

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, bletching.
 - ▶ Iron deficiency anemia, frank hemorrhage, or perforation.
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- ▶ 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

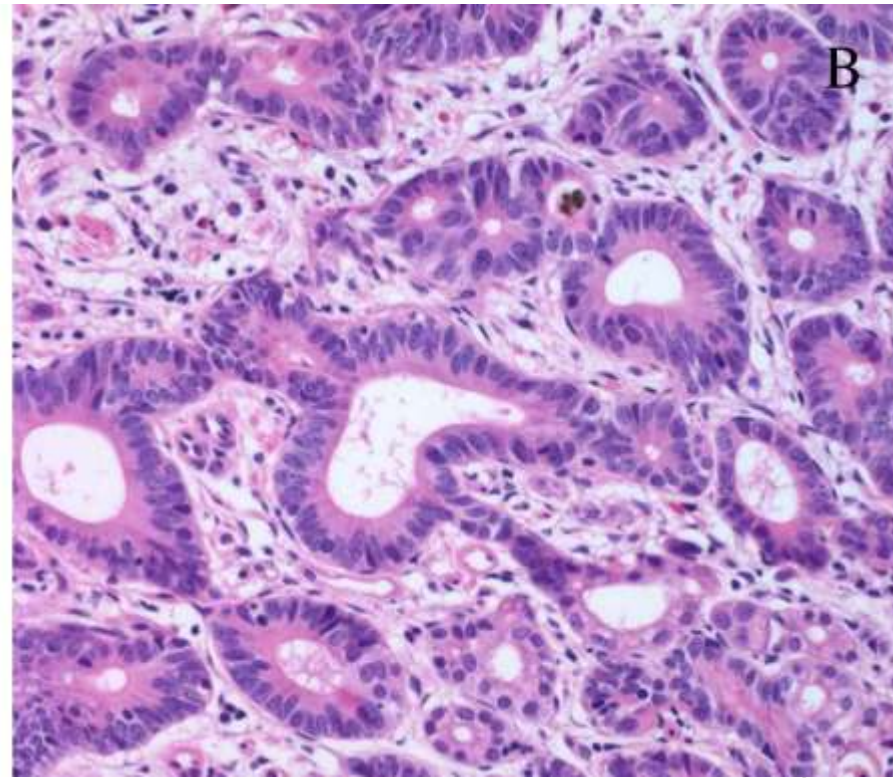
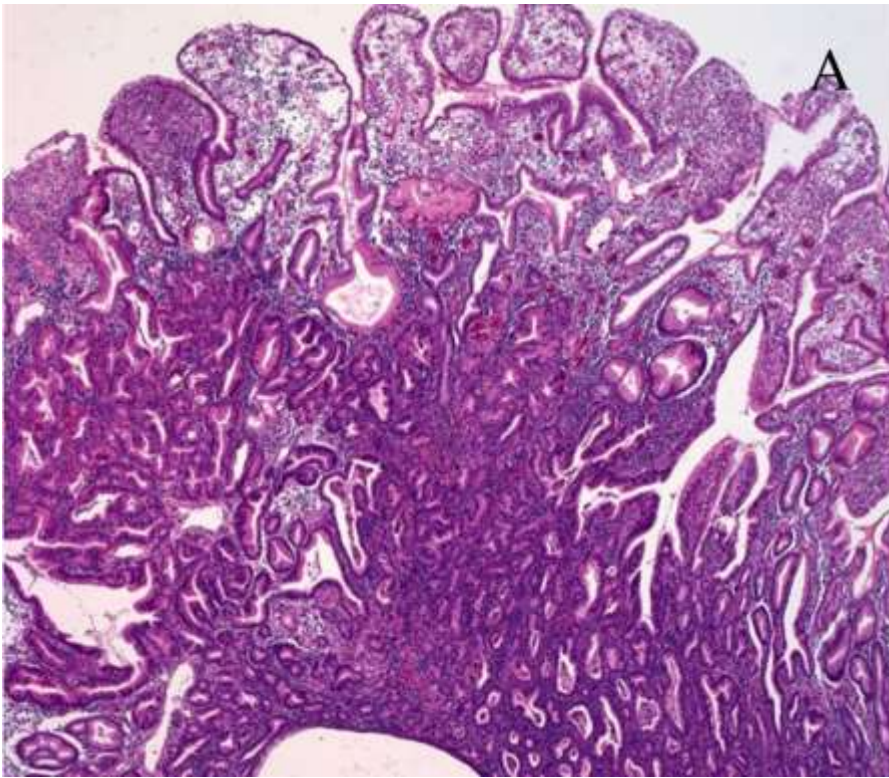
- ▶ Polyps: masses projecting above the level of adjacent mucosa
- ▶ Epithelial or stromal cell hyperplasia, inflammation, ectopia, or neoplasia.

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

Gastric Adenoma

- ▶ 10% of all polyps.
- ▶ Increase with age.
- ▶ M: eF = 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

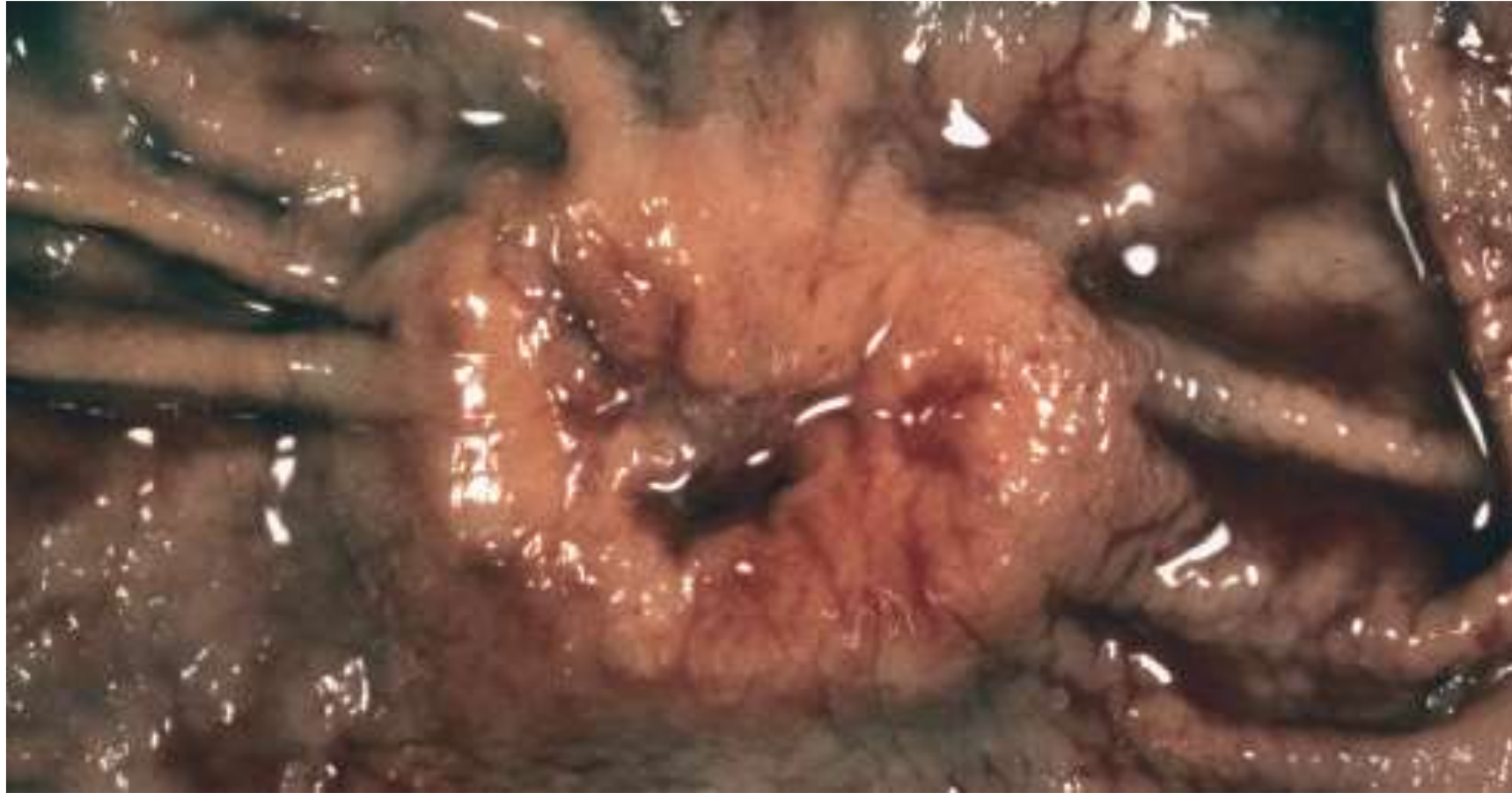
- ▶ Genetic alterations due to H.pylori associated chronic gastritis , lesser extent EBV (10%).
- ▶ Most cases are sporadic.
- ▶ Familial diffuse type cases: mutations in *CDH1* (E-cadherin).
- ▶ Sporadic diffuse type Ca: *CDH1* mutation in 50%.
- ▶ FAP: APC gene mutation, intestinal type cancer.
- ▶ Sporadic intestinal-type Ca: B catenin mutation
- ▶ P53 mutation in sporadic cancer of both types.

MORPHOLOGY

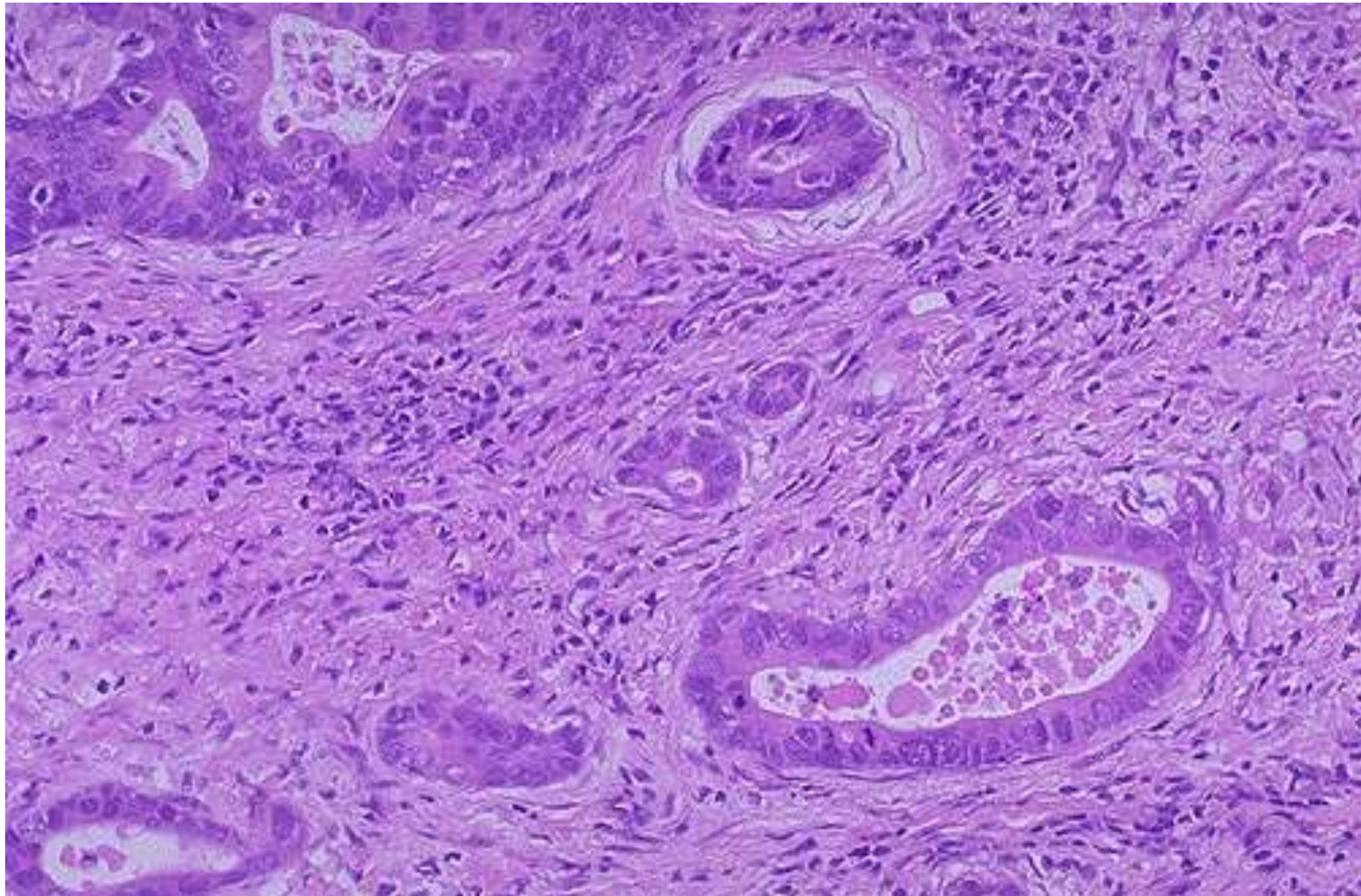
- ▶ Lauren classification: separates gastric cancers into intestinal and diffuse types.
- ▶ **Intestinal type:**
- ▶ Bulky.
- ▶ Exophytic mass or ulcer.
- ▶ Form glands.

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

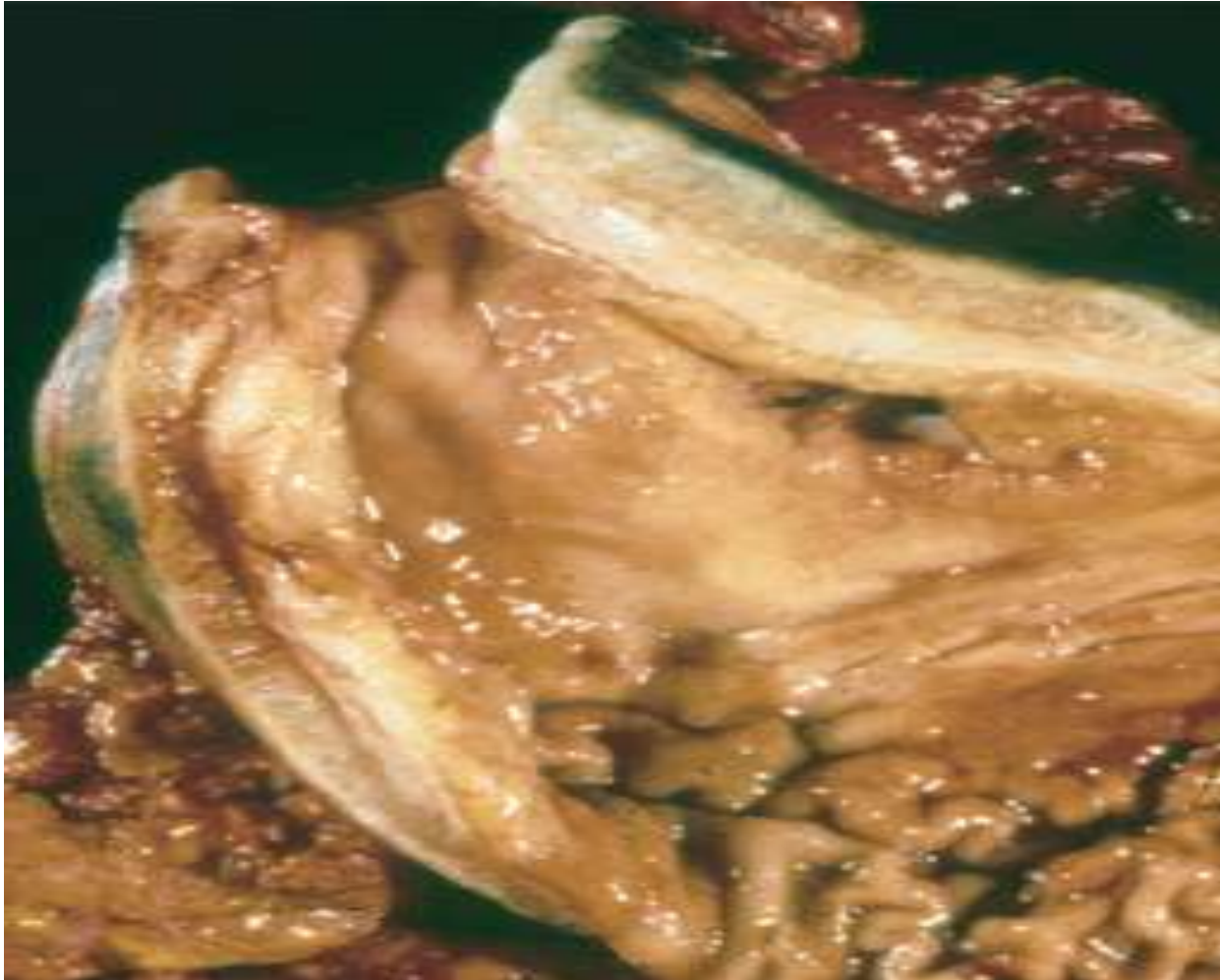
Intestinal type



Intestinal type

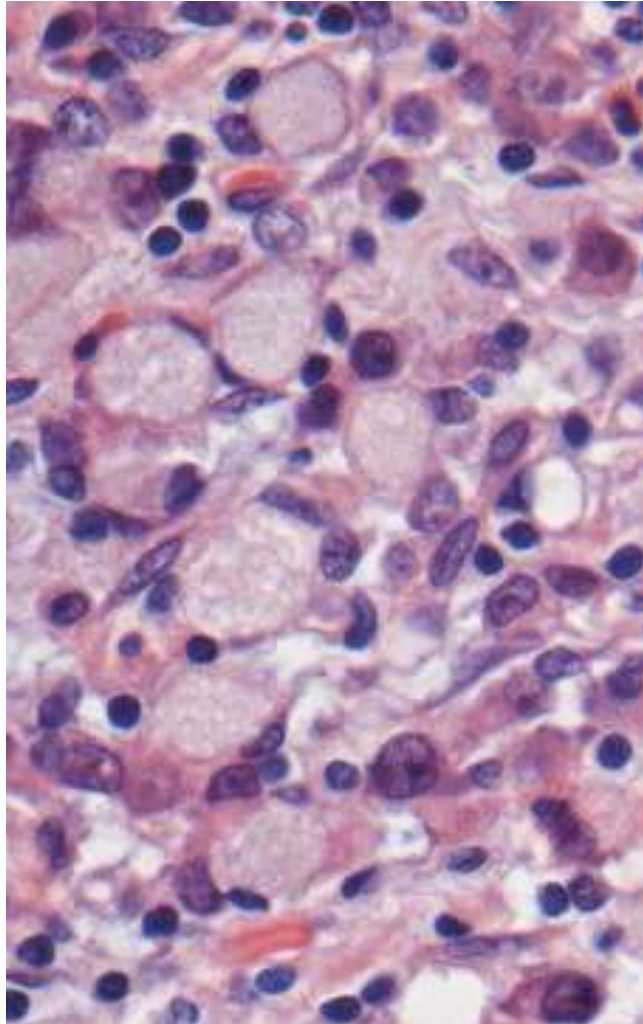


Linitis plastica

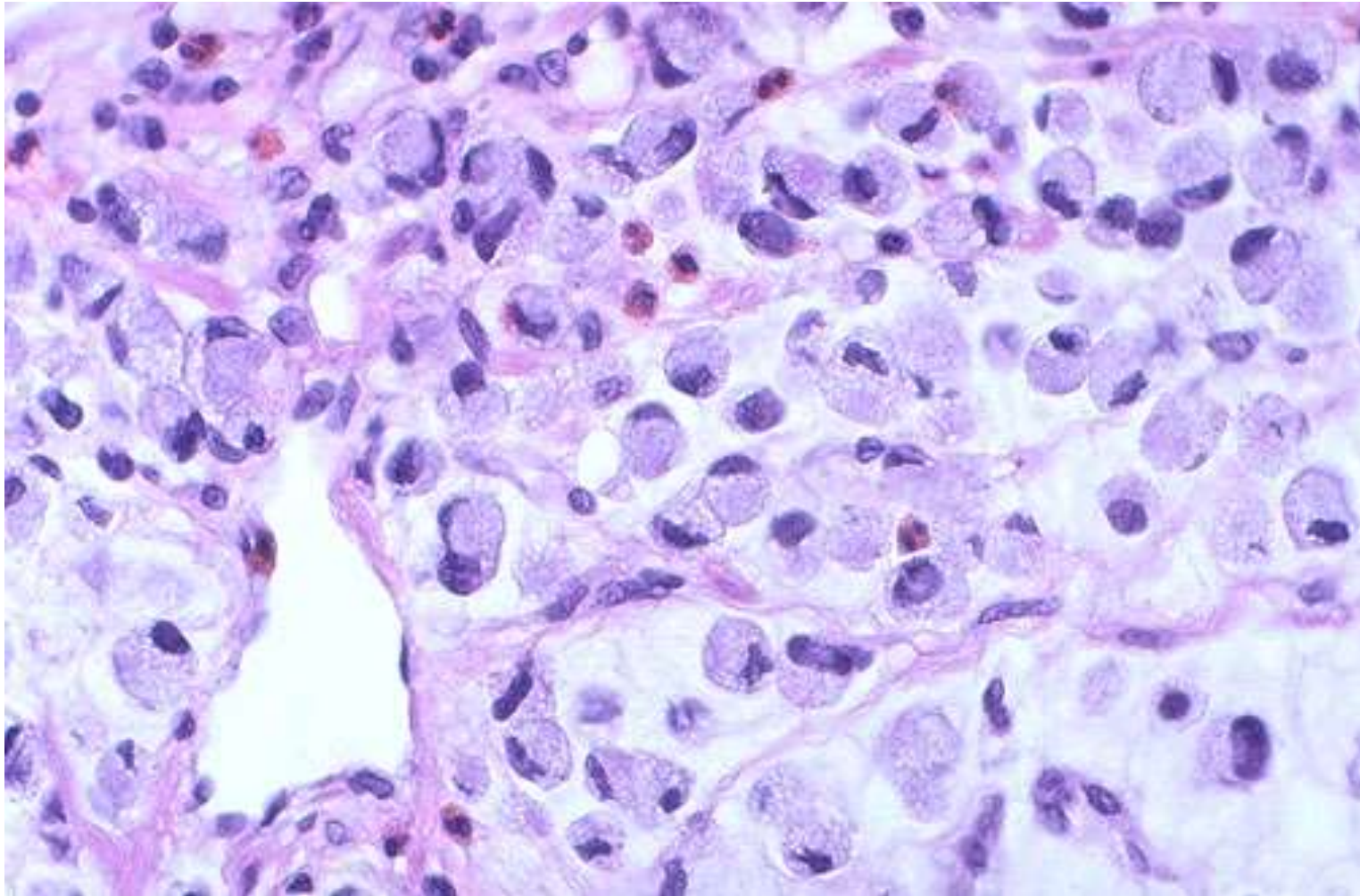


Signet ring cells:

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)

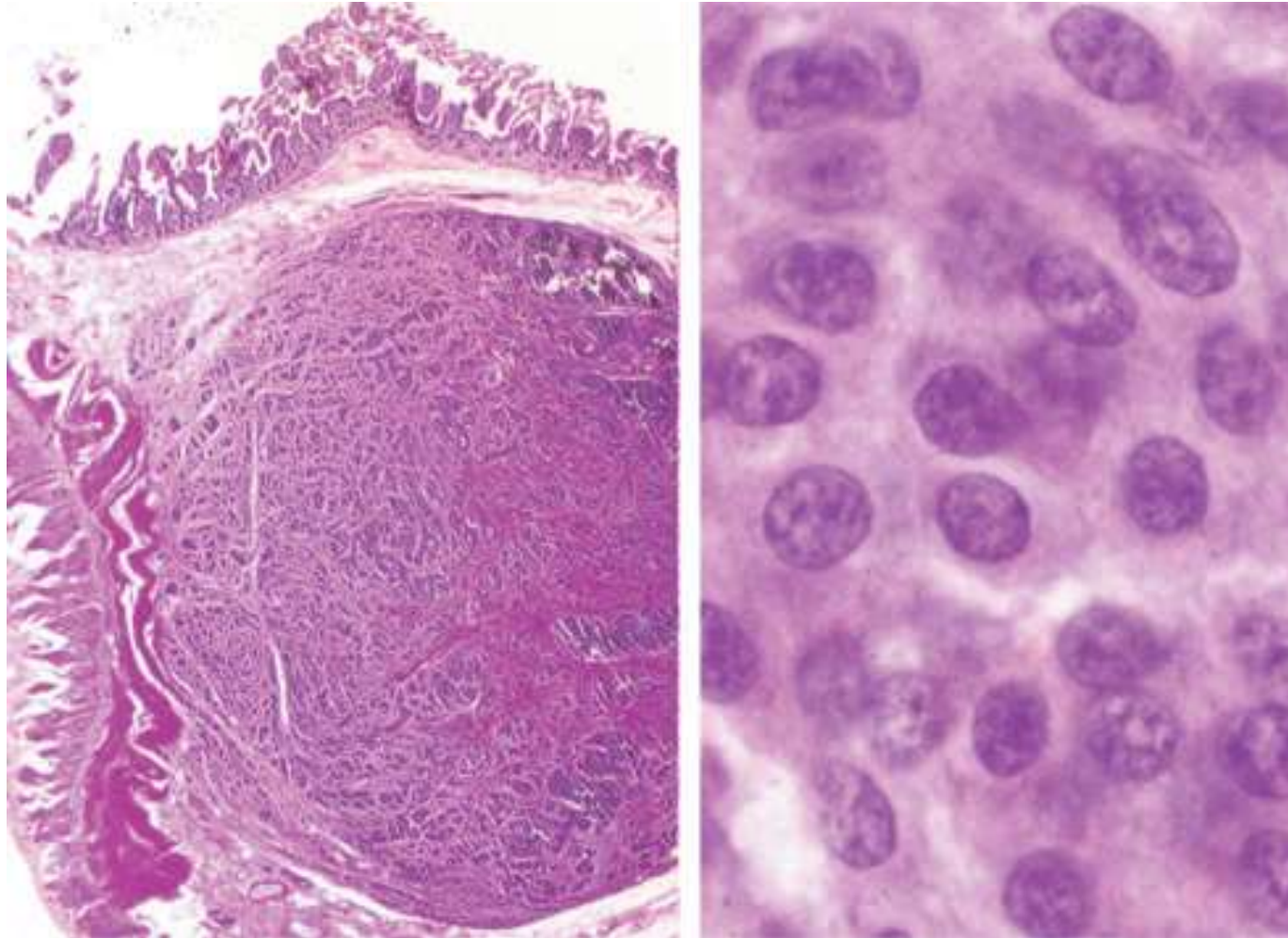
Lymphoma

- ▶ 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

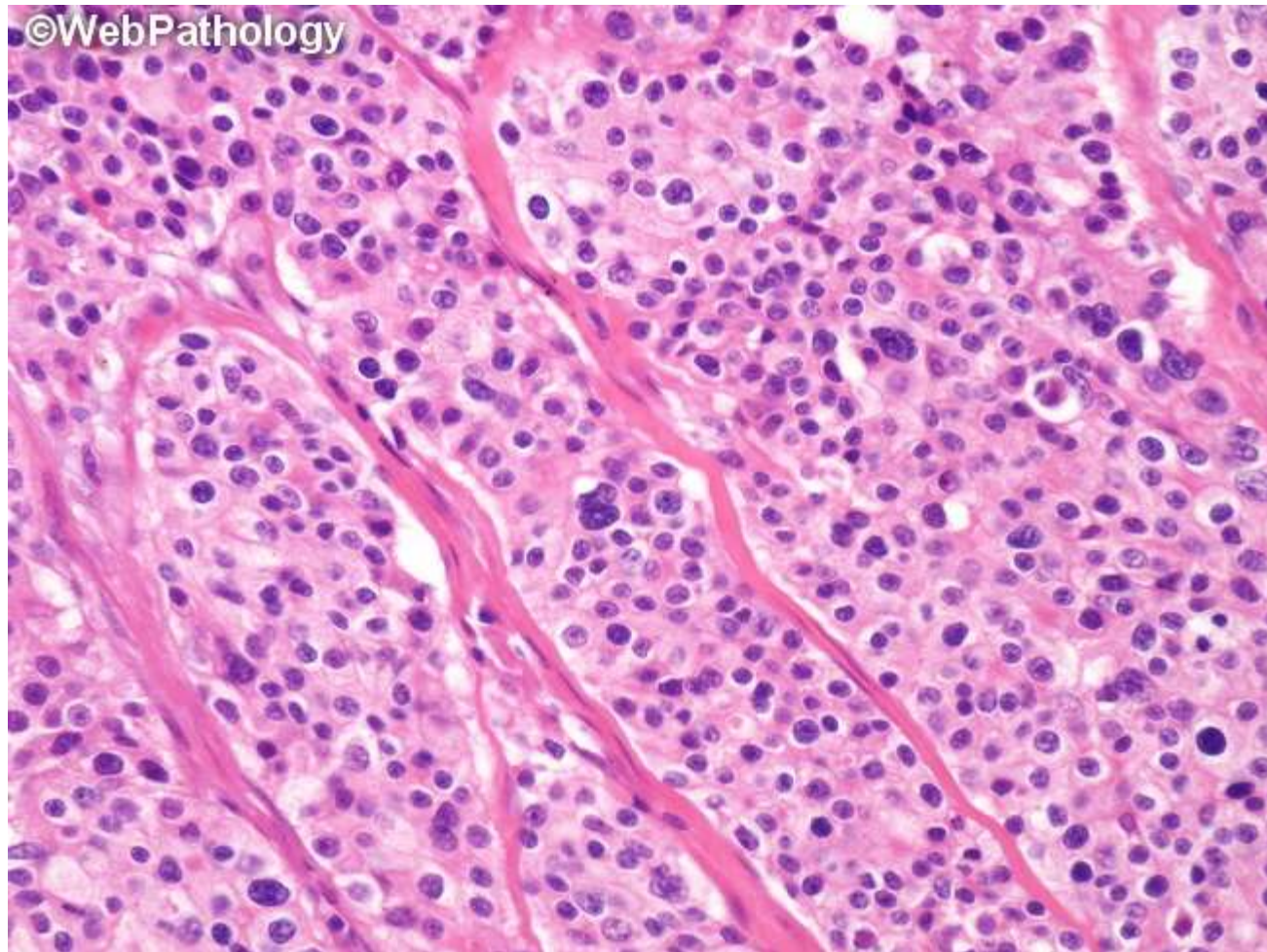
Neuroendocrine (Carcinoid) Tumor

- ▶ 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**