

Pathology of the stomach-part 2

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Peptic Ulcer Disease



- ▶ Most often is associated with *H. pylori* infection or NSAID use
- ▶ Imbalance between mucosal defenses and damaging forces.
- ▶ In USA, NSAID is becoming the most common cause of gastric ulcers: 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



- ▶ More than 70% of PUD cases are associated with *H. pylori* infection
- ▶ Only 5 -10% of *H. pylori*-infected individuals develop ulcers.
- ▶ **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

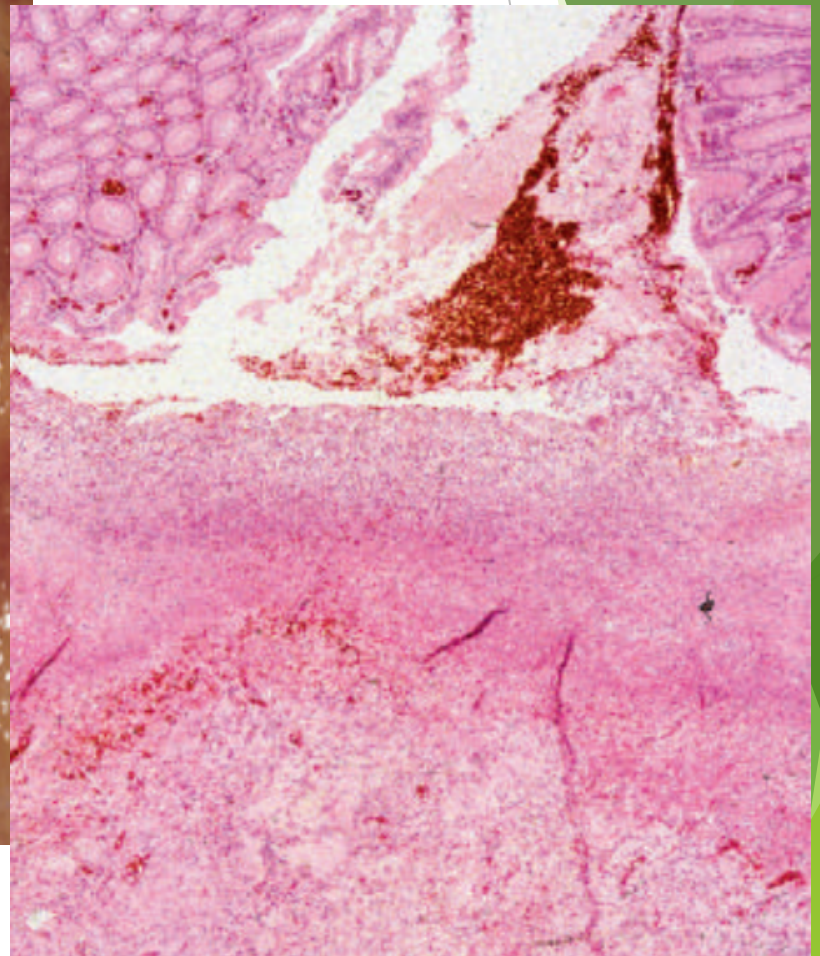
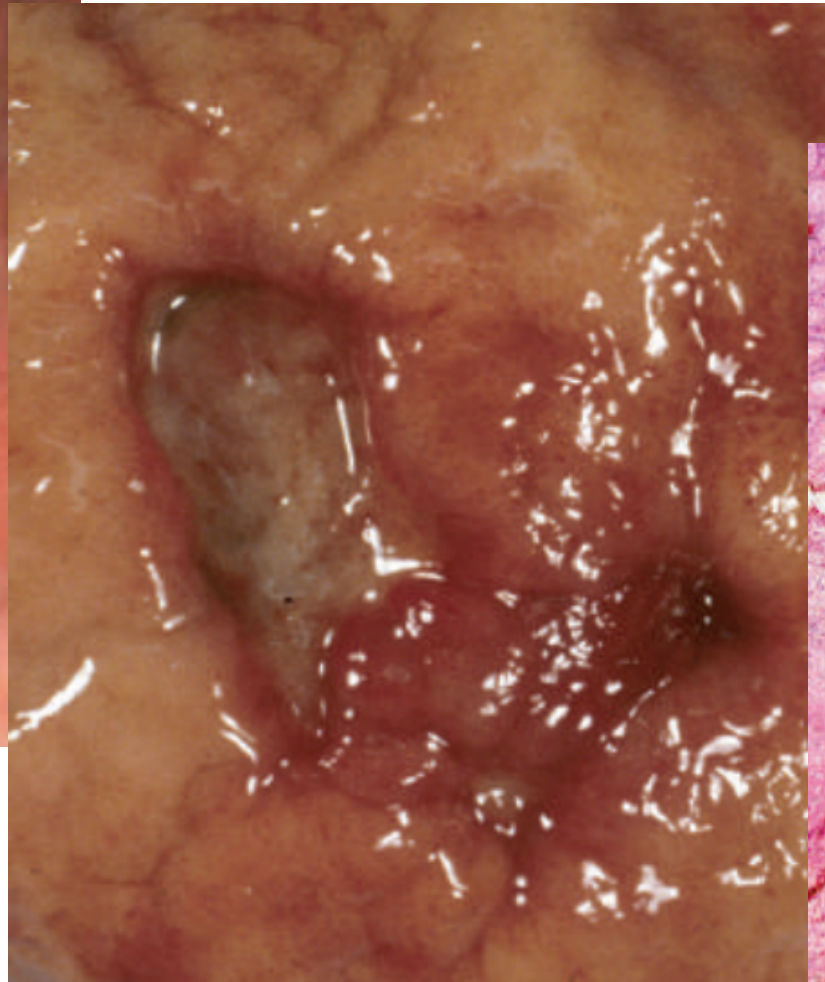
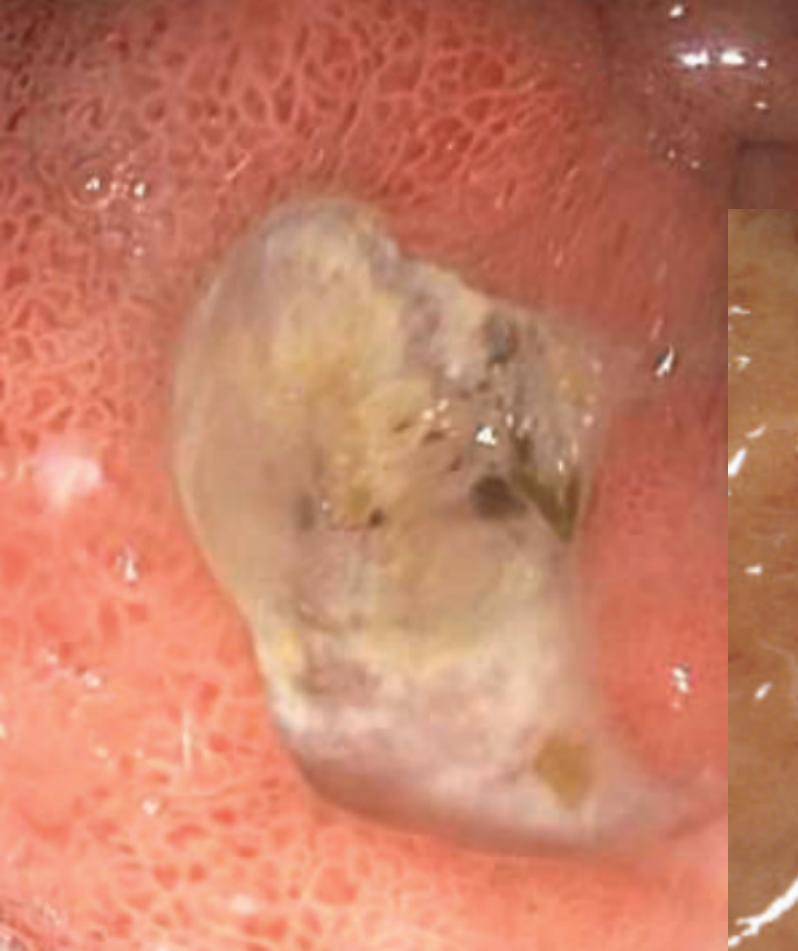


- ▶ Multiple peptic ulcerations
- ▶ Stomach , duodenum, even jejunum
- ▶ Caused by uncontrolled release of gastrin by a tumor (gastrinoma) and the resulting massive acid production.

MORPHOLOGY

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





Duodenal ulcer



Clinical Features

- ▶ Epigastric burning or aching pain
 - ▶ Pain 1 to 3 hours after meals at daytime
 - ▶ Worse at night, relieved by alkali or food
 - ▶ Nausea, vomiting, bloating, belching.
 - ▶ Iron deficiency anemia, frank hemorrhage, or perforation.
-
- ▶ 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
- ▶ Epithelial or stromal cell hyperplasia, inflammation, ectopia, or neoplasia.
- ▶ **Inflammatory and Hyperplastic Polyps**
- ▶ 75% of all polyps.
- ▶ Arise in a background of chronic gastritis
- ▶ Regress after H.pylori eradication.
- ▶ Risk of dysplasia if size > 1.5 cm.

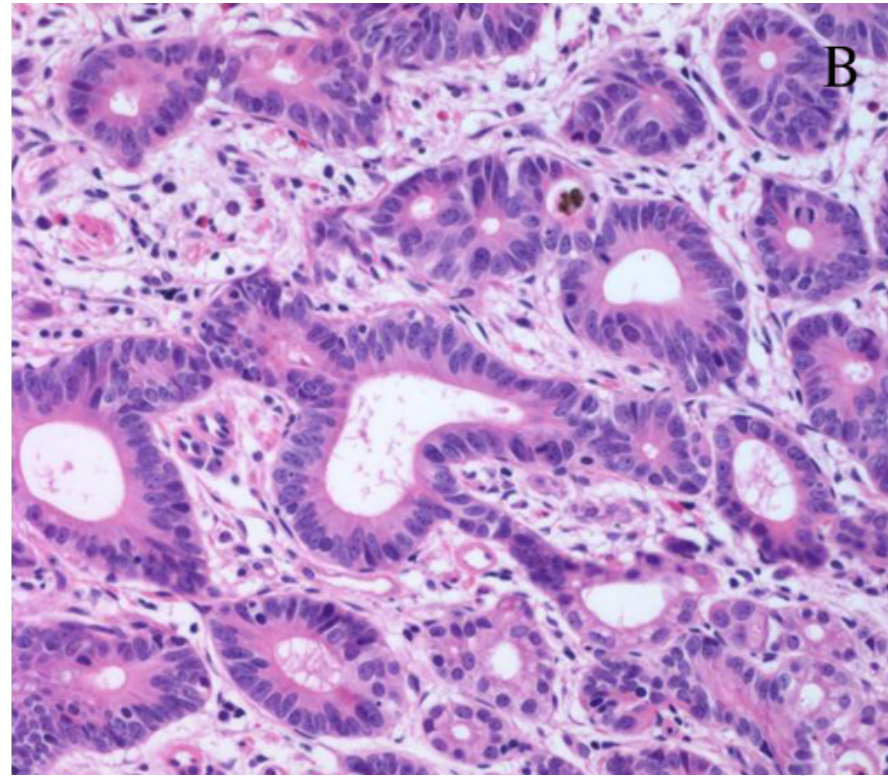
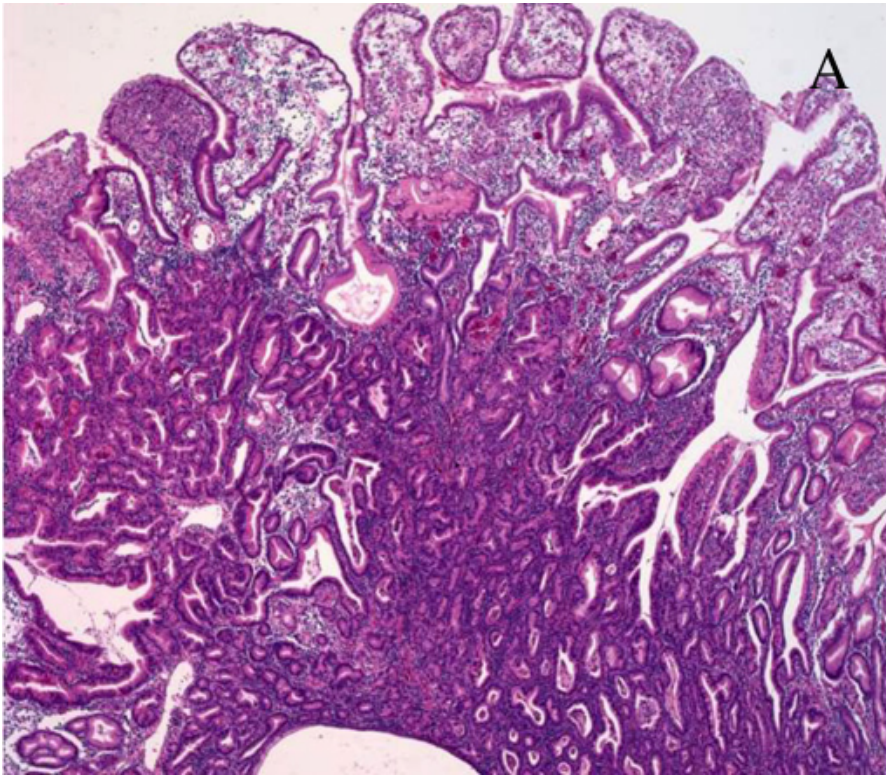


Gastric Adenoma

- ▶ 10% of all polyps.
- ▶ Increase with age.
- ▶ M:F = 3:1
- ▶ Background of chronic gastritis, atrophy and intestinal metaplasia.
- ▶ Dysplasia in all cases, 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.
- ▶ Rates vary markedly with geography (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 due to H.pylori associated chronic gastritis , lesser extent EBV (10%).
- ▶ Most cases are sporadic.
- ▶ Familial cases: mutations in *CDH1* (E-cadherin) >> diffuse type.
- ▶ Sporadic diffuse type Ca: CDH1 mutation in 50%.
- ▶ FAP: APC gene mutation, intestinal type cancer.
- ▶ Sporadic intestinal-type Ca: B catenin mutation
- ▶ P53 mutation in sporadic cancer of both types.



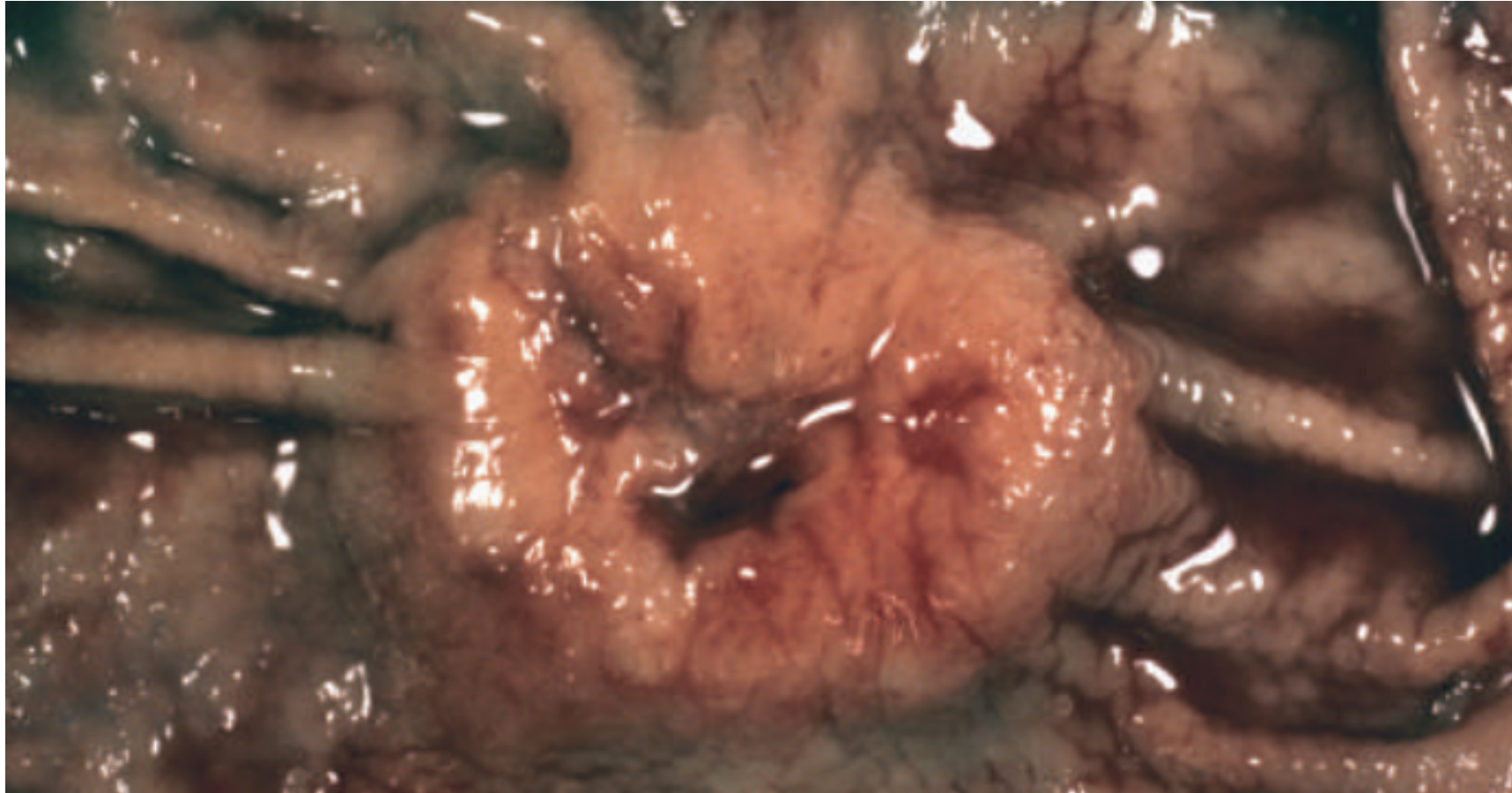
MORPHOLOGY

- ▶ Lauren classification: separates gastric cancers into intestinal and diffuse types.
- ▶ **Intestinal type:**
- ▶ Bulky.
- ▶ Exophytic mass or ulcer.
- ▶ Form glands.

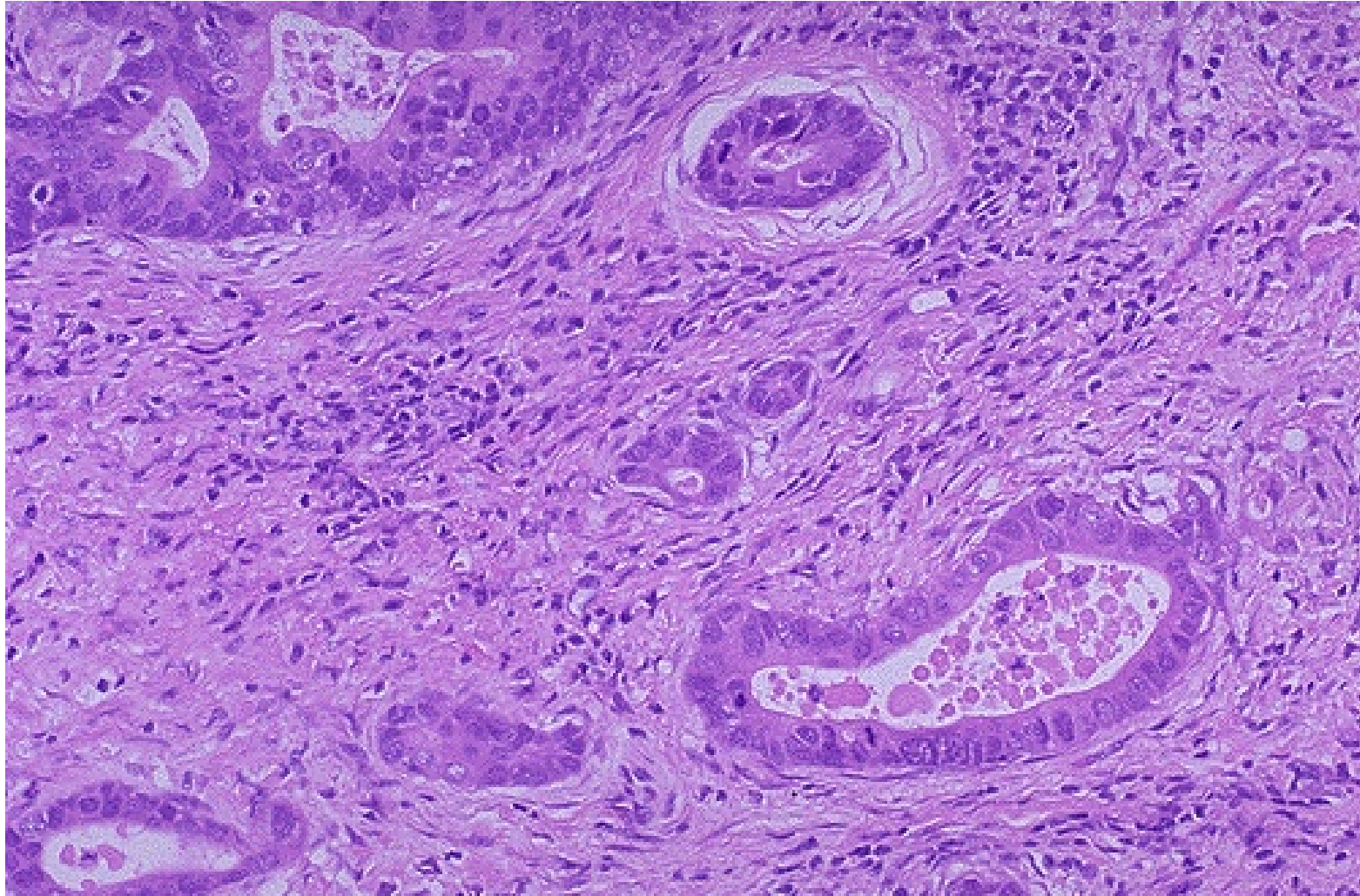
- ▶ **Diffuse gastric cancers**
- ▶ Infiltrative growth pattern
- ▶ Discohesive cells (signet ring cells)
- ▶ Desmoplastic reaction (thick wall, linitis plastica).



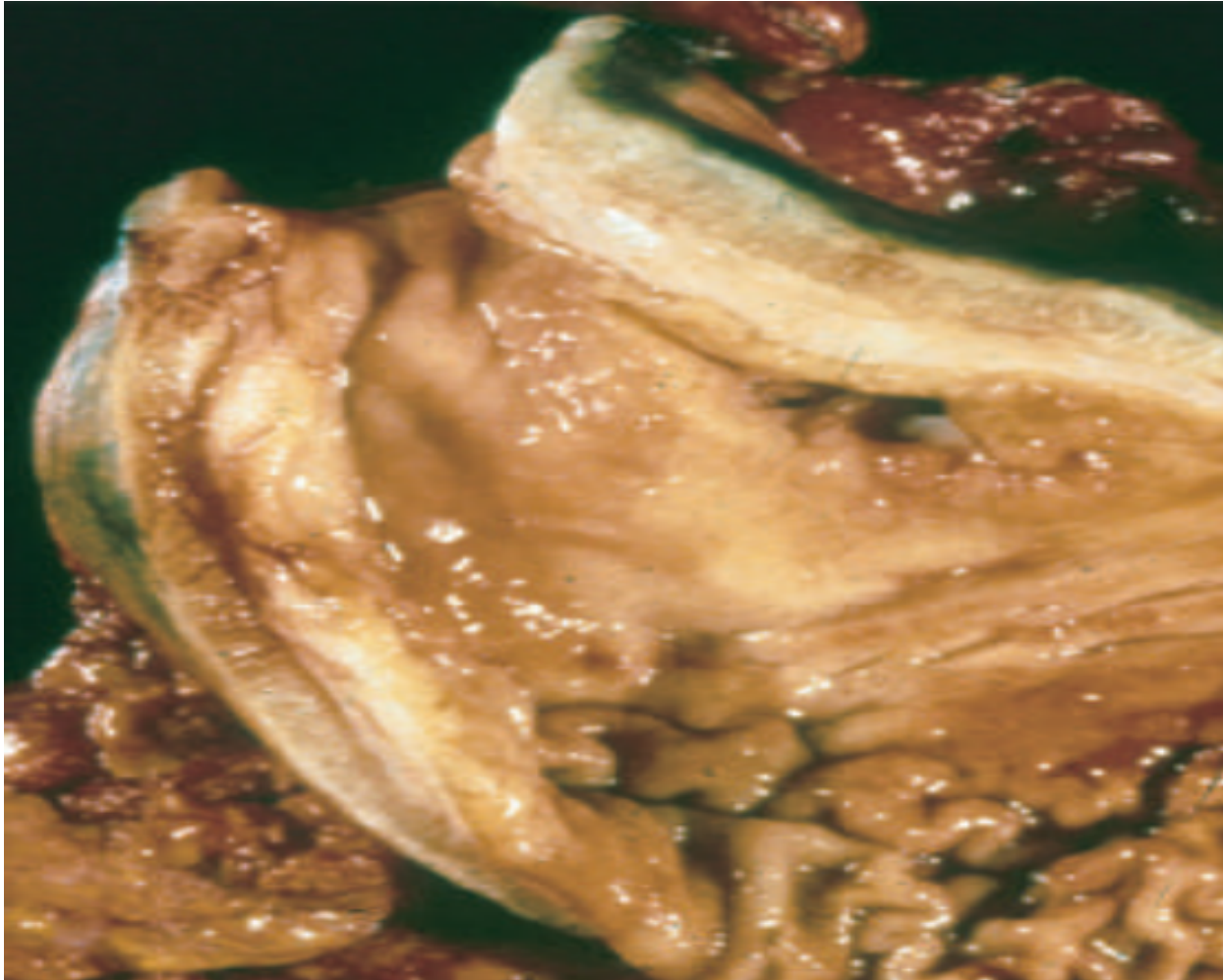
Intestinal type



Intestinal type

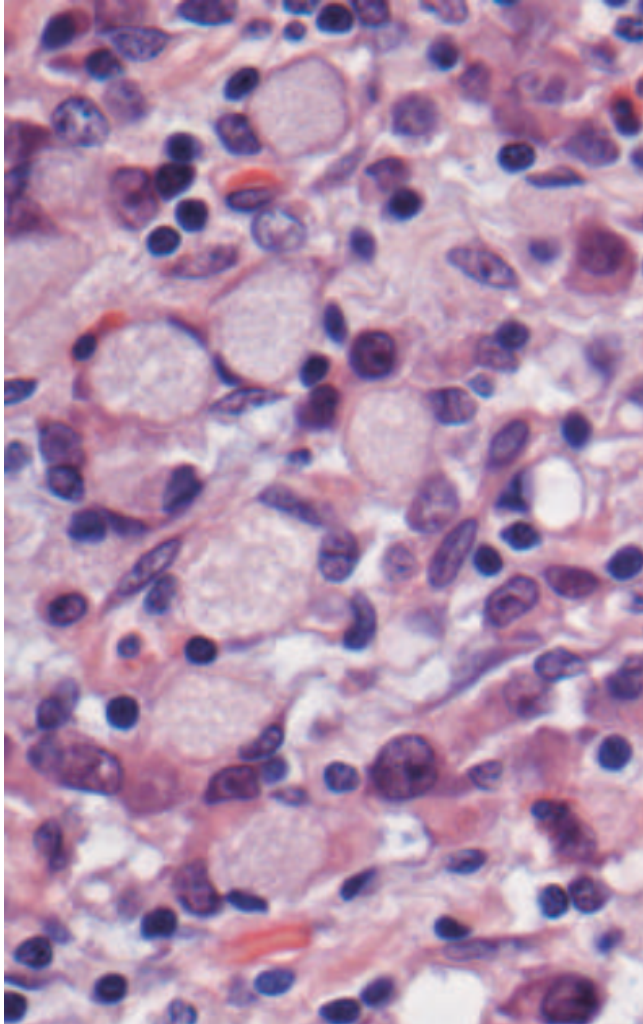


Linitis plastica

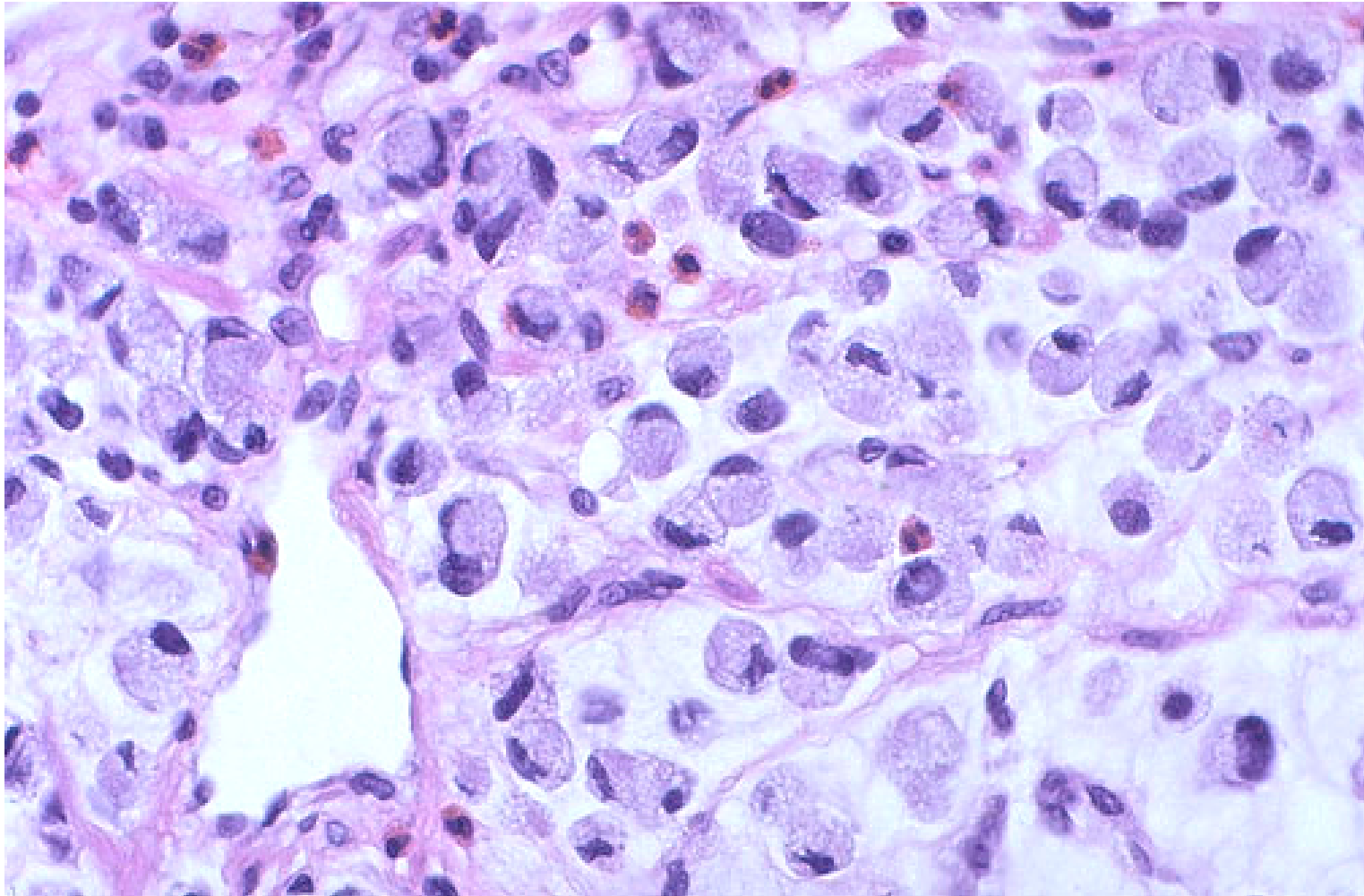


Signet ring cells:

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.



- ▶ Symptoms overlap with chronic gastritis, in addition to weight loss.
- ▶ 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 Dx at advanced stage.**
- ▶ 5 year survival 90% to 20% for early and advanced tumors, respectively.
- ▶ Tx: surgery, chemotherapy, targeted Tx (anti HER2)



Lymphoma



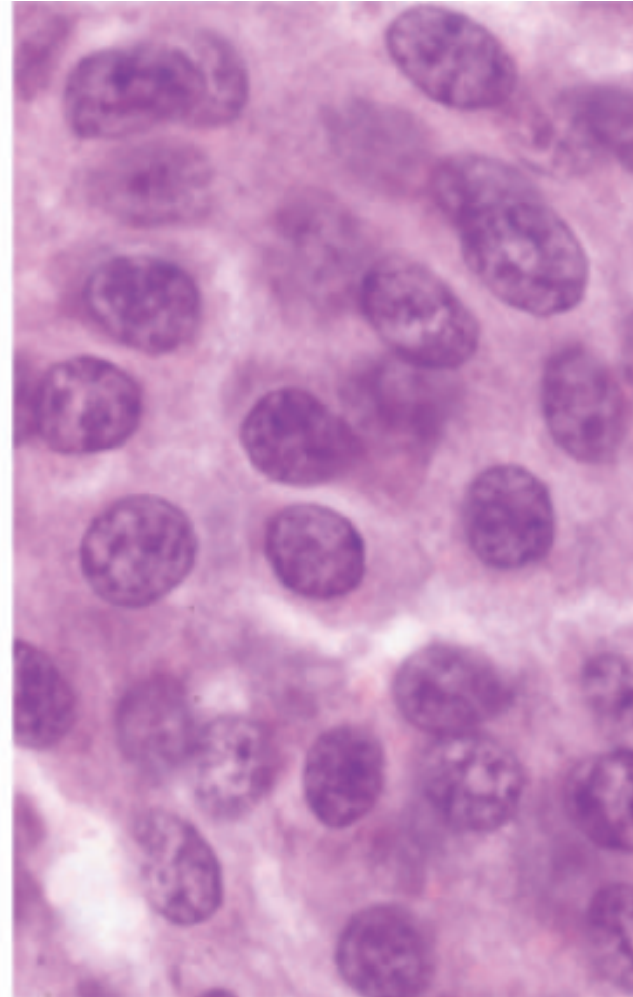
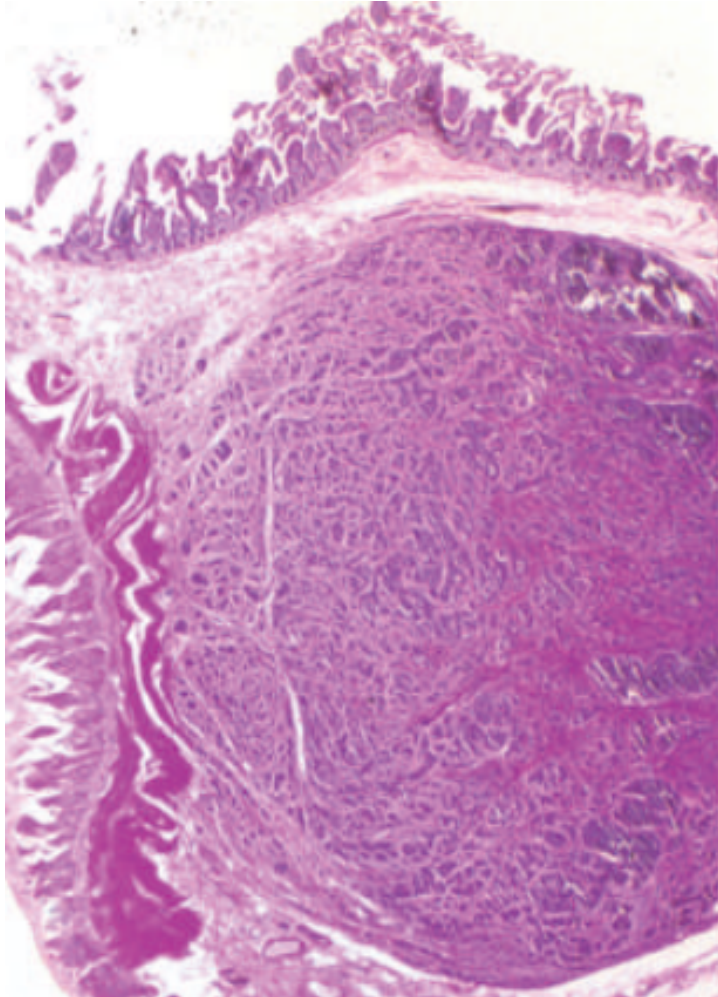
- ▶ Stomach is the most common site of extranodal lymphoma.
- ▶ 5% of all gastric malignancies.
- ▶ Most common type : indolent extranodal marginal zone B-cell lymphomas (*MALToma*)
- ▶ *Second most common lymphoma: diffuse large B cell lymphoma*

Neuroendocrine (Carcinoid) Tumor

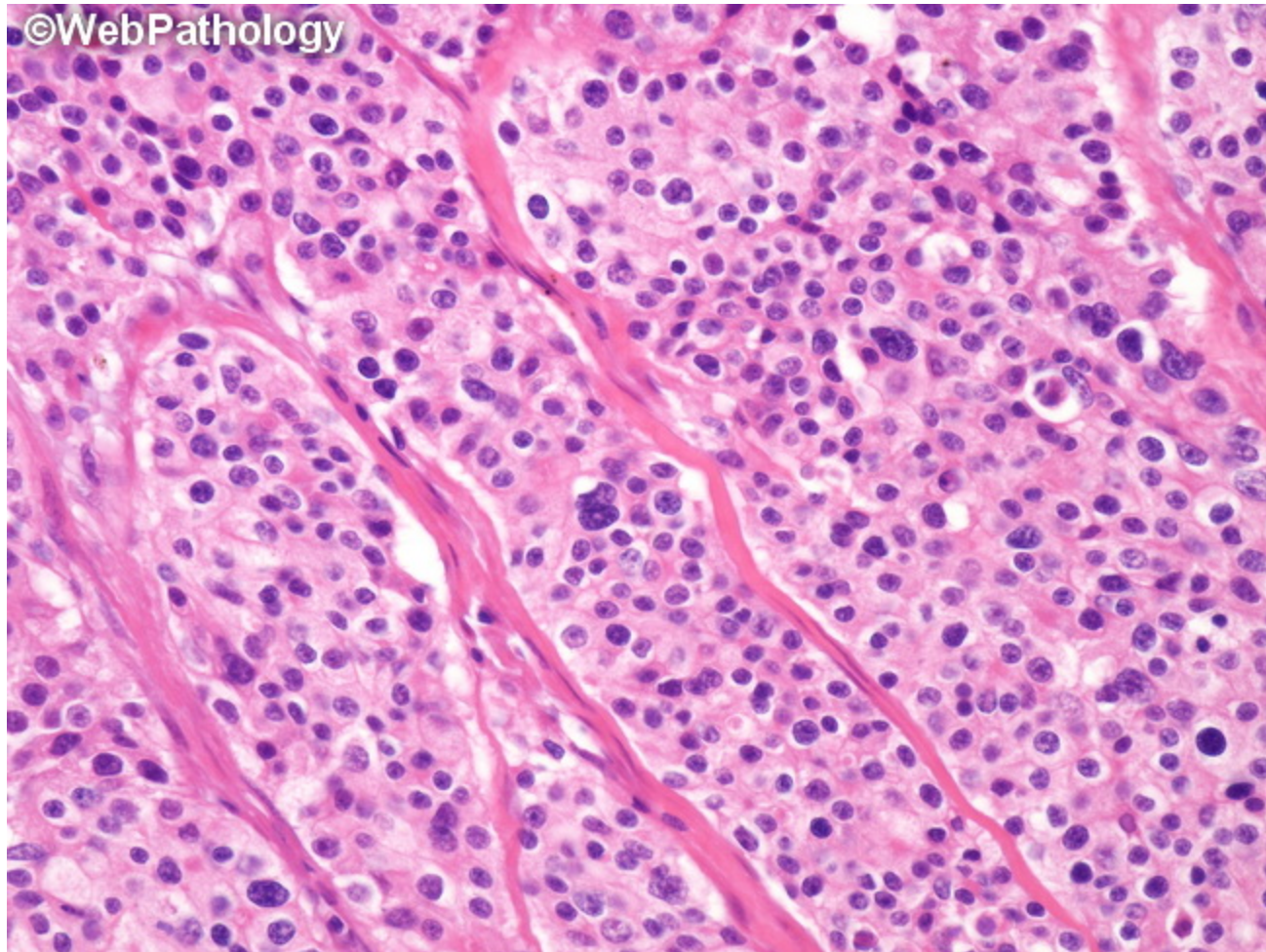


- ▶ Tumors arising from neuroendocrine-differentiated gastrointestinal epithelia (e.g., G cells).
- ▶ > 40% occur in the small intestine.
- ▶ Associated with endocrine cell hyperplasia, chronic atrophic gastritis, and Zollinger- Ellison syndrome
- ▶ Slower growing than carcinomas.

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