

PATHOLOGY OF THE STOMACH

DR. OMAR HAMDAN

GASTROINTESTINAL AND LIVER PATHOLOGIST
MUTAH UNIVERSITY

SCHOOL OF MEDICINE-PATHOLOGY DEPARTMENT
UNDERGRADUATE LECTURES 2023



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 (GERD) OR ECTOPIC GASTRIC MUCOSA (MECKEL'S DIVERTICULUM)

↳ in
gastric lining of
gastric mucosa

PATHOGENESIS

→ causes chronic > acute gastritis

- 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**

2. PPI

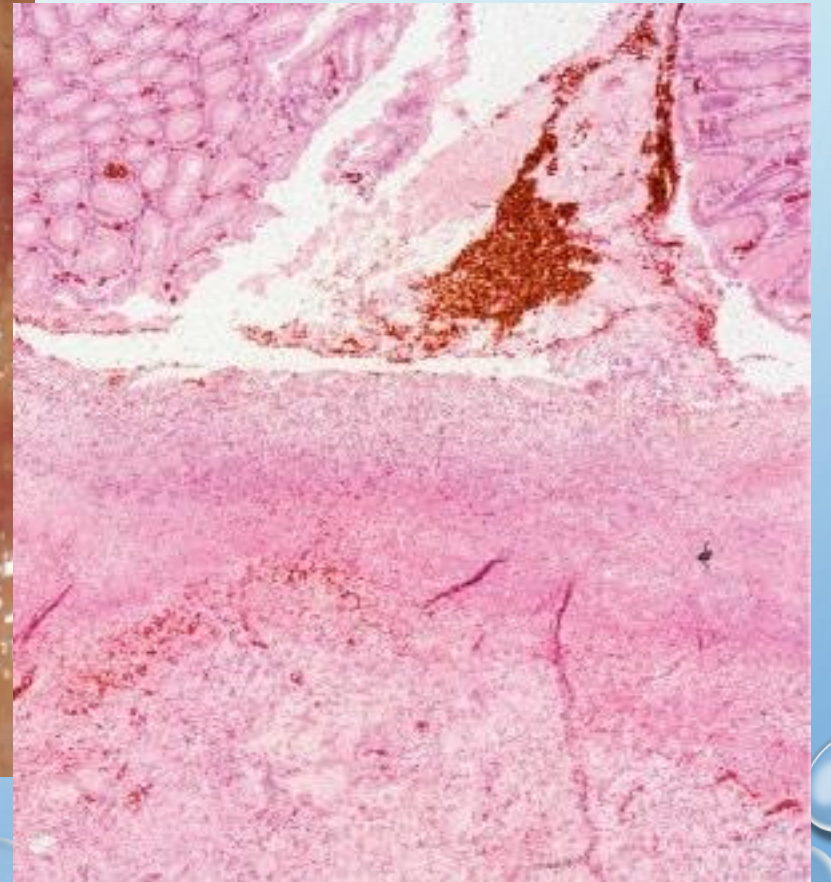
ZOLLINGER-ELLISON SYNDROME

- **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. , *could be multiple*
- ROUND TO OVAL, SHARPLY PUNCHED-OUT DEFECT
- BASE OF ULCERS IS SMOOTH AND CLEAN
- GRANULATION TISSUE.
- HEMORRHAGE & PERFORATION ARE COMPLICATIONS

↳ needs resection



Smooth & clean base of ulcer

DUODENAL ULCER



CLINICAL FEATURES

- Epigastric burning or aching pain, nausea, vomiting
- Pain 1 to 3 hours after meals at daytime
- Worse at night, relieved by alkali or food
- 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: *types*

Inflammatory and Hyperplastic Polyps

Gastric Adenoma

dysplasia

■ Gastric Adenocarcinoma

invasion to basement membrane

basem. mem. لغزاض او لغزاض

CIS or dysplasia

Intestinal and diffuse types

*by h. pylori
atrophy gastritis*

■ Lymphoma

MALToma. *assoc. w/ H. pylori*

■ Neuroendocrine (Carcinoid) Tumor *assoc. w/ atrophic gastritis*

■ Gastrointestinal Stromal Tumor

GASTRIC POLYPS

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

gastric adenoma

when finding duodenal mucosa in the stomach (heterotopia)

Inflammatory and Hyperplastic Polyps

- ❑ 75% of all polyps. *↑ adenoma*
- ❑ Arise in a background of chronic gastritis *atrophic*
- ❑ Regress after H.pylori eradication.
- ❑ Risk of dysplasia if size > 1.5 cm. *large*

الزيبان

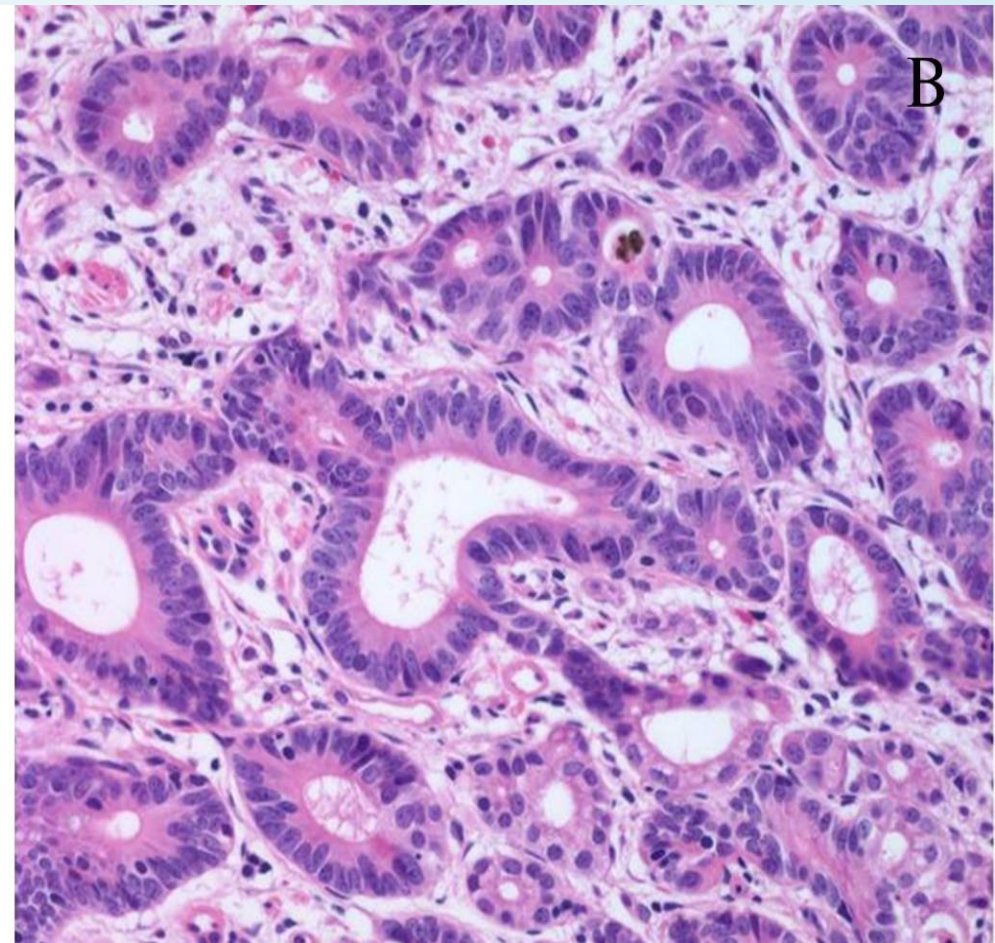
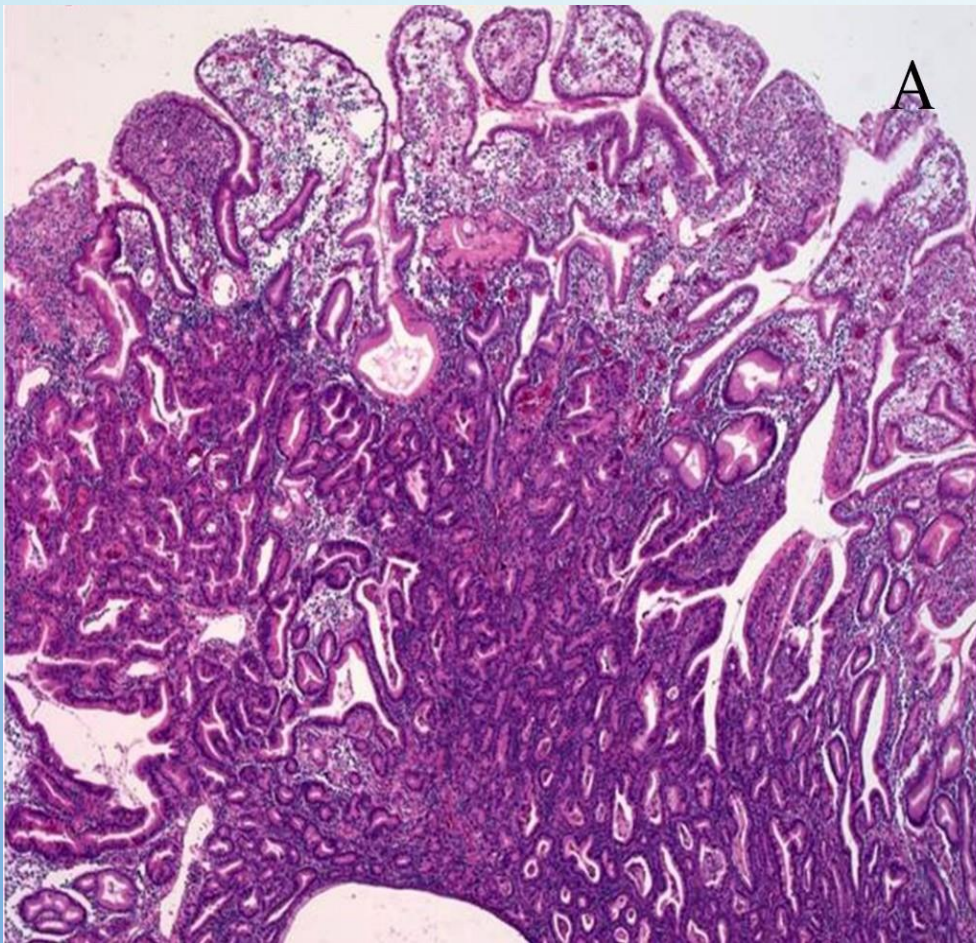
GASTRIC ADENOMA

- ❑ 10% of all polyps.
- ❑ Increase with age. *hyperplastic ↑ in young 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). *↑↑ size → ↑↑ risk*
- ❑ Risk of carcinoma higher than colonic adenoma. *gastric adenoma*
- ❑ 30% have concurrent CA.

*30% من اللي عندهم
adenoma*

*يكون عندهم adenocarcinoma
بنفس الوقت*

GASTRIC ADENOMA



↑ N:C ratio
hyperchromasia
prominent nuclei

▷ no invasion to muscularis mucosa or basement membrane + dysplastic glands

GASTRIC ADENOCARCINOMA

- ❑ 90% of all gastric cancers. *M.C.* *esoph. أما في ال. M.C. → SCC*
- ❑ 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.
- ❑ *peptic ulcer* PUD does not increase risk, *except chronic* except after surgery
- ❑ Two main types: intestinal and diffuse.

glandular

PATHOGENESIS

M.C. Factor

- ❑ 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%.
- Familial Adenomatous Polyposis
❑ FAP: APC gene mutation, intestinal type cancer. *Multiple or hundreds of adenomas*
- ❑ 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.

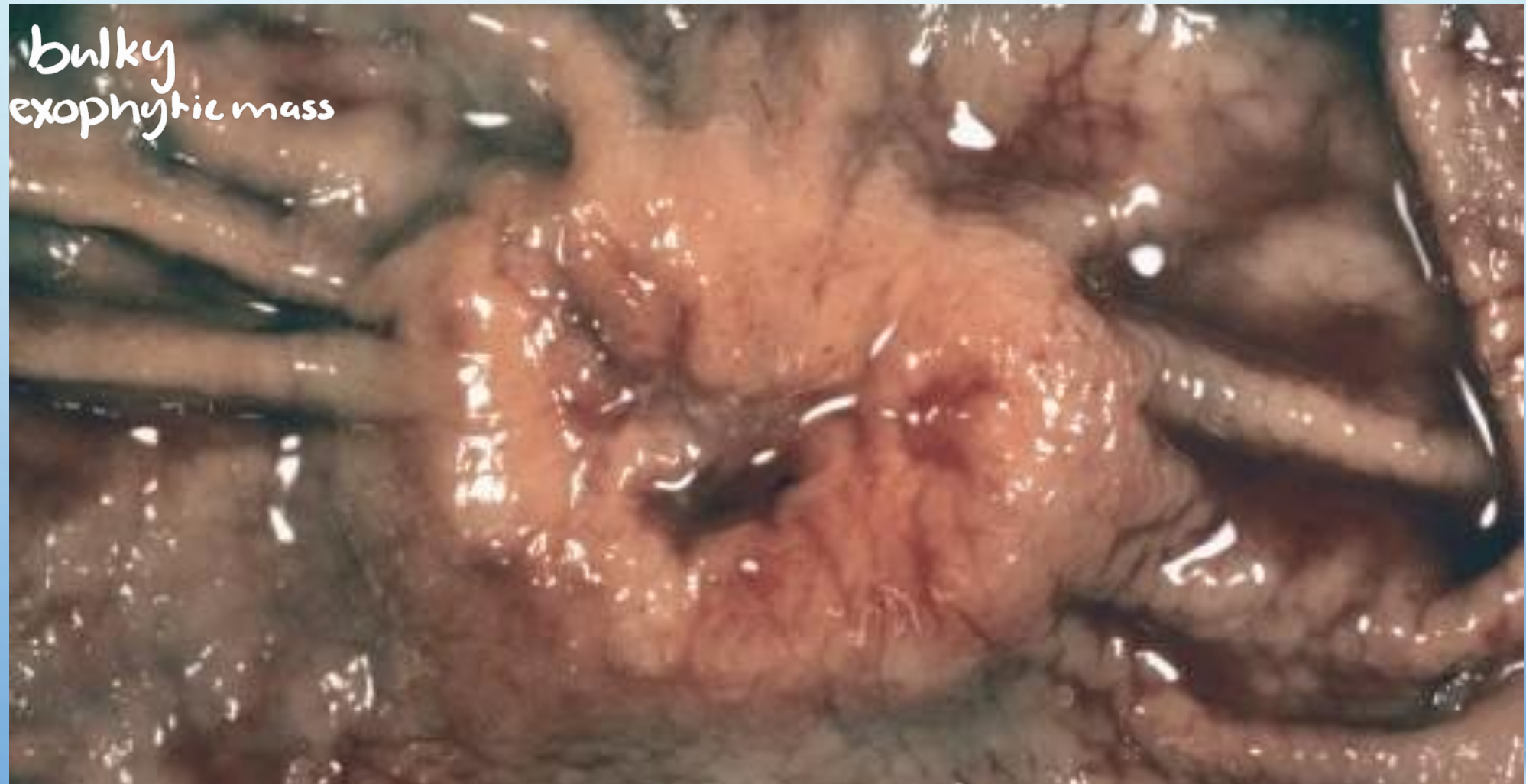
□ Diffuse gastric cancers

- Infiltrative growth pattern
- Discohesive cells (signet ring cells)
- Desmoplastic reaction (thick wall, linitis plastica)

+ ulcer

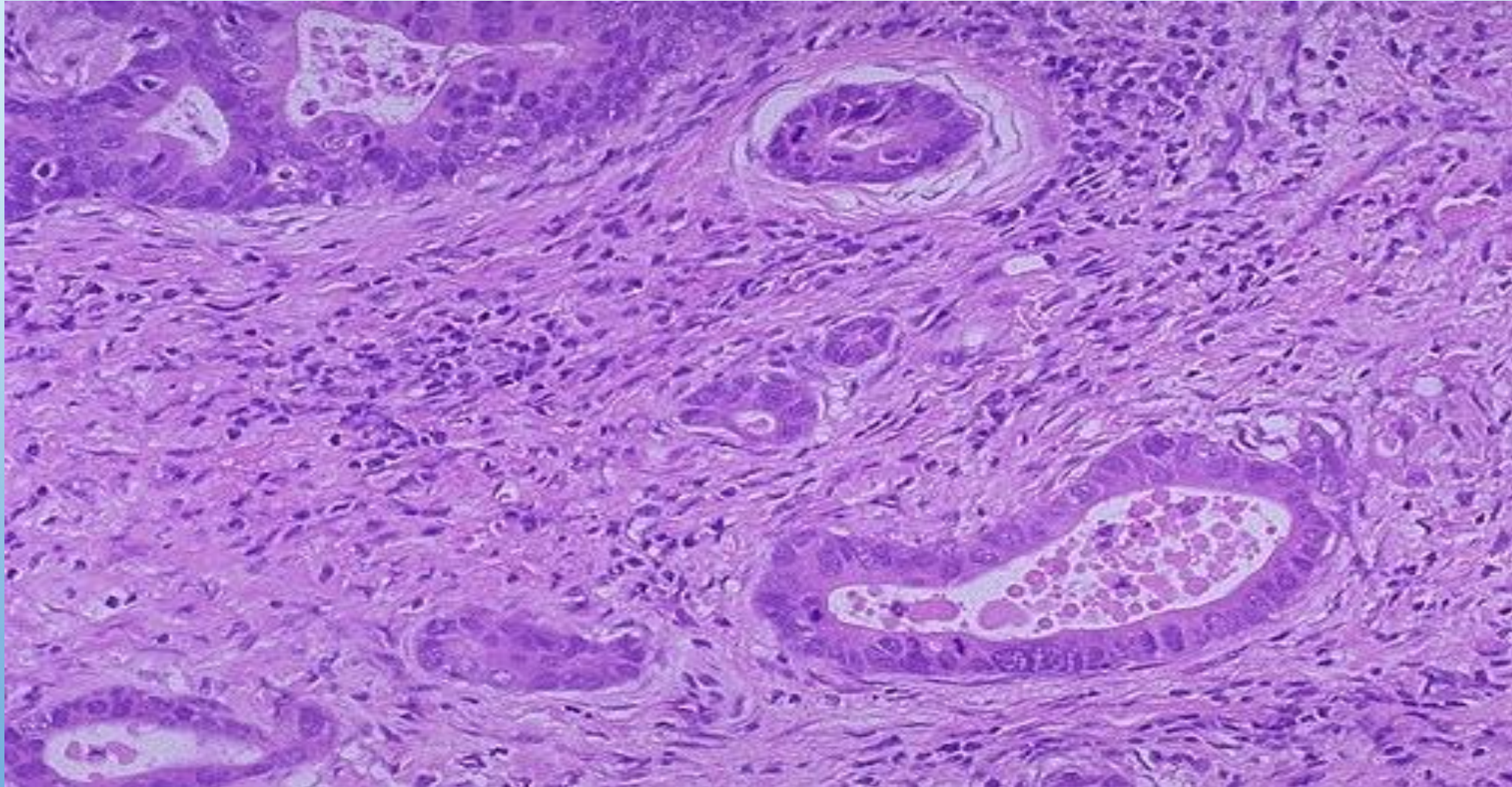
either
[intestinal type adenocarcinoma] biopsy
[or lymphoma] عثمان نعيم بينم

INTESTINAL TYPE



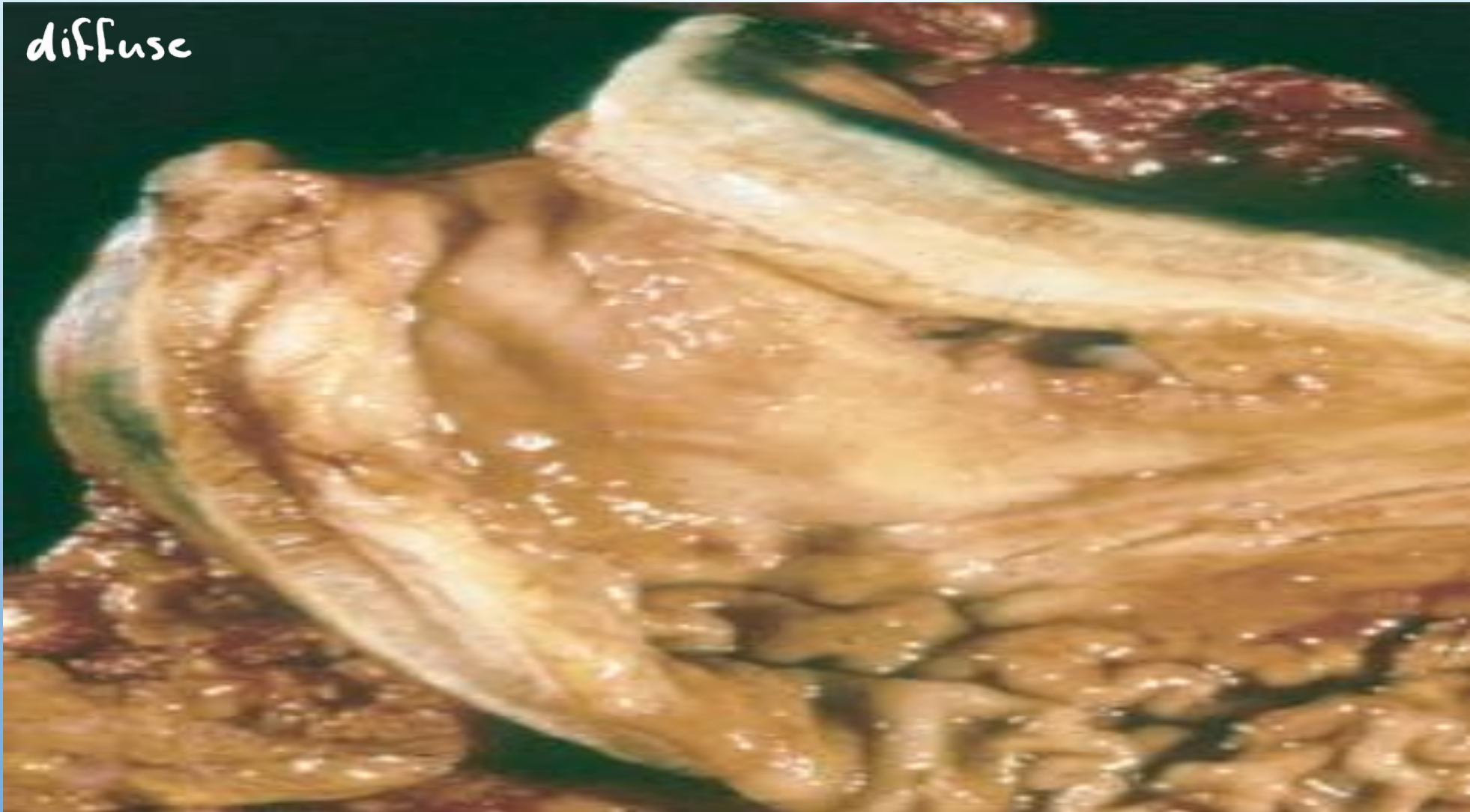
INTESTINAL TYPE

نفس شكل ال adenoma
بس وخرقة ال muscularis muc.
او basement mem.



LINITIS PLASTICA

diffuse



Signet ring cells:

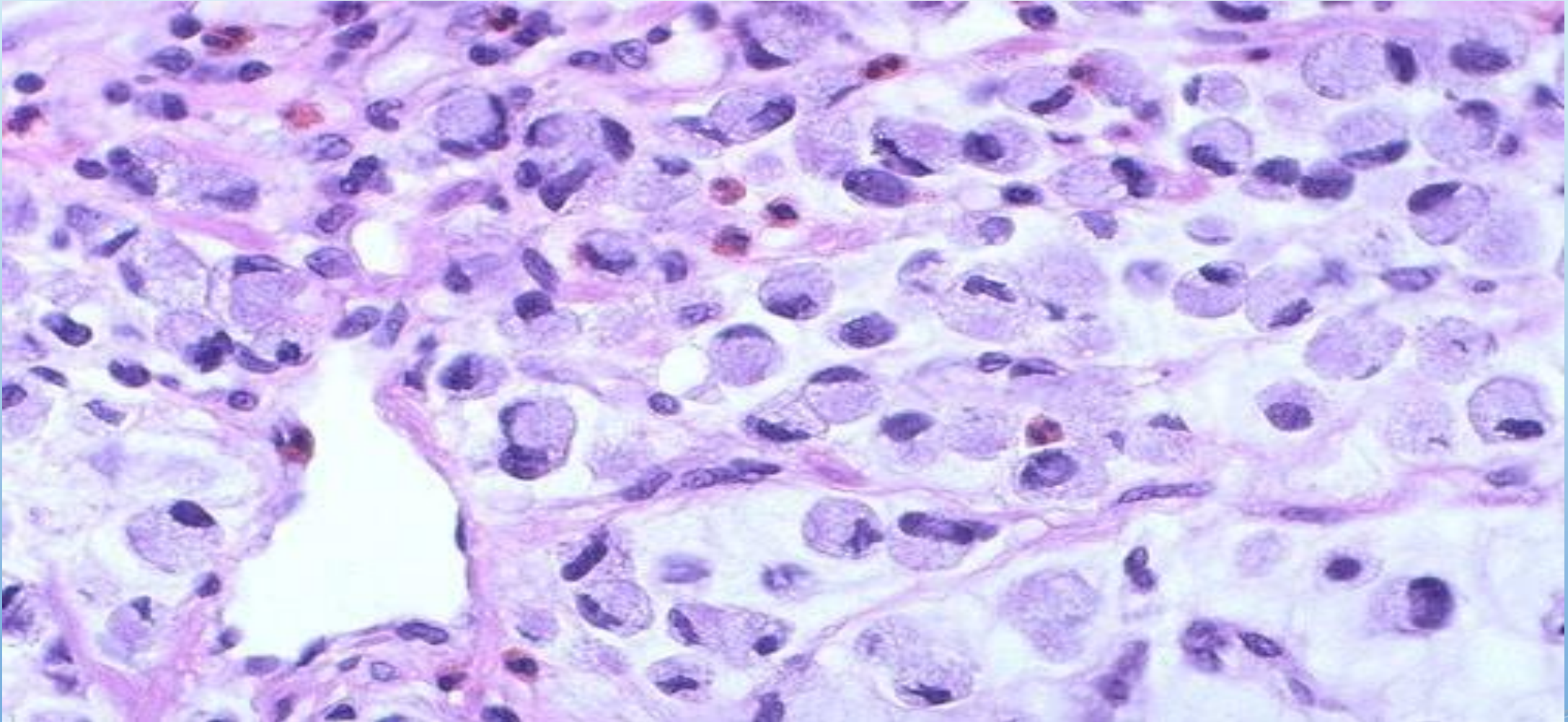
- large mucin vacuoles that expand the cytoplasm and ^{large} push the nucleus to the periphery,

diffuse



DIFFUSE TYPE, SIGNET RING CELLS

- كل cell لجال
- متش cohesive
- متش عاملين glands



CLINICAL FEATURES

❑ Intestinal-type gastric cancer

- High-risk areas : *Japan, Costa rica*
- Develops from precursor (adenoma, dysplasia)
- Mean age 55 yrs. *elderly*
- **M**:F 2:1

❑ Diffuse type gastric cancer:

- Incidence uniform across countries.
- No precursor lesion.
- M:F 1:1
- Younger age.

- N0: No regional lymph node metastasis (cancer has not spread to nearby lymph nodes).
- N1: Cancer has spread to one to three nearby lymph nodes.
- N2: Cancer has spread to four to nine nearby lymph nodes or lymph nodes in multiple regions.
- N3: Cancer has spread to ten or more nearby lymph nodes or to lymph nodes distant from the primary tumor.

- ❑ 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
 ↳ M.C. to the liver
- ❑ MOST CASES DIAGNOSED AT ADVANCED STAGE. 3,4
- ❑ 5 YEAR SURVIVAL 90% TO 20% FOR EARLY AND ADVANCED TUMORS, RESPECTIVELY.
- ❑ SURGERY, CHEMOTHERAPY, TARGETED TREATMENT (ANTI HER2)

TNM system
 ↳ mucosa → T1
 submucosa → T2
 muscularis propria → T3
 Serosa → T4

LYMPHOMA

M.C. site → L.N.

M.C. extranodal → in stomach

- ❑ STOMACH IS THE MOST COMMON SITE OF EXTRANODAL LYMPHOMA.
- ❑ 5% OF ALL GASTRIC MALIGNANCIES.
- ❑ MOST COMMON TYPE : ^{low grade} 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.

↑↑ in antrum
or in body
in case
of antralization

▷ good prognosis except if transformed to carcinoma

▷ type 1 assoc. w/ atrophic gastritis

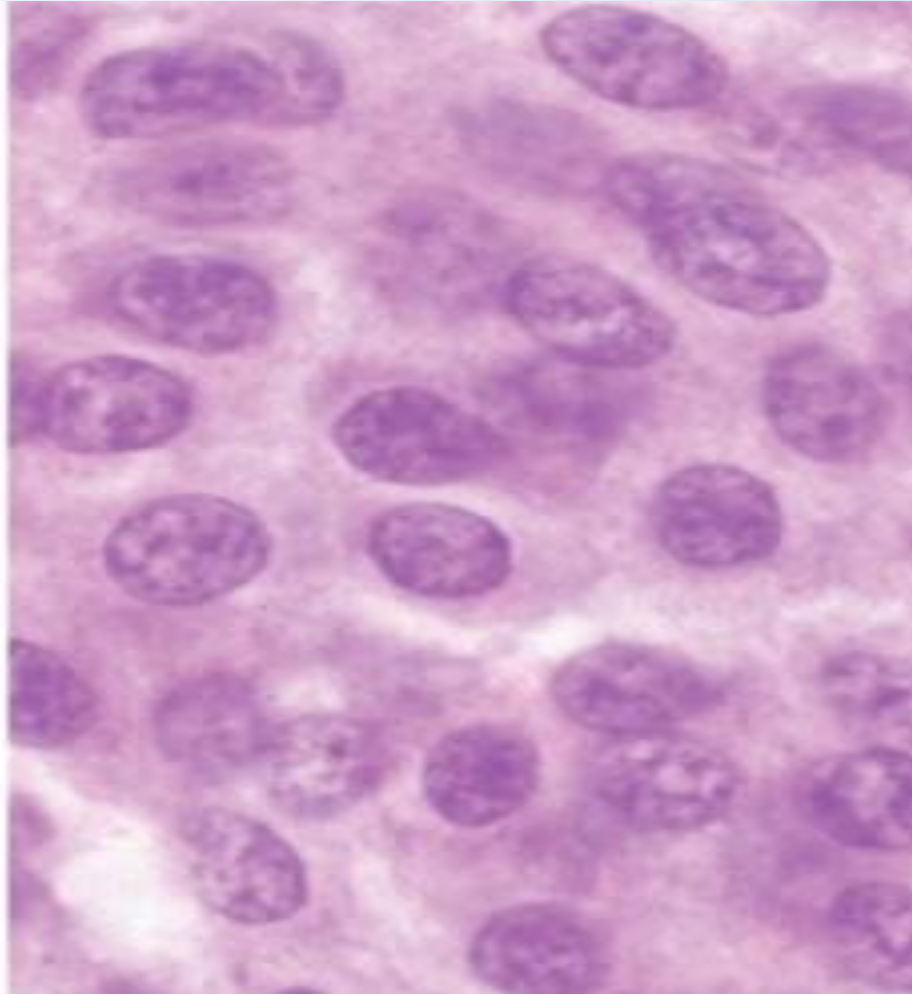
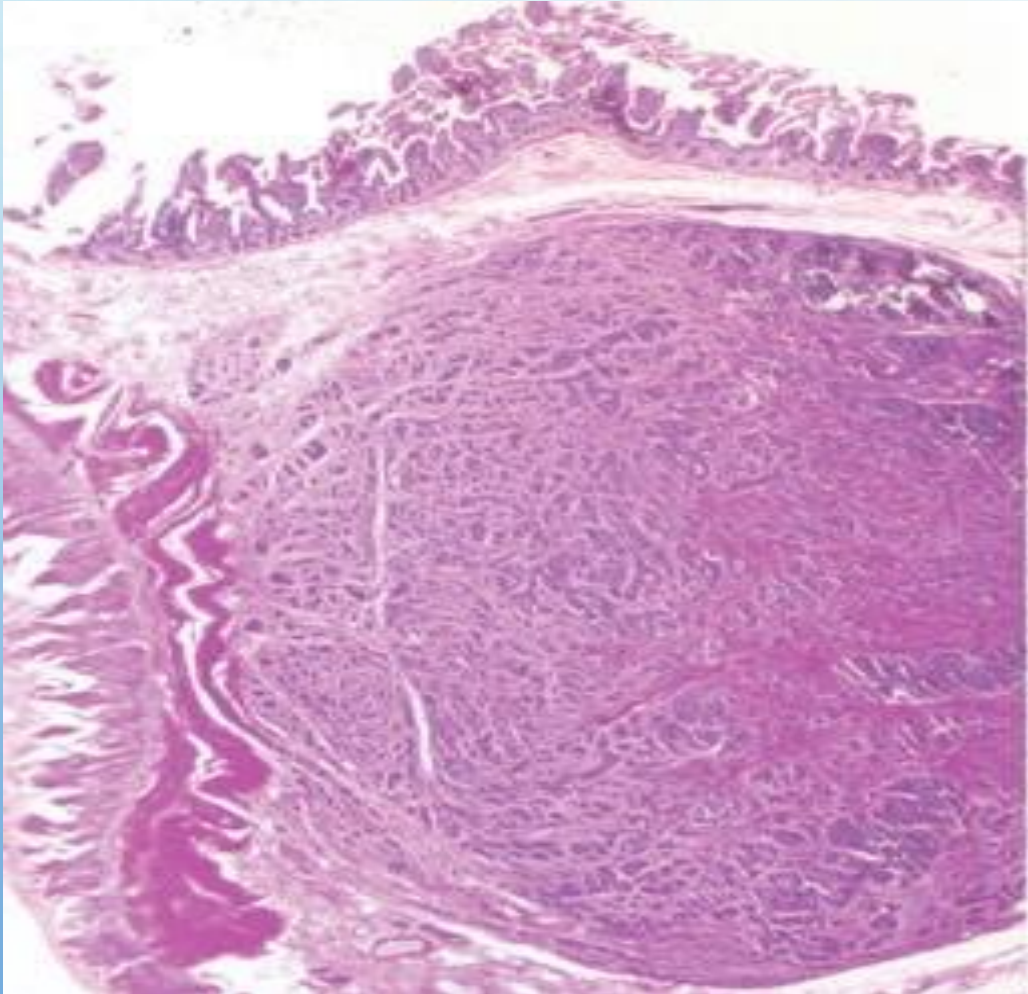
2 " " parietal cell hyperplasia

3 sporadic / poor prognosis / metastasizes } needs resection + chemotherapy

4 small cell carcinoma & large cell neuroendocrine carcinoma

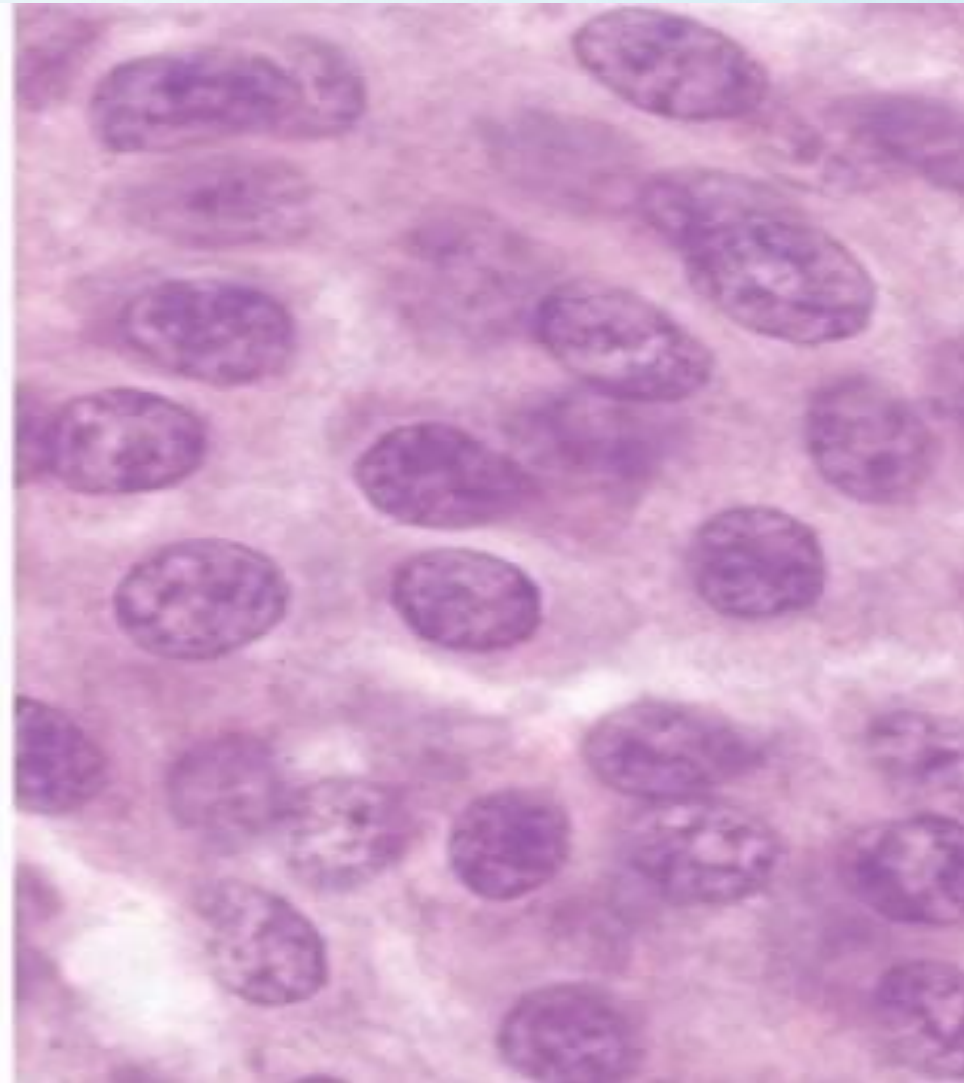
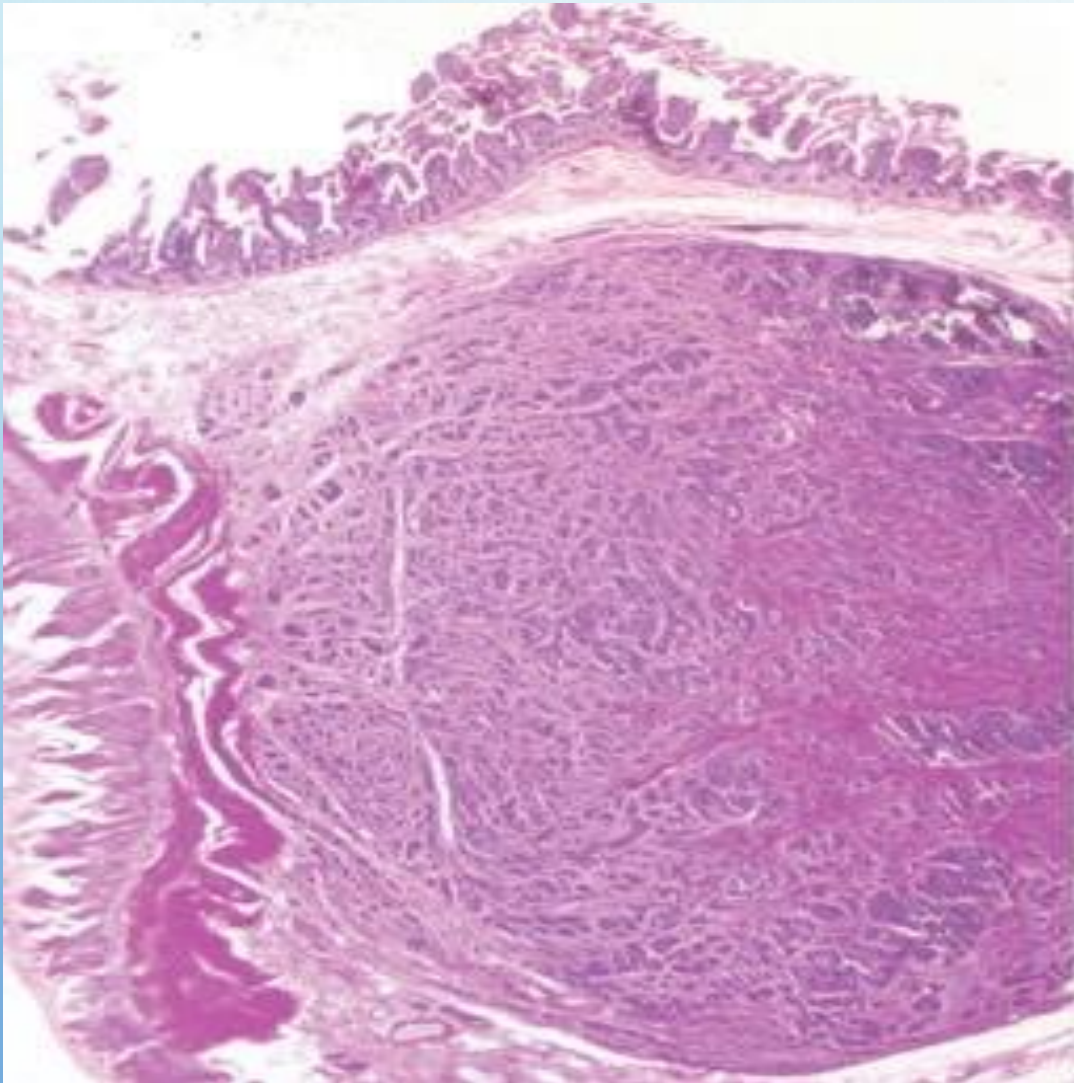
INTRAMURAL OR SUBMUCOSAL MASSES (SMALL POLYPOID LESIONS)

↳ mucosa is normal



Salt
& pepper
appearance
↳ dots
كَبِيرَةٌ + صَفِيرَةٌ

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



CARCINOID SYNDROME

Carcinoid tumor
دواء
neuroendocrine tumor

- ❑ Due to vasoactive ^{peptide} substances ^(VIP)
- ❑ Seen in 10% of cases.
- ❑ *Strongly associated with metastatic disease.*
- ❑ Cutaneous flushing, sweating, bronchospasm, colicky abdominal pain, diarrhea, and right-sided cardiac valvular fibrosis