Internal Medicine

PEPTIC ULCER

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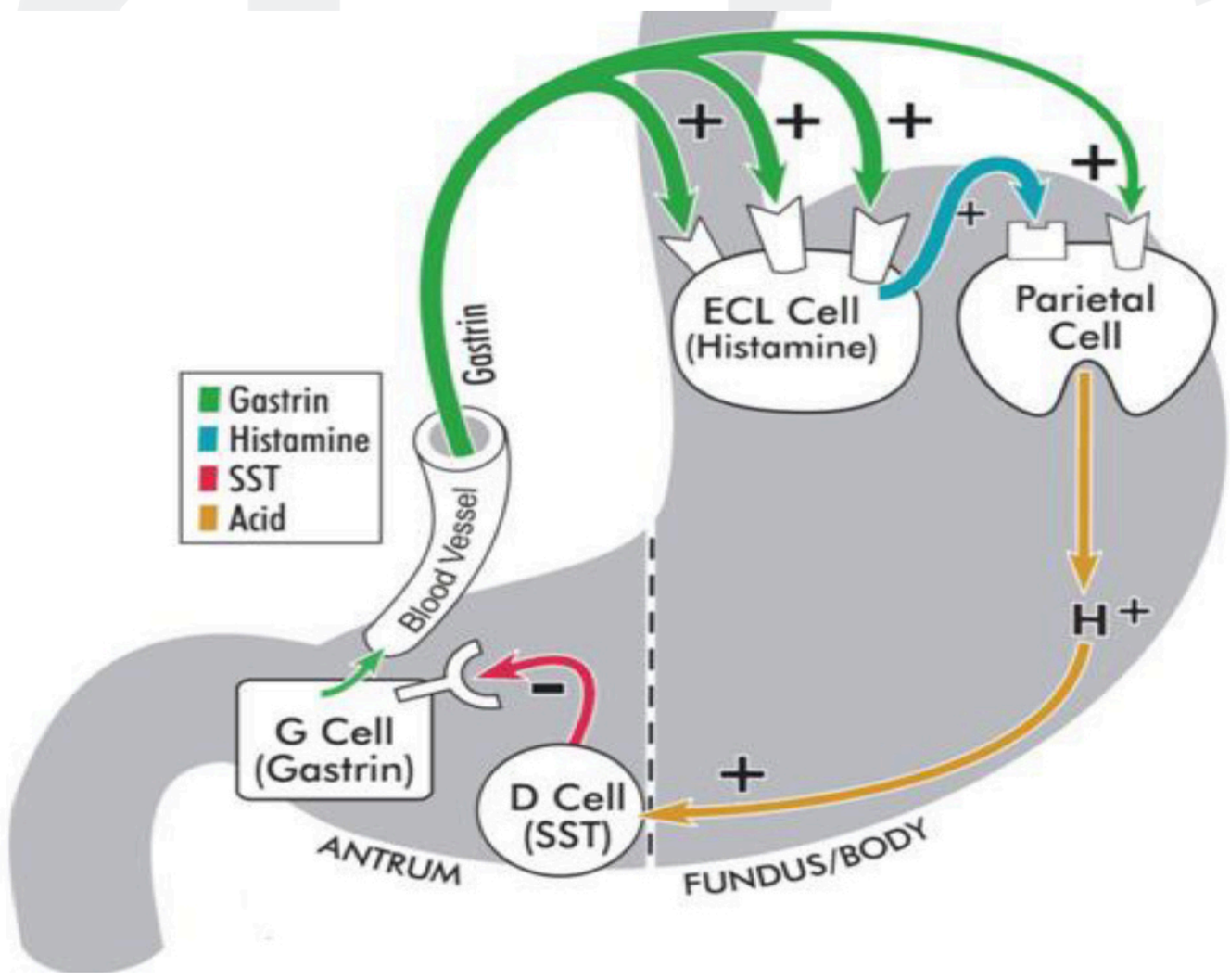
The stomach

- **The antral mucosa secretes bicarbonate and contains mucus-secreting cells and G cells, which secrete gastrin.**
- **Somatostatin is also produced by specialized antral cells (D cells).**
- **Mucus-secreting cells are present throughout the stomach and secrete mucus and bicarbonate.**
- **The ‘mucosal barrier’ , made up of the plasma membranes of mucosal cells and the mucus layer, protects the gastric epithelium from damage by acid.**
- **Prostaglandins stimulate secretion of mucus, and their synthesis is inhibited by inhibition of cyclo-oxygenase.**

- **The duodenal mucosa has villi like the rest of the small bowel, and also contains Brunner's glands that secrete alkaline mucus. This, along with the pancreatic and biliary secretions, helps to neutralize the acid secretion from the stomach**
- **Acid secretion is under neural and hormonal control.**
- **Both stimulate acid secretion through the direct action of histamine on the parietal cell.**
- **Acetylcholine and gastrin also release histamine via the enterochromaffin cells (ECL).**
- **Somatostatin inhibits both histamine and gastrin release and therefore acid secretion.**



The Major function of HCl is disinfection that’s why not easily gastritis occurs ,it considers the major disinfectant in upper GI , but still if there no HCl, no peptic ulcer occurs , so the main factor for creation peptic ulcer is H+ proton .
HCl secreted by parital cells , so anything stimulates the parietal cellc —> increase the risk of peptic ulcer

- Acid itself is not essential for digestion but does prevent some food-borne infections.
- Other major gastric functions are:

1. reservoir for food. The food remains from 4-6 hours
2. emulsification of fat and mixing of gastric contents.
3. secretion of intrinsic factor.
4. absorption (of only minimal importance).

Epidemiology of peptic ulcer disease

- The lifetime prevalence of peptic ulcer is around 5-10% (high prevalence).The incidence is decreasing
- The male-to-female ratio for duodenal ulcer varies from 5:1 to 2:1, while that for gastric ulcer is 2:1 or less.
- Both DUs and GUs are common in the elderly .
- There is considerable geographical variation, with peptic ulcer disease being more prevalent in developing countries related to the high H. pylori infection .
- Around 90% of duodenal ulcer patients and 70% of gastric ulcer patients are infected with H. pylori

Peptic ulcer disease: superficial injury to mucosa barrier of stomach or duodenum.
Superficial injury ranges from simple inflammation (gastritis and duodenitits) or gastric erosion (superficial break but involves just the mucosa layer) but if this erosion involves the submucosa layer we called it ulcer whether if it in stomach or duodenum .
The most common cause for peptic ulcer is H.pylori and NSAID

Pathology of peptic ulcer disease

- A peptic ulcer consists of a break in the superficial epithelial cells penetrating down to the muscularis mucosa; there is a fibrous base and an increase in inflammatory cells
- Erosions, by contrast, are superficial breaks in the mucosa alone
- The surrounding mucosa appears inflamed, hemorrhagic or friable (abnormal mucosa)
- GUs are most commonly seen on the lesser curve, but can be found in any part of the stomach.
- Peptic ulcers are seen without H. pylori, e.g. in patients on NSAIDs and in smokers

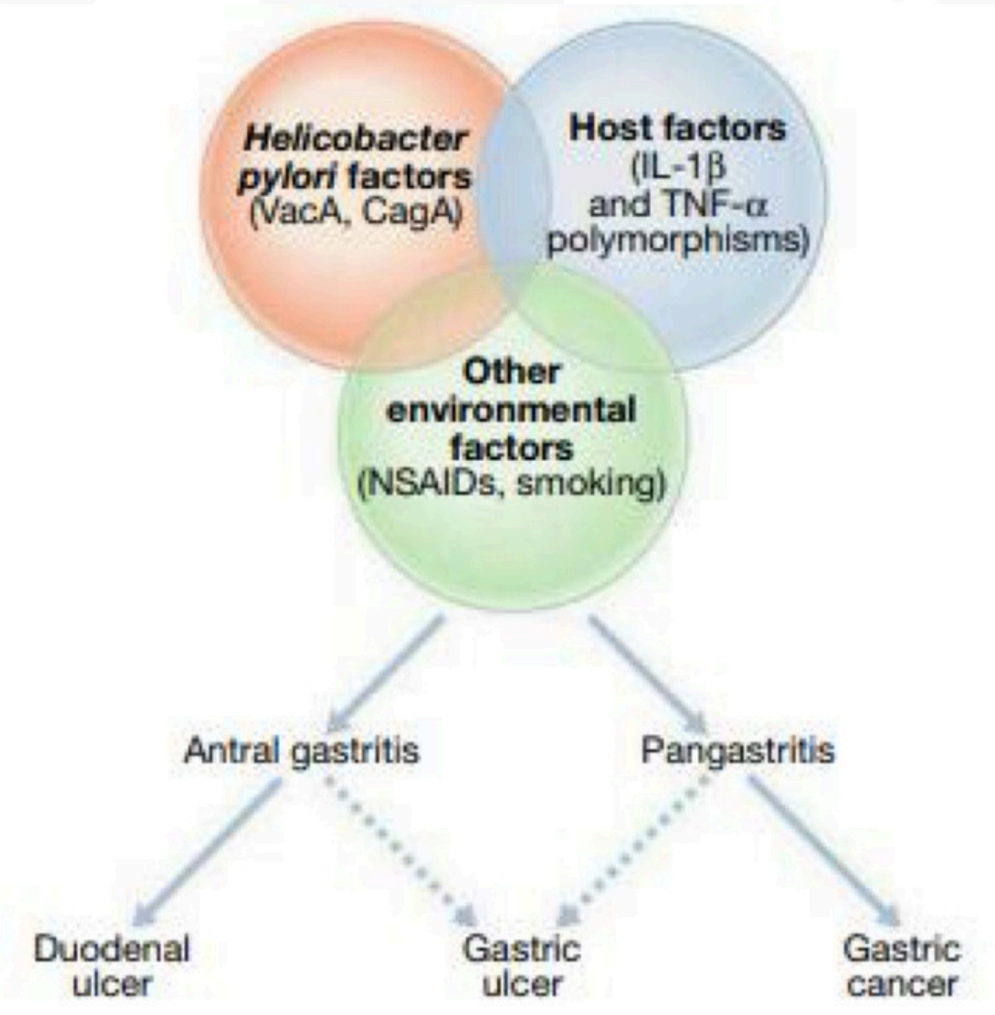
In 90-95% doudenal ulcer is caused by H.pylori, while the 60 -65% of gastric ulcer is caused by H.pylori and 35% from another causes like 15-20%NSAID (if there bleeding with it, there are probably ulcers in both stomach and duodenum) , gastric malignancy etc..depends on the patent status , age , risk factor ,etc...

Helicobacter pylori infection

- **H. pylori is Gram-negative and spiral, and has multiple flagella at one end, which make it motile, allowing it to burrow and live beneath the mucus layer adherent to the epithelial surface. Here the surface pH is close to neutral and any acidity is buffered by the organism's production of the enzyme urease.**
- **H. pylori is found in greatest numbers under the mucus layer in gastric pits, where it adheres specifically to gastric epithelial cells.**
- **It is protected from gastric acid by the juxtamucosal mucus layer which traps bicarbonate secreted by antral cells, and ammonia produced by bacterial urease.**

Its transition pathway is fecal-oral , so it's most common in young age due to poor hygiene.
Not necessary the gastritis occurs directly after H.pylori infection , it may occur after 5-10 years and it may not occur .

- **Urease : we don't have it in our body, so we use it to detect if person has H.pylori or not**



- **The prevalence of H. pylori is high in developing countries (80–90% of the population), and much lower (20–50%) in developed countries.**
- **Infection rates are highest in lower income groups.**
- **Infection is usually acquired in childhood; it may be fecal–oral or oral–oral**
- **Once acquired, the infection persists for life unless treated.**
- **The incidence increases with age, probably due to acquisition in childhood when hygiene was poorer, and not due to infection in adult life which is probably far less than 1% per year in developed countries.**

Causes of Gastritis

Acute gastritis (often erosive and haemorrhagic)
• Aspirin, NSAIDs • *Helicobacter pylori* (initial infection) • Alcohol • Other drugs, e.g. iron preparations • Severe physiological stress, e.g. burns, multi-organ failure, central nervous system trauma • Bile reflux, e.g. following gastric surgery • Viral infections, e.g. CMV, herpes simplex virus in HIV/AIDS (Ch. 14)
Chronic non-specific gastritis
• *H. pylori* infection • Autoimmune (pernicious anaemia) • Post-gastrectomy
Chronic 'specific' forms (rare)
• Infections, e.g. CMV, tuberculosis • Gastrointestinal diseases, e.g. Crohn's disease • Systemic diseases, e.g. sarcoidosis, graft-versus-host disease • Idiopathic, e.g. granulomatous gastritis

In acute it's caused by NSAID more than H.pylori unlike in the chronic gastritis.
The percentage of chronic gastritis is more common than acute .

- **Acute infection with H .pylori may cause a transient clinical illness characterized by nausea and abdominal pain that may last for several days and is associated with acute histologic gastritis with PMNs. After these symptoms resolve, the majority progress to chronic infection with chronic, diffuse mucosal inflammation (gastritis) characterized by PMNs and lymphocytes**
- **Results of infection:**

1. **Antral gastritis**

Most common and the simplest form of inflammation from H.pylroi .
It may progress to pangastritis (inflammation in all parts of stomach) , after that , it progresses to erosion and full ulceration.

2.Peptic ulcers (duodenal and gastric)

3.Gastric cancer

Antral gastritis

- **The usual effect of H. pylori infection**
- **It is usually asymptomatic, although occasionally**
- **patients without ulcers claim relief of dyspeptic symptoms after Helicobacter eradication.**
- **Antral gastritis causes hypergastrinemia due to gastrin release from antral G-cells.**
- **The subsequent increase in acid output is usually asymptomatic.**

Due to cytokines of inflammation, it will be partial cell hyperplasia —> more HCl and more acid —>more pain and symptoms.
If the patient doesn't get treatment of this active gastritis—> it converts to atrophic gastritis (atrophy of mucoua and parietal cell mass —>less acid —>less pain)which is highly associated with malignancy.

Duodenal Ulcer

- **H. pylori is causally associated with DU disease.**
- **In patients with DU 95% are infected with H. pylori in the antrum (antral gastritis) .**
- **In developed countries, the prevalence of H. pylori is rapidly declining. In the United States, the prevalence rises from less than 10% in non-immigrants under age 30 years to over 50% in those over age 60 years.**
- **The precise mechanism of duodenal ulceration is unclear, as only 15% of patients infected with H. pylori (50–60% of the adult population world-wide) develop duodenal ulcers.**
- **Factors that have been implicated include:**

1. Increased acid secretion because of increased parietal cell mass and increased gastrin secretion.
2. Smoking impairing mucosal healing.
3. Virulence factors such as Vac A (vacuolating toxin) and CagA (cytotoxic-associated protein) as well as urease and adherence factors.
4. Decreased inhibition of acid secretion; H. pylori- induced gastritis reduces somatostatin production in the antrum with loss of the negative feedback on gastrin secretion
5. Genetic susceptibility: duodenal ulcers are more common in patients who have blood group O .
6. Duodenal bicarbonate secretion is decreased by H.pylori inflammation and the damage and repair leads to gastric metaplasia which H. pylori colonizes, causing local release of cytokines and further damage.

It is not recommended to make a screening test about H.pylori that comes without clinical feature of gastritis, because it's cost, so instead we leave the patient without intervention unless he colpmplains from S&S.

Gastric Ulcer

- **Gastric ulcers are associated with a gastritis affecting the body as well as the antrum of the stomach (pangastritis) causing parietal cell loss and reduced acid production .**
- **The ulcers are thought to occur because of reduction of gastric mucosal resistance due to cytokine production by the infection or perhaps to alterations in gastric mucus.**

إضافة : جدول من كتاب step-up

TABLE 3-5 Duodenal Versus Gastric Ulcers

	Duodenal Ulcers	Gastric Ulcers
Pathogenesis	Caused by an increase in offensive factors (higher rates of basal and stimulated gastric acid secretion)	Caused by a decrease in defensive factors (gastric acid level is normal/low unless ulcer is pyloric or prepyloric)
Malignant potential	Low	High (5–10% are malignant)—should undergo biopsy to rule out malignancy
Location	Majority are 1–2 cm distal to pylorus and on posterior wall	Type I (most common, 70%): on lesser curvature
		Type II: gastric and duodenal ulcer
		Type III: prepyloric (within 2 cm of pylorus)
		Type IV: near esophagogastric junction
Age distribution	Tends to occur in younger patients (age <50)	Tends to occur in older patients (age > 60 years)
Risk factors	NSAIDs, *H. pylori* infection, smoking, alcohol	NSAIDs, *H. pylori* infection, smoking, alcohol
Other	**Pain occurs several hours after eating**	**Eating worsens pain**
	Nocturnal pain is more common than in gastric ulcers	Complication rates are higher than those of duodenal ulcers. There is a higher recurrence rate with medical therapy alone

Clinical features of peptic ulcer disease

The peptic ulcer disease coud be asymptomatic

- **The characteristic feature of peptic ulcer is burning epigastric pain.**
- **The relationship of the pain to food is variable .**

Gastric ulcer worse with food unlike the duodenal ulcer but this is not a specific difference to distinguish between them because the opposite could happen

- **The pain of a DU classically occurs at night (as well as during the day) and is worse when the patient is hungry .**
- **The pain of both gastric an duodenal ulcers may be relieved by antacids .**
- **Nausea may accompany the pain; vomiting is infrequent but often relieves pain .**
- **Anorexia and weight loss may occur, particularly with GUs.**
- **Persistent and severe pain suggests complications such as penetration into other organs. Back pain suggests a penetrating posterior ulcer .**
- **Severe ulceration can occasionally be symptomless, as many who present with acute ulcer bleeding or perforation have no preceding ulcer symptoms.**
- **Untreated, the symptoms of a DU relapse and remit spontaneously.**
- **The natural history is for the disease to remit over many years due to the onset of atrophic gastritis and a decrease in acid secretion.**
- **Examination is usually unhelpful; epigastric tenderness is quite common in non-ulcer dyspepsia.**

Diagnosis of Helicobacter pylori infection

- Serological tests detect IgG antibodies and are reasonably sensitive (90%) and specific (83%).
- IgG titers may take up to 1 year to fall by 50% After eradication therapy and therefore are not useful for confirming eradication or the presence of a current infection. Indicates about pervious infection but doesn't distinguish if it treated or not.
- 13C-Urea breath test is a quick and reliable test for H. pylori and can be used as a screening test .
- The measurement of 13CO2 in the breath after ingestion of 13C urea requires a mass spectrometer.
- The test is very sensitive (97%) and specific (96%).
- This test is suitable for testing for eradication of the organism, but may be falsely negative if patients are taking PPIs at the time.
- Stool antigen test is a specific immunoassay using monoclonal antibodies for the qualitative detection of H. pylori antigen. And it's easy and available
- The overall sensitivity is 97.6% with a specificity of 96%. It is useful in the diagnosis of H. pylori infection and for monitoring efficacy of eradication therapy.
- Patients should be off PPIs for 1 week but can continue with H2 blockers .

Invasive methods (Endoscopic) .

Used for patients who suspected or had :
-High risk of malignancy. -UGIB .
-who are with treatment more than 6th weeks and the symptoms still present

- Biopsy urease test: Gastric biopsies are added to a substrate containing urea and phenol red.

I can't take biopsy from duodenum

- If H. pylori are present, the urease enzyme that they produce splits the urea to release ammonia which raises the pH of the solution and causes a rapid color change.
- The test may be falsely negative if patients are taking PPIs or antibiotics at the time .
- Culture: Biopsies obtained can be cultured on a special medium, and in vitro sensitivities to antibiotics can be tested.
- Histology: H. pylori can be detected histologically on routine stained sections of gastric mucosa.

The most accurate from all investigations .

- **جدول إضافي كملخص**

Test Type	Method	Advantages	Disadvantages
Urea Breath Test	Patient ingests urea labeled with carbon isotope; exhaled air is analyzed for carbon dioxide	- Non-invasive- Highly accurate	- Requires special equipment- Cannot be used after treatment without waiting
Stool Antigen Test	Detects H. pylori antigens in stool	- Non-invasive- Can confirm eradication	- May be less accurate if the patient is on PPI or antibiotics
Serology Test	Detects antibodies to H. pylori in blood	- Simple and widely available	- Cannot distinguish current infection from past exposure
Endoscopic Biopsy Tests	Biopsy taken during endoscopy for: - Rapid urease test - Histology - Culture	- Highly accurate- Can diagnose and confirm malignancy	- Invasive- Requires endoscopy- Expensive
Culture	H. pylori is grown from a biopsy sample	- Confirms diagnosis- Guides antibiotic therapy	- Time-consuming- Requires specialized lab

General Rules

- **Patients under 50 years of age with typical symptoms of peptic ulcer disease who are H. pylori positive can start eradication therapy without investigation.**
- **Confirmation of the diagnosis and exclusion of cancer is required in older patients.**
- **Endoscopy is the preferred investigation. All GUs must be biopsied.**
- **Endoscopy is required in all patients with alarm symptoms:**

1. dysphagia
2. weight loss
3. protracted vomiting
4. anorexia
5. hematemesis or melena
6. persistent symptoms

- **Stopping smoking should be strongly encouraged as smoking slows mucosal healing.**
- **Patients with gastric ulcers should be routinely reendoscoped at 6 weeks to exclude a malignant tumor.**

Eradication therapy

- **Triple Therapy (14 days):**

1. **PPI .**
2. **Amoxicillin .**
3. **Clarithromycin .**

- **Quadruple Therapy (for resistance or failure):**

1.PPI .
2.Bismuth subsalicylate .
3.Tetracycline .
4.Metronidazole .

The most common side effect from these antibiotics is gi upset which cause poor compliance and fail the treatment.

- All patients with duodenal and gastric ulcers should have H. pylori eradication therapy .
- Eradication therapy is controversial in patients who have incidental H. pylori infection with no gastric or duodenal ulcer .
- Standard eradication therapies are successful in approximatel 90% of patients .
- Reinfection is very uncommon (1%) in developed countries .
- In developing countries reinfection is more common, as compliance with treatment may be poor and metronidazol resistance is high (> 50%) good compliance is essential.
- Oral metronidazole has frequent side-effects and bismuth chelate is unpleasant to take.
- Metronidazole, clarithromycin, amoxicillin, tetracycline and bismuth are the most widely used agents (metronidazole & clarithromycin are less efficient because of resistance)
- Resistance to amoxicillin (1–2%) and tetracycline (< 1%) is low.
- Quinolones such as ciprofloxacin, furazolidone and rifabutin are also used when standard regimens have failed 'rescue therapy'
- Bismuth suppresses H. pylori effectively .
- None of these drugs is effective alone; eradication regimens therefore usually comprise two antibiotics given with powerful acid suppression in the form of a PPI, all given for 1-2 weeks .
- Omeprazole 20 mg + clarithromycin 500 mg and amoxicillin 1 g – all twice daily.
- Omeprazole 20 mg + metronidazole 400 mg and
- clarithromycin 500 mg – all twice daily

Does مش مطلوب

- In eradication failures bismuth chelate (120 mg 4× daily), metronidazole (400 mg 3× daily), tetracycline (500 mg 4× daily) and a PPI (20–40 mg 2× daily) for 14 days is used .
- Sequential courses of therapy are being used in areas where resistance is high .
- The effectiveness of treatment for uncomplicated duodenal ulcer should be assessed symptomatically .

- If symptoms persist, breath or stool testing should be performed to check eradication .
- Patients with a risk of bleeding or those with complications, i.e. hemorrhage or perforation, should always have a 13C urea breath test or stool test for H. pylori 6 weeks after the end of treatment to be sure eradication is successful .
- Long-term PPIs may be necessary

Like in chronic non-specific gastritis and esophogeal disease.

Complications of peptic ulcer

- Hemorrhage .
- Perforation: The frequency of perforation of peptic ulceration is decreasing, DUs perforate more commonly than GUs, usually into the peritoneal cavity. Surgery is usually performed to close the perforation and drain the abdomen .
- Gastric outlet obstruction: The obstruction may be prepyloric, pyloric or duodenal. The obstruction occurs either because of an active ulcer with surrounding edema or because the healing of an ulcer has been followed by scarring.

إضافة : جدول من كتاب step-up

TABLE 3-7 Complications of Peptic Ulcer Disease

	Clinical Findings	Diagnostic Studies	Management	Other
Perforation Or Penetration	Acute, severe abdominal pain, signs of peritonitis, hemodynamic instability	CT scan is the most sensitive test (detects free abdominal air and can localize site of penetration)	Emergency surgery to close perforation and perform definitive ulcer operation	**Can progress to sepsis and death if untreated**
Gastric Outlet Obstruction	Nausea/vomiting (poorly digested food), epigastric fullness/early satiety, weight loss	Barium swallow, CT, and upper endoscopy	Initially, nasogastric suction; correct electrolyte/volume deficits; supplement nutrition. Endoscopic dilation or surgery is eventually necessary in some patients.	Most common with duodenal ulcers and type III gastric ulcers
GI Bleeding	Bleeding may be slow (leading to iron-deficiency anemia) or can be rapid and severe (leading to shock)	Upper GI endoscopy (diagnostic and therapeutic)	Resuscitation; diagnose site of bleed via endoscopy and treat; perform surgery or embolization for acute bleeds that require transfusion of ≥6 units of blood	**Peptic ulcer disease is the most common cause of upper GI bleeding**

Other H. pylori-associated diseases

- Gastric adenocarcinoma: The incidence of distal gastric cancer parallels that of H. pylori infection in countries with a high incidence of gastric cancer.
- Gastric B cell lymphoma: Over 70% of patients with gastric B cell lymphomas (mucosal-associated lymphoid tissue – MALT) have H. pylori. Eradication cures this typy of lymphoma.

The rest 30% need to to radio-therapy and they have a poor prognosis

Archive

1)The most common cause of peptic ulcer disease worldwide is?

A.NSAID use

B.Use of warfarin

C.Pylori infection

D.Varices from hepatitis B

E.Gastric benign tumors.

Answer:c

2)Wrong about peptic ulcer:

A.Associated with type A personality

B.Duodenal ulcer is associated with increased risk of malignancy.

C.Most common cause of upper GI bleeding

Answer:b

3)A 54-year-old man is investigated tor dyspepsia. An endoscopy shows a gastric ulcer and a CLO test done during the procedure demonstrates H. pylori infection. A course of H. pylori eradication therapy is given. Six weeks later the patients comes to review with great improvement of symptoms. What is the most appropriate next step?

a. Culture of gastric biopsy b. H. pylori serology.

b.Hydrogen breath test.

c.Urea breath test.

d.for assessing the effectiveness of H. pylori treatment.

e. Counseling and medical follow up.

Answer:d

4)A 33-year-old female patient reports to the outpatient clinic 6 weeks after completion of eradication therapy. She complains of epigastric pain and persistent vomiting. You conduct a urea breath test that comes back positive for H. pylori. One of the following is not a common cause of failure of eradication therap , Select one:

a .Noncompliance

b.Bacterial resistance.

c.Presence of complications.

d.Re-infection.

e.Heavy smoking .

Answer: d

5)All of the following can be used to confirm H.pylori eradication, except :

a.Stool antigens.

b.Urea breath test.

c.IgG serology.

d.Biopsy histology.

e.Cultures.

Answer:c

6. A young male takes diclofenac for his arthralgia, developing epigastric pain. His arthralgia has resolved. What is the best next step?

A) Stop diclofenac and initiate ibuprofen with PPI

B)Stop diclofenac and give PPI, then follow-up after one week

C) Urgent endoscopy

Answer: B (Stop the offending agent and treat with a PPI, followed by reassessment) .

7.**A patient with hematemesis. After resuscitation, what is the treatment of choice while waiting for endoscopy?**

A) Octreotide

B)Terlipressin

• Answer: Either A or B, depending on the clinical context (likely variceal bleeding as a cause) .

8.**A 19-year-old female complains of sore throat, headache, and fever. She was treated with amoxicillin for 2 days and developed a rash. What is the most likely diagnosis?**

A) Penicillin allergy

B)Infectious mononucleosis

C) Kawasaki disease

• Answer: B (Amoxicillin-induced rash is commonly associated with infectious mononucleosis) .

9.The best test to confirm successful eradication of H. pylori is?

• A) Biopsy and culture
• B) Urea breath test
• C) Stool antigen test
• D) Hydrogen breath test
• E) Biopsy urease test
• Answer: B or E (Urea breath test is commonly used to confirm eradication)

Mini-Ocse

Q1: Regarding this Upper Gl endoscopy, active antral bleeding, all of the following initial to do, EXCEPT? Then please mention the most common cause for this lesion

A. IV PPI

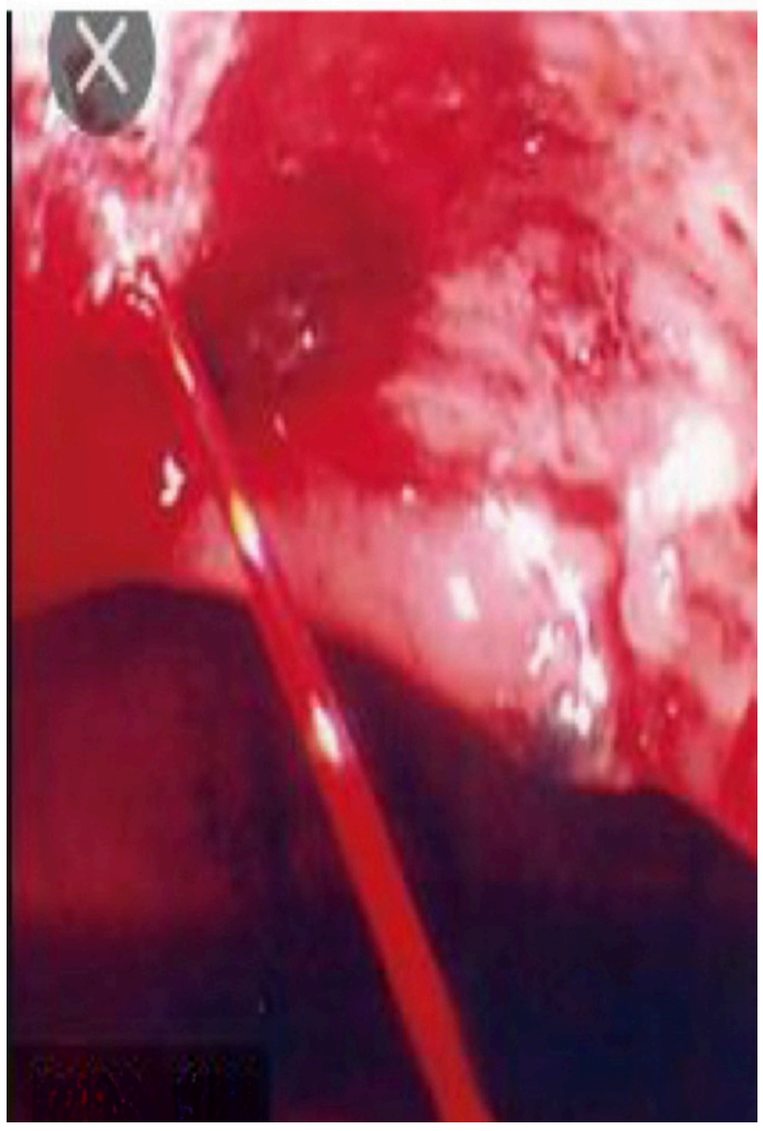
B. Thermal therapy

C. Mechanical Clips

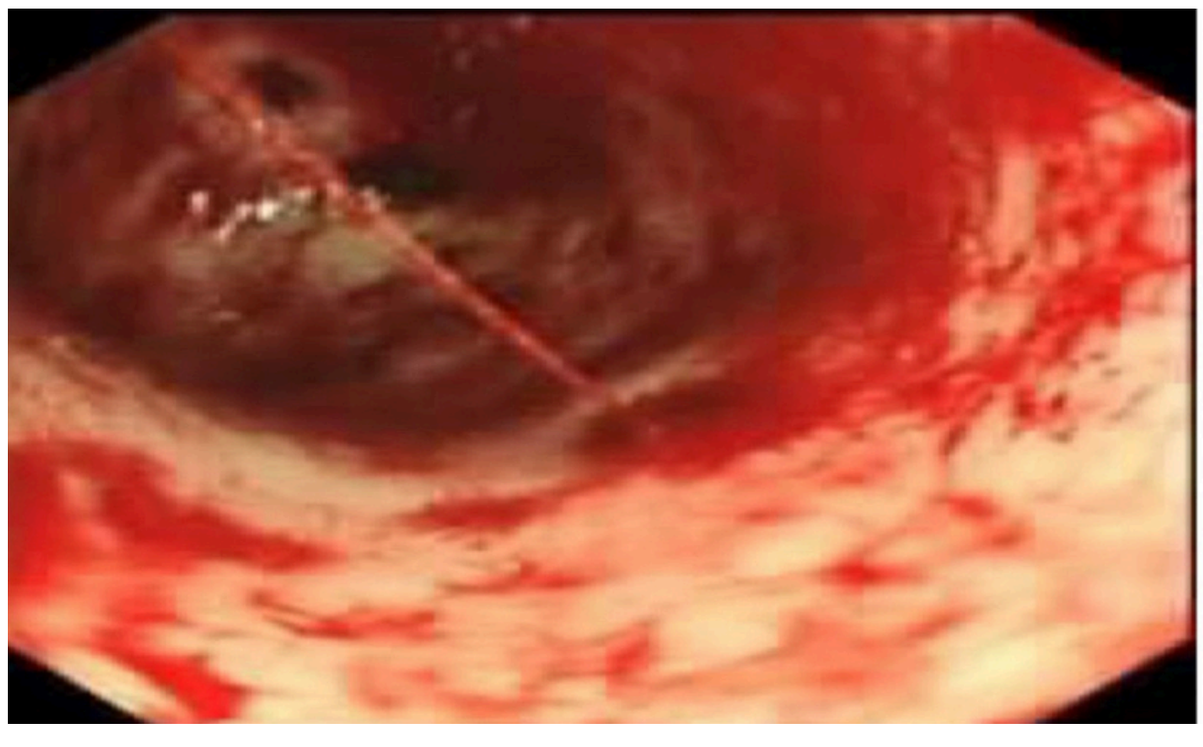
D. Adrenaline Injection

E. Surgery

* H Pylori infection is the most common cause



Q2) you did an endoscopy to a patient complaining of abdominal pain, hematemesis and melena. the image above is what you saw during the endoscopy.



- Describe what you saw ?

a) Oozing blood from vein

b)Spruting blood from an artery

- What is not important in the management of this patient ?

a) IV corticosteroids

b) endoscopic clipping

c) IV adrenalin

d) thermal coagulation

A male come to you complaining of recurrent epigastric pain.

What is the diagnosis?

Gastritis

•What treatment would you give him?

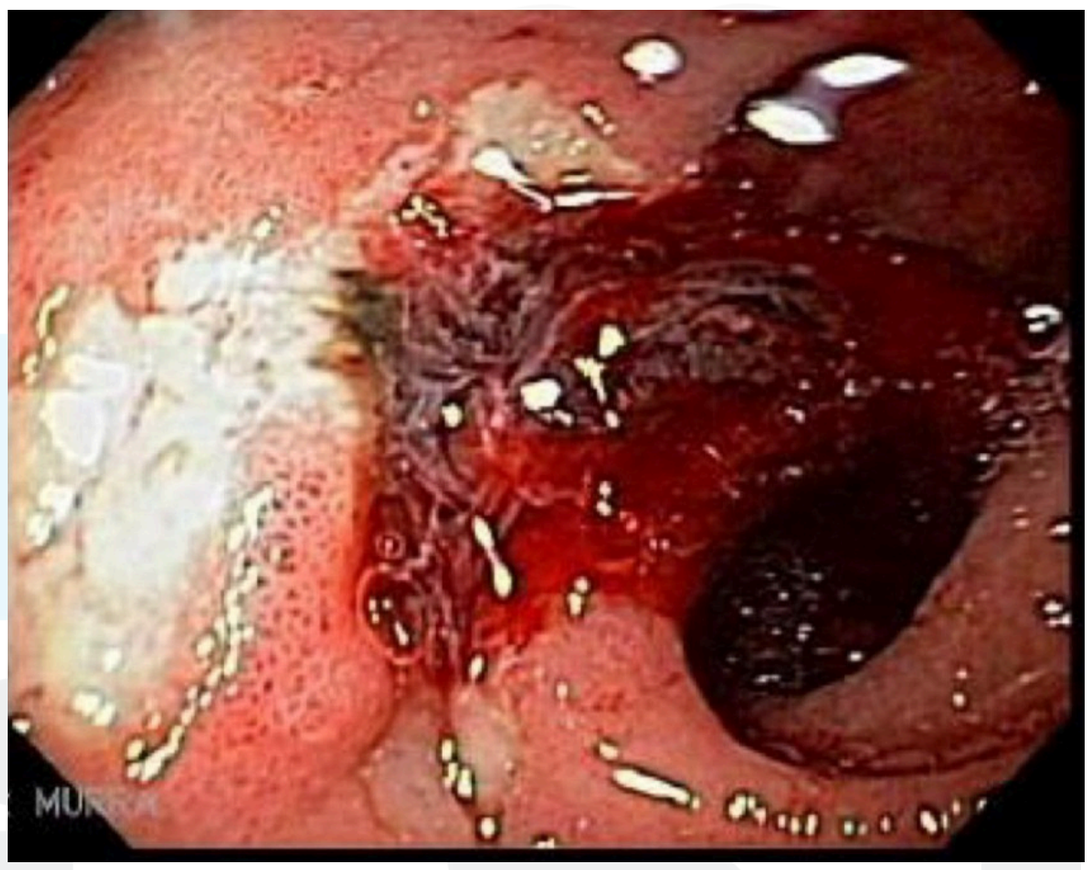
PPI

If he didn't improve on the previous medication,What might be the diagnosis?

Peptic ulcer (H.pylori)

And what is the treatment?

Triple therapy (PPI + 2 Ab) اكتبو هم من محاضرة د رامي



The same patient came after a while and on endoscopy you find this pic in duodenum

What do you see?

Bleeding duodenal ulcer

•Mention 4 laproscopic methods of treatment?

Epinephrine injection, clipping, thermal coagulation

Station 10: Patient presented with melena and hematemesis. This picture is from the antrum of the stomach. *not the same picture*

1) What is the diagnosis?

Peptic ulcer disease

1) What is the most common cause?

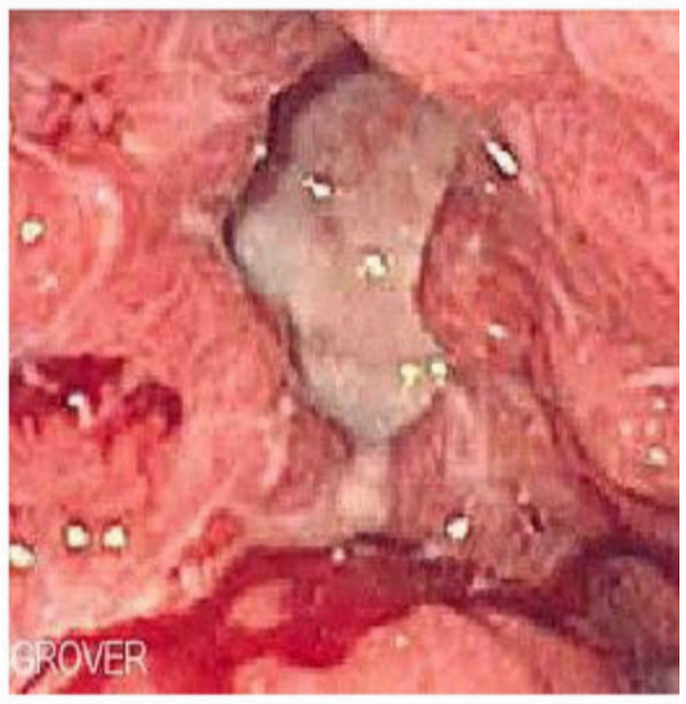
H. Pylori

1) What is the urgent management in case of massive GI bleeding?

Inection with epinephrine (adrenaline) .2-thermal coagulation
3- endoscopic clipping.

1) What are common complications?

Perforation – hemorrhage – gastric outlet obstruction



"إنكم لن تنالوا ماتحبون إلا بترك ماتشتهون ولن تدركوا ماتأملون إلا بالصبر على ما تكرهون"

الحسن البصري