Disorders of Esophagus 2nd year MBBS

Dr Saima Nadeem

Outline of Content

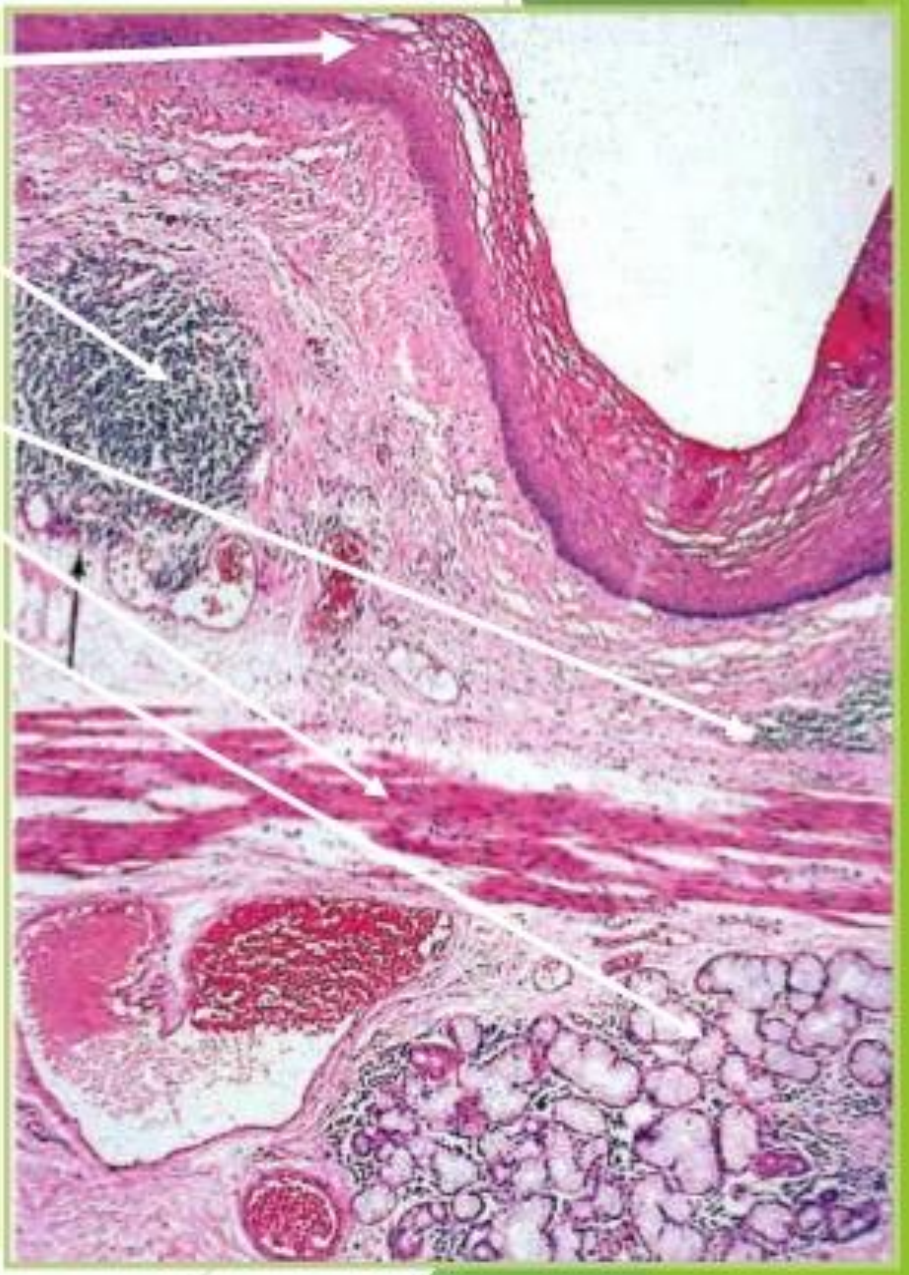
- Normal anatomy and histology
- Congenital and acquired malformations
- Lesions associated with motor dysfunction
- Esophagitis
- Barrett esophagus
- Esophageal varices
- Benign neoplasms and tumor-like lesions
- Malignant neoplasms and staging

Normal anatomy/physiology

- Muscular tube from pharynx (C6) to esophageal-gastric junction, about 25 cm long
- Endoscopy: defined as 15-40 cm from incisor teeth
- Two areas of increased intraluminal pressure that normally remain contracted at rest:
  - **Upper esophageal sphincter**: 3 cm segment at cricopharyngeus muscle
  - **Lower esophageal sphincter (LES):** 3-5 cm segment of thickened smooth muscle around diaphragmatic esophageal hiatus, just proximal to histologic EG junction

Normal Histology and Pathologic Correlations

- Mucosa: nonkeratinized squamous; basal zone is 10-15% of thickness
- Lymphocytes: CD8 T cells in epithelium; *CD4 T cells and B cells* in lamina propria
- Muscularis mucosa: smooth muscle between mucosa and submucosa
- Submucosal mucous glands: mainly proximal & distal esophagus
- Muscularis propria: skel. muscle upper 1/3 (voluntary swallow); sm. muscle lower 1/3; middle 1/3 mixed
- Myenteric nerve plexus: between circular inner and longitudinal outer layers of muscularis propria
- Serosa: mostly absent, facilitating spread of invasive tumors or infections into mediastinum



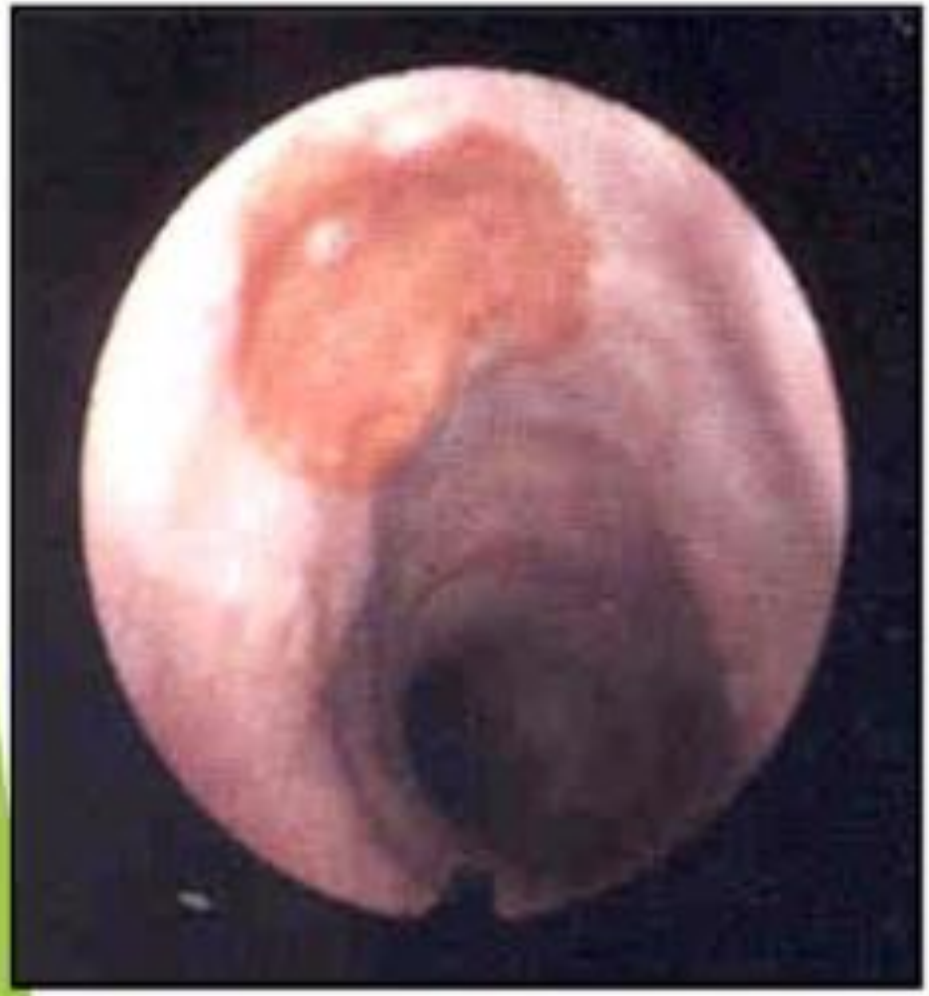
Congenital & Acquired Malformations

- Ectopias
- Atresias
- Stenoses
- Duplications
- Webs and Rings

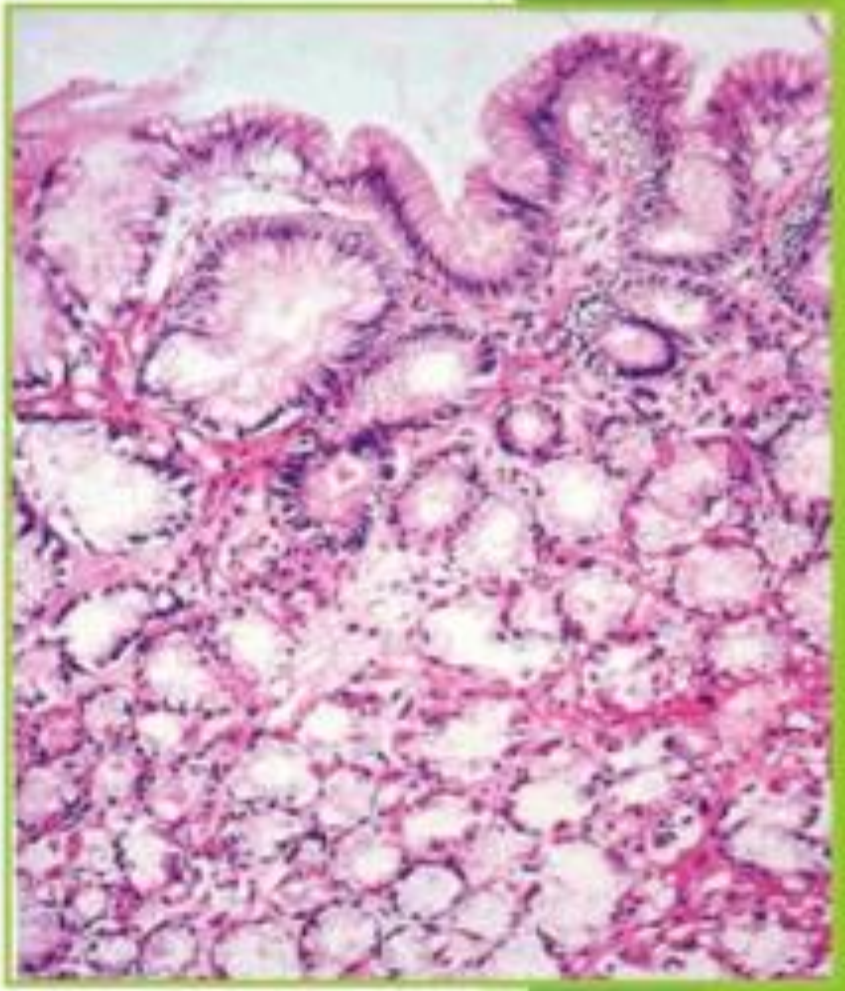
Congenital Malformations

- Ectopias; About 4% of persons by endoscopic exam
- "inlet patch" of gastric-type epithelium replaces squamous, just below upper esophageal sphincter
- Atresias; atresia = segment reduced to thin cord, no lumen
- • 1/1000 live births
- • usually near tracheal bifurcation, usually with associated tracheal-esophageal fistula
- • mechanism: failed septation of foregut
- • symptoms: regurgitation, paroxysmal choking, aspiration of liquid into lungs

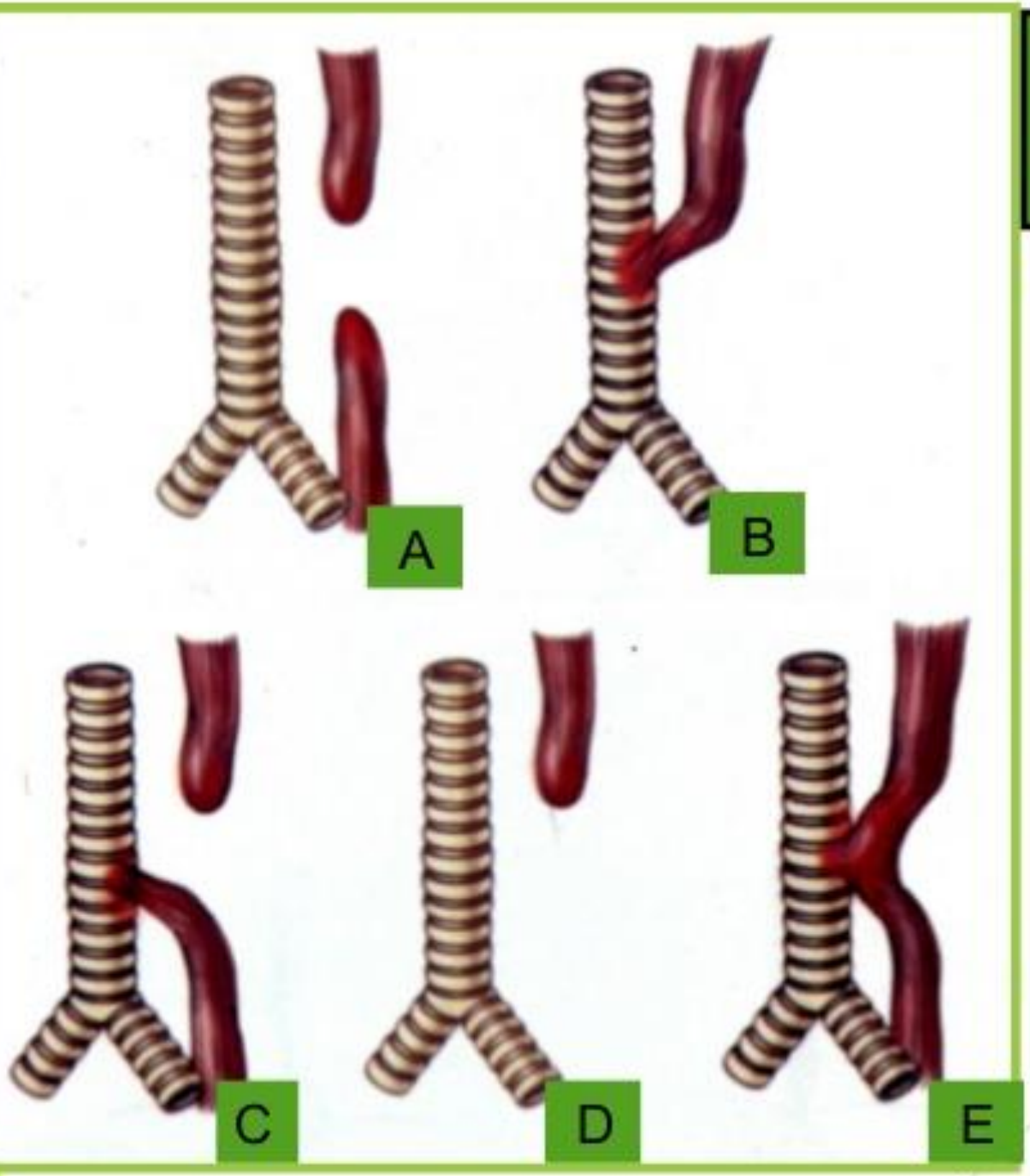
Ectopic gastric mucosa



Endoscopy: red patch within otherwise gray mucosa



Biopsy: normal appearing gastric-type mucosa



Atresia and tracheo-esophageal fistula:
5 types

Which two cause paroxysms of coughing upon baby's first feeding?

_____

Which one is the most common type, and causes immediate regurgitation upon baby's first feeding?

_____

All need immediate surgical correction

Achalasia

- **Swallowing disorder defined by 3 major problems**
  - Aperistalsis
  - Incomplete relaxation LES with swallowing
  - Increased *resting* tone of LES (impaired relaxation)
- **Pathogenesis:** normally, distal inhibitory neurons and interruption of cholinergic signals allow relaxation of LES. Degenerative failure of inhibitory neurons → impaired relaxation. Usually primary (idiopathic), but also secondary to malignancy, amyloidosis, sarcoidosis, Chagas disease
- **Symptoms:**
  - progressive dysphagia; nocturnal regurgitation of food
- **Treatment:** surgical myotomy with balloon dilation of LES
- **Sequelae:**
  - **5% develop squamous carcinoma**
  - epiphrenic diverticulum, aspiration pneumonitis

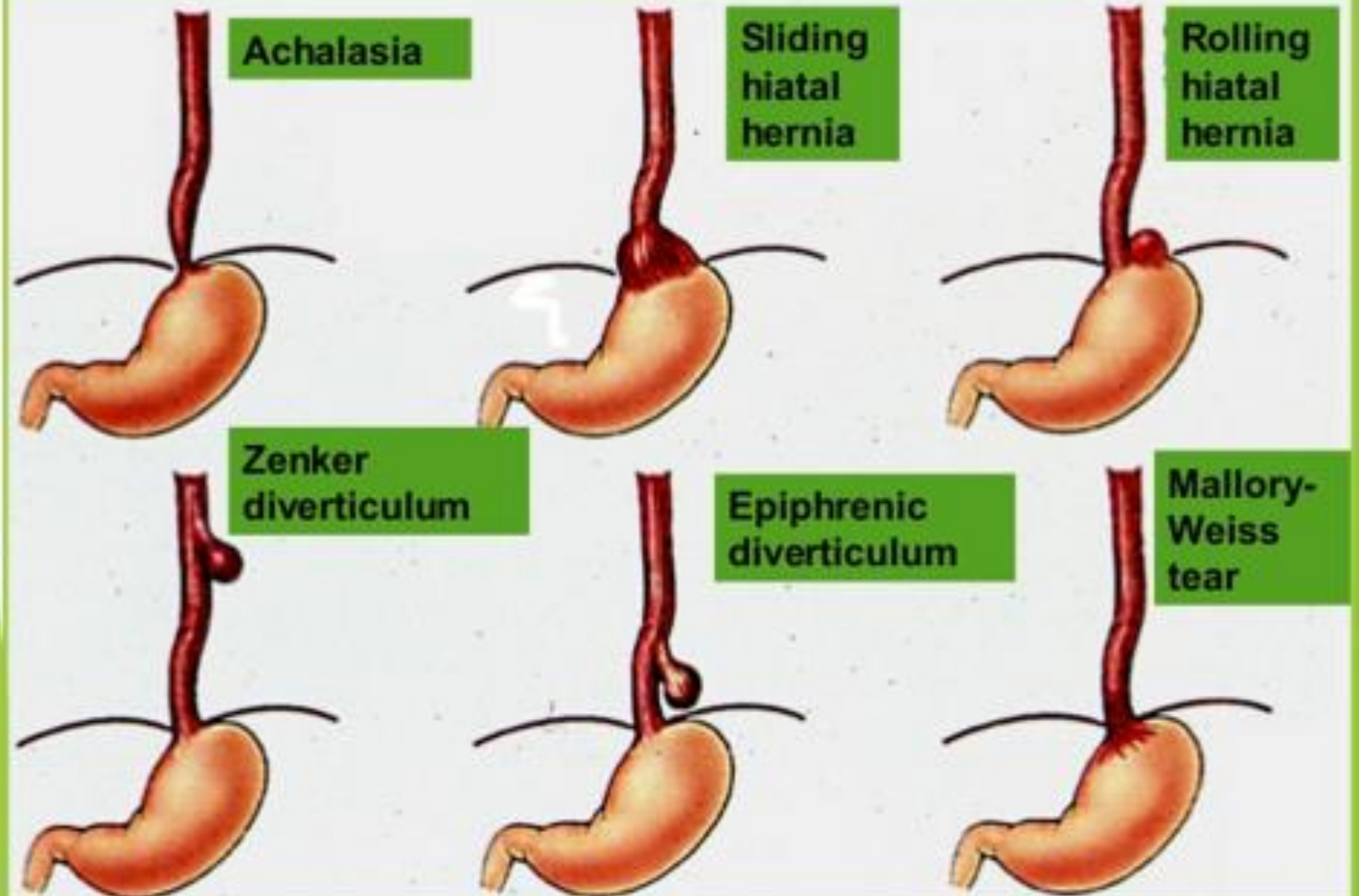
Achalasia

Pathology: progressive dilation of esophagus, proximal to an abnormal segment which is functionally denervated

Hiatal Hernia

- **Definition:** pouch of proximal stomach extending >2cm above diaphragmatic hiatus into thorax
- **Incidence:** **VERY COMMON**, 15-50% adults (depending on strictness of definition); incidence increases with age
- **Types**
  - Sliding: *95%;* stomach and esophagus bulge through hiatus together
  - Paraesophageal: *5%;* stomach alone herniates adjacent to esophagus
- **Complications**
  - Reflux esophagitis (to be discussed)
  - Incarceration: more likely in paraesophageal; uncommon in sliding
- **Treatment:** surgery for paraesophageal HH; degree of morbidity determines medical vs. surgical therapy for sliding

Lesions affecting motor function



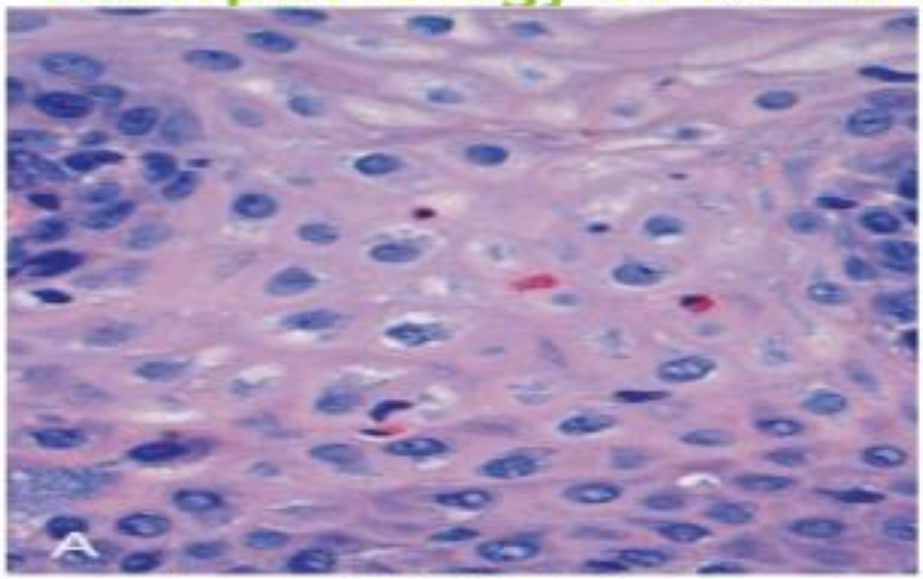
Esophagitis

- Reflux Esophagitis
- Infectious Esophagitis
- Chemical/Physical Esophagitis
- Eosinophilic Esophagitis

Reflux esophagitis

- **Def:** mucosal injury secondary to reflux of acidic gastric contents into lower esophagus; clinical term is GERD (gastroesophageal reflux disease)
- **Incidence:** 5% U.S. adults (millions of people!)
- **Clinical features:** "heartburn", chest pain mimicking MI, regurgitation, dysphagia
- **Complications:** ulceration, stricture, Barrett's metaplasia
- **Pathogenesis:** decreased LES tone or increased abdominal pressure
- **Risk factors**
  - sliding hiatal hernia
  - delayed gastric emptying $\Rightarrow$ increased gastric volume
  - obesity
  - CNS depressant drugs; EtOH abuse, smoking

Histopathology of Reflux Esophagitis



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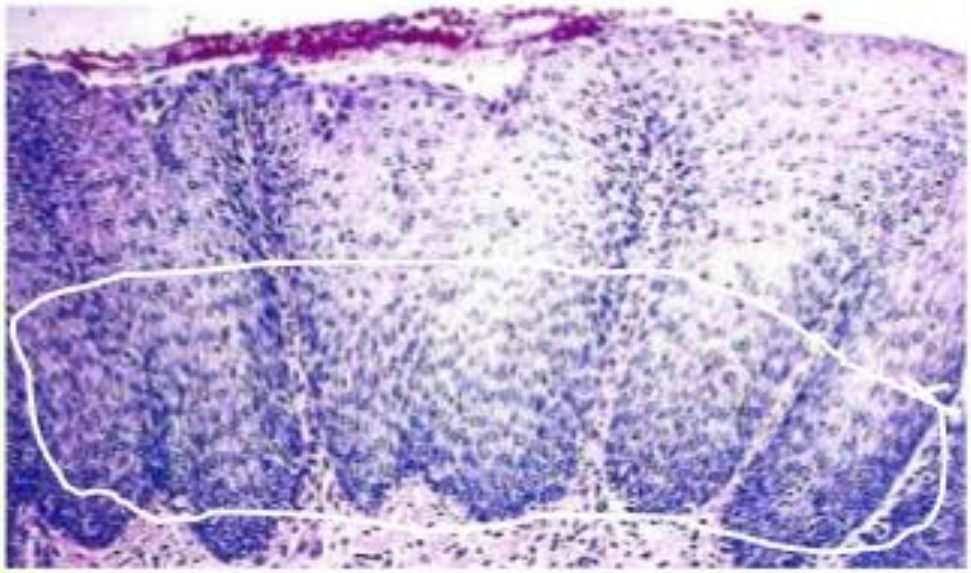


Evidence of mild acute injury:

• Reactive squamous hyperplasia • Scattered eosinophils or neutrophils within mucosa

More severe acute reflux injury:

mucosal ulceration

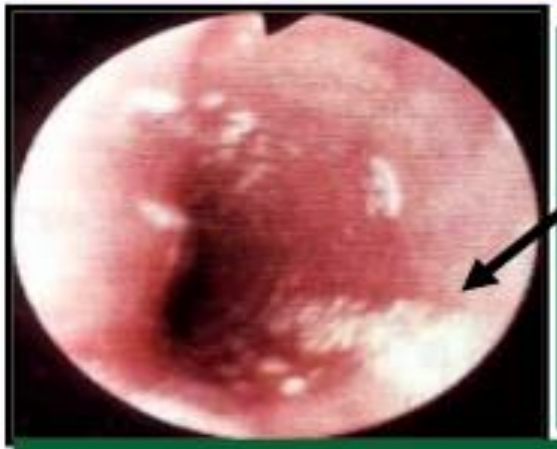
Evidence chronic reflux injury:

• basal zone hyperplasia (early)

• **Barrett** intestinal metaplasia (later)

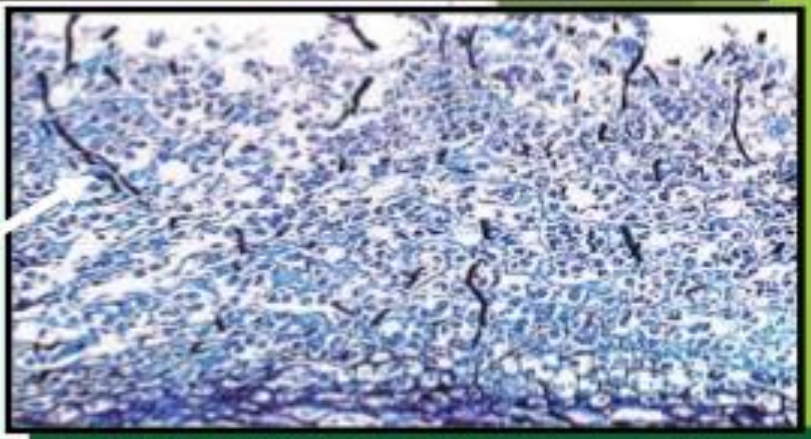
Chronic Reflux: hyperplastic basal layer comprises > 20% of mucosal thickness (normal basal layer is < 20% of mucosal thickness)

- most commonly seen in immunocompromised patients
- three organisms comprise >90% esophageal infections

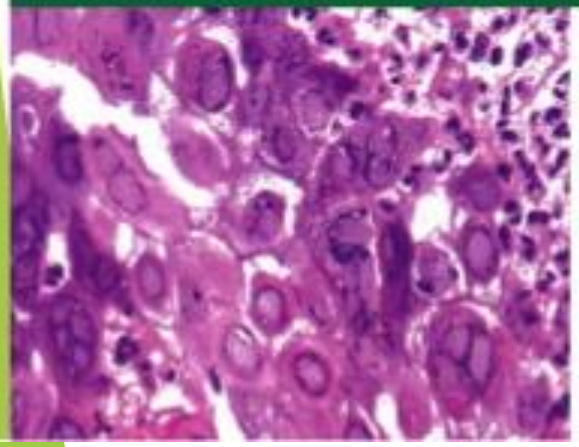


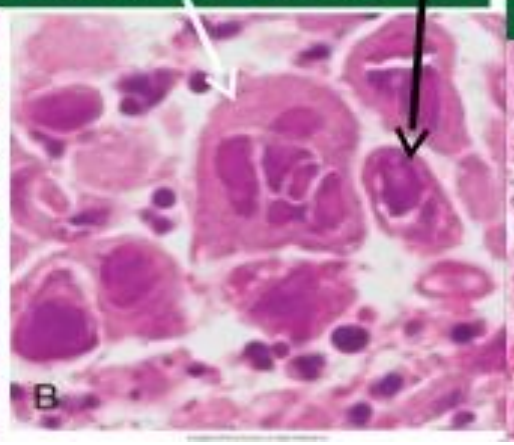
1) Candida:
Endoscopy shows white patches

Silver stain: pseudohyphae in squamous mucosa

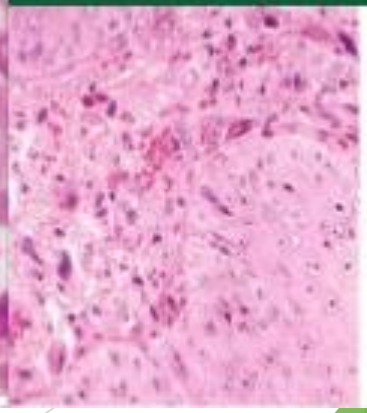


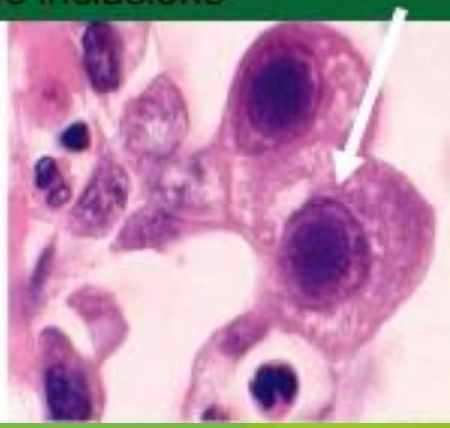
2) Herpes simplex, ground glass nuclei, intranuclear inclusions in squamous cells, multinucleated cells





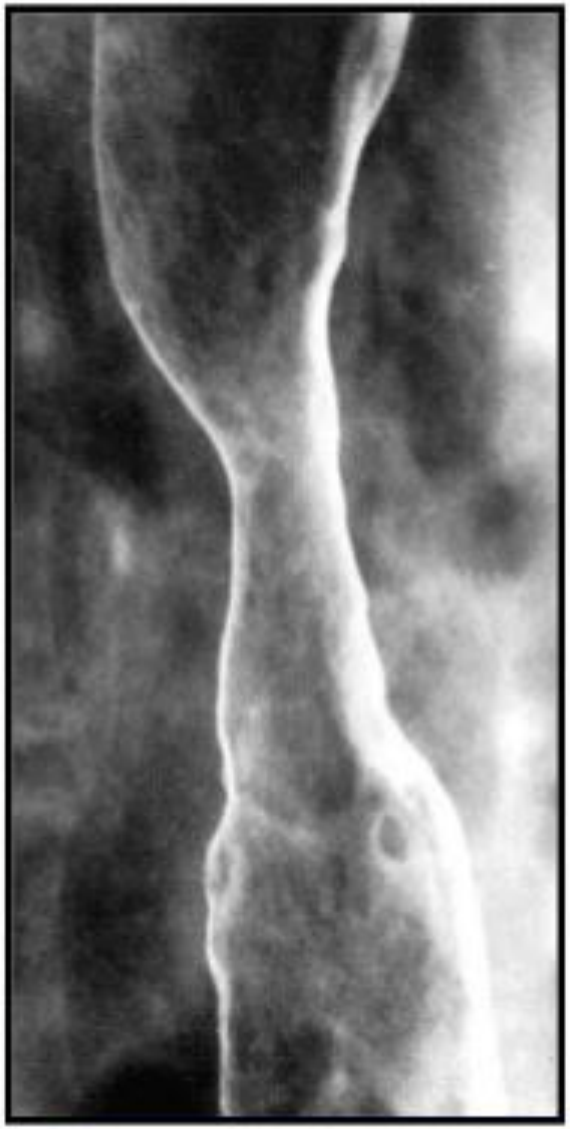
3) CMV, large intranuclear basophilic inclusions in endothelial or stromal cells; dot-like cytoplasmic inclusions





Chemical/Physical Esophagitis

Post-arsenic ingestion



Post-radiation Therapy (stricture)

Causes:

Ethanol abuse, heavy smoking

Acid or alkali (accidental or suicide attempt)

Very hot tea

Chronic uremia

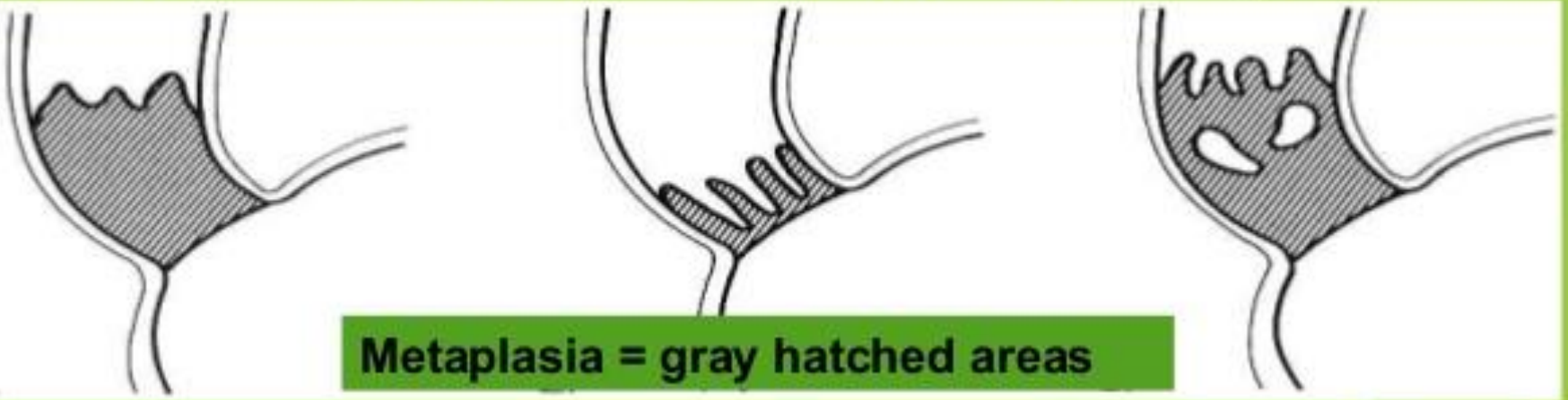
Chemotherapy

Post-radiation therapy for tumors

Barrett esophagus (BE)

- Definition (2 criteria):
  - (1) endoscopic evidence of **abnormal mucosa above EG junction** (clinical criterion)
  - (2) **intestinal metaplasia of squamous mucosa** in biopsies of esophagus (pathologic criterion)
- **Pathogenesis**
  - Precise molecular mechanisms unclear
  - Acid reflux ⇒ inflammation⇒ chronic mucosal injury ⇒ metaplasia into more acid-resistant epithelium
- **Clinical: BE** develops in 10-20% those with symptomatic chronic reflux esophagitis; usually presents ages 40-60 after years of chronic GERD.
- MAJOR CONCERN: **a minority of patients with BE develop epithelial dysplasia which may progress into adenocarcinoma. Life-long risk of adenocarcinoma is 10-15% in patients with BE, but this risk is 40x that of general population!**

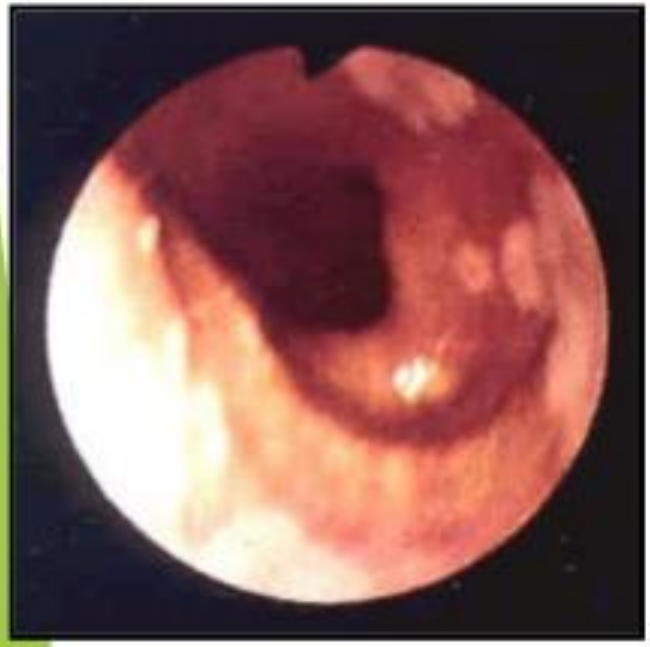
Barrett gross pathology: red granular mucosa

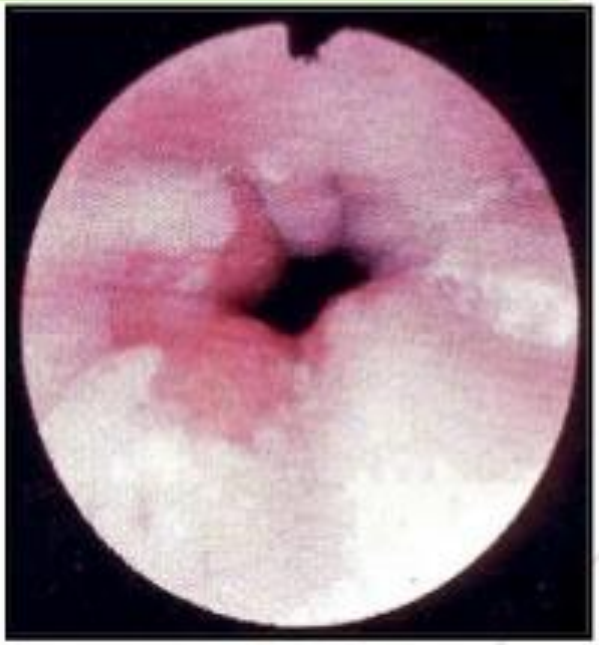


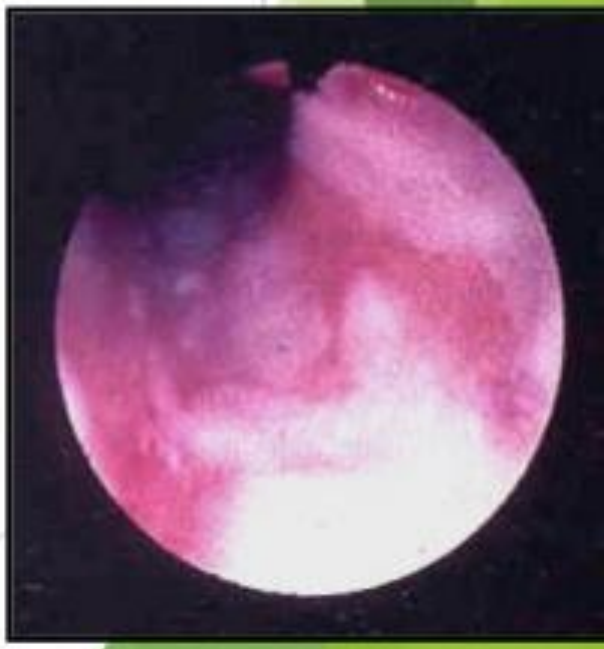
Long segment (>3cm)

Short segment
(< 3cm, near EG jct)

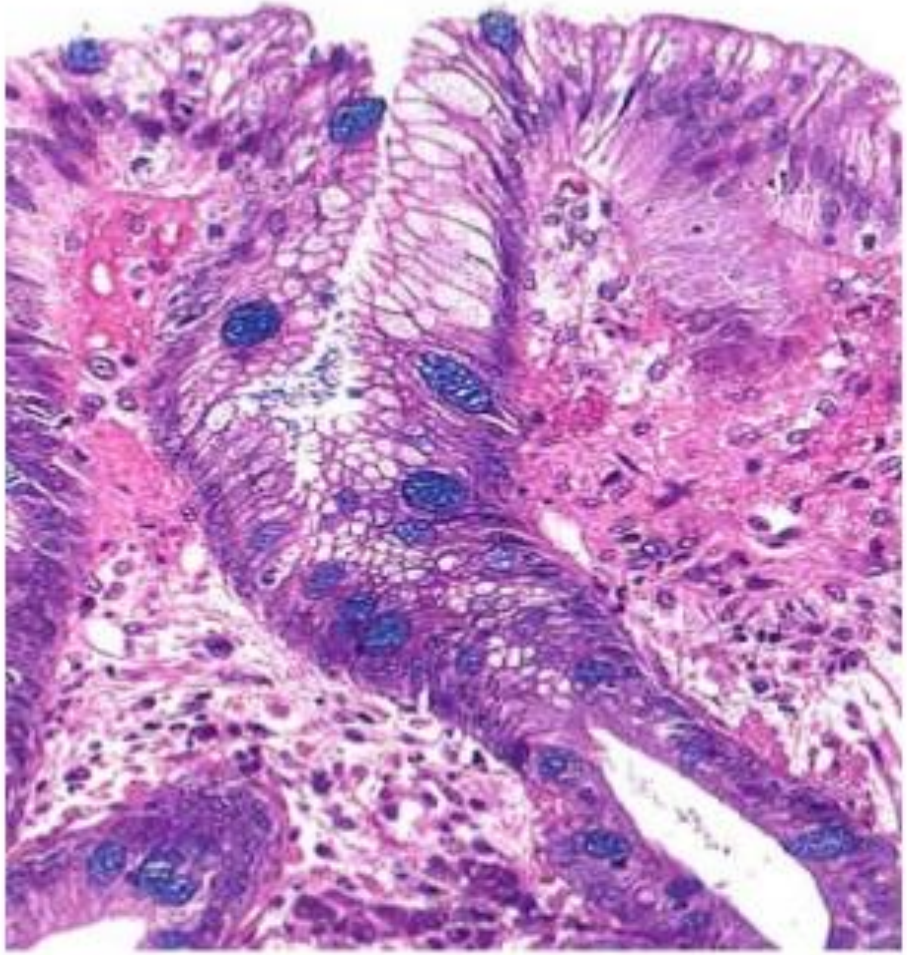
Long segment

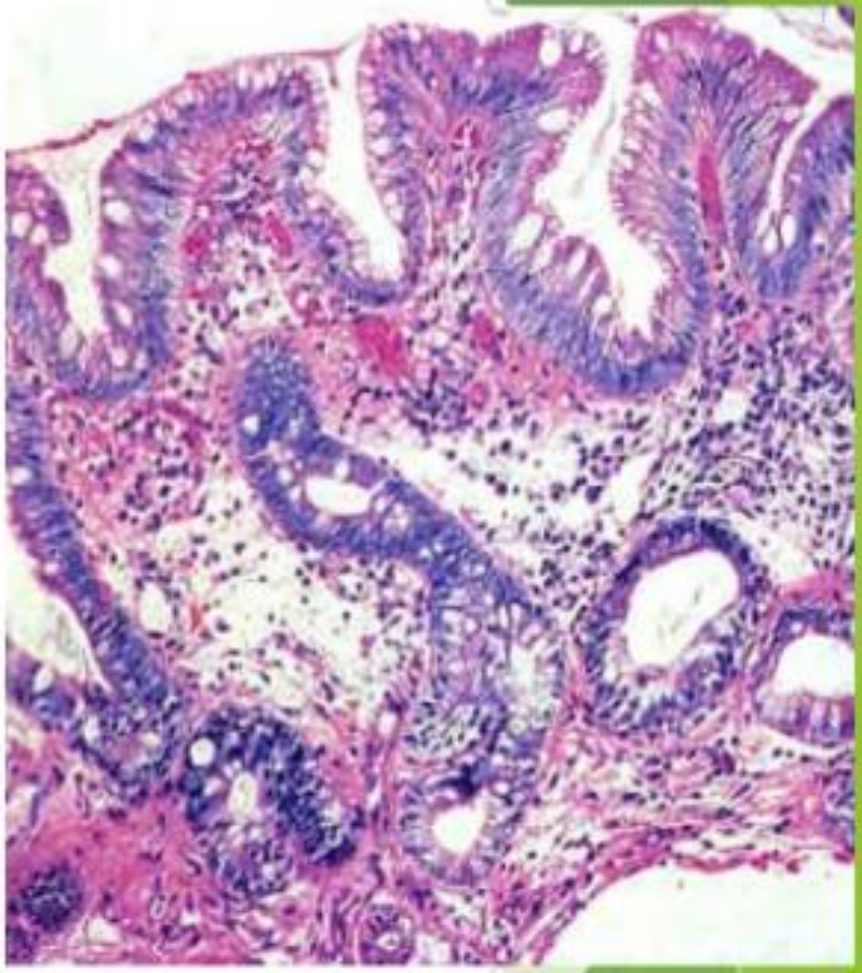






Barrett esophagus: histopathology 1

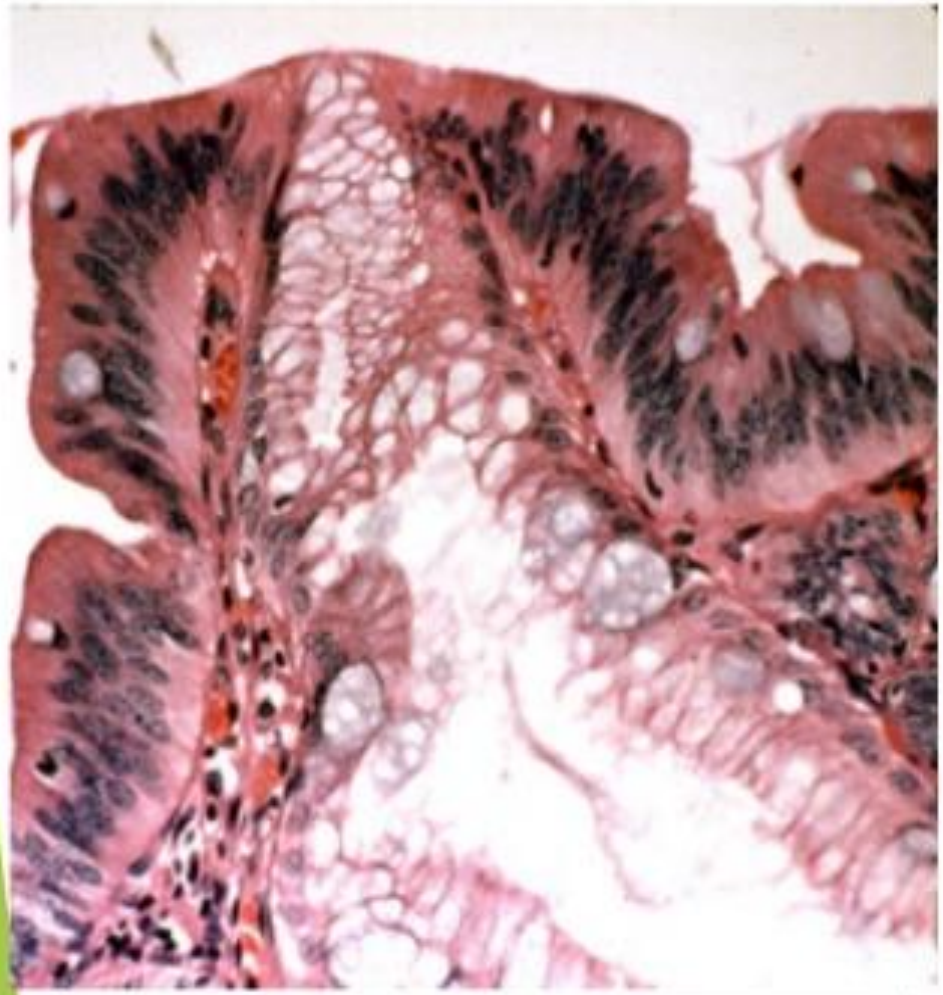




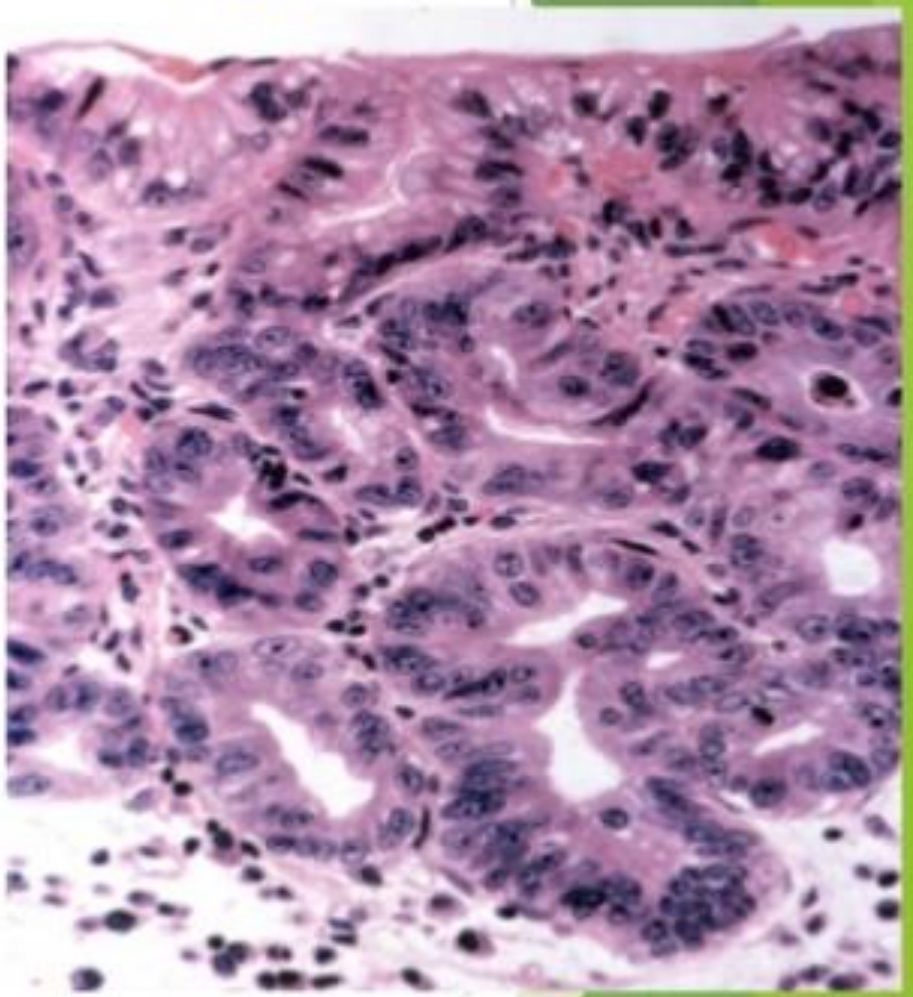
Diagnosis: intestinal metaplasia, negative for dysplasia

Diagnosis: intestinal metaplasia, indefinite for dysplasia (reactive inflammatory changes vs. low-grade dysplasia

Barrett's: histopathology 2



Diagnosis: intestinal metaplasia with low grade dysplasia



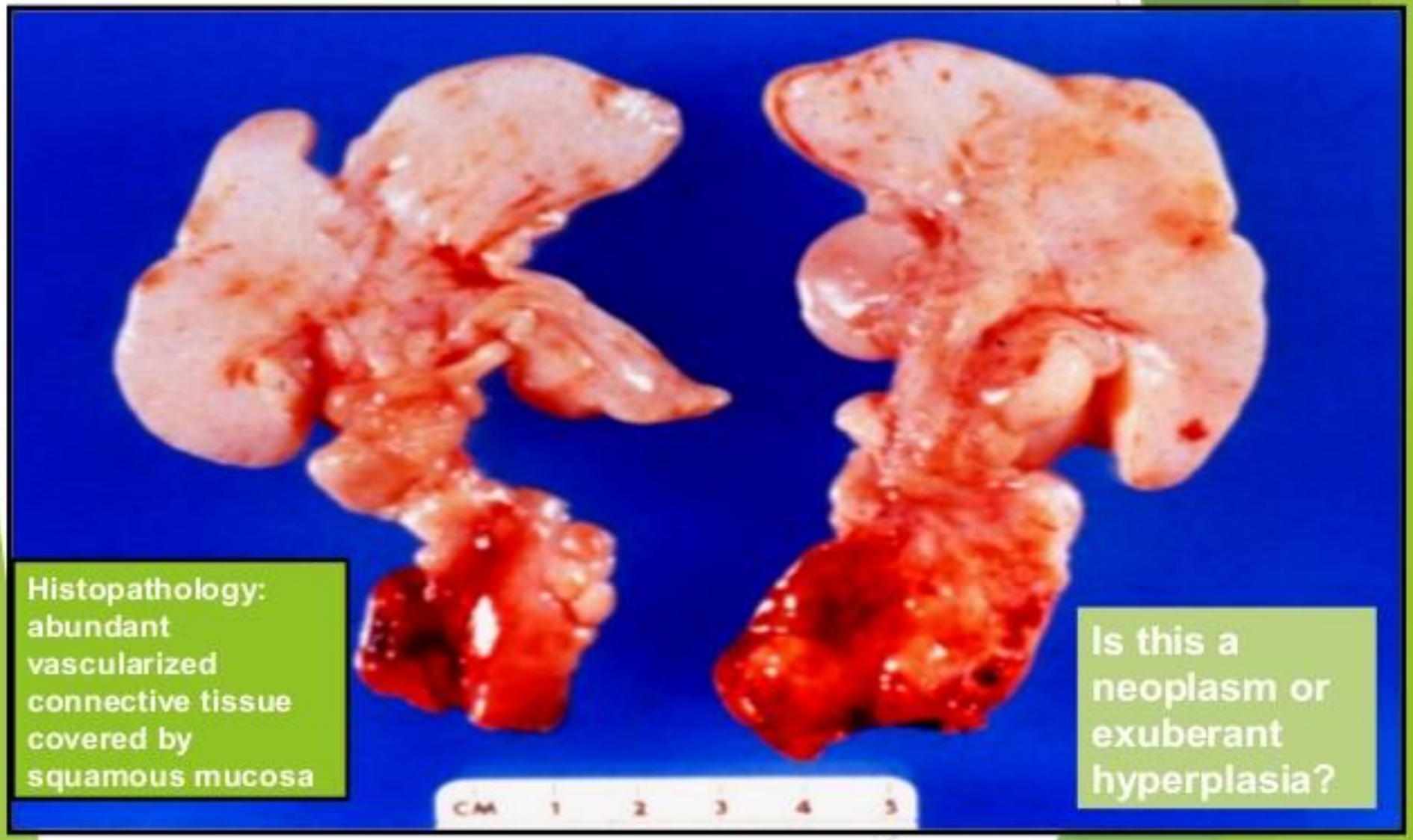
Diagnosis: intestinal metaplasia with high grade dysplasia

Benign neoplasms & tumor-like lesions

- Esophageal benign neoplasms are mostly of mesenchymal origin (non-epithelial): leiomyomas, lipomas, hemangiomas, neurofibromas.
- Two distinctive lesions:
  - **Fibrovascular polyp**
  - **Squamous papilloma**

Fibrovascular polyp

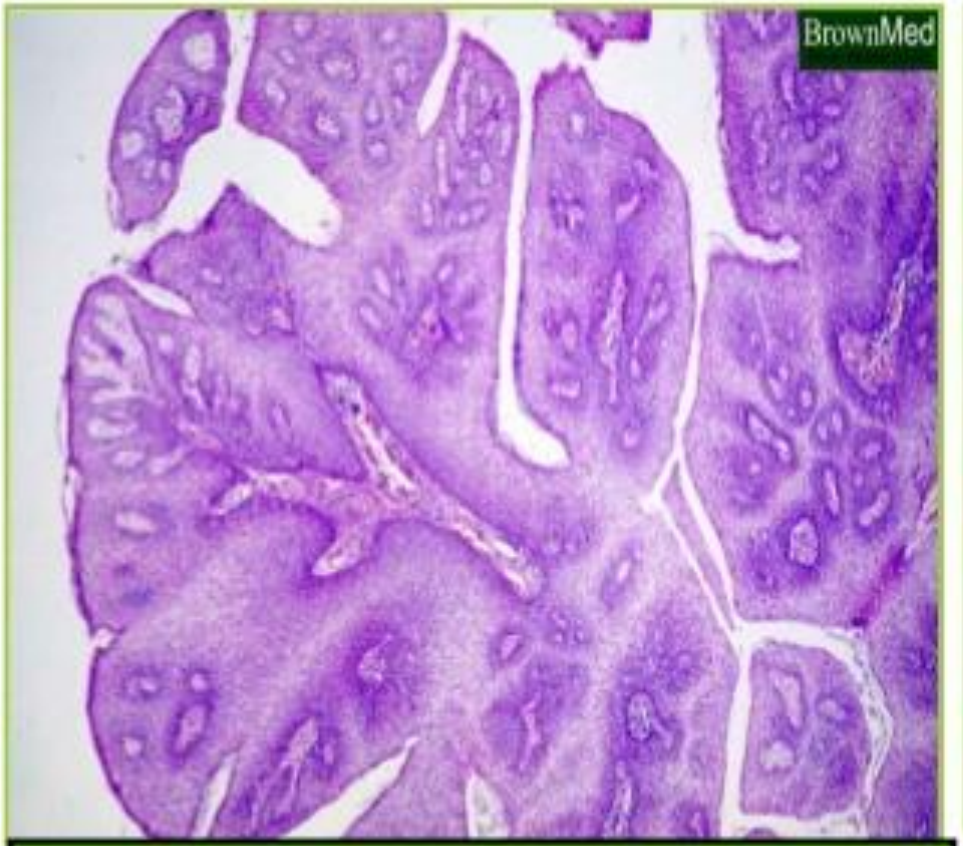
Presentation: dysphagia; lesion usually in upper 1/3 esophagus



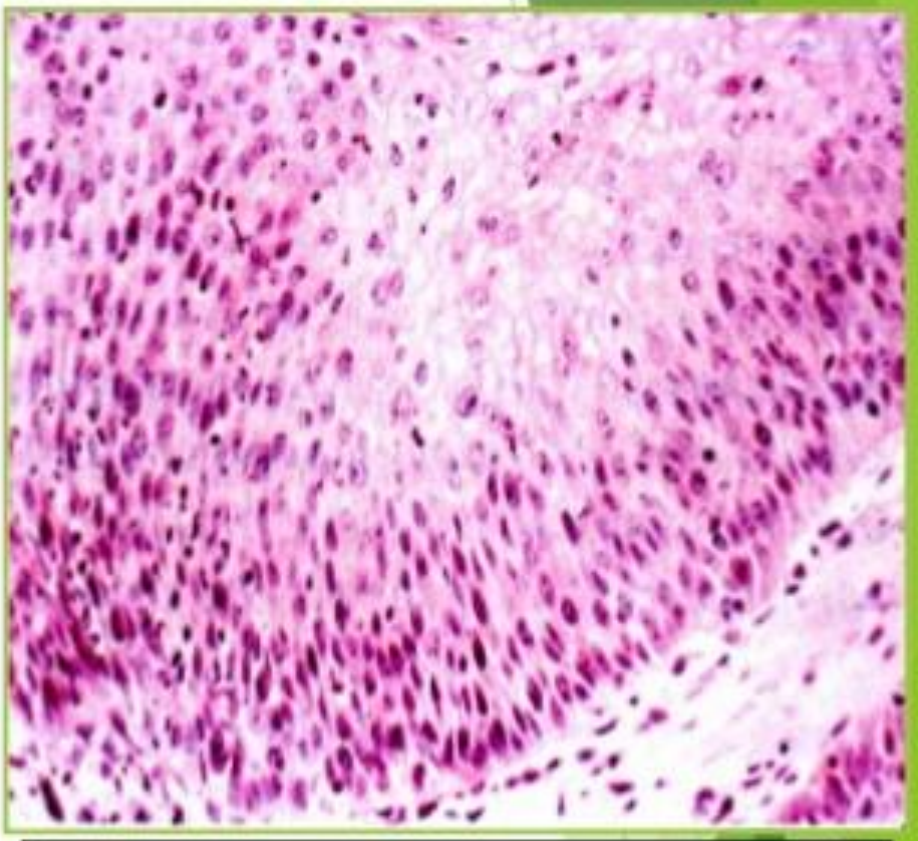
Histopathology: abundant vascularized connective tissue covered by squamous mucosa

Is this a neoplasm or exuberant hyperplasia?

Squamous papilloma



Low magnification: fronds of thickened squamous epithelium supported by connective tissue cores



Some have HPV-related cytologic changes or evidence of HPV DNA by in-situ hybridization methods

If squamous papilloma identified, respiratory tract should be examined for HPV-related papillomatosis (especially children)

Esophageal Carcinoma

- •Squamouscell carcinomas •Adenocarcinomas •Worldwide, squamouscell carcinomas constitute 90% of esophageal cancers, but in the United States there has been a very large increase (three-to fivefold in the last 40 years) in the incidence of adenocarcinomas associated with Barrett esophagus.

SquamousCell Carcinoma

- •Mucosal epithelial dysplasia •Carcinoma in situ •Invasive cancer •Polypoidexophyticmasses that protrude into the lumen; •Necrotizing cancerous ulcerations that extend deeply and sometimes erode into the respiratory tree, aorta, or elsewhere; •Diffuse infiltrative neoplasms

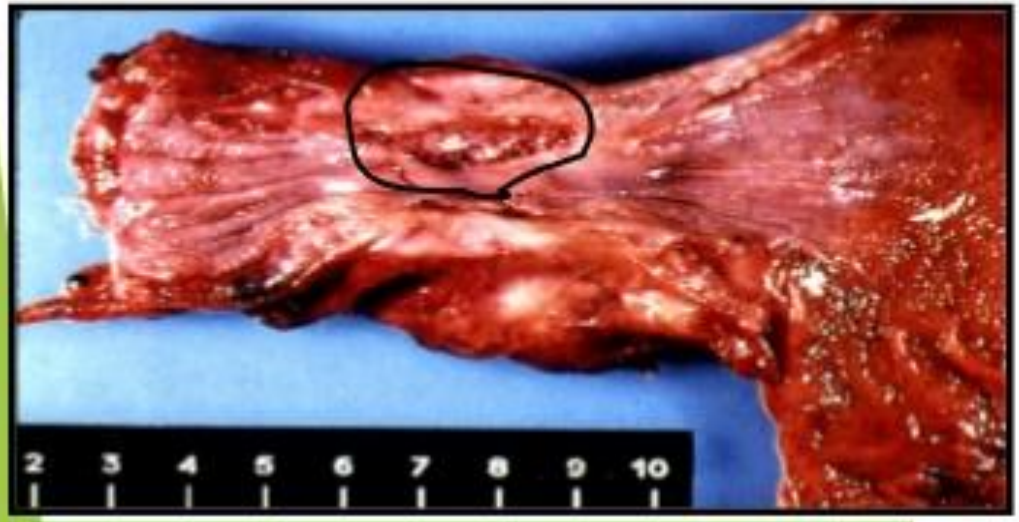
- A,Large ulcerated squamous cell carcinoma of the esophagus. B,Low power view of cancer invasion of the submucosa.

A

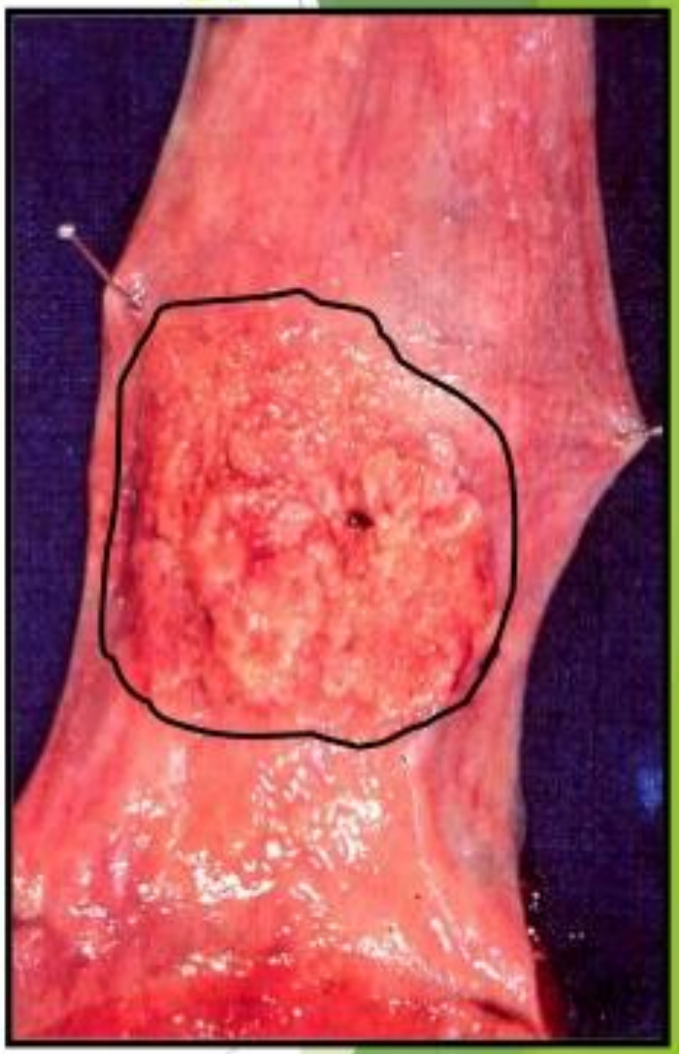
B

Squamous CA: gross pathology

Exophytic polypoid (obstructing lesion)



Ulcerated stricture (dysphagia)

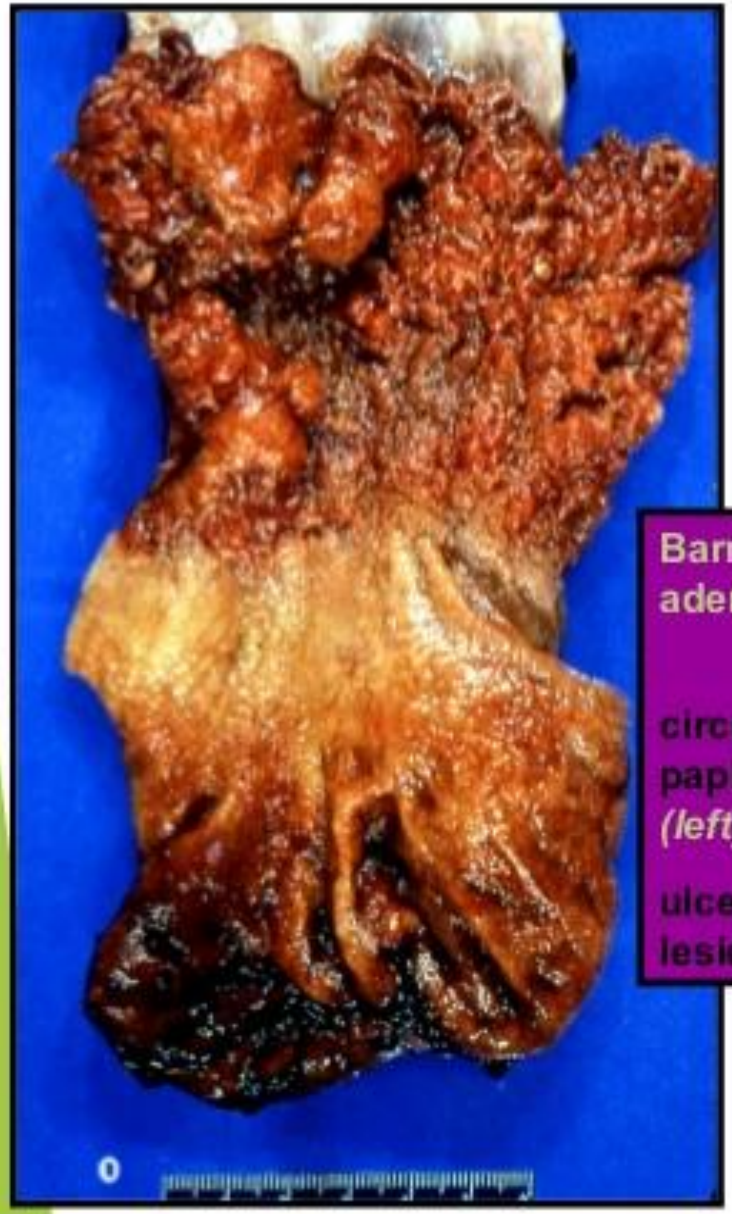


Early, superficial T1 lesion, good prognosis

Adenocarcinoma

- •Barrett esophagus is the only recognized precursor of esophageal adenocarcinoma. •Large nodular masses •Deeply ulcerative •Diffusely infiltrative features •Mucin-producing glandular tumors
- **Clinical Features**
- •Esophageal carcinoma is insidious in onset and produces dysphagiaand obstruction gradually and late. •Weight loss, anorexia, fatigue, and weakness appear, followed by pain, usually related to swallowing. •Diagnosis is usually made by imaging techniques and endoscopic biopsy. •Surgical excision is rarely curative. •Esophageal cancer confined to the mucosa or submucosais amenable to surgical treatment.

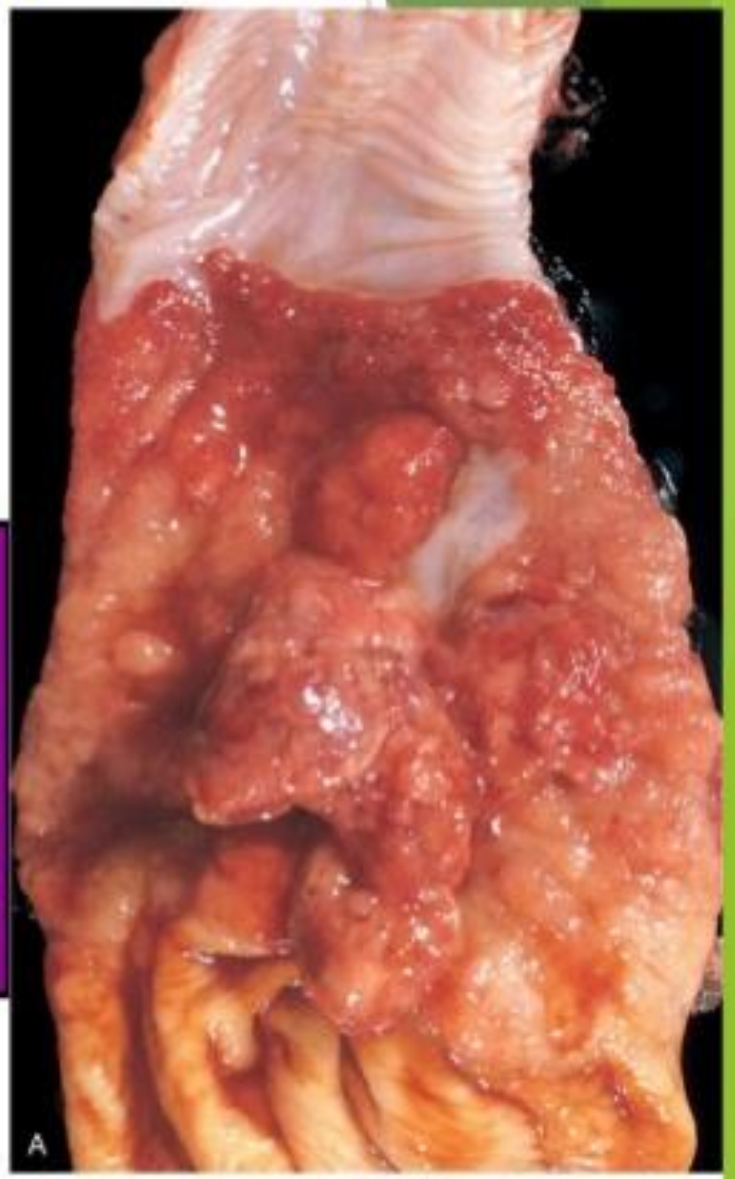
Adenocarcinoma: gross pathology



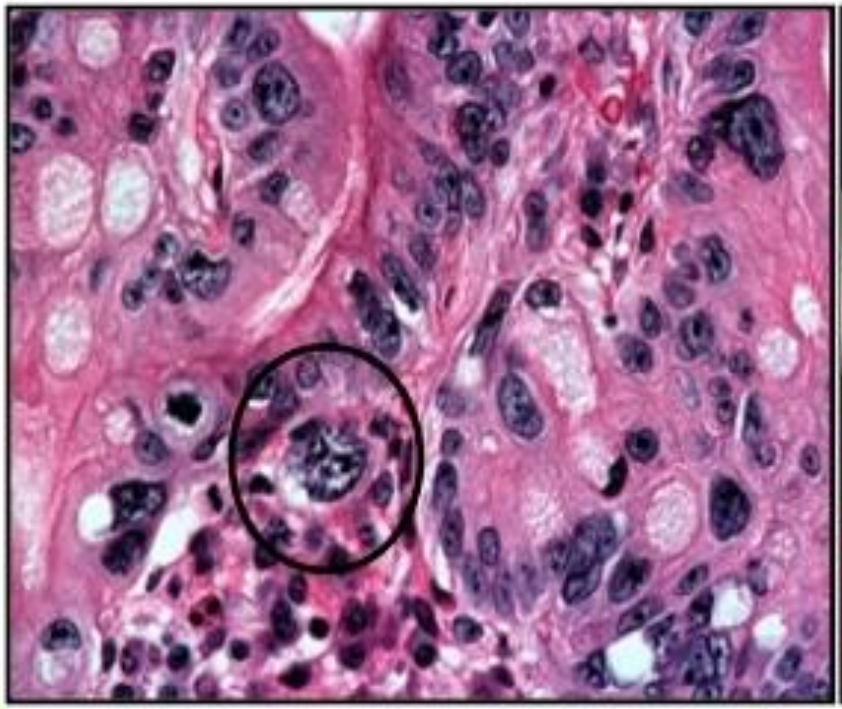
Barrett associated adenocarcinoma:

circumferential papillary lesion *(left)*

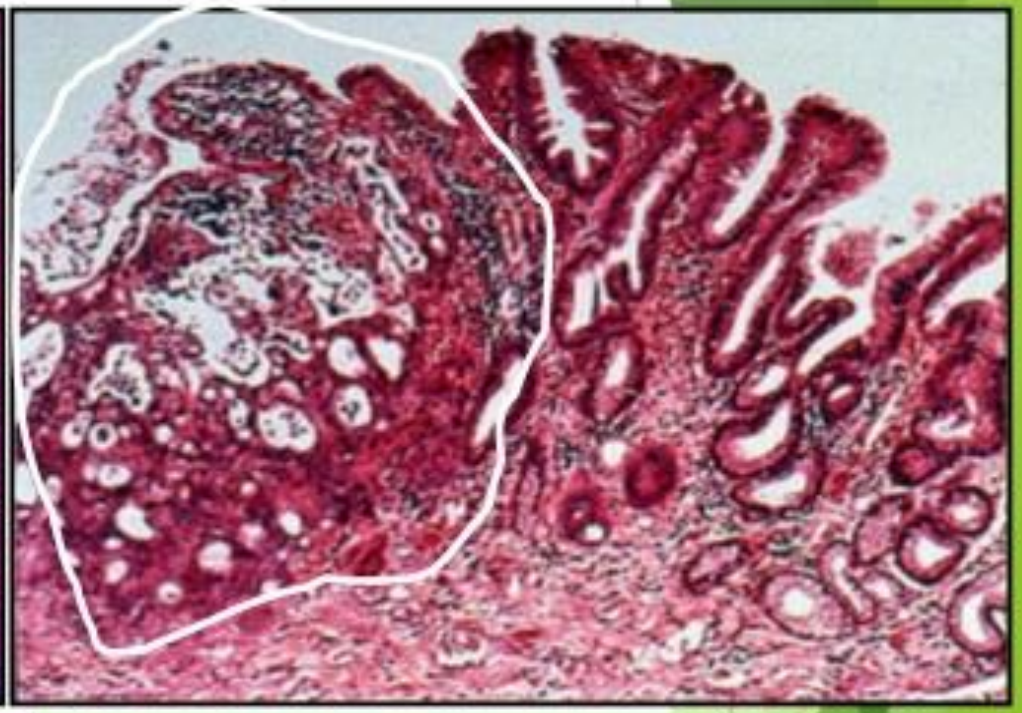
ulcerated polypoid lesion *(right)*



Adenocarcinoma: early invasive lesions developing in setting of high grade dysplasia



High-grade dysplasia with single dysplastic cell invading lamina propria (intramucosal adenocarcinoma = T1)



Adenocarcinoma invading submucosa, T1 lesion (circled), arising in Barrett intestinal metaplasia with high-grade dysplasia (right half)

left photo courtesy University of Washington department pathology;
right photo courtesy University of Pittsburgh
department pathology

Invasive Adenocarcinoma arising in Barrett esophagus

Intestinal metaplasia with dysplasia (red)

Malignant glands invading into submucosa (black)

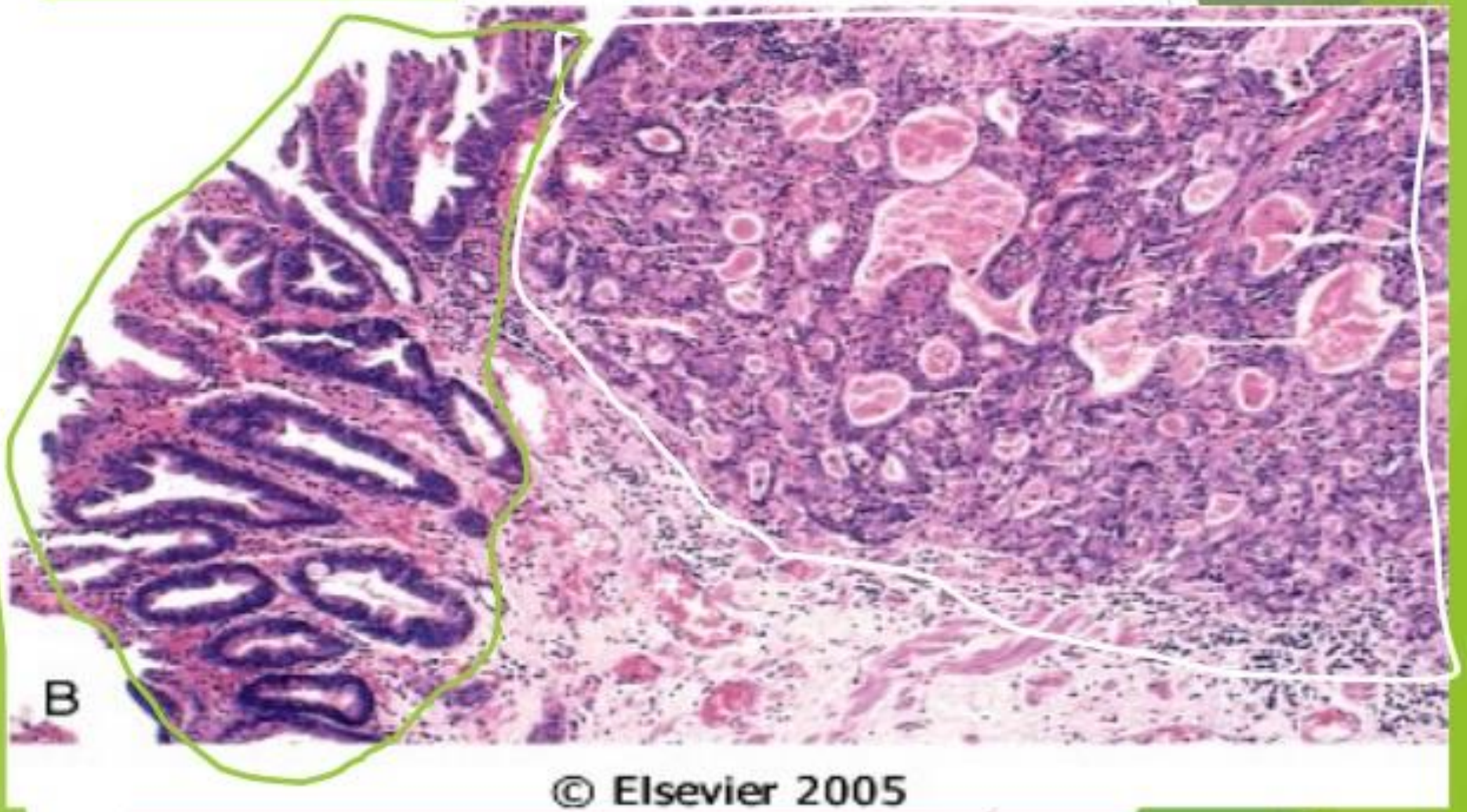


Fig. 17-11B, Pathologic Basis of Disease, 7th ed, Elsevier 2005

Malignant neoplasms of esophagus: overview

- Malignant tumors of esophagus comprise 6% of all gastrointestinal cancers, but account for 10% GI cancer mortality
- Problem: often asymptomatic until late, when they are deeply invasive or already metastatic
- **Worldwide:** 90% squamous / 10% adenocarcinoma
- **U.S.:** 50% squamous / 50% adenocarcinoma; incidence of adenocarcinoma rising steadily since 1970, almost always arising in Barrett esophagus

Squamous Carcinoma	Descriptor	Adenocarcinoma
M:F = 4:1; high incidence Iran, China, Puerto Rico (environmental initiators)	Epidemiology	M:F = 7:1; >95% from Barrett metaplasia; <5% from submucosal glands
Initiators: environmental carcinogens; promoters: nutritional deficiencies (vitamins A, B1, B2, B6, trace metals)	Pathogenesis	**Barrett dysplasia:** early mutation or overexpression of p53; amplfication cERB-B2, cyclin D, cyclin E
Ethanol, tobacco, achalasia, chronic esophagitis, Plummer-Vinson syndrome	Clinical Risk Factors	**chronic reflux esophagitis** tobacco, obesity
20% upper third 50% middle third 30% lower third	Anatomic Distribution	>95% lower third
5 yr. survival: 5-10% --75% 5 yr. survival if T1 lesion --25% 5 yr. survival for all cases subjected to surgery	Prognosis	**5 yr. survival: 25%** >80% 5 yr. survival with esophagectomy for T1 lesion

Staging esophageal carcinoma

TNM classification of oesophageal tumours

TNM classification[1]

T – Primary Tumour

TX	Primary tumour cannot be assessed
T0	No evidence of primary tumour
Tis	Carcinoma in situ
T1	Tumour invades lamina propria or submucosa
T2	Tumour invades muscularis propria
T3	Tumour invades adventitia
T4	Tumour invades adjacent structures

N – Regional Lymph Nodes

NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Regional lymph node metastasis

M – Distant Metastasis

MX	Distant metastasis cannot be assessed
M0	No distant metastasis
M1	Distant metastasis
	For tumours of lower thoracic oesophagus
	M1a Metastasis in coeliac lymph nodes
	M1b Other distant metastasis
	For tumours of upper thoracic oesophagus
	M1a Metastasis in cervical lymph nodes
	M1b Other distant metastasis
	For tumours of mid-thoracic oesophagus
	M1a Not applicable
	M1b Non-regional lymph node or other distant metastasis

Stage Grouping

Stage 0	Tis	N0	M0
Stage I	T1	N0	M0
Stage IIA	T2	N0	M0
	T3	N0	M0
Stage IIB	T1	N1	M0
	T2	N1	M0
Stage III	T3	N1	M0
	T4	Any N	M0
Stage IVA	Any T	Any N	M1a
Stage IVB	Any T	Any N	M1b


Thank You!