L1 Summary pathology

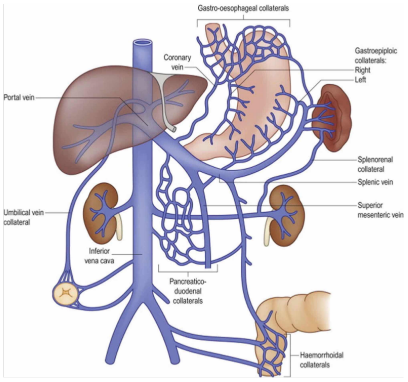
Diseases of esophagus

1- obstruction →

- mechanical
  - Congenital
    - atresia
    - fistula
    - Agenesis
    - duplications
  - acquired
    - stenosis
- Functional
  - Achalasia
    - primary achalasia
      most Common
    - secondary achalasia

حكت الدكتورة انها بتهتم بال macroscopic images
not microscopic ones.

2- Vascular disease →



the normal case

blood from GIT
↓
portal vein
↓
*liver (detoxification)
↓
inferior vena cava

Varices

*Disease impedes portal circulation.
↓
portal hypertension
↓
Collateral channels in distal esophagus
↓
shunt of blood from portal to systemic
↓
dilated collaterals
↓
varices

★ الـ Varices بكون الها asymptomatic لكن ممكن يحصلها rupture بعدين → hematemesis → bloody vomiting & death

Causes of portal hypertension → cirrhosis
→ hepatic schistosomiasis

3- Esophagitis →

1. esophageal lacerations
2. mucosal injury
3. infections → page 3
4. eosinophilic esophagitis
5. reflux esophagitis.

1 esophageal ulcerations

- Mallory weiss tears most common and present with hematemesis
- Cause → severe retching & prolonged vomiting.

Gastroesophageal musculature doesn't relax
↓
antiperistaltic contractions
↓
stretch
↓
tears.

- heal quickly no surgical intervention

2 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) → graft vs host disease

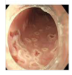
الأعراض → ulceration, acute inflammation
self-limited pain, odenophagia

hemorrage , stricture (mostly accompanied with stenosis) or perforation in severe cases

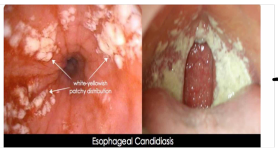
3- infectious esophagitis

- viral (HSV, CMV)
- fungal (Candida >>> mucor mycosis & aspergillosis)
- bacterial 10%

HSV:
- punched out ulcers
- multinucleated epithelial cells
- nuclear viral inclusions
- degenerative epithelial cell ulcers



CMV:
- shallower ulcers
- Megalo cells (large)
- nuclear & cytoplasmic inclusions in stromal, endothelial cells.

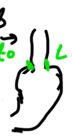


→ the microscopic appearance of Candida infection

4- reflux esophagitis

(GERD) * most frequent cause of esophagitis

*pathogenesis :-



esophagus (sensitive to acids), LES, stomach

the normal state ← الحالة الطبيعية

protective forces :- mucin, bicarbonate, high LES tone.

LES = lower esophageal sphincter

← (pathogenesis) الحالة المرضية

- LES tone ↓ occurs due to → alcohol, tobacco, CNS depressants
- abdominal pressure ↑ " " " → obesity, ...
- idiopathic (unknown cause)

* morphology
  - macro → severity (unremarkable → simple hyperemia)
  - micro →
    - eosinophils infiltration → neutrophils infiltration (more severe)
    - Basal zone hyperplasia
    - Elongation of lamina propria papillae

هون مش متأكدة من المعنى ١٠٠٪ بس عشان ايجيب الحفظ سهل ←

- Basal zone ---→ يعني محيط الخلية يزداد ويتبين أكبر
- Elongation ---→ هاد CT موجود مباشرة تحت ال epithelium

*clinical features →
- age >40
- may occurs in infants & children.
- heartburn & dysphagia
- regurgitation
- Rarely! severe chest pain → like angina

*Treatment → PPI

* Complications →
- hematemesis → vomiting blood
- melena → black stool (blood in stool)
- esophageal ulcerations
- strictures → like stenosis
- Barret esophagus

reflux → Barret → Cancer

5- Eosinophilic esophagitis

* chronic immune mediated disorder

* most patients are atopic (asthma عنده مثلاً) or modest peripheral eosinophilia.

symptoms
* → food impaction & dysphagia (adults)
  → feeding intolerance (children) & GERD like symptoms

* rings in upper & mid esophagus

* numerous eosinophils, and far from GEJ →

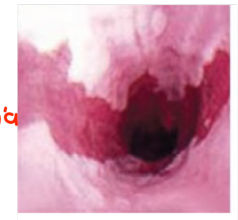
Treatment (TX)
- Dietry restriction
- Corticosteroids
- PPIx (refractory to PPI)

* a Complication of chronic GERD is Barret esophagus: intestinal metaplasia into the esophagus squamous mucosa

10% of symptomatic GERD patients → Barret

metaplasia → dysplasia → adenocarcinoma

- morphology →
  - red tongues upward from GEJ
  - Gastric intestinal metaplasia
  - Goblet cells
  - +/- Dysplasia
  - intramucosal Carcinoma.



management → periodic surveillance endoscopy for screen dysplasia.

→ dysplasia (high grade) / adenocarcinoma → intervention

Esophageal tumors

adenocarcinoma

half of Barret cases

risk factors → dysplasia associated Barret
- smoking
- obesity
- radio Tx

- Geographic & racial variations.

metaplasia → dysplasia → adenocarcinoma (Barret)

pathogenesis
- genetic & epigenetic variations
- chromosomal abnormalities
- TP53 variations

Morphology →

Early: Flat/raised patches (distal third) → later: exophytic infiltrative masses

Clinical features →
- Pain or difficulty swallowing
- Progressive weight loss
- Chest pain → GERD شبيه
- Vomiting.
- Advanced stage at diagnosis: 5-year survival <25%.
- Early stage: 5-year survival 80%

Squamous Cell Carcinoma

- Risk factors:
- Alcohol
- Tobacco use
- Poverty
- Caustic injury
- Achalasia .
- Plummer-Vinson syndrome → disorder with iron deficiency anemia
- Frequent consumption of very hot beverages
- Previous radiation Tx

pathogenesis → alcohol & tobacco (western countries)
- → polycyclic hydrocarbons
- → nitrosamines
- → Fungal infested food
- → HPV infection

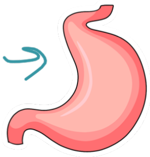
morphology →
- middle third
- polypoid, ulcerated or infiltrative
- wall thickening & lumen narrowing
- invade (mediastinum, bronchi, aorta, pericardium).

squamous dysplasia / CIS → moderately to well differentiated invasive SCC

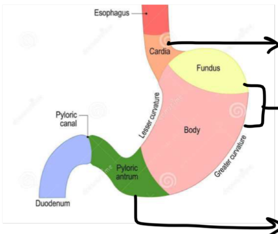
intramural tumor nodules

clinical features →
- Dysphagia
- Odynophagia
- Obstruction
- Weight loss and debilitation
- Impaired nutrition & tumor associated cachexia
- Hemorrhage and sepsis if ulcerated.
- Aspiration via a tracheoesophageal fistula
- Dismal Px: 5 year survival <9%

Pathology of the stomach →



part 1

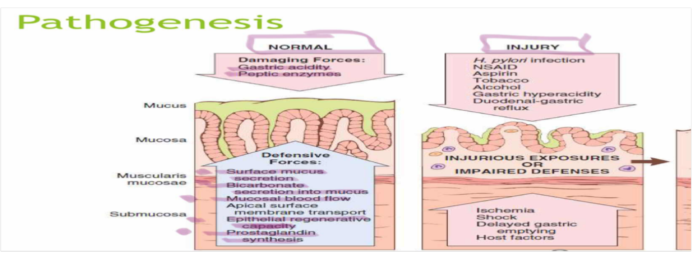


→ mucin secreting Foveolar cells.
→ parietal cells (HCl) / chief cells (pepsin)
→ neuroendocrine G cells (gastrin)

تذكروا من الفسيو انو ال Gastrin يحفز افراز ال Hcl
(فسيو ال GI
مش الدذو 🤐)

Gastric diseases

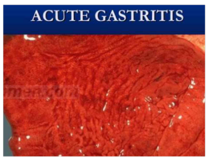
- inflammatory
  - Gastritis
    - Acute gastritis
    - chronic gastritis
  - ulcers
    - acute gastric ulcers
- Neoplastic



→ For all inflammatory gastric diseases → افهموها رح تسهّل
حفظ كثير شغلات

acute gastritis (gastropathy)

↓ neutrophils ✓ — ↓ no inflammation



Causes → NSAID, alcohol, hip & stress_induced

clinical features → Can be asymptomatic

H. pylori اولها اللي بتجي

chronic لحدين تتحول الى

causes الاكثر انتبهوا لذلك

morphology →

* Hyperemia (redness).
* edema, Congestion.
* intact epithelium.
* neutrophils, lymphocytes & plasma cells not prominent
* Active inflammation is not necessarily.

Pathogenesis →

① NSAIDs (cox1, cox2) → PGE2, I2
② uremic patients & H. pylori → ammonia ↑ and bicarbonate transport ↓
③ hypoxia (blood flow)
④ old age (mucin & bicarbonates)
⑤ chemotherapy (cellular renewal)
⑥ Direct injury → harsh chemicals, alcohol, NSAID, radiation

* acute gastritis with/may develop → erosions / bleeding → تستمر نهايته الحالة

acute erosive hemorrhagic gastritis

* prostaglandins E2 & I2 → stimulate nearly all defense mechanisms.

* Both selective Cox 2 inhibitors & nonselective Cox inhibitors can result in gastropathy

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stress related mucosal disease

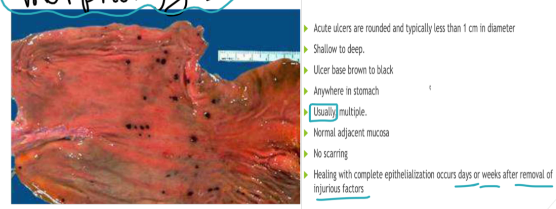
acute gastric ulcers

the name shows that it's caused by physiological stress → trauma, extensive burns, intracranial disease ...

Acute gastric ulcers

- stress ↓ shock, sepsis, trauma ↓ pathogenesis ↓ mostly due to ischemia caused by:
  ① hypotension ② vasoconstriction ③ systemic acidosis (low intracellular PH)
- Curling ↓ proximal duodenum — severe burns / severe trauma
- Cushing → intracranial problems — high risk of perforation — duodenum, esophagus & stomach ↓ pathogenesis ↓ Direct vagal stimulation → acid hypersecretion.

morphology →



clinical features →

- Melena → black stool
- Coffee ground hematemesis → vomiting with blood

PPI for prophylaxis

perforation complication.

→ the stomach is the source of the blood so it is affected by many factors to be black in color like acidity

Chronic gastritis

Causes → H. pylori most common
→ autoimmune less that 10%
→ less common → Chronic NSAIDs
→ radiation injury
→ chronic bile reflux

① H. pylori gastritis →
↓
G-ve
.acute is subclinical
. majority of gastric ulcers & chronic gastritis
mostly cause doudenal ulcers.

→ Antral gastritis with ↑ Acl → peptic ulcer
→ pangastritis → hypochlorhydria.

Complication → intestinal metaplasia & increased risk of gastric Cancer.

pathogenesis by H. pylori virulence Factors →
→ Flagella
→ urease
→ Adhesins
→ toxins

Morphology →
biopsy → H. pylori & neutrophils, plasma cells, lymphocytes & macrophages

MALT lymphoma → lymphoid aggregates.
adenocarcinoma → (intestinal metaplasia → dysplasia → ↑risk of adenocarcinoma)

Diagnosis → serology
→ stool
→ urea breathtest
→ biopsy
→ culture
→ PCR

Tx → antibiotics & PPI

② Autoimmune gastritis →
Antibodies against parietal cells & serum intrinsic factor

pepsingen I ↓ , HCL ↓ (achlorhydria)
↓ Antral endocrine cells hyperplasia (hypergastrinemia)
→ كورپسی‌ها parietal ها cells so spares the antrum

intrinsic factor → vitamin B12 defficiency ↓ megaloplastic anemia.

*Due to damage of some Chief cells → reduced pepsinogen

Morphology → Damage of oxyntic (acid-producing) mucosa.
→ thinning, atrophy & loss of rugal folds
→ lymphocytes, plasma cells, macrophages, neutrophils less likely

intestinal metaplasia → dysplasia → Carcinoma
neuroendocrine cells hyperplasia → tumors.

60 years, Female أكثر
often with other autoimmune diseases

peptic ulcer disease →

mostly by H. pylori & by NSAIDs — the most Common use of gastric ulcers in USA.
→ more than 70%

any part of GIT exposed to acidic gastric juices.

Site → mostly antrum & upper doudenum
→ Esophagus (GERD)
→ Ectopic gastric mucosa (meckel diverticulum)

may be also in

pathology of the stomach part 2 →

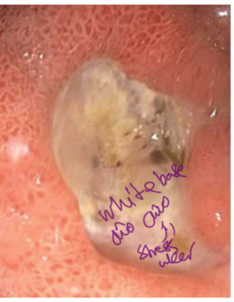
Pathogenesis →
*No acid No ulcer

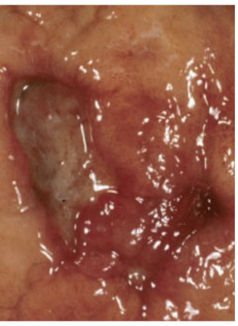
Cofactors: smoking, chronic NSAIDs, high-dose corticosteroids, alcoholic cirrhosis, COPD CRF, hyperparathyroidism.

Hyperacidity caused by:
① H. pylori ② Hypergastrinemia as in Zollinger-Ellison syndrome
③ parietal cell hyperplasia ④ Excessive vagal stimulation

Zollinger Ellison syndrome
Cause: uncontrolled release of gastrin by a tumor
↓
massive acid secretion
↓
multiple peptic ulceration in stomach, doudenum & jejunum

Morphology → 4:1, proximal doudenum : stomach
>80% Solitary





Sharply punched out defect

Base of the ulcer is smooth and clean

Granulation tissue → the background is not healthy mucosa.

Complications → hemorrage & perforation

Clinical Features →

- worse at night, relieved by alkali & Food.
- bloating & belching
- iron defficiency anemia, Frank hemorrage or perforation.

Tx → Surgery for Complications
→ H. pylori eradication

بدا تتخلص من السبب

Gastric polyps & tumors →

Gastric polyps
- epithelial / stromal cell hyperplasia
- inflammation
- neoplasia
- ectopia

→ inflammatory & hyperplastic polyps →
- 75% of all polyps
- in a background of chronic gastritis.
- when H. pylori infection is eradicated → it regresses
- risk of dysplasia if > 1.5 cm

→ Gastric adenomas

Adenomas are the least common type of stomach polyp but the type most likely to become cancerous

- 10% of all polyps
- increase with age
- males > females
- in a background of chronic gastritis, atrophy, intestinal metaplasia.
- Dysplasia in all cases (low-high) ← dysplasia لازم يكون في

dysplasia should be found with Gastric adenoma
nuclei → enlarged, ugly, hyperchromatic

Cancer ← mitosis الـ ببين
يقهر بالحالات
Cancer
dysplasia أكثر من adenoma

- risk of adeno Carcinoma depending on size
- risk of Carcinoma in gastric adenoma > risk of carcinoma in colonic adenoma.

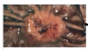
Gastric adeno Carcinoma →

- 90% of gastric cancer
- problem →
  - its early symptoms mimic gastritis → leads to late diagnosis
  - but if we do screening → early detection
- rates vary geographically.
- PUD doesn't increase risk except after surgery.
- Background of :- mucosal atrophy & intestinal metaplasia
  - نفس الـ adenoma
  - precursor كولها آتية

Gastric adenocarcinoma
- intestinal
  - pathogenesis
  - sporadic
    - P53 mutation
    - B Catenin mutation
  - Familial
    - APC gene mutation in FAP
  - * H. pylori chronic gastritis, EBV (lesser extent) → genetic alterations cause intestinal type
- diffuse
  - sporadic
    - P53
    - 50% CDH1 (E. Cadherin)
  - Familial
    - CDH1 (E Cadherin)

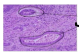
Cont.....

morphology (lauren classification)



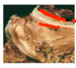
→ intestinal due to the mass

- ① intestinal
  - underlying intestinal metaplasia
  - Bulky
  - Forms glands
  - Exophytic mass / ulcer.

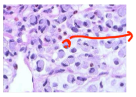


→ glands & necrosis center → intestinal

- ② diffuse
  - intestinal growth pattern (within the wall)
  - Discohesive cells (signet ring cells)
  - Desmoplastic reaction (thick wall & linitis plastic)



→ linitis plastica (thick wall) → diffuse



→ signet ring cell

clinical Features →

both types in general → similar to chronic gastritis & cachexia.

intestinal →
- in high risk areas (varies geographically)
- Develops from precursor (adenoma) → dysplasia with intestinal metaplasia
- M:F → 2:1
- mean age 55 years.

DiFFuse → (very bad prognosis)
- uniform incidence across countries.
- No precursor lesion.
- M:F → 1:1
- younger age

- the drop in incidence applies only to the intestinal type
- now incidence of intestinal ~ of diffuse → after drop

prognostic Factors →
- T-Stage → depth of invasion (عمق اختراق)
- extent of metastasis → nodal / distant

early diagnosis → 5 year survival 90%

late diagnosis → " " " 20%

lymphoma

- 5% of gastric malignancies
- Stomach → most common site of extranodal lymphoma
  - most common lymphoma → indolent extranodal marginal zone B-Cell lymphomas → low grade lymphoma.
  - 2nd most common lymphoma → diffuse large B cell lymphoma (aggressive

neuroendocrine (carcinoid) tumor

- arising from neuroendocrine differentiated cells (e.g → G cells) — associated with carcinoid syndrome (sometimes)
- 40% in small intestines but also in the stomach.
- associated with chronic atrophic gastritis, endocrine cell hyperplasia & Zollinger Ellison syndrome.

→ submucosal masses (small polypoid lesions)

Smooth chromatin (salt & pepper)

الخلايا تتميز بـ nesting pattern والأنوية

كالفلفل والملح

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

Carcinoid Syndrome →
- In 10% of neuroendocrine tumor cases
- strongly associated with metastatic disease especially to the liver
- symptoms due to vasoactive amines production

Cutaneous flushing, sweating, bronchospasm, colicky abdominal pain. diarrhea, and right-sided cardiac valvular fibrosis.

Cutaneous flushing →