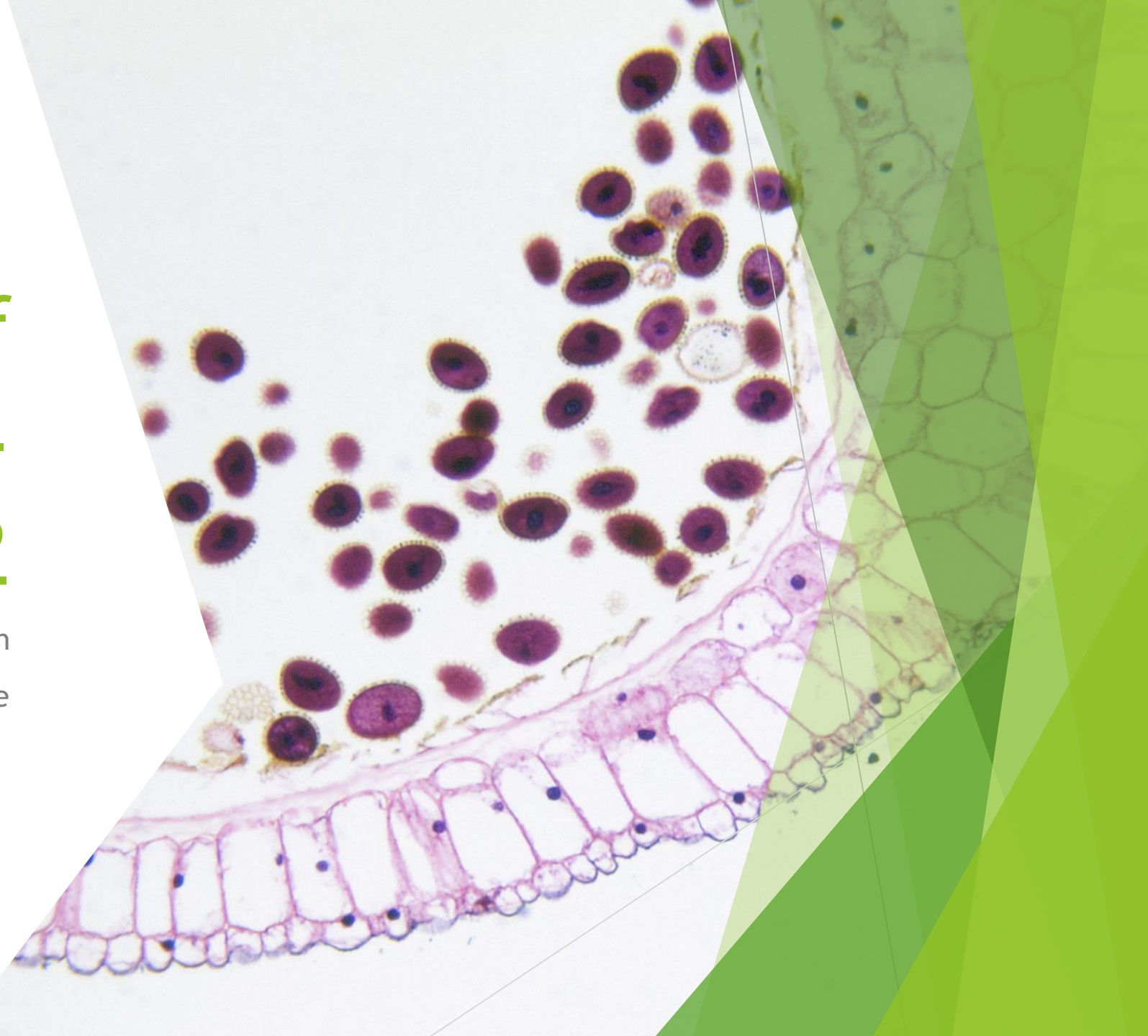
# Pathology of the stomach-2

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)

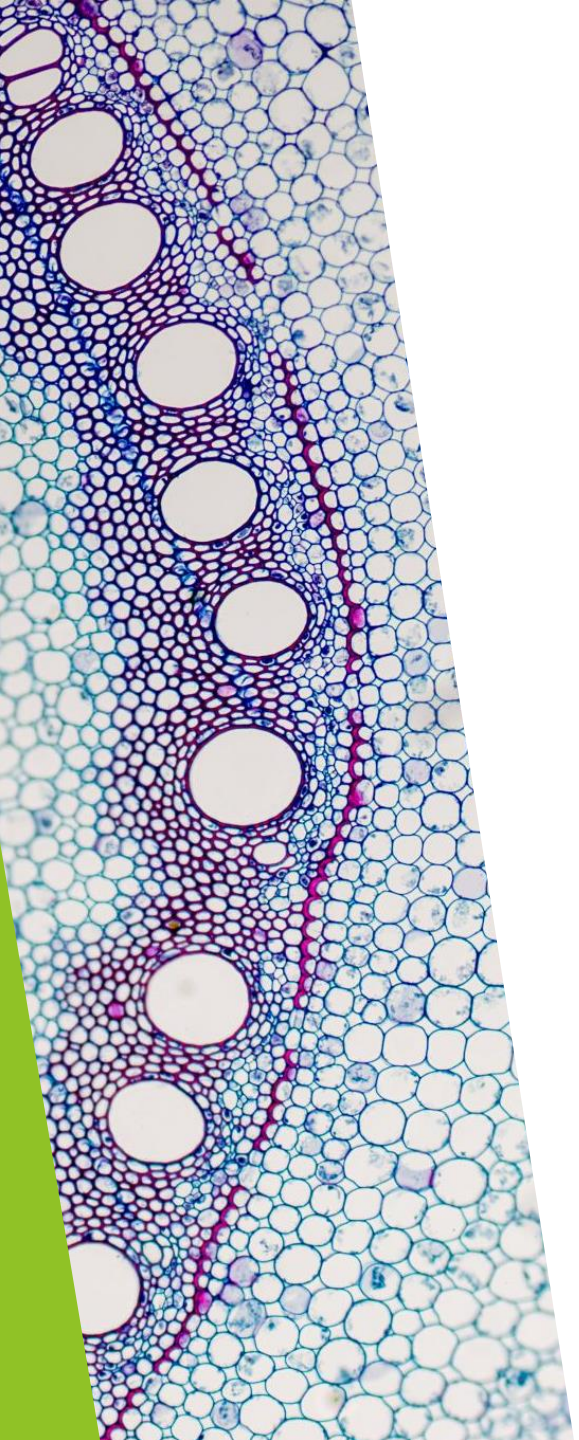
# Pathogenesis of PUD:

- > 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

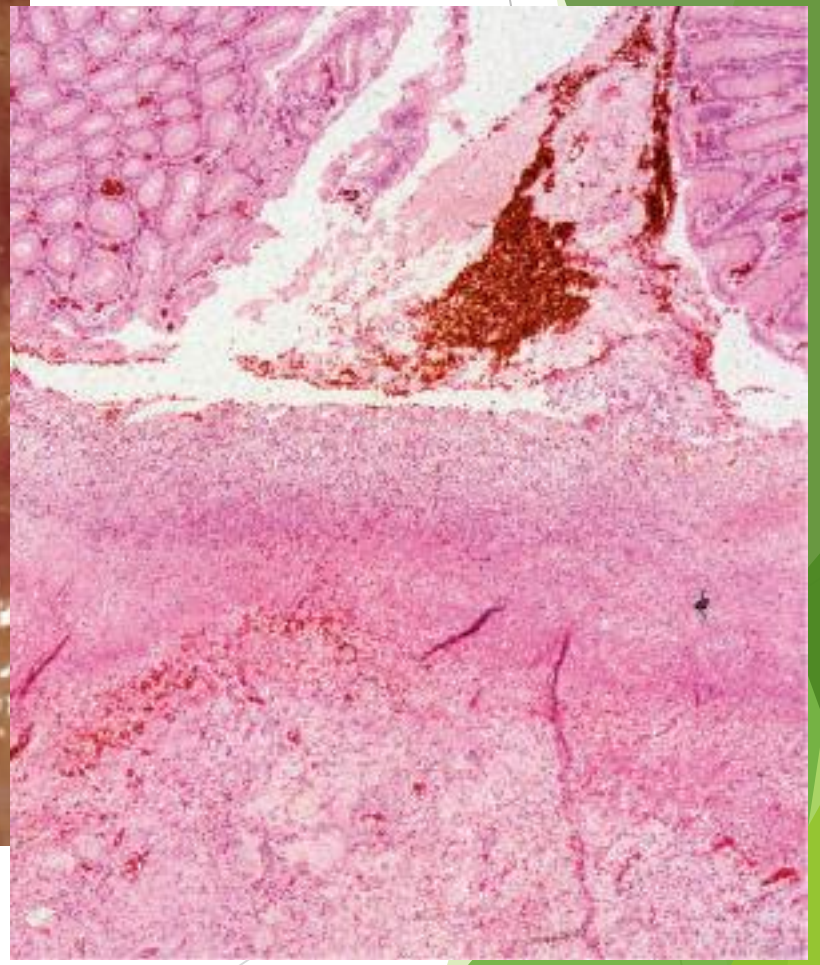
# Zollinger-Ellison syndrome

- 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

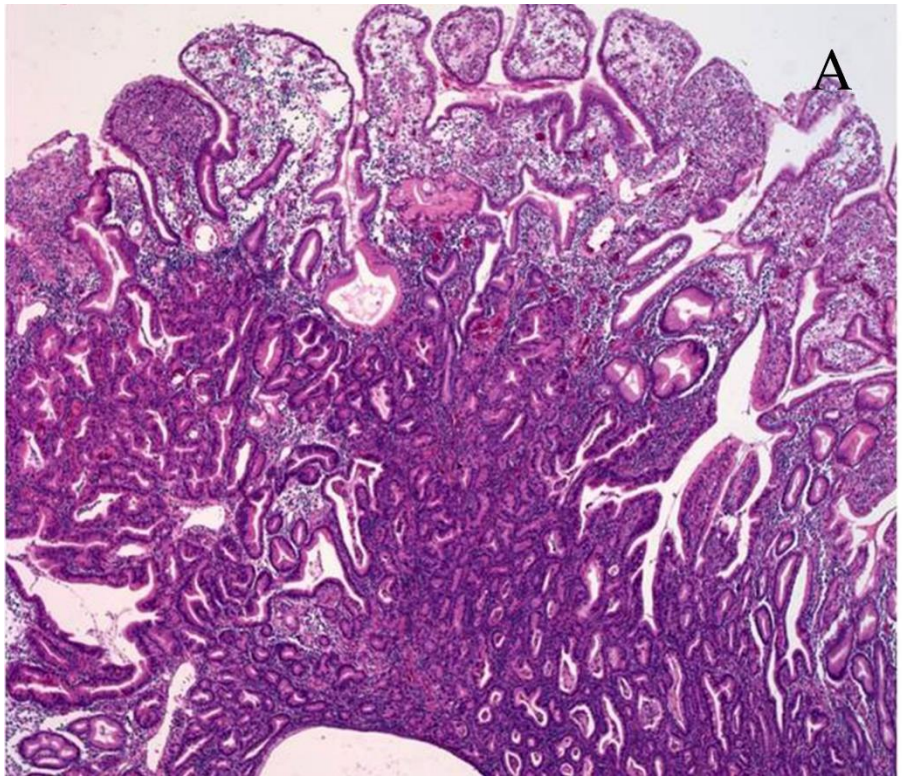
- Polyps: masses projecting above the level of adjacent mucosa

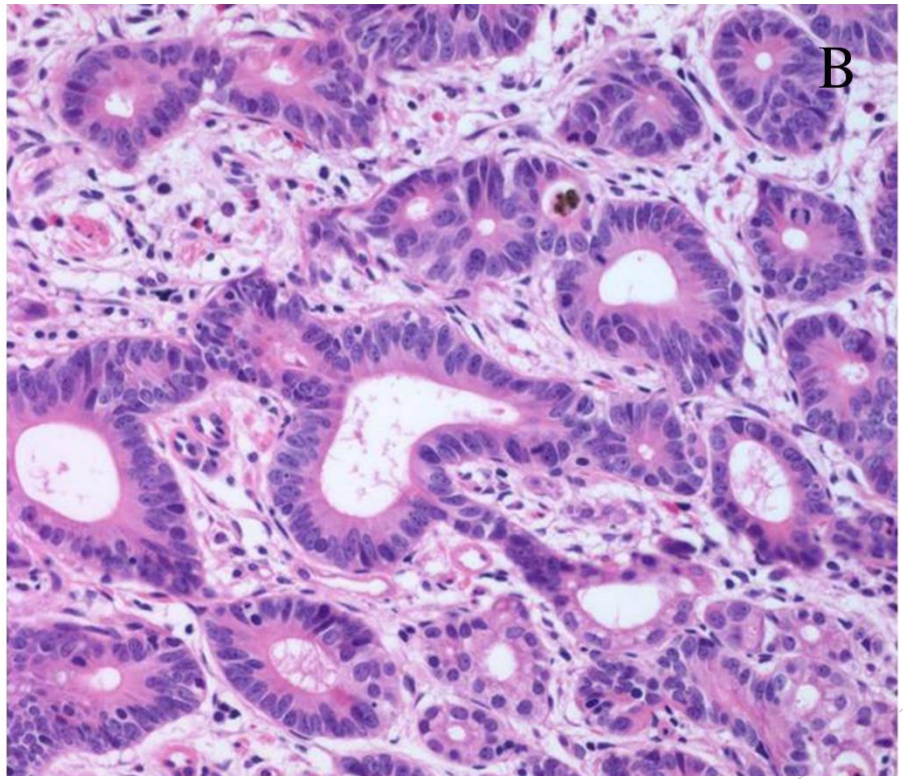
- **Inflammatory and Hyperplastic Polyps**
- 75% of all polyps.
- Arise in a background of chronic gastritis
- Regress  after H.pylori eradication.

# 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.

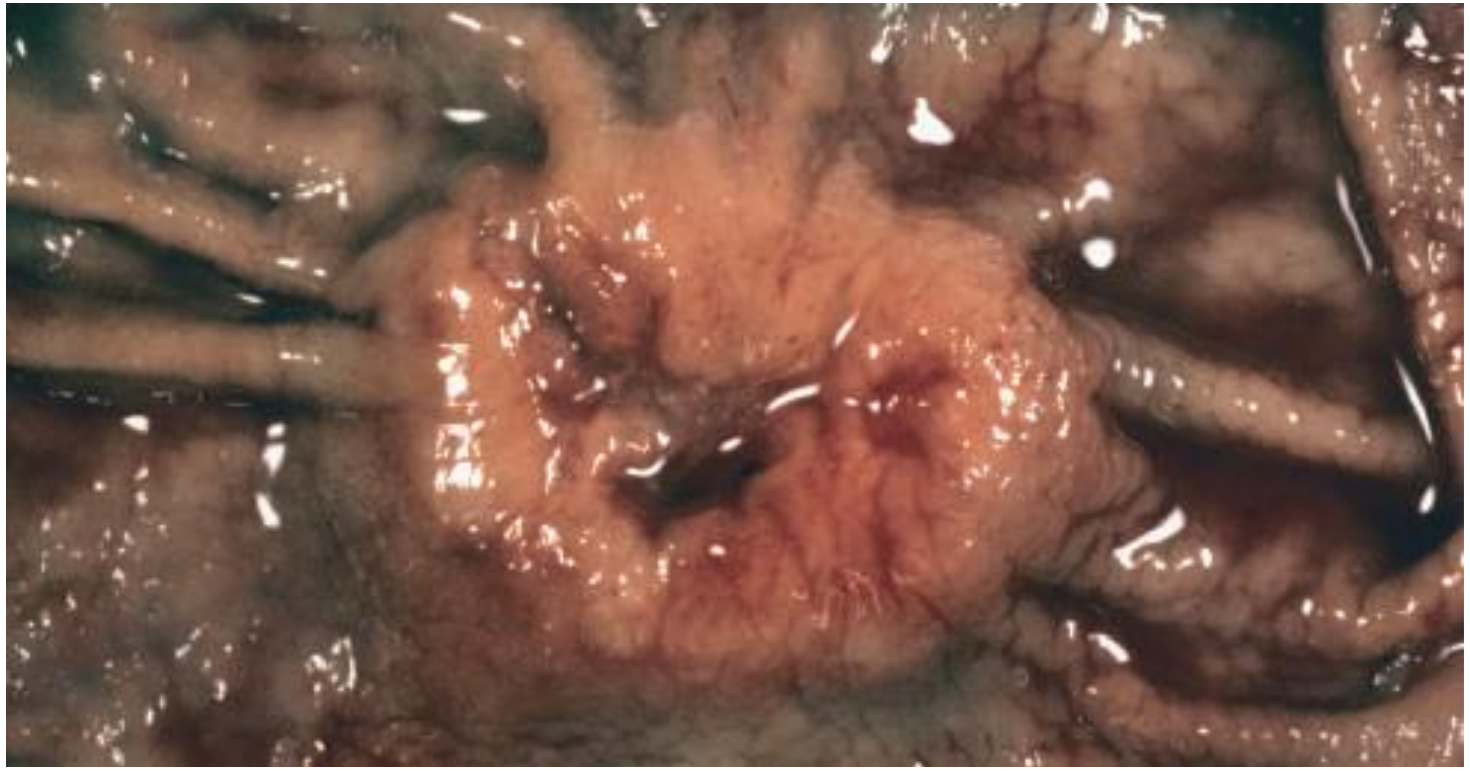
- Familial diffuse type: germline mutations in *CDH1* (E-cadherin).
- Sporadic diffuse type: somatic CDH1 mutation in 50%.
- Familial intestinal type cancer: FAP, APC gene mutation.
- Sporadic intestinal-type Ca: B catenin mutation

- 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

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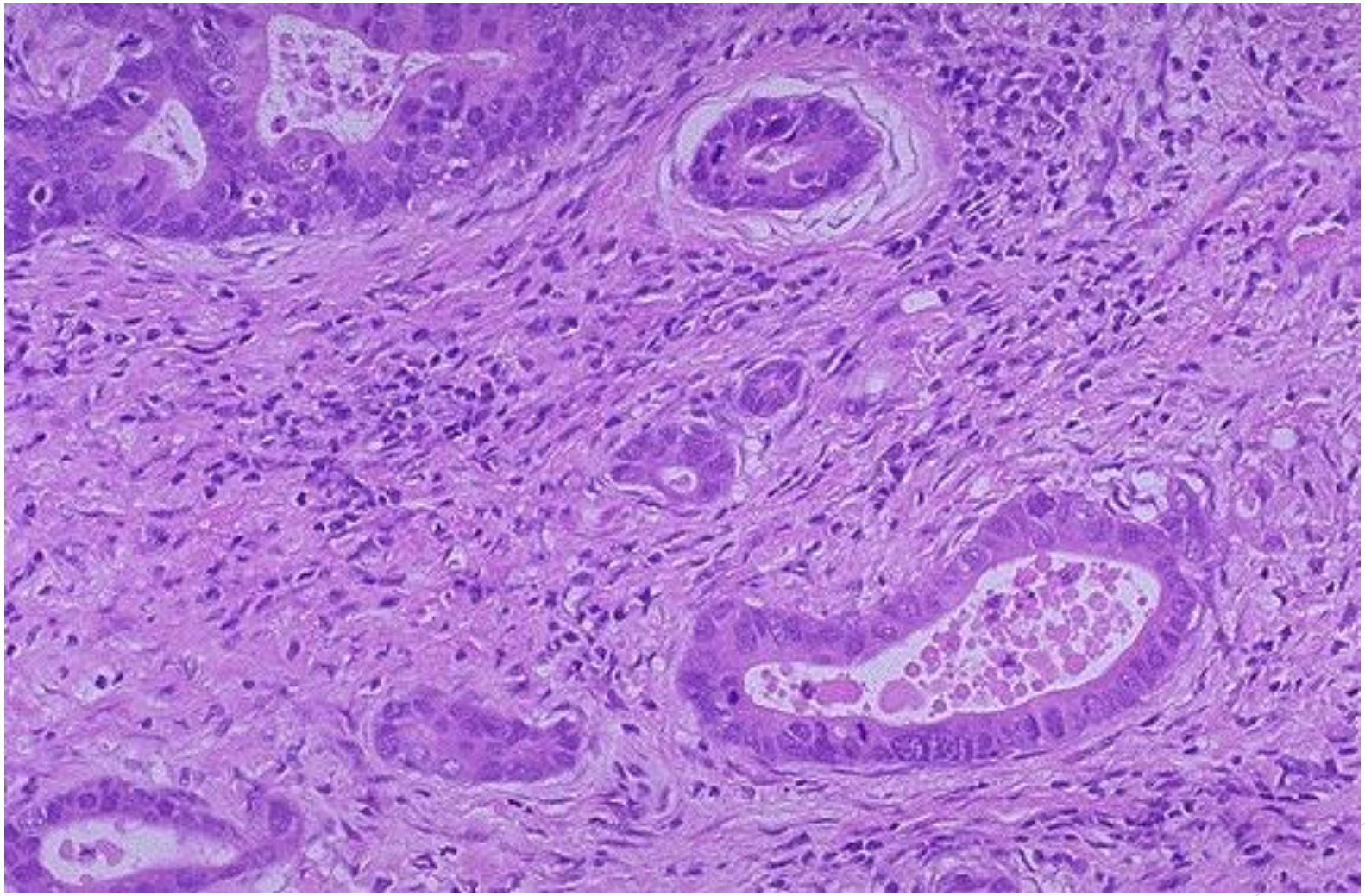
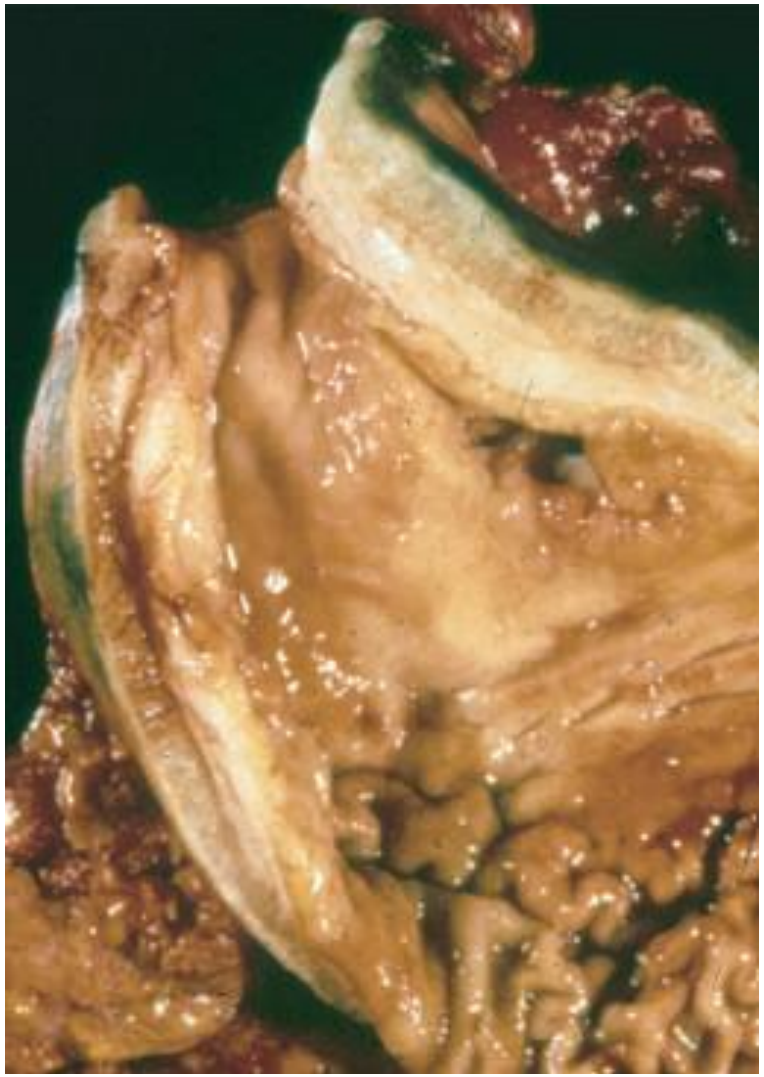
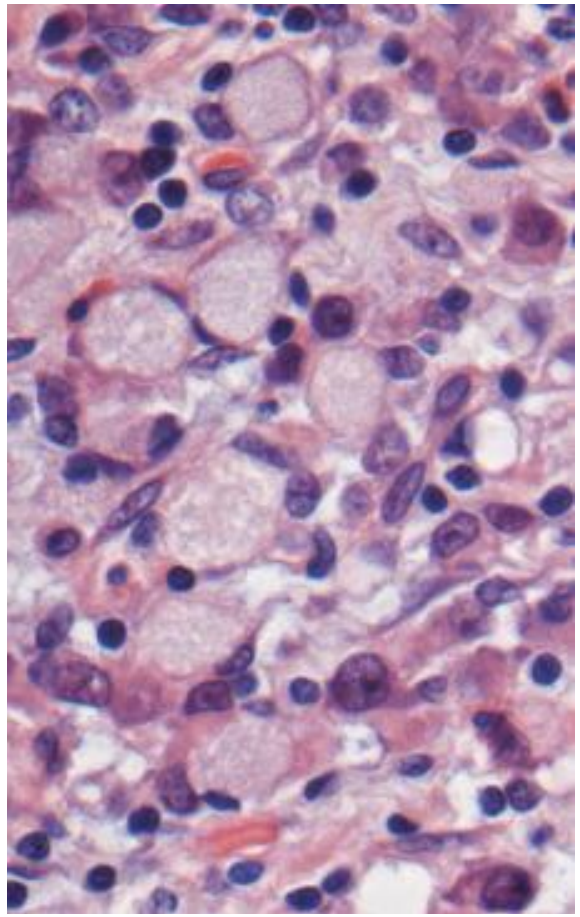
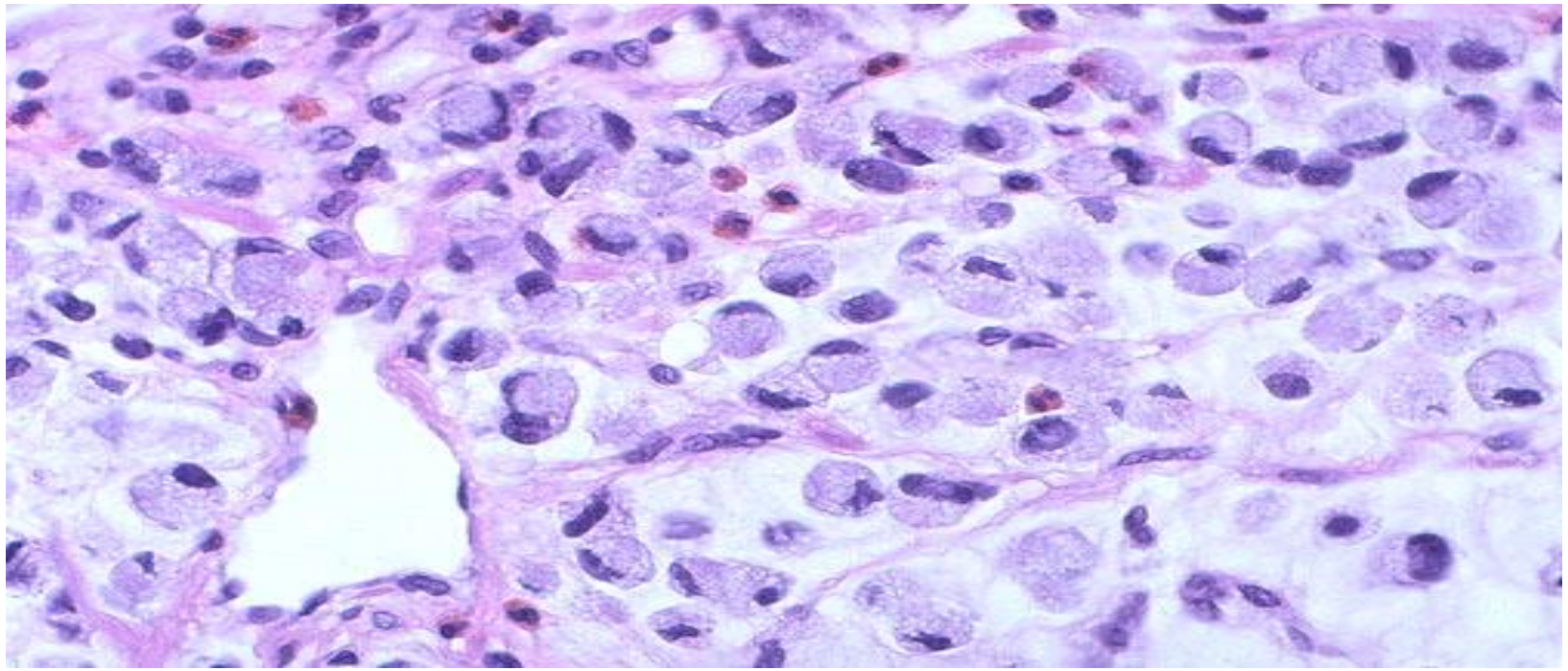


# Linitis plastica





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



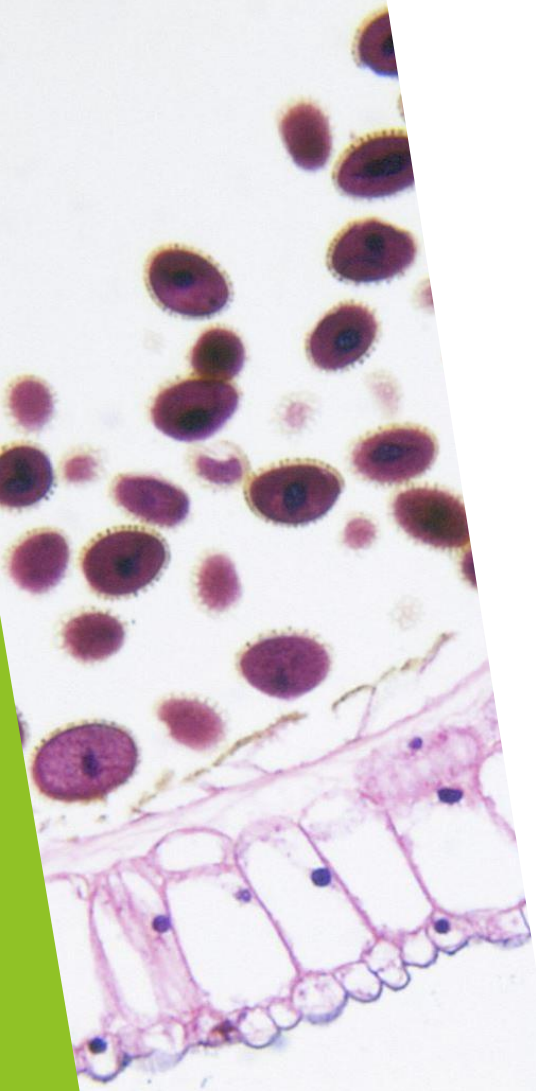
# Diffuse type, signet ring cells

# 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**

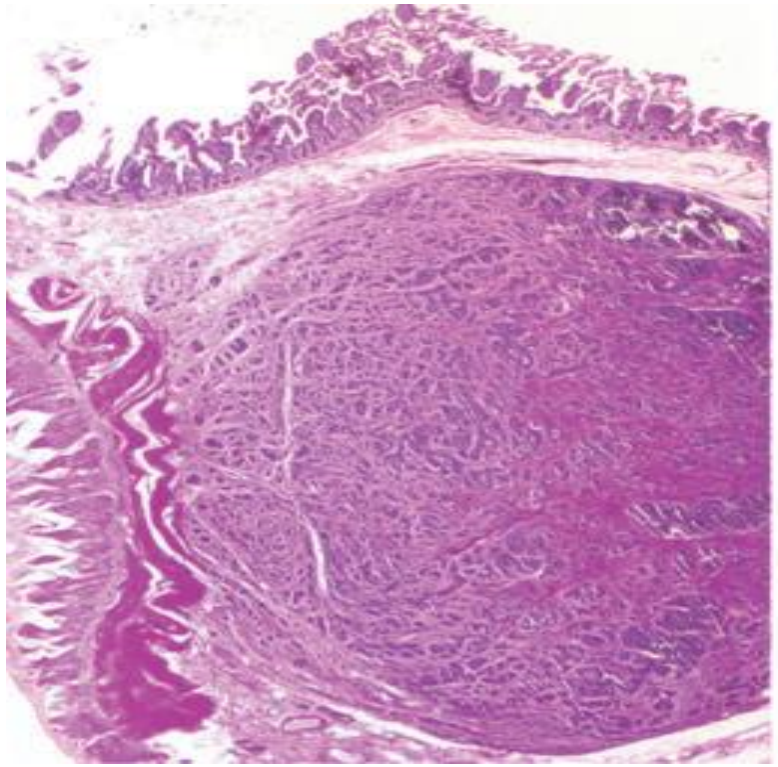
- **Most cases discovered at advanced stage.**
- 5-year survival 90% to <30% for early and advanced tumors, respectively.
- Tx: surgery, chemotherapy, targeted Tx (anti HER2)

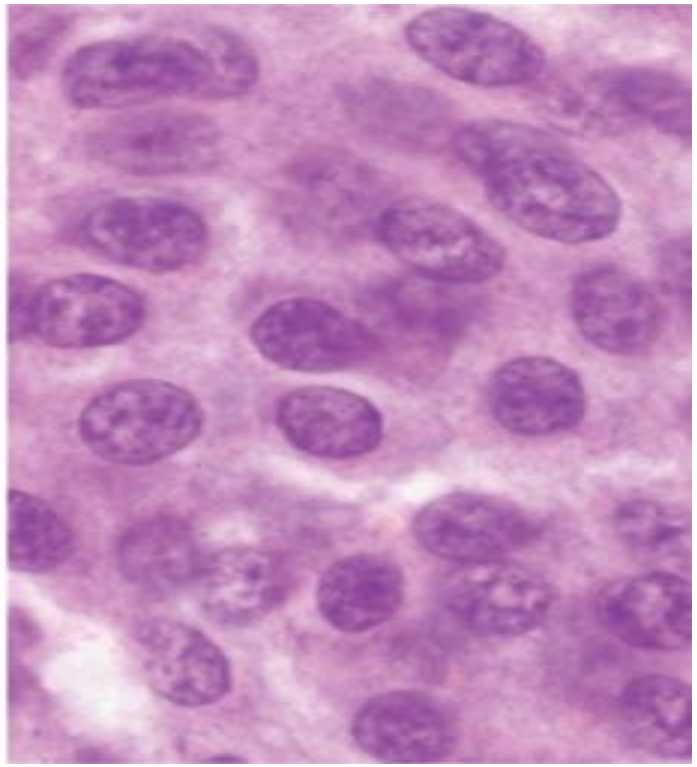
# Lymphoma

- **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

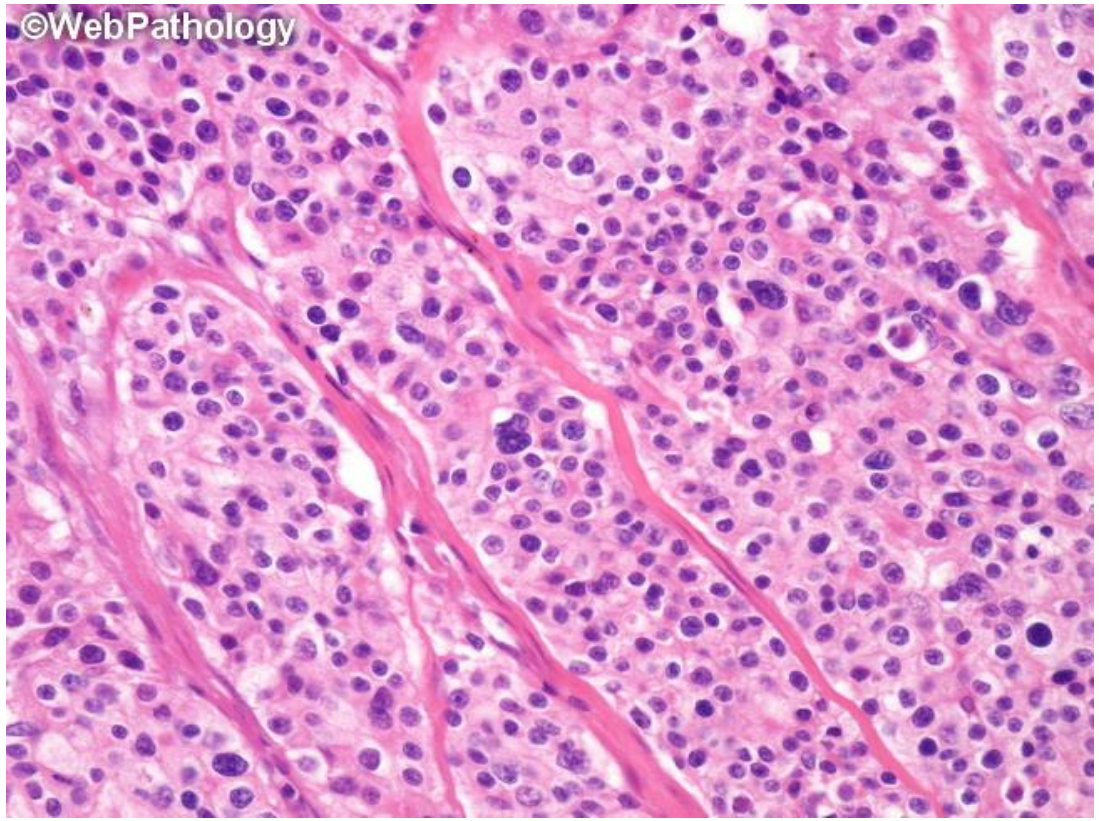
- Tumors arising from neuroendocrine-differentiated gastrointestinal epithelia (e.g., G cells).
- **> 40% occur in the small intestine**.
- Associated with endocrine cell hyperplasia, chronic atrophic gastritis, and Zollinger- Ellison syndrome
- **Slower growing than carcinomas**.





# 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**