# Lec 1: disease of esophagus

- Diseases that affect the esophagus:

1. Obstruction: mechanical or functional.

2. Vascular diseases: varices.

3. Inflammation: esophagitis.

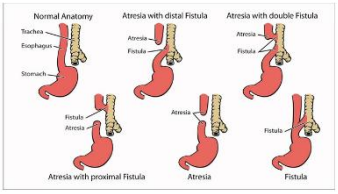
4. Tumors

## Mechanical Obstruction

Congenital or acquired

Examples: Atresia -Fistulas - Duplications - Agenesis (v rare) – Stenosis

### Atresia




* Thin, non-canalized cord replaces a segment of esophagus.
* Most common location: at or near the tracheal bifurcation
* +-fistula (upper or lower esophageal pouches to a bronchus or trachea

* Clinical presentation: Shortly after birth: regurgitation during feeding
Needs prompt surgical correction (rejoin).

*Complications if w/ fistula:
Aspiration - Suffocation - Pneumonia - Severe fluid and electrolyte imbalances.

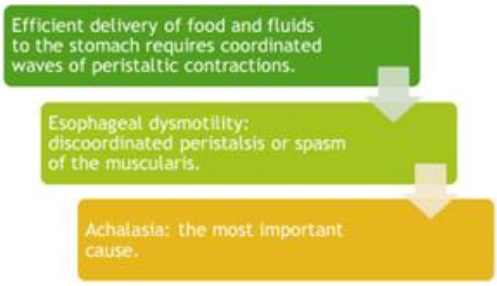
### Esophageal stenosis

* Acquired>>>Congenital
* Fibrous thickening of the submucosa & atrophy of the muscularis propria.
*Due to inflammation and scarring
*Causes: Chronic GERD / Systemic sclerosis / Irradiation / Ingestion of caustic agents

*Clinical presentation : Progressive dysphagia.
Difficulty eating solids that progresses to problems with liquids

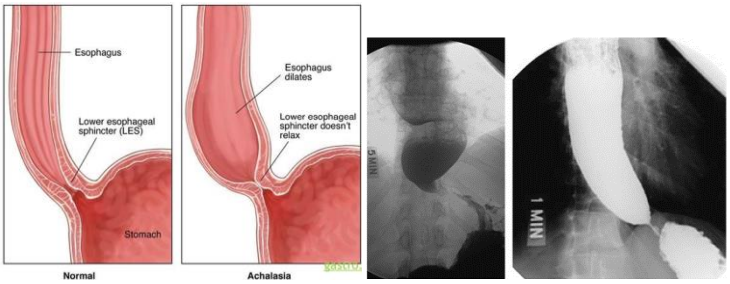
## Functional Obstruction

### Achalasia




*Triad: Incomplete LES relaxation- Increased LES tone
Esophageal aperistalsis.

*Primary >>>secondary




### Primary achalasia

*Degeneration of distal esophageal inhibitory neurons

*Idiopathic

*Most common

### Secondary achalasia

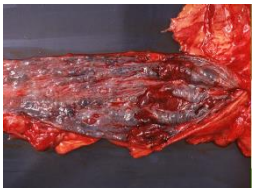
* loss of neural innervation due ton damage in:

- esophagus
- Vagus nerve
- Dorsal motor nucleus of vagus

- **Chagas disease**, Trypanosoma cruzi infection>>destruction of the myenteric plexus>> failure of LES relaxation>> esophageal dilatation.

**Clinical presentation* : Difficulty in swallowing - Regurgitation - Sometimes chest pain.

## Vascular diseases: Esophageal Varices



* Tortuous dilated veins within the submucosa of the distal esophagus and proximal stomach.

*Diagnosis by endoscopy or angiography.

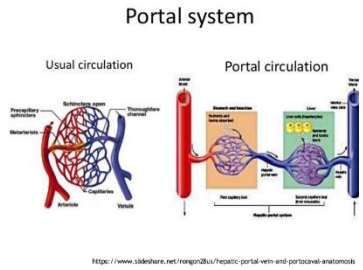
**Pathogenesis:*

1 -Portal circulation: blood from GIT>>portal vein>>liver (detoxification)>>inferior vena cava.

2- Diseases that impede portal blood flow >> portal hypertension >>esophageal varices

3-Distal esophagus : site of Porto-systemic anastomosis

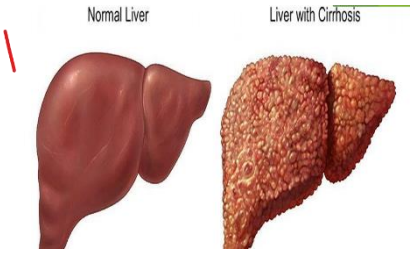
4- Portal hypertension>>collateral channels in distal esophagus>>shunt of blood from portal to systemic circulation>>dilated collaterals in distal esophagus>>varices




*Causes of portal hypertension :

- Cirrhosis is most common Alcoholic liver disease.

- Hepatic schistosomiasis 2nd most common worldwide




**Clinical Features:*

*1*- Often asymptomatic.

2-Rupture leads to massive hematemesis and death

3- 20% of patients die from the first bleed despite interventions.

4- Death due to hemorrhage, hepatic come, and hypovolemic shock

5- Rebleeding in 60%

## ESOPHAGITIS

* Esophageal Lacerations.

* Mucosal Injury

* Infections

*Reflux Esophagitis

* Eosinophilic Esophagitis

### Esophageal Lacerations

*Mallory Weiss tears are most common → Due to severe retching or forceful prolonged vomiting → Present with hematemesis → Gastric contents in vomitus >>>stretching>>>tear

Linear lacerations → longitudinally oriented → Cross the GEJ → Superficial → Heal quickly , no surgical intervention


### Chemical Esophagitis

*Damage to esophageal mucosa by irritants:

- Alcohol

-Corrosive acids or alkalis

-Excessively hot fluids

-Heavy smoking

-Medicinal pills (doxycycline and bisphosphonates)  Iatragenic (chemotx, radiotx , GVHD)

*** *Clinical symptoms &* morphology :**

- Ulceration and acute inflammation

-Only self-limited pain, odynophagia (pain with swallowing)

- Hemorrhage, stricture, or perforation in severe cases

## Infectious esophagitis

Mostly in debilitated or immunosuppressed

-Viral (HSV, CMV)

-Fungal (candida >>> mucormycosis & aspergillosis)

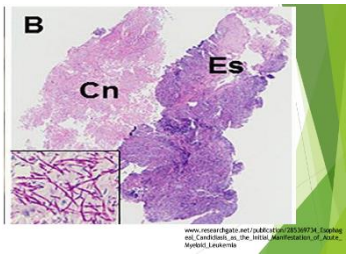
-Bacterial: 10%

- **Candidiasis :**

-Adherent.

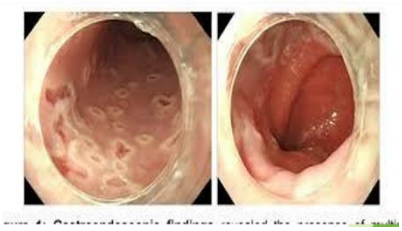
- Gray-white pseudo membranes

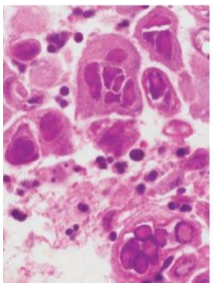
- Composed of matted fungal hyphae and inflammatory cells

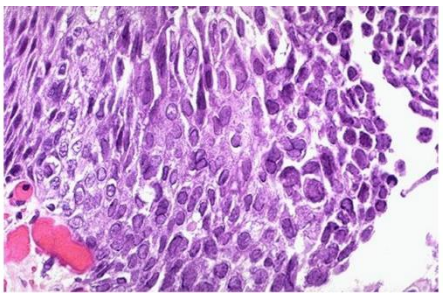




- **Herpes viruses** : Punched-out ulcers

- Histopathologic: Nuclear viral inclusions -Degenerating epithelial cells ulcer edge - Multinucleated epithelial cells



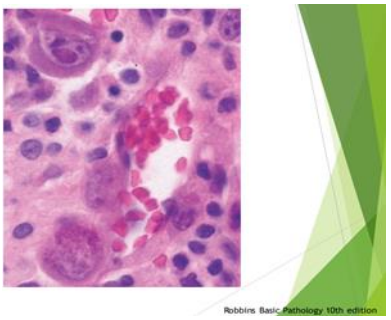




- **CMV** :

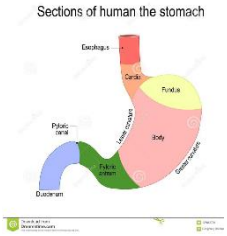
-Shallower ulcerations.

- Biopsy: nuclear and cytoplasmic inclusions in capillary endothelium and stromal cells.( Mega cells).



# Lec (2 ) : Gastric diseases 1

*Gastric diseases*: 1-Inflammatory. 2-Neoplastic .



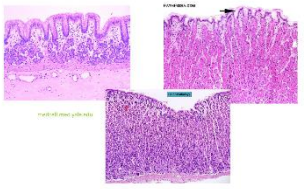

*Normal anatomy & histology:*

- 4 mains parts: cardia, fundus, body, antrum (pylorus).

- Cardia: mucin secreting foveolar cells.

-Body and fundus: parietal cells (HCL) and chief cells (pepsin).

-Antrum: neuroendocrine G cells (gastrin).



*Inflammatory conditions:

1-Acute gastritis

2-Chronic gastritis

3-Acute gastric ulcer.

4-Chronic peptic ulcer

***ACUTE GASTRITIS and gastropathy:**

**Acute gastritis**: Mucosal injury, neutrophils present.

**Gastropathy:** regenerative, no/rare inflammation.

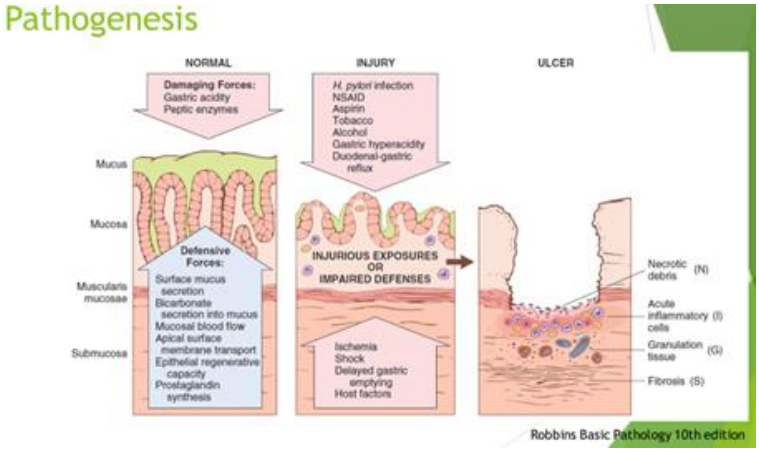
**Causes of gastropathy**: NSAIDs, alcohol, bile, and stressinduced

**Clinical features**:

-Asymptomatic

-Epigastric pain, nausea, vomiting.

**Severe**: erosions, ulcers, hematemesis, melena




## Pathogenesis of gastropathy, acute and chronic gastritis:

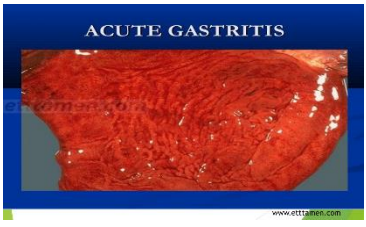
*Imbalance between protective and damaging forces

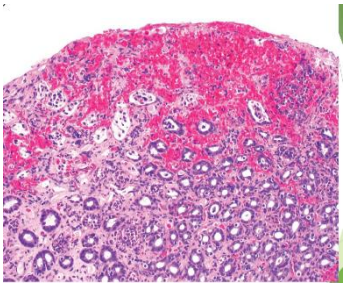
*Main causes:
1-NSAIDs (COX1 and COX2 inhibitors)
2-Uremic patients (ammonia inhibit bicarbonate transport)
3-H pylori (urease produces ammonia)
4-Aging (reduced mucin and bicarbonate secretion)
5-Hypoxia (high altitudes)
6-Harsh chemicals, (acids or bases) (direct epithelial injury)
7-Alcohol, NSAIDs, radiation therapy (direct mucosal damage)
8-Chemotherapy (inhibit DNA synthesis and cellular renewal)

### prostaglandins E2 and I2:

*Stimulate nearly all the defense mechanisms including

1. Mucus and bicarbonate secretion
2. mucosal blood flow
3. Epithelial restitution



### MORPHOLOGY

- Hyperemia (redness).

-Edema and slight vascular congestion

- Neutrophils, lymphocytes, and plasma cells are not prominent.

-Neutrophils : Active inflammation (gastritis) .

- Intact surface epithelium if mild.

**-Acute erosive hemorrhagic gastritis (Advanced)**

## Stress-Related Mucosal Disease

*Severe physiologic stress :

1-Trauma

2-Extensive burns

3-Intracranial disease

4-Major surgery

5- Serious medical disease

6-Critically ill patients

***Stress ulcers:** critically ill patients with shock, sepsis, or severe trauma.

*** Curling ulcers**: proximal duodenum , severe burns or trauma.

***Cushing ulcers:** stomach, duodenum, or esophagus, CNS injury as stroke, high risk of perforation.

### Pathogenesis

***Stress related injury:** Mostly due to Local ischemia caused by:

1-Systemic hypotension.

2-Decreased blood flow (Splanchnic vasoconstriction)

3-Systemic acidosis (lower intracellular PH ).

4-COX2 expression is protective

***CNS injury and Cushing ulcers:** Direct vagal stimulation, acid hypersecretion

### MORPHOLOGY

-Spectrum (Shallow to deep).

-Acute ulcers are rounded and typically < 1 cm.

-Ulcer base brown to black.

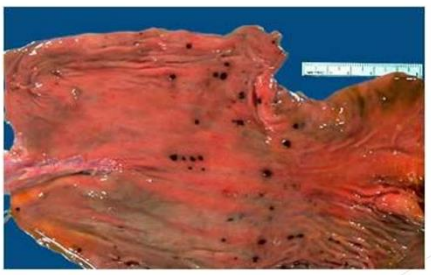
-Multiple, anywhere in stomach

- Normal adjacent mucosa

-No scarring

-Healing with complete epithelialization occurs days or weeks after removal of injurious factors

Stress ulcers



**Clinical features**

-Nausea, vomiting,

-Melena

-Coffee -ground hematemesis

-Perforation complication.

-Prophylaxis with proton pump inhibitors

-Outcome depends on severity of underlying cause

**CHRONIC GASTRITIS**

***Causes:**

1-Helicobacter pylori associated gastritis: most common.

2-Autoimmune atrophic gastritis: less than 10% of cases.

***Less common :**

Chronic NSAID -- Radiation injury -- Chronic bile reflux.

**Clinical features :**

-Nausea and upper-abdominal discomfort

-Vomiting

- Hematemesis uncommon

-Less severe but more prolonged symptoms

## Helicobacter pylori Gastritis

*Discovery of the association of H.pylori with peptic ulcer disease was a revolution.

*Spiral or curved, G-ve, bacilli.

*In almost all duodenal ulcers and majority of gastric ulcers or chronic gastritis.

*Epidemiology:

- Poverty, poor sanitation. Acquired in childhood, persists to adult-life.

- Acute infection is subclinical

Pathogenesis:

Non-invasive, adapted to live in the mucus layer:

-**Flagella**: allow motility.

**-Urease**: split urea to ammonia, protect bacteria from acidic pH.

- **Adhesins:** bacterial adherence to foveolar cell

**-Toxins:** (CagA) mucosal damage

## Pathogenesis :

Starts as Antral gastritis >>stimulate G cells >> increased acid production >> peptic ulcer

If severe: spread to body with atrophy (damage .Parietal cells)

Intestinal metaplasia and increased risk of gastric cancer

## MORPHOLOGY

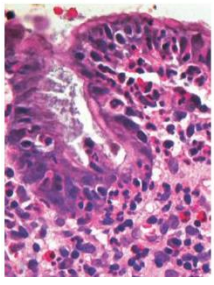
-**Gastric antral biopsy:** H. pylori in mucus layer.

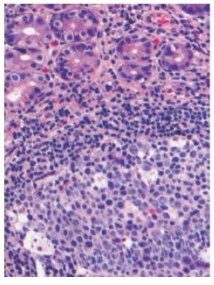
-Regenerative changes (hyperplastic polyps)

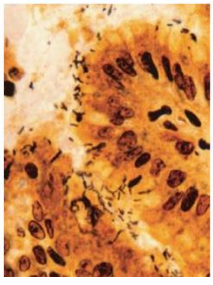
-Neutrophils, Plasma cells, lymphocytes & macrophages.

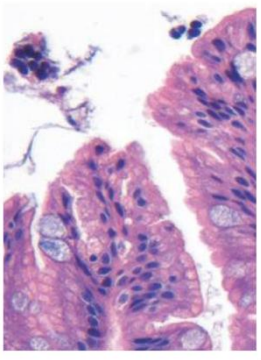
**-Lymphoid aggregates>>> increased risk of MALT lymphoma.**

**-Intestinal metaplasia (goblet cells)>>> dysplasia >> increased risk of adenocarcinoma**







### Diagnosis and treatment

-Serologic test: anti-H .pylori antibodies.

-Stool test for H.pylori.

-Urea breath test.

-Gastric antral biopsy (rapid urease test during endoscopy)

-Bacterial culture.

-PCR test for bacterial DNA.

-*Treatment:* combinations of antibiotics and PPI (triple therapy)

## Autoimmune Gastritis

-Antibodies to parietal cells and intrinsic factor in serum.

-Reduced serum pepsinogen I levels

- Antral endocrine cell hyperplasia

-Vitamin B12 deficiency >>> pernicious anemia and neurologic changes

-Impaired gastric acid secretion (achlorhydria)

-Marked hypergastrinemia

- Spares the antrum

### Pathogenesis

*Immune-mediated loss of parietal cells >>> reductions in acid and intrinsic factor secretion.

*Acid reduction >>> Hyperplasia of antral G cells >>> hypergastrinemia

*Deficient intrinsic factor >> deficient ileal VB12 absorption >> pernicious anemia

### MORPHOLOGY

-Damage of the oxyntic (acid-producing) mucosa.

-Diffuse atrophy, thinning of wall, loss of gastric folds

- Lymphocytes, plasma cells, macrophages, less likely neutrophils.

**-Intestinal metaplasia >>> dysplasia >> carcinoma.**

**-G- cell hyperplasia >>> carcinoids**

## Clinical features

- 60 years, slight female predominance.

-Often associated with other autoimmune diseases

-Dyspepsia

-Anemia (VB12 or iron)

Table 15.2 Characteristics of *Helicobacter pylori*–Associated and Autoimmune Gastritis

| Feature | *H. pylori*–Associated | Autoimmune |
|---|---|---|
| Location | Antrum | Body |
| Inflammatory infiltrate | Neutrophils, subepithelial plasma cells | Lymphocytes, macrophages |
| Acid production | Increased to slightly decreased | Decreased |
| Gastrin | Normal to markedly increased | Markedly increased |
| Other lesions | Hyperplastic/inflammatory polyps | Neuroendocrine hyperplasia |
| Serology | Antibodies to *H. pylori* | Antibodies to parietal cells ($H^+$,$K^+$-ATPase, intrinsic factor) |
| Sequelae | Peptic ulcer, adenocarcinoma, lymphoma | Atrophy, pernicious anemia, adenocarcinoma, carcinoid tumor |
| Associations | Low socioeconomic status, poverty, residence in rural areas | Autoimmune disease; thyroiditis, diabetes mellitus, Graves disease |

Robbins Basic Pathology 10th edition

## Complication of chronic gastritis

**1-Peptic ulcer**

**2-Mucosal atrophy**

**3-Intestinal Metaplasia**

**4-Dysplasia**

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