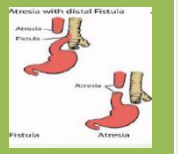
Diseases of the esophagus

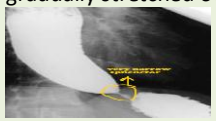
1 . **Obstruction: mechanical** (Atresia, Fistulas, Duplications Agenesis (v rare), Stenosis) **or functional** (problem in innervation)

2 . **vascular diseases: varices**

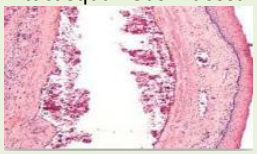
3 . **Inflammation: esophagitis** (Esophageal Lacerations, Infectious [viral, fungal &bacterial] esophagitis, Reflux Esophagitis, Eosinophilic Esophagitis)

4 . **Tumors**: adenocarcinoma & squamous cell carcinoma (both are malignant tumors)

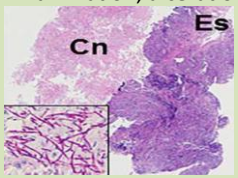
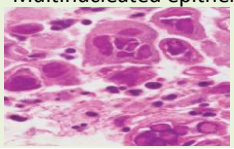
1-obstruction								
Disease	**Definition**	**Age group**	**Site**	**Cause**	**Diagnosis**	**Treatment /management**	**Complications**	**notes**
***Atresia (mechanical)** 	Thin, noncanalized cord replaces a segment of esophagus.	neonates	Most common location: **at or near the tracheal bifurcation**	**Congenital** abnormality	**Clinically**: regurgitation during feeding (Shortly after birth)	-surgical correction **(rejoin).**	**If it is associated with fistula** **-**Aspiration (breathing foreign objects into airways, usually food, saliva or stomach contents). -Suffocation Pneumonia. -Severe fluid and electrolyte imbalances.	Usually associated with a fistula (connection between two hollow spaces) connecting the upper or lower esophageal pouches to a bronchus or to the trachea.
Esophageal Stenosis (mechanical)	Narrowing of the esophageal lumen.			**-Due to inflammation and scarring** 1. Chronic GERD. 2. Irradiation. 3. Ingestion of caustic agents.	**Clinically:** Dysphagia (difficulty in swallowing) is usually the main symptom with stenosis. **Microscopically:** Fibrous thickening of the submucosa & atrophy of the muscularis propria (mucosa is intact).		Difficulty eating solids that progresses to problems with liquids.	Acquired >>> Congenital.
Achalasia (functional)	It is characterized by a triad: 1-Incomplete LES relaxation. 2-Increased LES tone. 3-Esophageal aperistalsis (food passes under the		**Distal esophagus**	**Primary achalasia (most common):** Caused by failure of distal esophageal inhibitory neurons and is, by definition, <u>idiopathic.</u> -**Secondary achalasia:** Degenerative changes in neural innervation (Intrinsic, Vagus nerve, dorsal motor nucleus of vagus) by Chagas disease, Trypanosoma cruzi infection **which** causes destruction of the myenteric plexus, failure of	1-Manometric study> measures the pressure and muscle tone across the gastroesophageal sphincter. 2-barium swallow then the X-rays track its path through the digestive system and we will notice: **1.** Normal peristatic movement is not seen. **2.** LES and the GEJ are narrowed, producing **"bird's**	*focus on relaxing the LES with swallowing -Endoscopic balloon dilatation of LES (pneumatic dilation).		

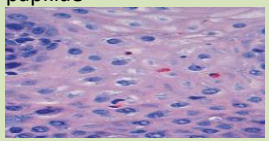
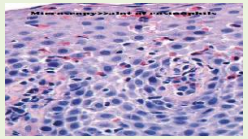
	effect of Gravity only).			LES relaxation, and esophageal dilatation.	**beak"** appearance. **3.** The esophagus above the narrowing is often dilated (enlarged) as the esophagus is gradually stretched over time.  **Clinically:** -Difficulty in swallowing -regurgitation -sometimes chest pain			
Achalasia-like disease (functional)	If one of the triad arms is absent, we diagnose the condition as "achalasia-like disease"			-Diabetic autonomic neuropathy **(the most common cause).** -Infiltrative disorders like malignancy, amyloidosis, or sarcoidosis. - Dorsal motor nuclei lesions (produced by **polio** or surgical ablation).				

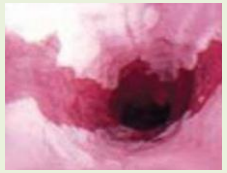
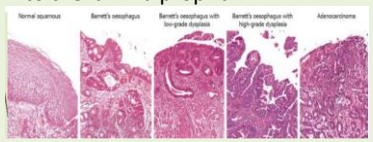
2-vascular diseases

Disease	definition	site	cause	pathogenesis	Clinical features	Morphology	Complications	Notes
Esophageal Varices	Tortuous dilated veins	within the submucosa of the distal esophagus and proximal stomach	***portal hypertention due to:** -Cirrhosis (most common) including hepatitis infection& alcoholic liver diseases. - **Parasitic infection: Hepatic schistosomiasis** is the 2nd most common cause.	•Diseases that impede portal blood flow> **Portal hypertension** > Shunt of blood from portal to systemic circulation> Collateral channels in distal esophagus > **Dilated collaterals** in distal esophagus >**Varices**.	Often asymptomatic. -But their rupture can lead to massive **hematemesis** and death.	**Macroscopically:** Markedly distended veins in the distal esophagus  **Microscopically:** Dilated varices beneath intact squamous mucosa 	-The most serious complication of esophageal varices is severe bleeding which if left untreated can be fetal and often responsible for **hypovolemic shock**.	**-**Why distal esophagus? There is a specific type of anastomosis that occurs between the veins of the portal circulation and those of the systemic circulation called <u>Porto-systemic anastomosis.</u> -50 % of patients die from the first bleed despite interventions. -Rebleeding in 20 %. *bleeding is unpredictable -medical emergency.

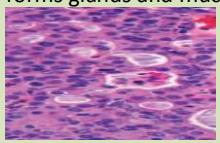
3-Esophagitis*								
Disease	**Definition**	**site**	**cause**	**pathogenesis**	**Clinical features**	**Morphology**	**Complications**	**notes**
***Esophageal Lacerations**	**Mallory-Weiss tears are most common**	**at the gastroesophageal junction.**	severe retching or prolonged vomiting	failure of gastroesophageal musculature to relax prior to antiperistaltic contraction associated with vomiting> stretching> Gastric contents cause the esophageal wall to stretch and tear.	- hematemesis (fresh blood usually)	**Macroscopically:** Superficial ,linear and longitudinally oriented crossing the GEJ.		-Heal quickly , no surgical intervention
***Chemical esophagitis**	Damage of the stratified squamous mucosa of the esophagus by a variety of irritants		-Alcohol. -Corrosive acids or alkalis. -Excessively hot fluids. -Heavy smoking. -Medicinal pills: like doxycycline and bisphosphonates **(causing a pill-induced esophagitis).** -Iatrogenic (illness caused by medical treatment): chemotx , radiotx		-Only self- limited pain, odynophagia (pain with swallowing).	The morphologic changes consist of ulceration and acute inflammation	Hemorrhage, stricture, or perforation in severe cases.	

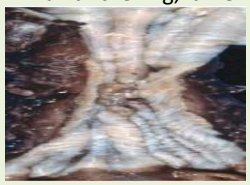
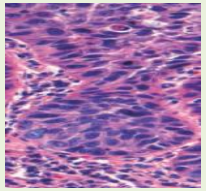
Disease		cause	Clinical features	morphology	treatment	notes
***Infectious esophagitis**	**Fungal esophagitis**	Candida (the most common)>> **candidiasis,** Mucormycosis & Aspergillosis.	-dysphagia -odynophagia	**-Macroscopically:** -Adherent. -Gray white pseudo-membranes  **-Microscopically:** inflammation, ulceration, and candida hyphae  	Antifungal medications	- Mostly in debilitated or immunosuppressed patients -candida is part of normal flora , but it does no harm when the patient is Immunocompetent.
	Viral esophagitis	**HSV>herpetic esophagitis**		**Macroscopically:** - punched out (deep, heated-up rounded edges) ulcers  **Microscopically:** -Nuclear viral inclusions -Degenerating epithelial cells ulcer edge -Multinucleated epithelial cells & ground-glass appearance of the nuclei 		**<u>- HSV infects the squamous cells (epithelial cells).</u>** - Mostly in debilitated or immunosuppressed patients.
		CMV		**Macroscopically:** Presence of shallow ulcers (very superficial) **Microscopically:** -enlarged cells -nuclear inclusions -cytoplasmic inclusions  .		**<u>-CMV infects the stromal fibroblasts and the endothelial cells lining the capillaries under the mucosa.</u>** - Mostly in debilitated or immunosuppressed patients.

Disease	Age group	site	Causes & pathogenesis	Clinical features	morphology	treatment	complications	notes
Reflux esophagitis (GERD)	-Most common over 40 years. -May occur in infants and children.	**Lower esophagus**	1-**Decreased lower esophageal sphincter tone** (causes>>CNS depressants, alcohol, and smoking.) 2-**Increase abdominal pressure causing reflux of gastric content into the lower esophagus.** causes>> pregnancy obesity, hiatal hernia, delayed gastric emptying and increased gastric volume, tumors, ascites and gases (irritable bowel syndrome**)).** 3- **idiopathic**	**In adults:** ***(usually at night because the patient is in a supine position)*** **-heartburn** (Most frequent symptom). - **Dysphagia** (in more severe cases). -Regurgitation of sour tasting gastric contents. -Rarely: Severe chest pain, mistaken for heart disease. **In infants:** -crying (from pain of heartburn) -regurgitation -vomiting -failure to thrive (no increase in weight)	**Macroscopically:** -Redness(hyperemia) depends on severity  **Microscopically**: ***at least 2 of them should exist to diagnose*** -Eosinophils infiltration (the earliest change) -Followed by neutrophils (more severe) -Basal zone hyperplasia -Elongation of lamina propria papillae 	proton pump inhibitors	-Esophageal ulceration -Hematemesis -Melena (black colored stool due to **upper** GI bleeding) -Strictures -Barrett esophagus (precursor of Ca.)>the most important complication.	-Most common cause of esophagitis. -Most common complaint by patients. -Squamous epithelium is **sensitive** to acids but the esophagus has some **Protective forces**>>mucin and bicarbonate, high LES tone. -Barret esophagus: stratified squamous epithelium converted to columnar or glandular epithelium (intestinal or gastric type).
Eosinophilic Esophagitis	Can happen in children &adults	**Upper and mid esophagus**	-Mostly allergic in nature due to food that contain soy products. - Can happen to infants due to an allergy to milk.	**In adults:** -Food impaction (stuck in the esophagus) -dysphagia **In children:** Feeding intolerance or GERD like symptoms.	**Macroscopically:** Rings in the upper and mid esophagus.  **Microscopically:** -numerous eosinophils within epithelium, far from the GEJ (to differentiate it from the reflux type) 	- Dietary restrictions (cow milk and soy products). -Topical or systemic corticosteroids. -Refractory to PPIs.		-Chronic immune mediated disorder - Most patients are atopic (atopy refers to the genetic tendency to develop allergic diseases such as atopic dermatitis, allergic rhinitis, and asthma) or have modest peripheral eosinophilia.

Disease	Age group	site	Causes & pathogenesis	Morphology	Treatment /management	complications	notes
Barrett Esophagus (complication of GERD)	40-60 yrs. Males>>females	Extends upward starting from GEJ	**Chronic GERD** (for years)>> metaplasia in squamous epithelium (which is very fragile and can not handle acidity) transforms into columnar epithelium that is more resistant to acid (glandular epithelium that can be gastric type or intestinal type epithelium).	**Macroscopically**: -red tongues extending upward from the GEJ  **Microscopically:** -Gastric or intestinal metaplasia. - Presence **of goblet cells** (intestinal type) - **+-Dysplasia**: low grade then high grade - Intramucosal carcinoma: invasion into the lamina propria 	-Periodic surveillance endoscopy with biopsy to screen for dysplasia (Barrett is reversible and can regress with treatment). very important to protect the patient from getting carcinoma. -High grade dysplasia & intramucosal carcinoma needs interventions (surgical resection for example).	- Direct precursor of esophageal adenocarcinoma	-10% of individuals with **symptomatic GERD** -0.2- 1% of people with barret progress to **dysplasia** & **adenocarcinoma**

4-Esophageal tumors (very bad tumors☹)

	Age group	site	Causes& risk factors	pathogenesis	Morphology	Clinical features	complications	notes
Adenocarcinoma	**40-60 yrs. Males>>females**	Distal third of the esophagus	-Background of Barrett esophagus and long-standing GERD **-risk factors:** -dysplasia associated Barrett -smoking -obesity -radiotherapy	*From Barrett > dysplasia > adenocarcinoma. • Acquisition of genetic and epigenetic changes. • Chromosomal abnormalities and TP53 mutation. When mutations accumulate, the process becomes irreversible.	**Macroscopically:** -EARLY: flat or raised patches -LATE: exophytic infiltration masses  **Microscopically:** forms glands and mucin 	-Pain or difficulty swallowing -Progressive **weight loss** (**ALARMING SYMPTOM**) -Chest pain -Vomiting		-Advanced stage at diagnosis: 5-year survival < 25% (bad prognosis). -EARLY STAGE: 5-year survival 80%. -Geographic & racial variation (developed countries).

Squamous cell carcinoma		middle esophagus (50% of cases) although it can occur in the lower esophagus.	**Risk factors:** *THE TWO MOST IMPORTANT RISK FACTORS: **alcohol and smoking** • Poverty • Caustic injury • **Achalasia** • Plummer-Vinson syndrome: Associated with iron deficiency and anemia • Frequent consumption of very hot beverages • Previous radiation therapy (Increases risk for many cancers)	• In western countries**: alcohol and tobacco use** • Other areas: **polycyclic hydrocarbons, nitrosamines, fungus-contaminated foods** • **HPV infection implemented in high risk regions**.	**Macroscopically:** *Polypoid, ulcerated or infiltrative • Wall thickening, lumen narrowing  **Microscopically:** -Pre-invasive: Squamous dysplasia & CIS (precursors of squamous cell carcinoma). -Well to moderately differentiated invasive SCC. -Intramural tumor nodules 	Dysphagia • Odynophagia • Obstruction • Weight loss —> very important in cancers • Debilitation • Impaired nutrition and tumor associated cachexia • Hemorrhage and sepsis if ulcerated • Aspiration via a tracheoesophageal fistula	-invade surrounding structures in advanced stages (mediastinum, bronchi, pericardium, aorta). -metastasis through lymphatics. *Upper 1/3 (location of the tumor): cervical lymph nodes • Middle 1/3: mediastinal, paratracheal and tracheobronchial lymph nodes. • Lower 1/3: gastric and celiac lymph nodes.	-Not associated with Barrett esophagus) -Comes from squamous epithelial cells.

Diseases of the stomach

1-Inflammatory :*acute gastritis

***acute gastric ulcers**

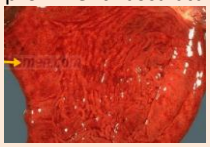
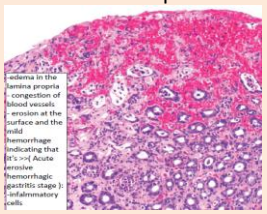
***chronic gastritis**

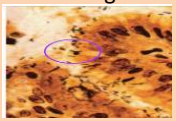
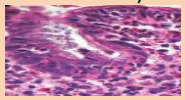
***chronic peptic ulcer**

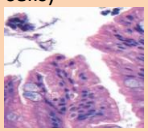
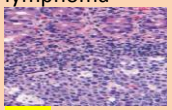
2-Gastric polyps:*inflammatory & hyperplastic polyps

***gastric adenomas**

3-Gastric tumors: *Gastric adenocarcinoma *lymphoma *neuroendocrine tumor *gastrointestinal stromal tumor

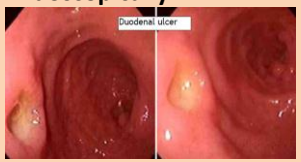
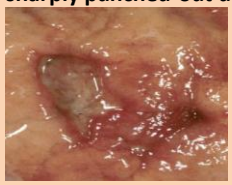
1-inlammatory								
Disease	**site**	**cause**	**pathogenesis**	**Clinical features**	**Morphology**	**treatment**	**complications**	**notes**
Acute gastritis & gastropathy **(differ just in microscopic appearance)**		-NSAIDs -Uremic patients, H pylori infected patients -Old age. -Hypoxia -Harsh chemicals, (acids or bases) -Alcohol -radiation therapy -Chemotherapy -reflux of bile from deudenum to stomach after certain procedure -stress-induced	***Imbalance between protective and damaging forces:** **Main causes (damaging forces):** -NSAIDs → work by inhibiting COX → decrease PGs synthesis which work as protective factors - Uremic patients (renal failure patients) and *H. pylori* infected patients ,H. pylori produces urease enzyme that splits urea into ammonia>> interferes with the transport of bicarbonate to the mucous layer. ***Decreased concentration of bicarbonate → decreased protective effect** **-Old age,** because mucus and bicarbonate secretions are decreased with age . -**Hypoxia** whether caused by ischemia or high altitude. *Hypoxia and decreased oxygen supply to the mucosa would lead to a decrease in the protective factors* -**Harsh chemicals** cause direct epithelial injury and damage > like acids or bases in suicidal attempts or accidental ingestion. **-Alcohol, NSAIDs, and radiation therapy** cause direct injury to epithelial cells. -**Chemotherapy**. *By Interference with DNA synthesis and mitotic capacity. It affects the GIT through decreasing proliferation of cells or causing direct damage.	**Depend on severity:** -Asymptomatic **OR** -epigastric pain -nausea -vomiting.	Endoscopically : mild hyperemia and edematous mucosa with prominent vasculature  Microscopically: -hyperemia , congestion of the vessels and edema in the lamina propria. -Neutrophils, lymphocytes, and plasma cells are not prominent.(there is no inflammatory cells in gastropathy) -Intact surface epithelium 		-Advanced: Erosions and hemorrhage, **acute erosive hemorrhagic gastritis.**	-Presence of neutrohpils doesn't mean it's acute , it means that there Is an active inflammation so neutrophils can be seen in acute &chronic gastritis -The difference between acute and chronic is mainly the duration. **-Acute gastritis: Mucosal injury, neutrophils present.** **-Gastropathy: regenerative changes in the mucosa due to damage, but no inflammation (and inflammatory cells).**

disease		site	cause	pathogenesis	Clinical features	Diagnosis	treatment	complications	notes
Acute gastric ulcers		**-In curling ulcer>>** Proximal duodenum **in cushing ulcer>>** stomach, duodenum, or esophagus	Severe physiologic stress: -Trauma -Extensive burns -Intracranial disease -Major surgery -Serious medical disease -Critically ill patients **Stress ulcer:** critically ill patients with shock, sepsis, or severe trauma **Curling ulcers:** severe burns or trauma. **Cushing ulcers:** intracranial disease	**Stress ulcer:** **Local ischemia.** Which can follow: • Systemic hypotension or heart failure. • Locally reduced blood flow due to Splanchnic vasoconstriction. (blood supply to the GI) *Systemic acidosis → lower PH of cells → acidosis in the cells damage them **Cushing ulcers:** **Direct vagal nerve stimulation,** like in cases of increased intracranial pressure>>causes acid hypersecretion.	*Severely and critically ill patient in the ICU, or traffic road accidents *Nausea, *vomiting *Melena *Coffee - ground hematemesis	**-NO biopsies** -rounded and typically less than 1 cm in diameter -Shallow to deep. -Ulcer base **brown** to **black** **-Usually multiple.** -Normal adjacent mucosa -No scarring 	-Healing with complete re-epithelialization occurs days or weeks **after removal of injurious factors** **-for critically ill patients>>** Prophylaxis with proton pump inhibitors	-high risk of perforation of **cushing ulcer**	**3 types:** **-Stress ulcers**. COX2 expression is protective. **-Curling ulcers** **-Cushing ulcers.** ***Differ in>** *cause+location* *the main differences between the acute peptic ulcer and the chronic peptic ulcer are :-the surrounding mucosa : **-acute →normal** **-chronic →abnormal** **-Acute →no scarring , chronic →scarring** **-Acute →multiple , Chronic →single ulcer**
Chronic gastritis (most common causes: (H.pylori, autoimmune) Less common: **-Chronic NSAID use Radiation injury.** **-Chronic bile reflux**	**H.pylori Associated gastritis**	**Antrum of the stomach**	**-H.pylori**: Spiral or curved, G-ve, bacilli	They prefer living in the antrum of the stomach in the mucus layer and cause **Antral gastritis>>** stimulation of the G-cells of antrum> increased gastrin hormone production → activation of parietal cells → increased acid production >> peptic ulcer. -it's usually non-invasive,It has developed many mechanisms to protect itself from the acidic environment like: ***Flagella**: allow motility. ****Urease**: split urea to ammonia,* protect bacteria from acidic pH. ****Adhesins**:* bacterial adherence to foveolar cells ****Toxins**: CagA,* for ulcer or cancer development	- Acute infection is subclinical -Nausea -upper-abdominal discomfort -Vomiting -Hematemesis uncommon. **Less severe but more prolonged symptoms than acute gastritis**	***Invasive>> Endoscopically:** - Most important feature is hyperemia. **Microscopically:(biopsy)** (Antrum is the best place to obtain a biopsy) -**H.pylori** can be demonstrated with H&E stain or other specialized stains like giemsa  **-inflammatory response in the mucosa>>** ***Neutrophils** within the lamina propria or attacking glands of antrum and causing small abscesses (in active disease).  ▪ Plasma cells, lymphocytes	Combinations of antibiotics (at least 2) and PPIs.	**-Increase risk of :** ***adeno carcinoma** ***MALT lynphoma** ***pangastritis >>** Inflammation spreads all over the stomach affecting even the body and the fundus and damage to the parietal cells>>hypo-secretion of acid	-Present in almost all duodenal ulcers. -Majority of gastric ulcers or chronic gastritis. - More common with poverty, household crowding, limited education, poor sanitation - **cytotoxin associated gene A** encodes (CagA) and aids in ulcer or cancer development by causing damage to epithelial cells. -In duodenal ulcer or duodenitis, the bacteria would still be in the stomach, however the hyper acidity is what causes the problem

						& macrophages found in the lamina propria (The amount of these cells depends on the severity of chronic gastritis). -In long standing disease we might see Intestinal metaplasia (intestinal epithelium with goblet cells)  -In more severe cases we can observe Lymphoid aggregates >> MALT lymphoma  -PCR **Non-invasive:** -**Serologic test** (blood test): anti-H. pylori antibodies (IgA, IgG). - **Stool test** for H. pylori -**Urea breath test**			
	Auto immune atrophic gastritis	**body & fundus**	Antibodies against parietal cells and intrinsic factor in serum.	-loss of parietal cells>> reduction in acid and secretion >>reflex hypergastrinemia, which is mediated by hyperplasia of antral G cells -Reduction in intrinsic factor due to cells and auto-ABs directed against it>> Deficient intrinsic factor >> deficient ileal VB12 absorption >> megaloblastic anemia which has many neurological manifestations. -Some chief cells damage in the body of the stomach >> reduced pepsinogen production	-60 years, slight female predominance. -Often associated with other autoimmune diseases (Hashimoto thyroiditis, type 1 DM, or Graves disease of the thyroid - neurological manifestations -Nausea and upper-	-Reduced serum pepsinogen **I** levels -achlorhydria -Vitamin B12 deficiency > pernicious anemia and neurologic changes -marked *hypergastrinemia* **Microscopically:** Preferred biopsy site is the body or the fundus NOT the antrum -Damage of the oxyntic (acid-producing) mucosa -Diffuse atrophy, thinning of wall, loss of rugal folds (due to loss of acid producing cells and their damage) -Antral endocrine cell hyperplasia		*Intestinal metaplasia (due to achlorhydria) >>> dysplasia >> **adenocarcinoma.** *Neuroendocrine (G-cell) cell hyperplasia >**neuroendocrine tumors.**	-less common than H.pylori chronic gastritis (10%) -Minority of patients develop **megaloblastic anemia**, but it's a very important point to differentiate between autoimmune gastritis and helicobacter pylori gastritis -Intrinsic factor binds to vitamin B12 and aids in its absorption in the distal ilium.

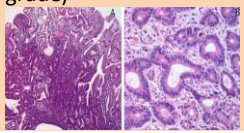
					abdominal discomfort -Vomiting Hematemesis uncommon	-Lymphocytes, plasma cells, macrophages, less likely neutrophils.			

please refer to table in slide#32 (Pathology of the stomach part-1)

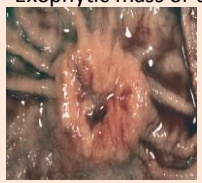
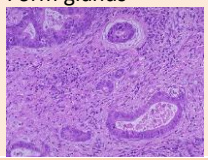
Disease	site	cause	pathogenesis	Clinical features	Morphology	treatment	complications	notes
Peptic Ulcer Disease	-Any portion of the GIT exposed to acidic gastric juices -Most common in **gastric antrum, first part of duodenum.**	-Most often is associated with **H. *pylori*** infection or **NSAID** use -**cofactors** that can cause peptic ulceration (not main causes)>> **-smoking -chronic NSAIDs -high-dose corticosteroids -alcoholic cirrhosis -COPD -CRF hyperparathyroidism**	**-Gastric acid (hyperacidity) is fundamental in pathogenesis** caused by: *H. pylori. *Parietal cell hyperplasia. *Excessive secretory response (vagal) *Hypergastrinemia as in *Zollinger-Ellison syndrome* * (hypergastenemia) -hyperacidity> chronic gastritis> peptic ulcer	-Epigastric burning or aching pain -Pain 1 to 3 hours after meals at daytime -Worse at night, relieved by alkali or food -Nausea, vomiting, bloating, bletching. -Iron deficiency anemia caused by chronic blood loss from ulcers	**Endoscopically :**  -solitary (single) ulcer except in cases like Zollinger-Ellison syndrome where you can see multiple ulcerations. -Round to oval in shape **and sharply punched-out defects.**  -Base of ulcer is smooth and clean. -granulation tissue **Microscopically:** intact mucosa on the periphery of the ulcer. At the center the epithelium is lost and new blood vessels inflammatory cells, and hemorrhage can be seen 	-Current therapies are aimed at H.pylori eradication -Surgery reserved for complications.	-Hemorrhage(So the patient will complain hematemesis and melena) -Perforation (the patient comes with severe abdominal pain, peritonitis, rigid abdomen and this need immediate surgical correction)	-ex: Esophagus in (GERD) or ectopic gastric mucosa (Meckel diverticulum) **-More than 70% of PUD cases** are associated with **H.pylori infection** **-only 5-10% of H.pylori infected individuals develop ulcers, and many of them complain only from chronic gastritis.** -Proximal duodenum is more affected than stomach (4:1) -Anterior duodenal wall is most affected site of proximal duodenum ---------- *Zollinger-Ellison syndrome ✓ **Characterized by multiple peptic ulcerations.** ✓ Can develop in **stomach , duodenum and even jejunum** "if there is excessive acid secretion" ✓ Caused by **uncontrolled release of gastrin by tumor (gastrinoma) and the resulting massive acid production.** ----------

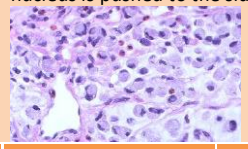
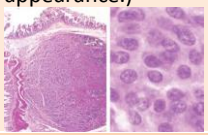
2-Gastric Polyps

Disease	Patients	cause	morphology	Risk	treatment	notes
Inflammatory &hyperplastic		**background of chronic gastritis**	-no dysplasia	-non -neoplastic(most of the time these polyps are very	Regress spontaneously after H.pylori eradication (as we know	- It is a reactive condition -They constitute about 75% of all

polyps				small and there is no risk to have neoplasia or dysplasia -Risk of dysplasia if the size of polyp > 1.5 cm.	H.pylori is the most commn cause of chronic gastritis)	polyps
Gastric Adenoma	Increase with age, and Males are affected more than Females (3:1).	background of chronic gastritis, atrophy and intestinal metaplasia	Dysplasia in all cases (low or high grade) 	Precancerous(neoplastic) >Risk of adenocarcinoma related to the size mainly (if greatest > 2cm). Also related to the grade of dysplasia		-10% of all polyps. -When we diagnose gastric adenoma in a biopsy, there is a risk that 30% of the patients have concurrent gastric adenocarcinoma.

3-Tumors

Disease	types	cause	pathogenesis	Affected group	Morphology	Clinical features	treatment	notes
Gastric Adenocarcinoma	**Intestinal type**	Background of mucosal atrophy and intestinal metaplasia -PUD does not increase risk, except after surgery. -Genetic alterations due to H.pylori associated chronic gastritis , lesser extent EBV (10%).	**Familial cases:** APC gene mutation associated with FAP. **Sporadic cases:** B-catenin mutation + P53 mutation.	-Mean age 55 yrs. -Males>> Females (2:1))	**Endoscopically :** -Bulky -Exophytic mass or ulcer  **Microscopically:** Form glands 	-The symptoms are not specific for cancer (they can be seen in chronic gastritis and PUD) *Weight loss and cachexia are alarming. Predominant in high risk areas (like Japan , Costa Rica and Chile .. etc) -Usually develops from precursors (adenoma, dysplasia)	*surgery *chemotherapy *targeted therapy (anti HER2)	Comprises 90% of all gastric cancers - In USA rates dropped > 85%, BUT increased rate of cardia cancer due to GERD & obesity -The drop in gastric cancer incidence applies only to the intestinal type - **Most powerful prognostic factors:** 1-depth of invasion 2-extent of nodal 3-distant metastasis at the time of diagnosis
	Diffuse type		**Familial cases :** mutations in CDH1 (E-cadherin) **Sporadic cases:** CDH1 mutation in 50% +P53 mutation	-Younger groups are affected. -Males = Females	**Endoscopically :** - Infiltrative growth pattern (non mass forming tumor)>This will lead to thickening of gastric mucosa - strong desmoplastic reaction> thickening of the wall of the stomach >**linitis plastica** (thick &rigid wall)  **Microscopically:** - discohesive cells (due to E-cadherin gene mutation) and form **signet ring cells** (large droplets of mucus &the	-The symptoms are not specific for cancer (they can be seen in chronic gastritis and PUD) *Weight loss and cachexia are alarming. -Incidence is uniform across all countries. -Usually no precursor lesion (genetic abnormality only)		

					nucleus is pushed to the side of the cell) 		
Disease	**types**	**site**	**Morphology**		**cause**	**Clinical features**	**notes**
Lymphoma	1-indolent extranodal marginal zone Bcell lymphomas (MALToma)> **most common** **2-** diffuse large B cell Lymphoma **Second most common**	most found in lymph nodes. However, they can be found somewhere else (extranodal) →(Stomach is the most common site of extranodal)					-5% of all gastric malignancies.
Neuroendocrine (Carcinoid) Tumor		-**More than 40% occur in the small intestine** -arise from neuroendocrine cells that are present in gastric mucosa	**Microscopically:** -Intramural or submucosal masses (small polypoid lesions) -under the microscope we will see **neuroendocrine cells** (their nuclei showing salt and pepper chromatin appearance.) 		associated with -endocrine cell hyperplasia -chronic atrophy gastritis and Zollinger-Ellison syndrome		- it is not a gastric polyp nor adenoma, this polypoid growth is due to a submucosal nodule of tumor composed of neuroendocrine cells -**Slower growing** than carcinomas, thus the name (carcinoids). **- Carcinoid tumors can be associated with carcinoid syndrome***
***carcinoid syndrome**					-production of vasoactive substances by neuroendocrine cells -only seen with **metastatic carcinoid (neuroendocrine) tumor**	-Cutaneous flushing (the patients face is very red) -excessive sweating -bronchospasm -colicky abdominal pain -diarrhea -right-sided cardiac valvular fibrosis	-only seen in 10% of patients with carcinoid tumors

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GOOD LUCK