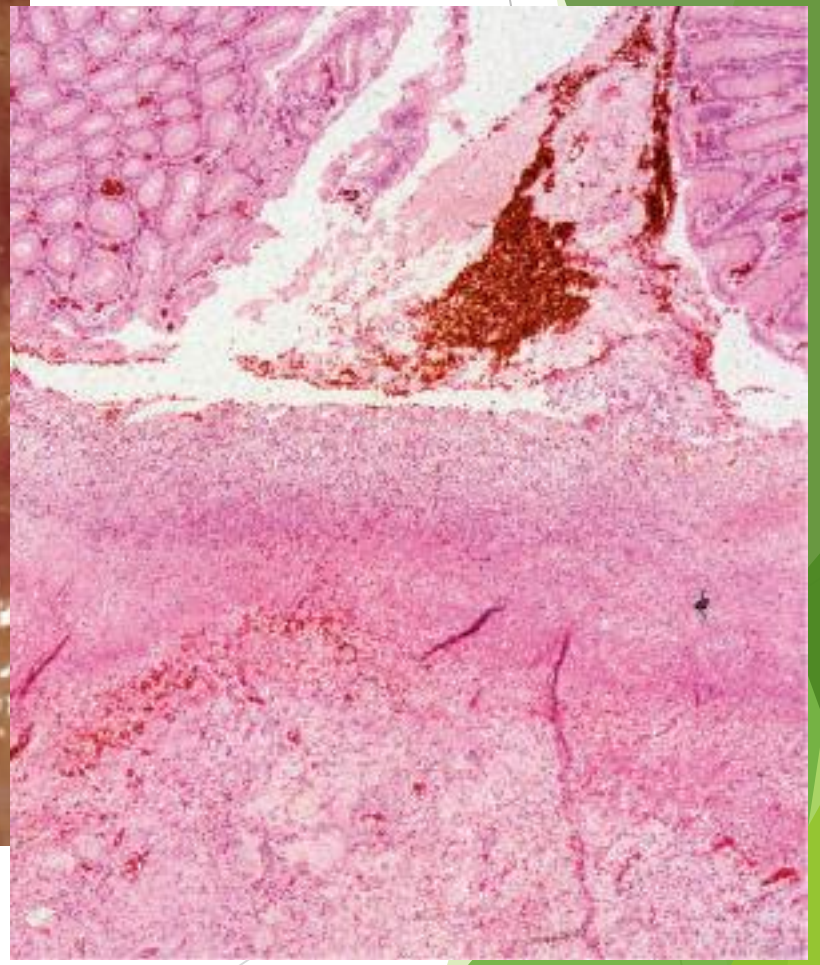
- Multiple peptic ulcerations
- Stomach , duodenum, even jejunum
- Caused by uncontrolled release of gastrin by a tumor (gastrinoma) and the resulting massive acid production.

MORPHOLOGY



- 4:1, proximal duodenum : stomach.
- Anterior duodenal wall or antrum.
- **>80% solitary**.
- Round to oval, sharply punched-out
- **Base of ulcers is smooth and clean**
- Granulation tissue.
- Hemorrhage & Perforation are complications.





Robbins Basic Pathology 10th edition

Duodenal ulcer

Clinical Features

- Epigastric burning or aching pain
- Complication: Iron deficiency anemia, frank hemorrhage, or perforation.
- Pain 1 to 3 hours after meals at daytime
- Worse at night, relieved by alkali or food
- Nausea, vomiting, bloating, bletching.

- Current therapies are aimed at H.pylori eradication.
- Surgery reserved for complications.

GASTRIC POLYPS AND TUMORS

- Gastric Polyps:
- Inflammatory and Hyperplastic Polyps
- Gastric Adenoma

- Gastric Adenocarcinoma
- intestinal and diffuse types

- Lymphoma
- MALToma.

- Neuroendocrine (Carcinoid) Tumor
- Gastrointestinal Stromal Tumor

Gastric polyps

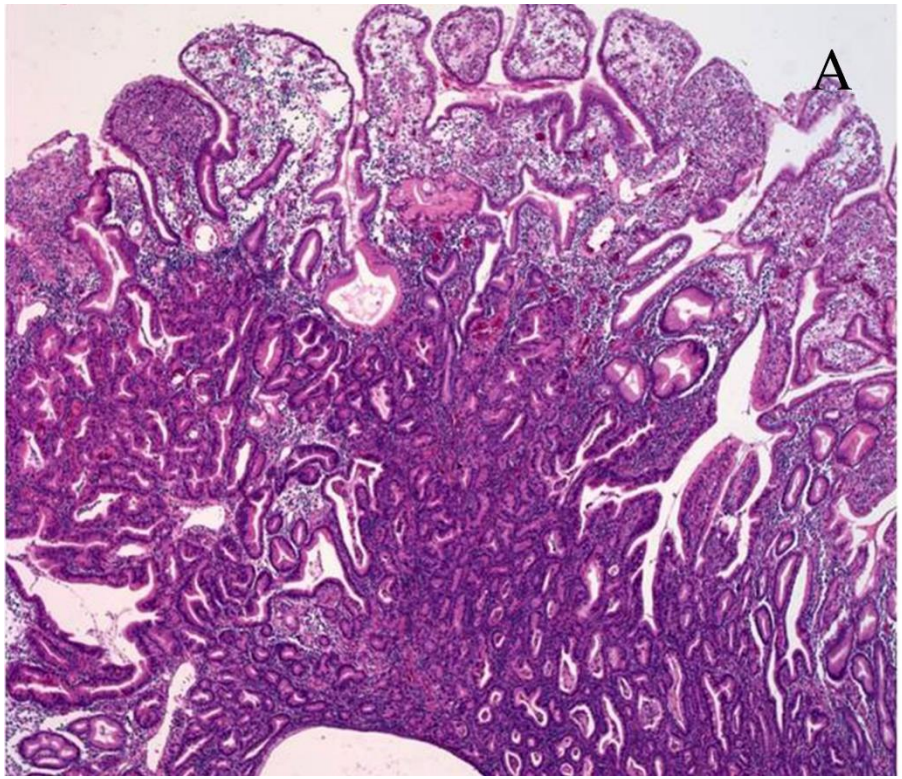
- Polyps: masses projecting above the level of adjacent mucosa

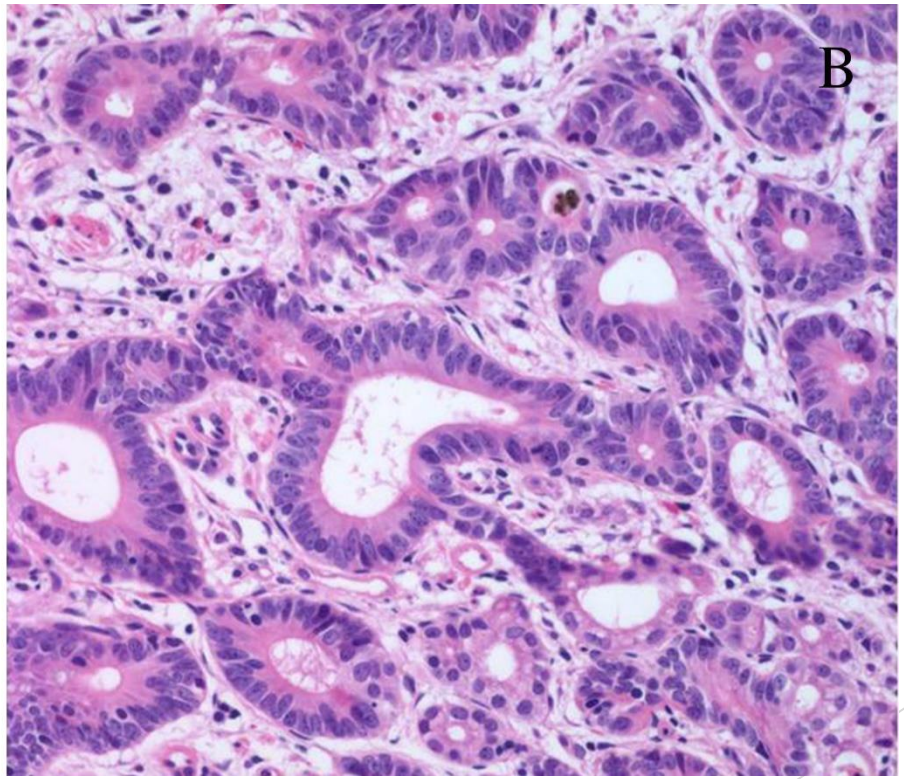
- **Inflammatory and Hyperplastic Polyps**
- 75% of all polyps.
- Arise in a background of chronic gastritis
- Regress after H.pylori eradication.

Gastric Adenoma

- 10% of all polyps.
- Increase with age.
- M: F = 3:1
- Background: chronic gastritis, atrophy and intestinal metaplasia.
- **Dysplasia, low- or high-grade.**
- Risk of adenocarcinoma related to the size (greatest if > 2cm).
- **Risk of carcinoma higher than colonic adenoma.**
- 30% have concurrent CA.

Gastric adenoma





Gastric Adenocarcinoma

- 90% of all gastric cancers.
- Early symptoms mimic gastritis >>> late diagnosis.
- Marked geographic variation (Japan, Costa Rica, Chile).
- Screening >> early detection.
- Background of mucosal atrophy and intestinal metaplasia.
- PUD does not increase risk, except after surgery

- **In USA rates dropped > 85%, BUT increased rate of cardia cancer due to GERD & obesity.**
- **Two main types: intestinal and diffuse.**

Pathogenesis

- Genetic alterations (H.Pylori associated chronic gastritis , lesser extent EBV (10%).
- Most cases are sporadic.

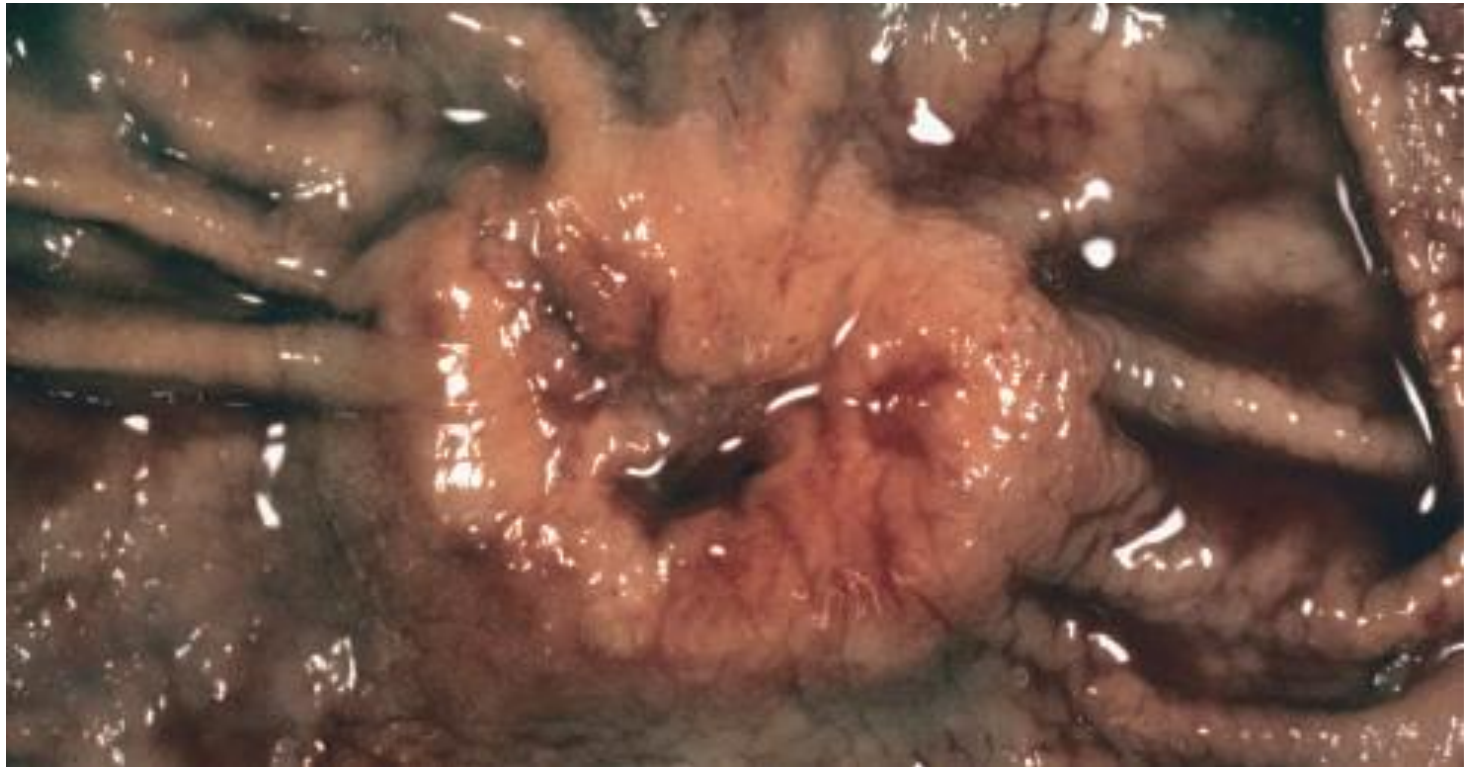
- Familial diffuse type: germline mutations in *CDH1* (E-cadherin).
- Sporadic diffuse type: somatic CDH1 mutation in 50%.
- Familial intestinal type cancer: FAP, APC gene mutation.
- Sporadic intestinal-type Ca: B catenin mutation

- Sporadic cases: P53 mutation + HER2 amplification.

MORPHOLOGY

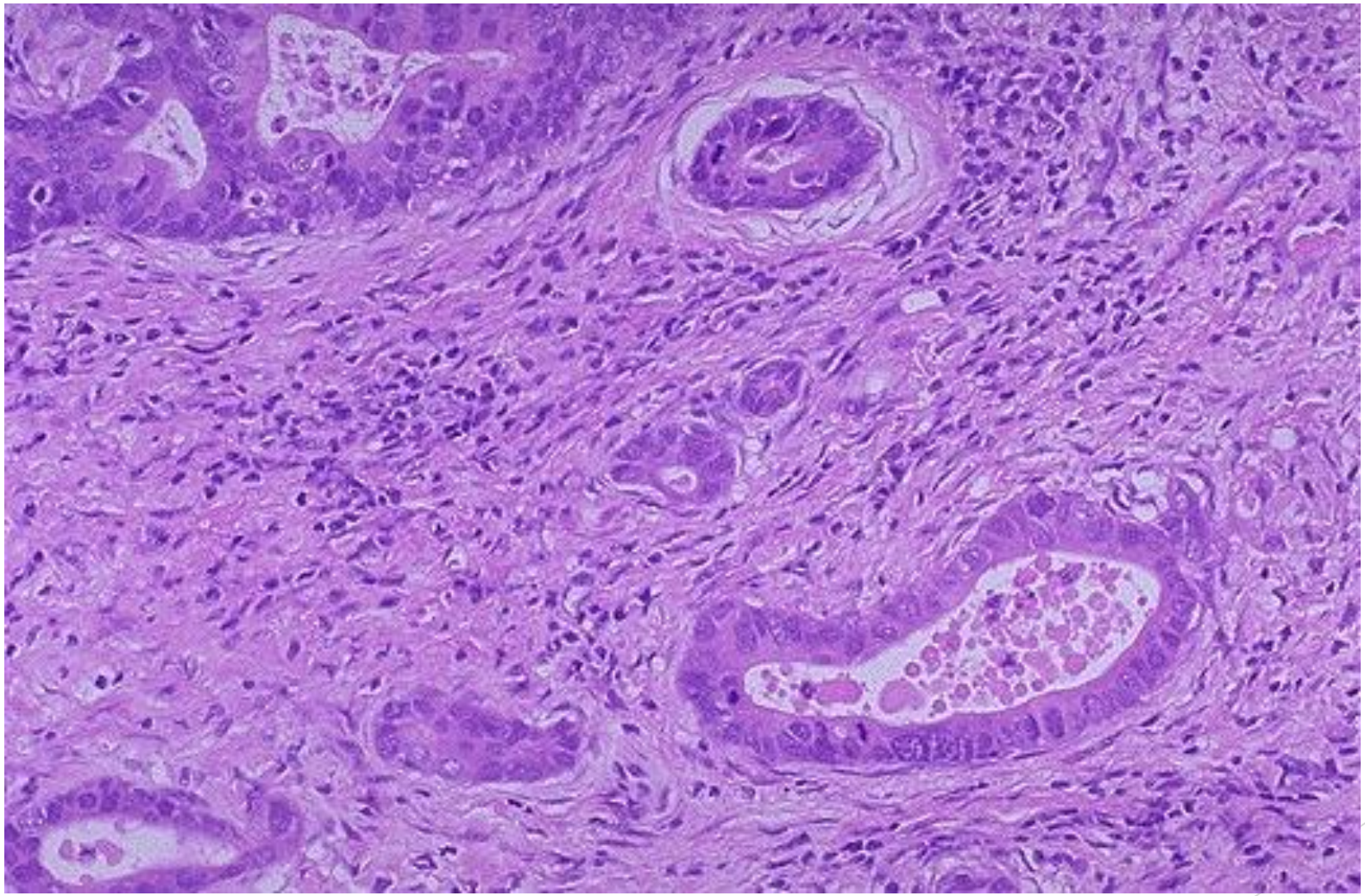
- Lauren classification: separates gastric cancers into
- **Intestinal type:**
- Bulky.
- Exophytic mass or ulcer.
- Form glands.

- **Diffuse type:**
- Infiltrative growth pattern
- Discohesive cells (signet ring cells)
- Desmoplastic reaction (stiffens wall, flat ruge, linitis plastic).

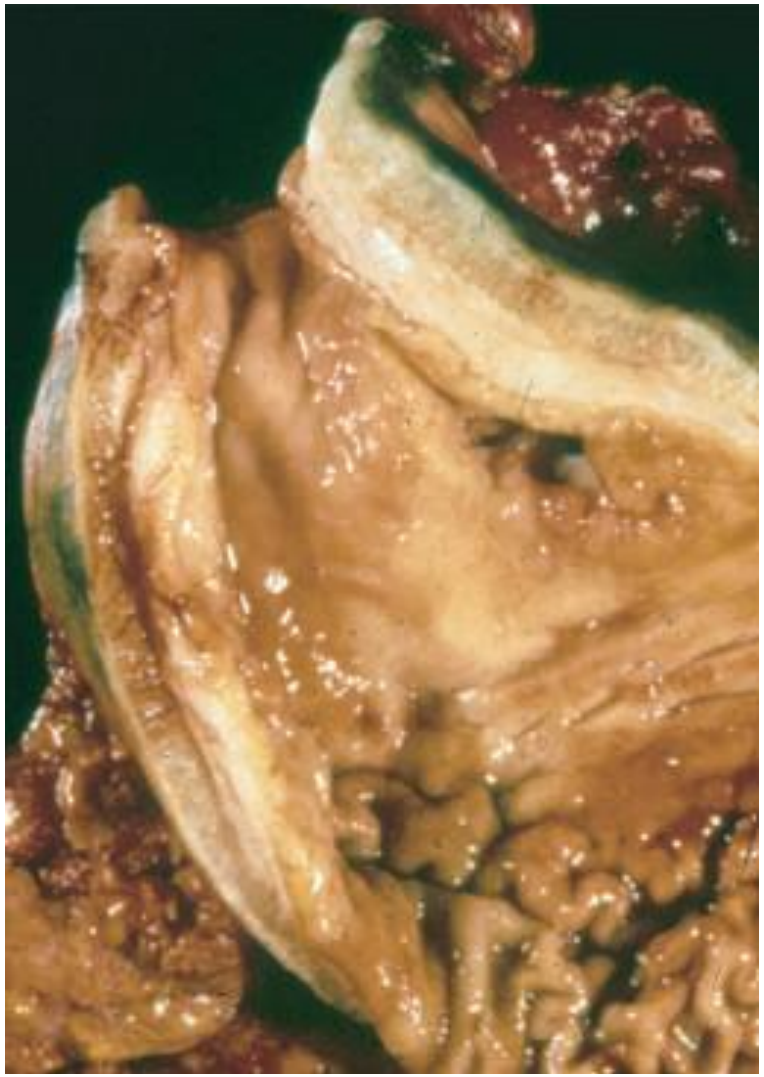


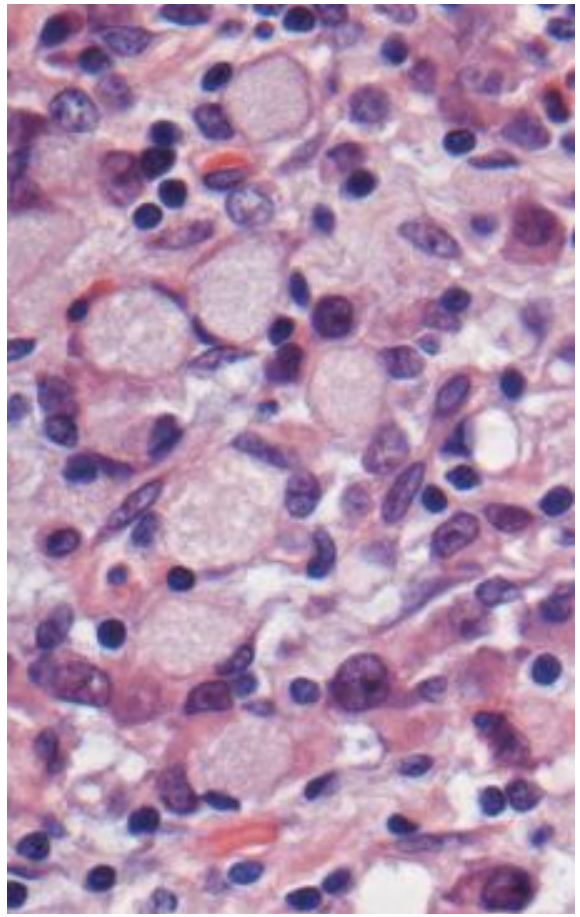
Intestinal type

Intestinal type

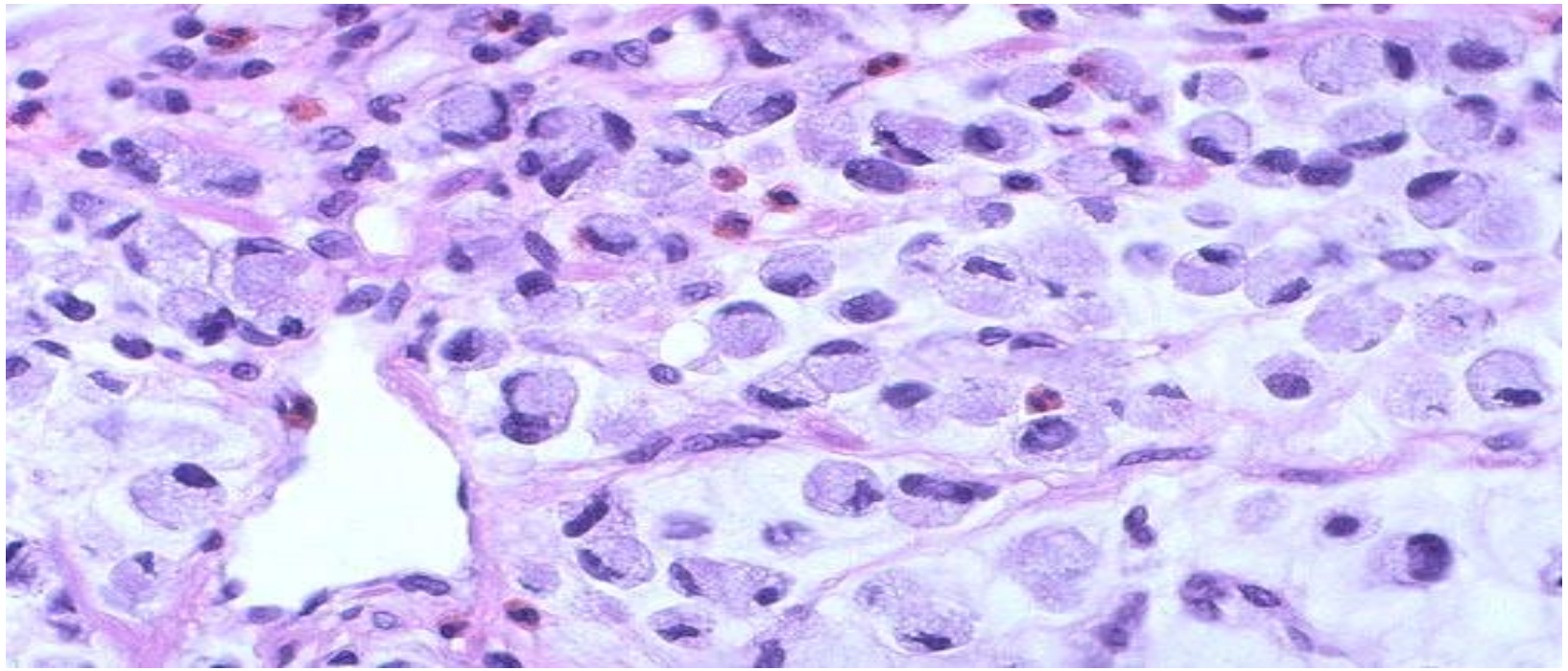


Linitis plastica





Signet ring cells:
large mucin vacuoles that expand the cytoplasm and push the nucleus
to the periphery,



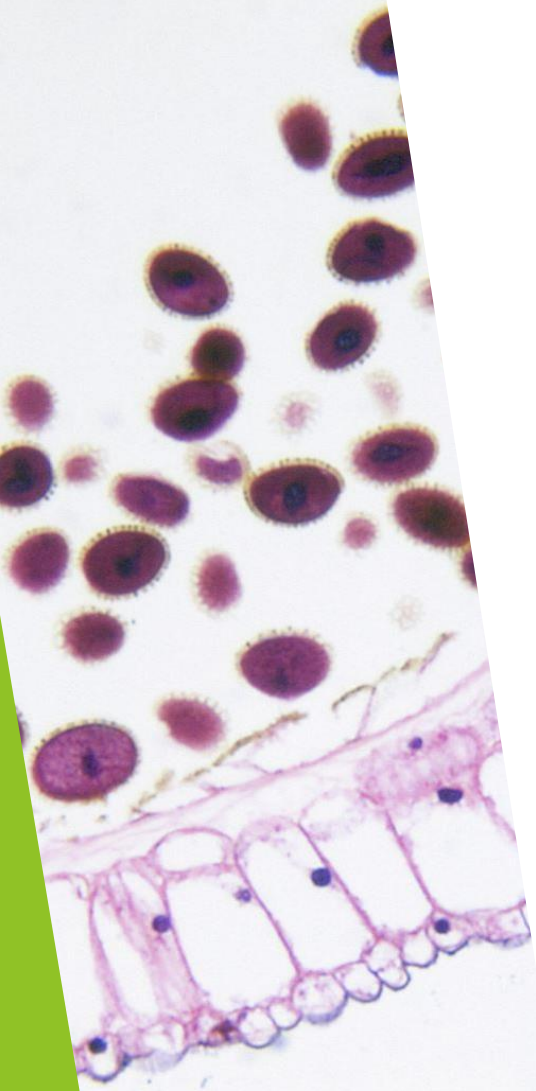
Diffuse type, signet ring cells

Clinical Features

- **Intestinal-type gastric cancer**
- High-risk areas
- Develops from precursor (adenoma, dysplasia associated w/ intestinal metaplasia)
- Mean age 55 yrs.
- M:F 2:1

- **Diffuse type gastric cancer:**
- Incidence uniform across countries.
- No precursor lesion.
- M:F 1:1
- Younger age.

Clinical features:



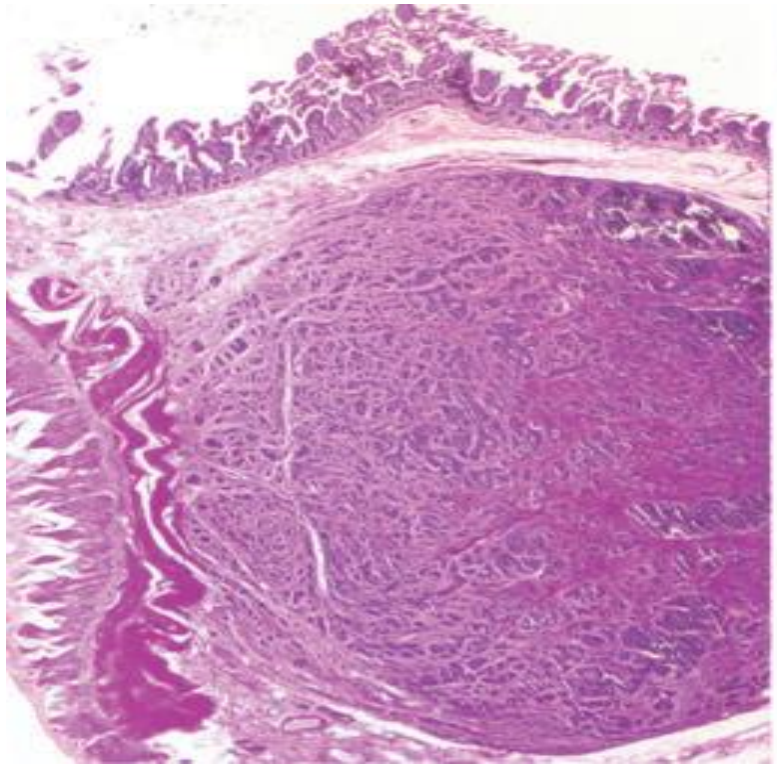
- The drop in gastric cancer incidence applies only to the intestinal type.
- Incidences of intestinal and diffuse types are now similar in some regions.
- **Most powerful prognostic factors: depth of invasion & extent of nodal and distant metastasis at the time of diagnosis**
- **Most cases discovered at advanced stage.**
- 5-year survival 90% to <30% for early and advanced tumors, respectively.
- Tx: surgery, chemotherapy, targeted Tx (anti HER2)

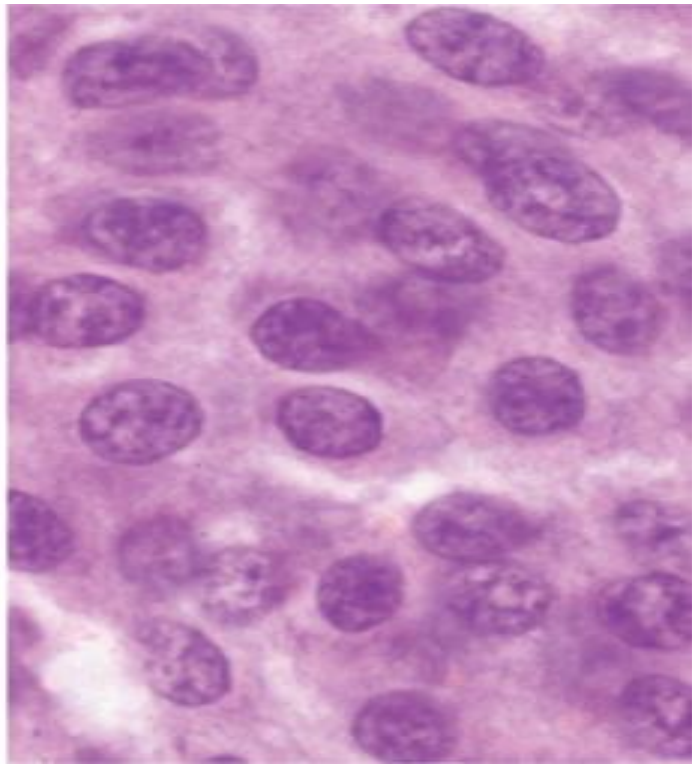
Lymphoma

- **Stomach is the most common site of extranodal lymphoma.**
- 5% of all gastric malignancies.
- Most common type : extranodal marginal zone B-cell lymphomas (MALToma) (indolent)
- Second most common lymphoma: diffuse large B cell lymphoma (aggressive)

Neuroendocrine (Carcinoid) Tumor

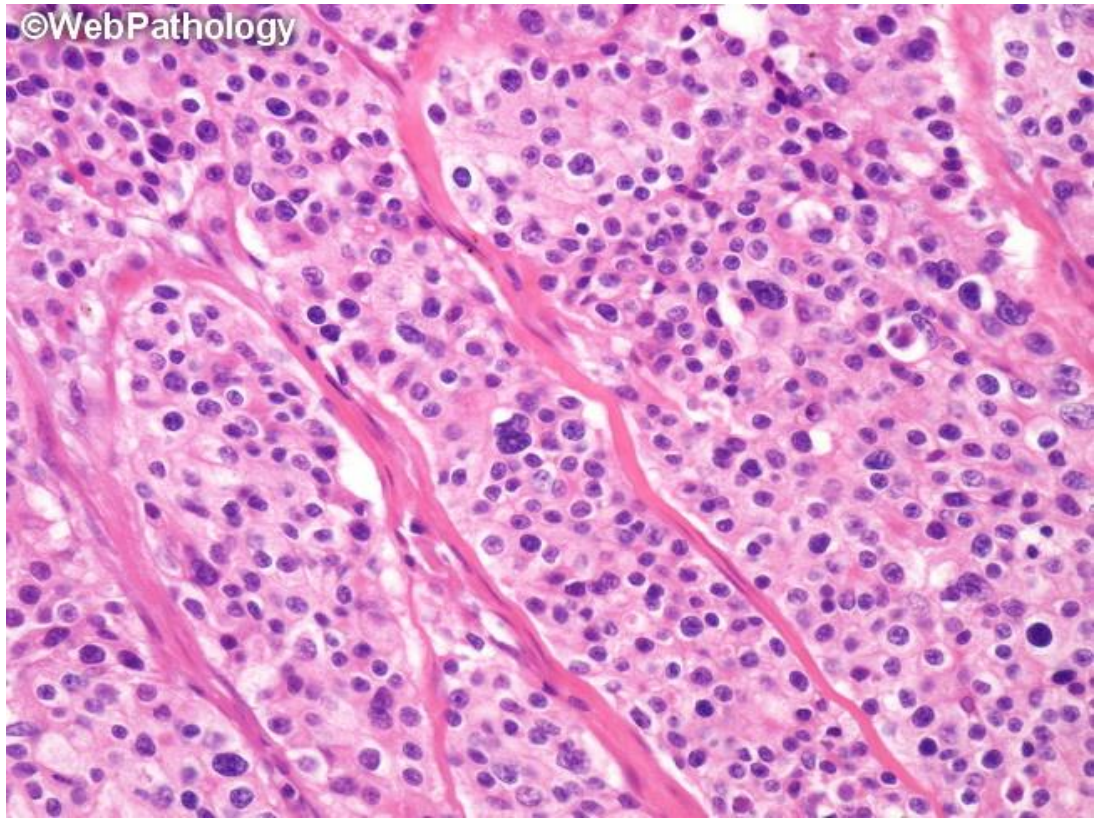
- Tumors arising from neuroendocrine-differentiated gastrointestinal epithelia (e.g., G cells).
- **> 40% occur in the small intestine**.
- Associated with endocrine cell hyperplasia, chronic atrophic gastritis, and Zollinger- Ellison syndrome
- **Slower growing than carcinomas.**





Intramural or submucosal masses (small polypoid lesions)

Islands, trabeculae, strands, glands, or sheets of uniform cells with scant, pink granular cytoplasm and salt and pepper chromatin.



carcinoid syndrome

Due to vasoactive substances

Seen in 10% of cases.

strongly associated with metastatic disease.

Cutaneous flushing, sweating, bronchospasm, colicky abdominal pain, diarrhea, and right-sided cardiac valvular fibrosis