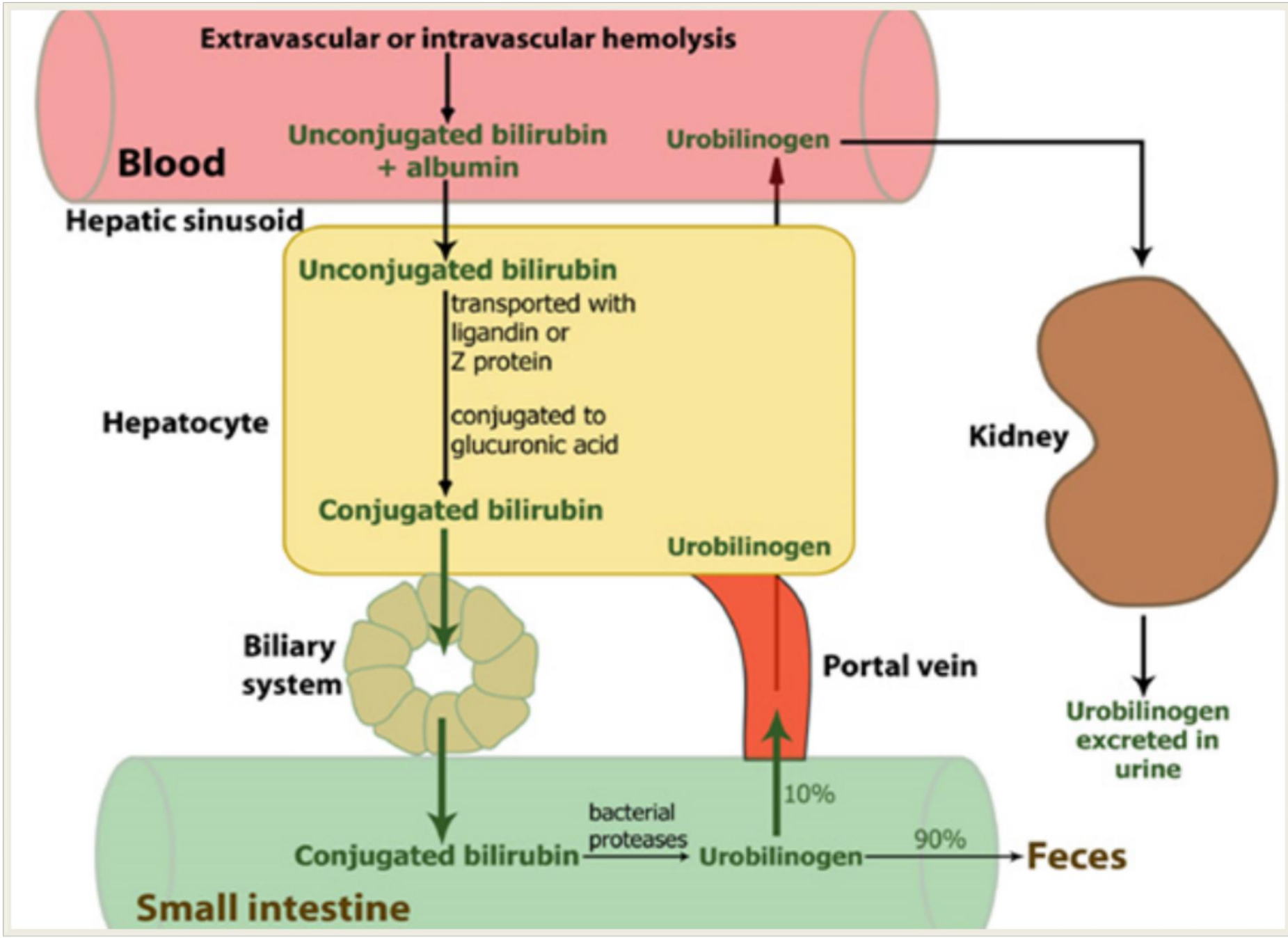
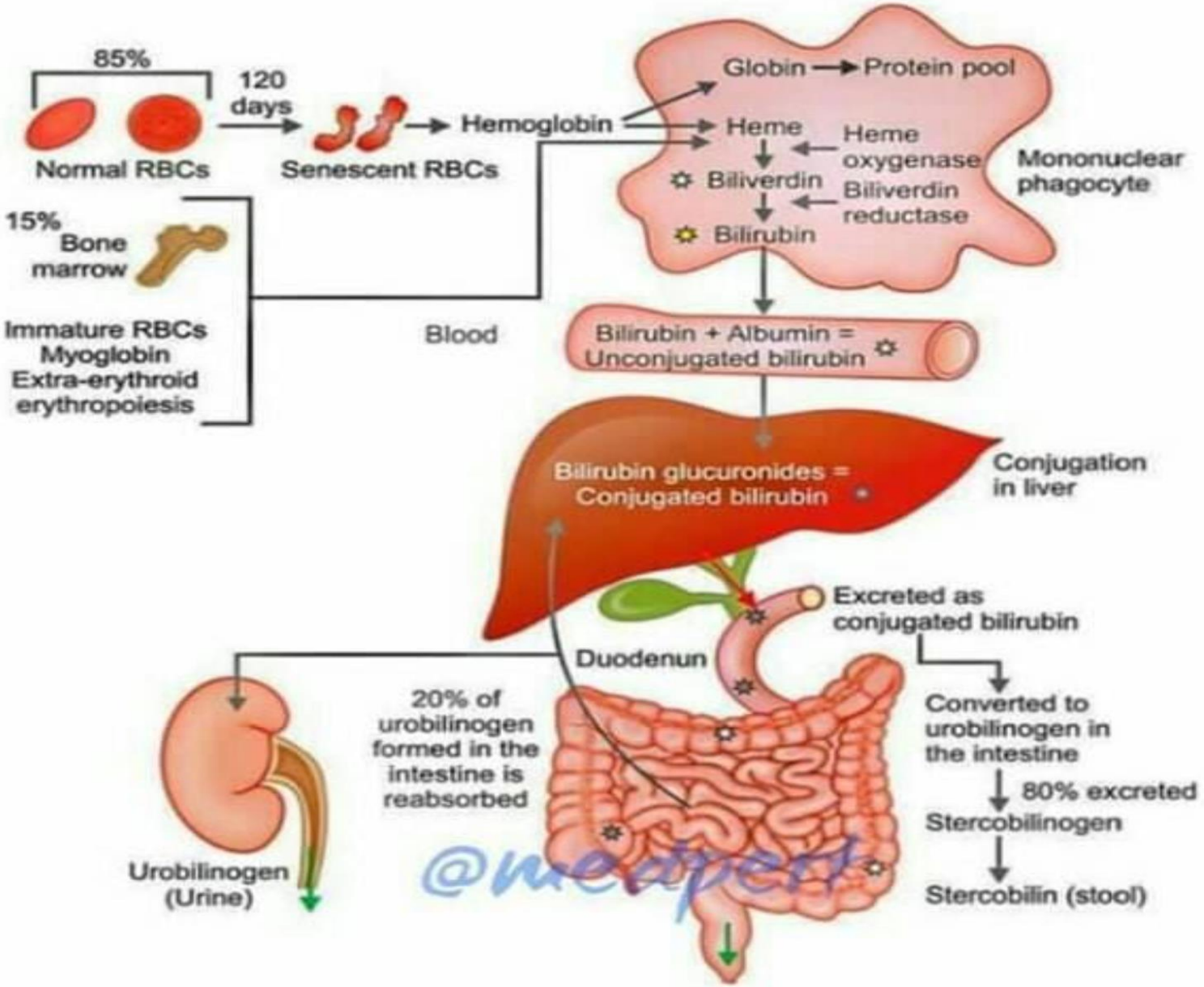
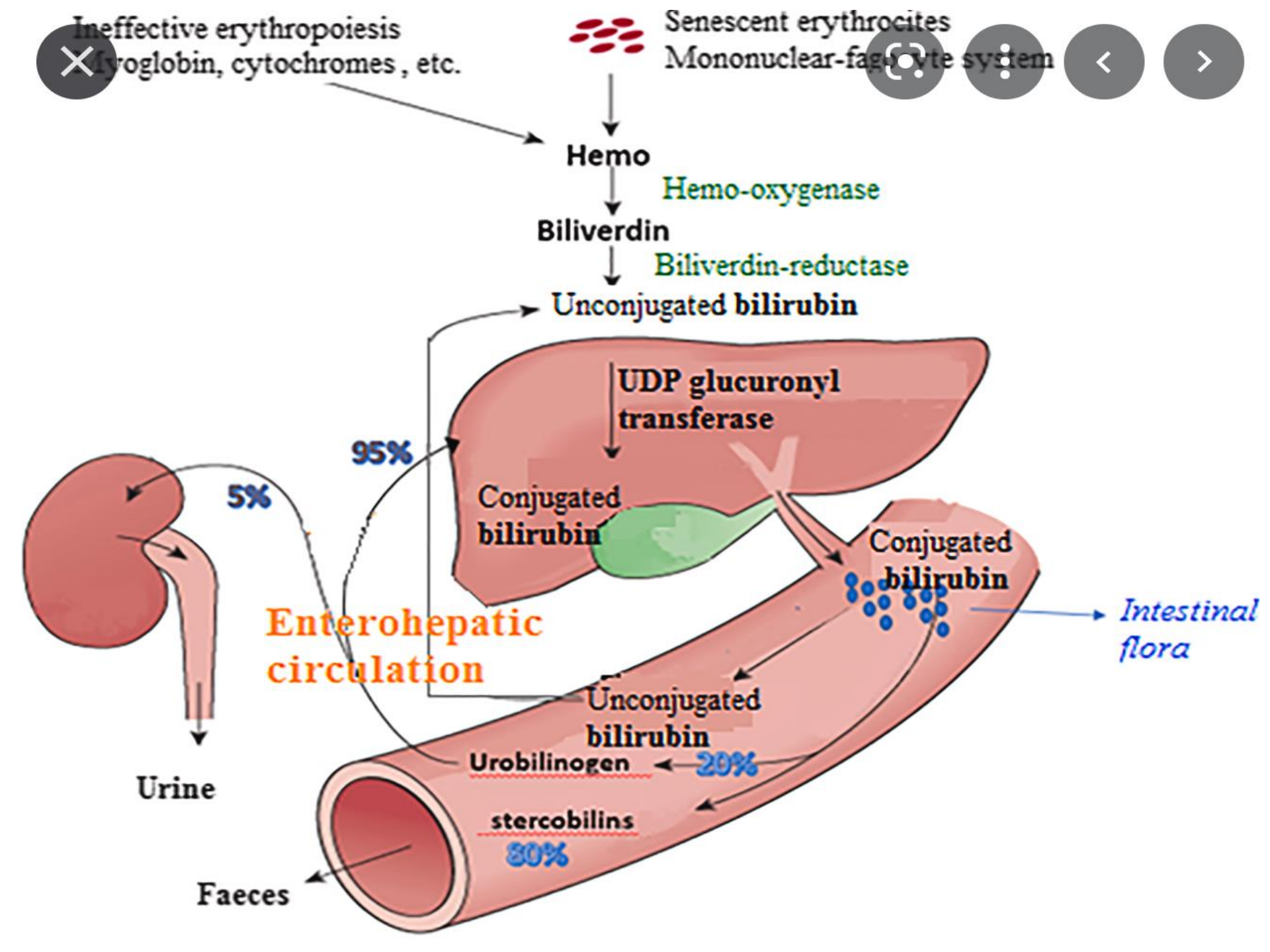
Bile Pigments

- Hb of RBCs is phagocytozed by RES → Heme + Globin.
- Heme ring is opened → Iron is stored in the liver.
- The remaining part of heme is converted to the Green pigment biliverdin → reduced into bilirubin → blood, combine with albumin (haemobilirubin, unconjugated, indirect or free bilirubin)→ liver where albumin is detached, while bilirubin is conjugated with glucuronic acid (Conjugated or direct bilirubin).
  - Conjugated bilirubin is actively transported into the bile canaliculi → golden yellow color of liver bile → Small intestine is converted to urobilinogen → most urobilinogen is converted to sterocoblinogen→Stool (sterocobilin, brown color of stool).
  - 10% enter the general circulation →(urobilinogen) 5%→ kidneys → urine (urobilin).


Extravascular or intravascular hemolysis
Blood
Unconjugated bilirubin
+ albumin
Urobilinogen
Hepatic sinusoid
Unconjugated bilirubin
transported with
ligandin or
Z protein
Hepatocyte
conjugated to
glucuronic acid
Conjugated bilirubin
Urobilinogen
Kidney
Biliary
system
Portal vein
Urobilinogen
excreted in
urine
10%
bacterial
proteases
Conjugated bilirubin
Urobilinogen
90%
Feces
Small intestine

Bilirubin Metabolism




Ineffective erythropoiesis
Myoglobin, cytochromes , etc.
Senescent erythrocites
Mononuclear-phagocyte system
Hemo
Hemo-oxygenase
Biliverdin
Biliverdin-reductase
Unconjugated bilirubin
UDP glucuronyl transferase
95%
5%
Conjugated bilirubin
Conjugated bilirubin
Intestinal flora
Enterohepatic circulation
Unconjugated bilirubin
Urobilinogen
20%
Urine
stercobilins
80%
Faeces

Jaundice

- **Definition:** ***Yellow discoloration of skin and mucus membranes due to presence of excess level of bilirubin (free or conjugated).***

	Hemolytic jaundice	Hepatocellular J	Obstructive J
Causes	Excessive hemolysis of RBCS Hemolytic anemia, drugs, Autoimmune disease	Liver disease Infection viral hepatitis Chemicals chloroform Drugs	Cholestasis Intrahepatic cirrhosis Extra-hepatic GBS Carcinoma stricture
Mechanism	↑ Production of free bill	Liver cannot uptake Conjugate and excreate bill	Liver conjugate but cannot excrete bill to intestine
Blood Bill Bile salts	Haem billi↑ ↑ Absent	Both ↑ Present	Chole bill ↑ ↑ Present
Urine Billi Color	Absent normal	Present Chole billi Dark brown	Present Chole Billi Very dark brown
Stool	Very dark stool	Pale stool	Very pale stool

Physiology of Gastrointestinal Disorders

- ***Disorders of Swallowing and of the Esophagus:***
- **Paralysis of the Swallowing Mechanism :**
- **Damage to the *Fifth, Ninth, or Tenth* cranial nerve**
- ***Poliomyelitis* or *encephalitis.***
- **Paralysis of the swallowing muscles, *muscle dystrophy* , *myasthenia gravis* or *botulism.***

- ***When the swallowing mechanism is partially or totally paralyzed***

- **Swallowing cannot occur.**
- **Failure of the glottis to close food passes into the lungs instead of the esophagus .**
- **Failure of the soft palate and uvula to close the posterior nares so that food refluxes into the nose during swallowing.**

Aspiration under GA.

Achalasia and Mega esophagus

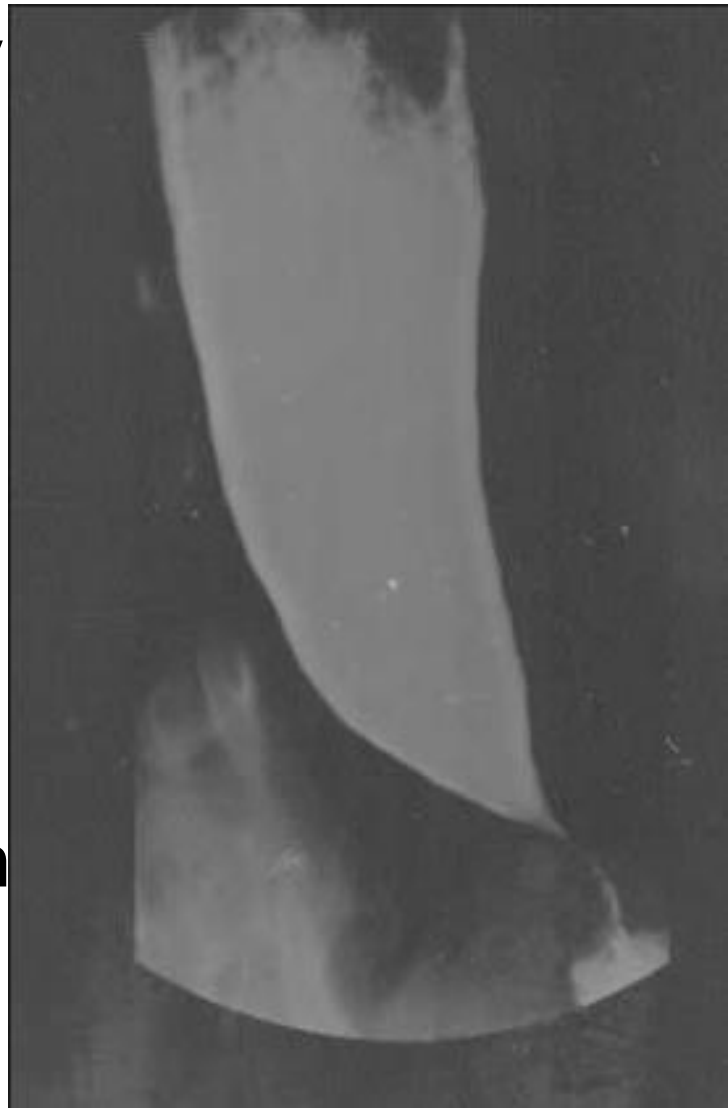
Definition: ***Aprestalsis of muscles of body of esophagus and failure of relaxation of lower esophageal sphincter .***

- **Food fails to pass from the esophagus into the stomach.**
- ***Causes:*** **Damage of the Myenteric plexus in the lower two thirds of the esophagus.**

Muscles remains spastically contracted ,loss receptive relaxation" of the G.E sphincter.

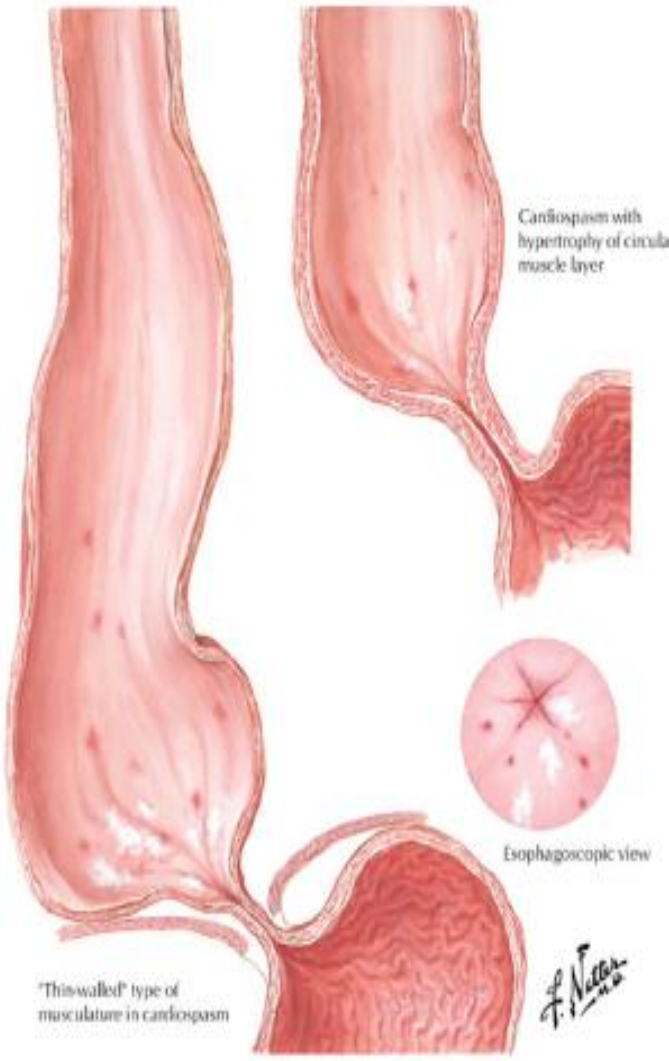
- **Over long periods the esophagus becomes markedly enlarged until it often can hold as much as 1 liter of food, which becomes putridly infected during the long periods of esophageal stasis. The infection may also cause ulceration of the esophageal mucosa, severe substernal pain or even rupture and death**

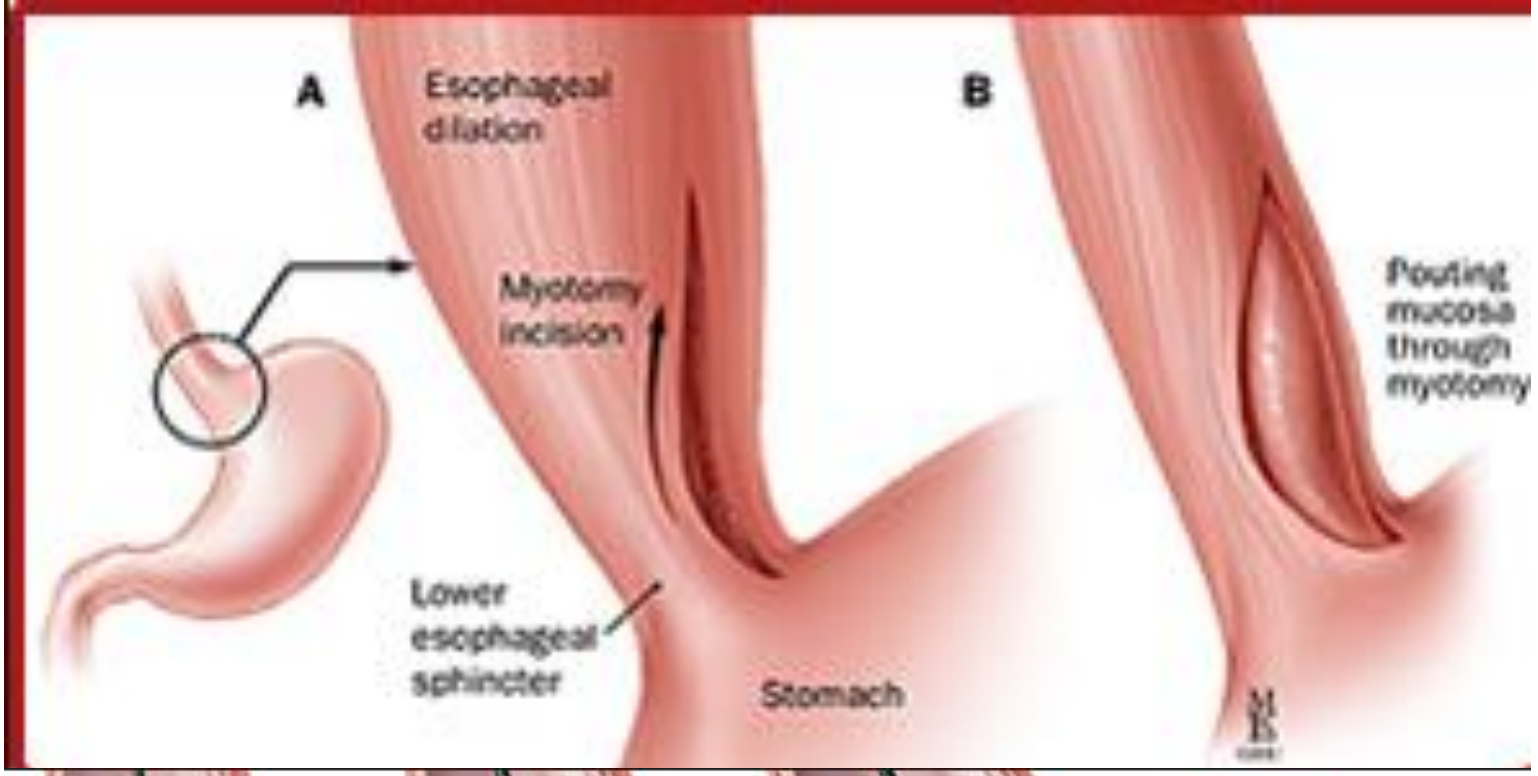
Mega esophagus.

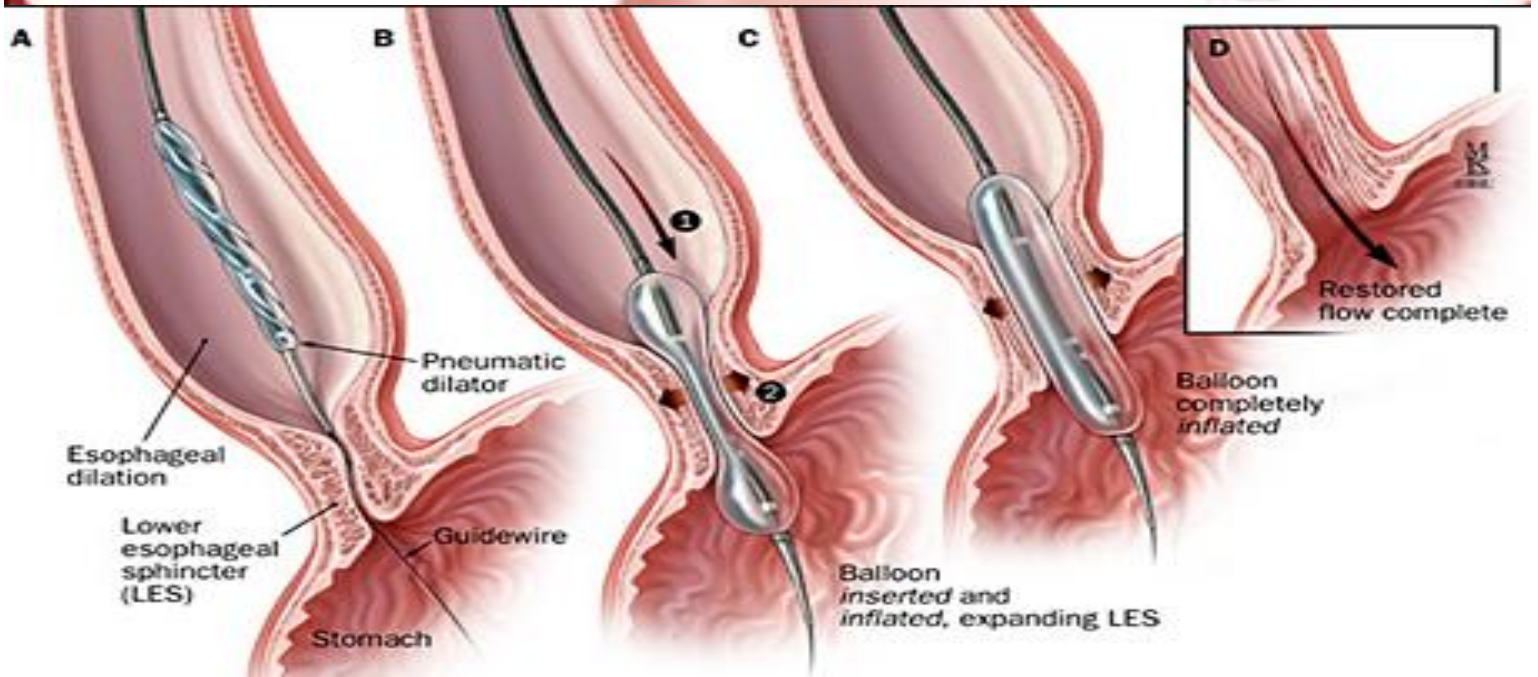


Achalasia

- Primary esophageal motility disorder.
- Peak incidence 20 -50 y.
- Cause progressive dysphagia to solids and liquids.
- Regurgitation undigested food
- Chest pain.
- Loss of weight.
- Increase risk of esophageal cancer.




A
Esophageal dilation
Myotomy incision
Lower esophageal sphincter
Stomach
B
Pouting mucosa through myotomy


A
Esophageal dilation
Lower esophageal sphincter (LES)
Pneumatic dilator
Guidewire
Stomach
B
1
2
Balloon inserted and inflated, expanding LES
C
Balloon completely inflated
D
Restored flow complete

Disorders of the Stomach

- ***Gastritis*** **Inflammation of the Gastric Mucosa**
- **Gastritis is caused by chronic *Bacterial infection* of the gastric mucosa.**
- **Damage to the protective gastric mucosal barrier by *Alcohol, Aspirin , NSAIDS .Steroids, Viniger .***
- ***Gastric Barrier and Its Penetration in Gastritis:***
- **low level of stomach absorption is mainly due to two specific features of the gastric mucosa:**

(1) It is lined with highly resistant mucous cells that secrete viscid and adherent mucus.

(2) It has tight junctions between the adjacent epithelial cells*. "Gastric Barrier."*

- **The gastric barrier normally is resistant enough to diffusion of highly concentrated hydrogen ions of the gastric juice.**

- **In gastritis, the permeability of the barrier is greatly increased. The H^+ diffuse into mucosa causing damage and atrophy.**

- **It also makes the mucosa susceptible to digestion by the peptic digestive enzymes, thus frequently resulting in a *Gastric ulcer.***

Chronic Gastritis Can Lead to Gastric Atrophy and Loss of Stomach Secretions

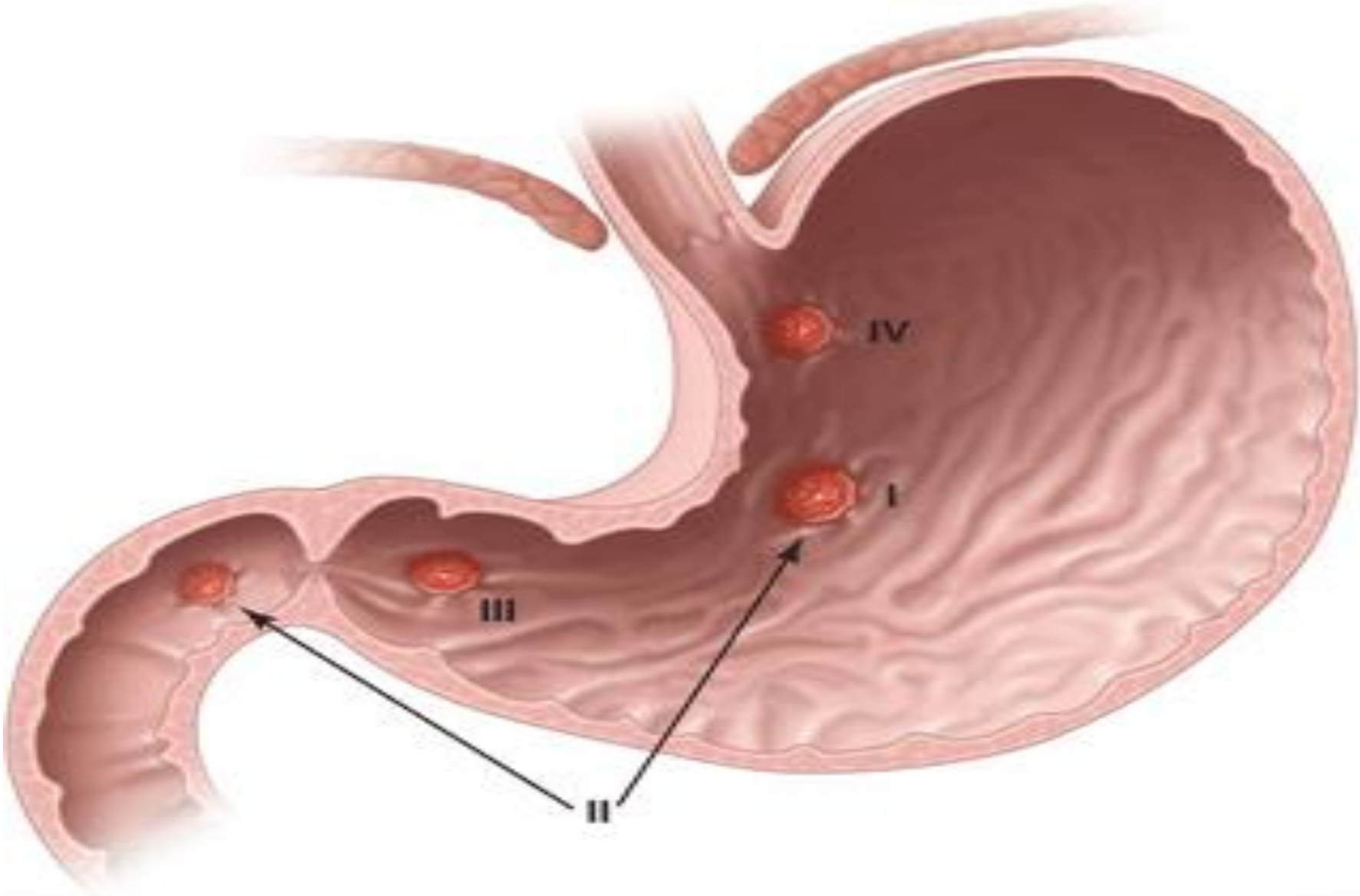
Achlorhydria (and Hypochlorhydria):

- ***Achlorhydria:*** **means simply that the stomach fails to secrete hydrochloric acid; it is diagnosed when the pH of the gastric secretions fails to decrease below 6.5 after maximal stimulation.**
- **Hypochlorhydria: means diminished acid secretion. When acid is not secreted, pepsin also usually is not secreted; even when it is, the lack of acid prevents it from functioning because pepsin requires an acid medium for activity.**

Gastric Atrophy May Cause Pernicious Anemia

- **In the absence of intrinsic factor, only about 1/50 of the vitamin B_{12} is absorbed. And, without intrinsic factor, an adequate amount of vitamin B_{12} is not made available from the foods to cause young, newly forming red blood cells to mature in the bone marrow. The result is *Pernicious Anemia.***

Types of gastric ulcers



- ***A Surface Breach*** **of mucosal lining of GIT (excoriated area of stomach or intestinal mucosa) occurring as a result of *acid and pepsin* attack.**
- ***Sites:***
  - **Duodenum (DU)**
  - **Stomach (GU)**
  - **Oesophagus**
  - **Gastro-Enterostomy stoma *(Marginal ulcer).***
  - **Related to ectopic gastric mucosa (e.g. in Meckel's diverticulum).**
  - **Acute peptic ulcer Like acute erosion but breaching muscularis mucosa.**

Peptic Ulcer

Causes:

1. High acid and peptic content
2. Irritation
3. Poor blood supply
4. Poor secretion of mucus
5. Infection, *H. pylori*

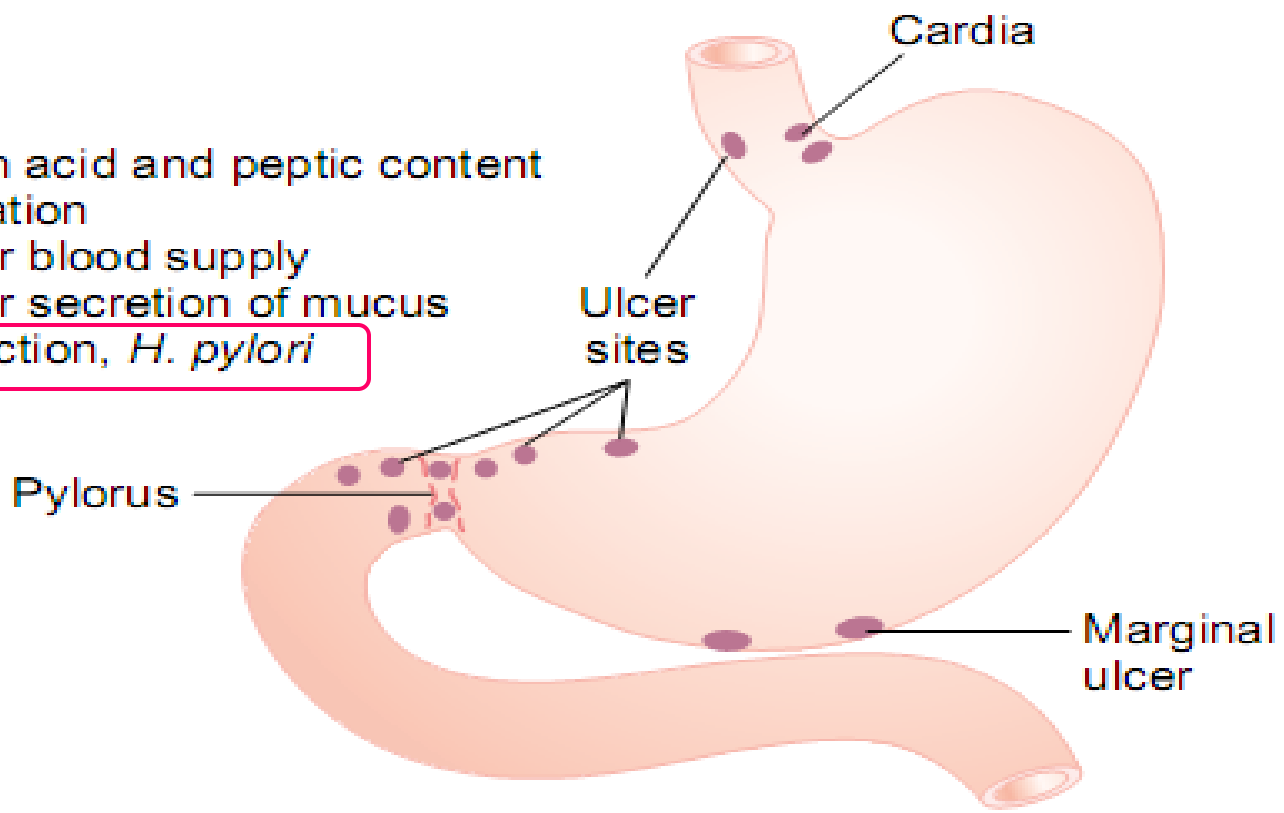


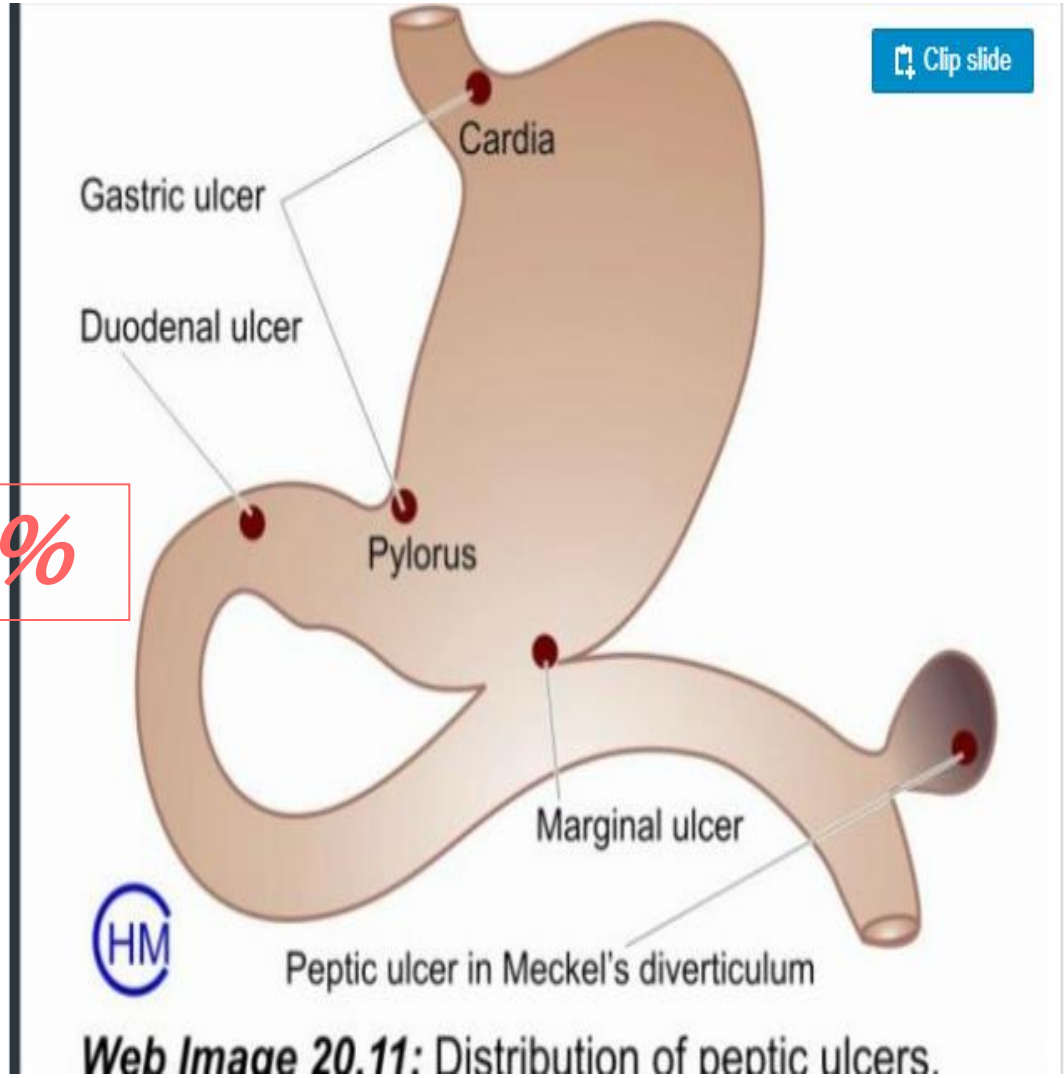
Figure 66–1

Peptic ulcer. *H. pylori*, *Helicobacter pylori*.

Sites of PUD

- **Duodenum:80%**
- ***Gastric:* 15%**
- ***D1, Stomach:* 4%**
- ***O-G Junction :***
- ***Meckel's D:***
- ***Marginal :***

1 %



Web Image 20.11: Distribution of peptic ulcers.

Basic Cause of Peptic Ulceration

The usual cause of peptic ulceration is an *Imbalance* between the Rate of secretion of gastric juice and the Degree of protection afforded by

- **The gastro duodenal mucosal barrier .**
- **The neutralization of the gastric acid by duodenal juices.**

MUCUS : **all areas normally exposed to gastric juice are well supplied with mucus glands(compound mucous glands in the lower esophagus plus the mucous cell coating of the stomach mucosa, the mucous neck cells of the gastric glands, the deep pyloric glands that secrete mainly mucus, and, finally, the glands of *Brunner's of the upper Duodenum*, which secrete a highly alkaline mucus).**

ALKALINE SECRETIONS

- **The duodenum is protected by the *Alkalinity of small intestinal secretions.***
- ***Pancreatic secretion,* which contains large quantities of $Nahco_3$ that neutralize the Hcl of the gastric juice, also *Inactivating Pepsin* and preventing digestion of the mucosa.**
- **In addition, large amounts of bicarbonate ions are provided in the secretions of the large Brunner's glands in the first *few centimeters of the duodenal wall* and In bile coming from the liver.**

Aggressive Factors

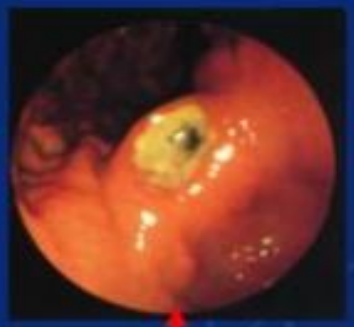
Acid/Pepsin

- H. pylori infection
- NSAIDs
- Smoking

Defensive Factors

- Mucus-bicarbonate barrier
- Barrier of apical membrane
- Mucosal blood flow
- Prostaglandins
- Epithelial cell restitution

I Aggressive Factors ↑



Defensive Factors ↓ II

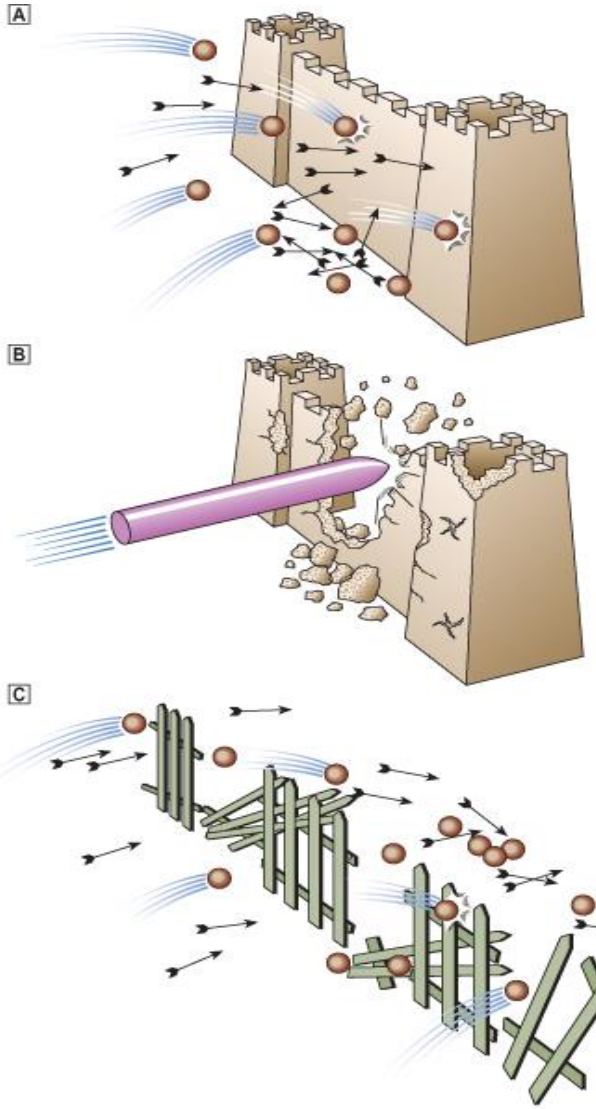
III Aggressive Factors ↑ + Defensive Factors ↓

REFLEXES

- ***Two feedback control mechanisms*** **normally ensure that this neutralization of gastric juices is complete.**
- **When excess acid enters the duodenum, it inhibits gastric secretion and peristalsis in the stomach, both by nervous reflexes and by hormonal feedback from the duodenum, thereby *decreasing the rate of gastric emptying.***
- **The presence of acid in the small intestine liberates *Secretin* from the intestinal mucosa, which then passes by way of the blood to the pancreas to promote rapid secretion of pancreatic juice.**

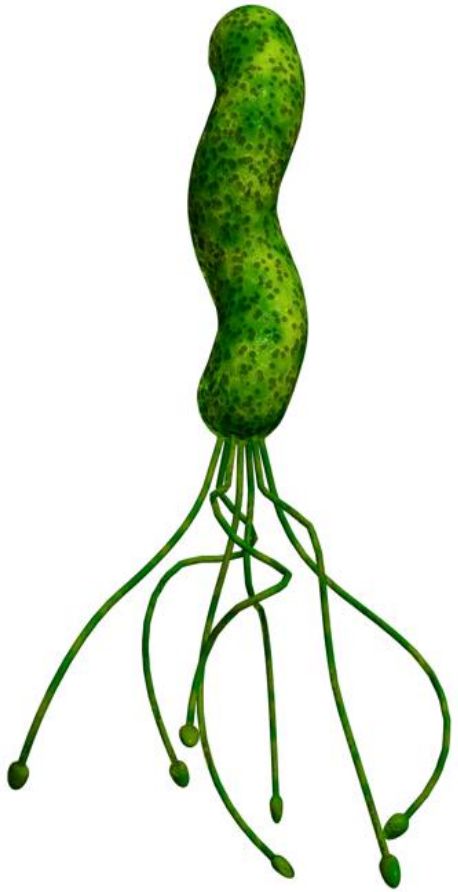
Causes

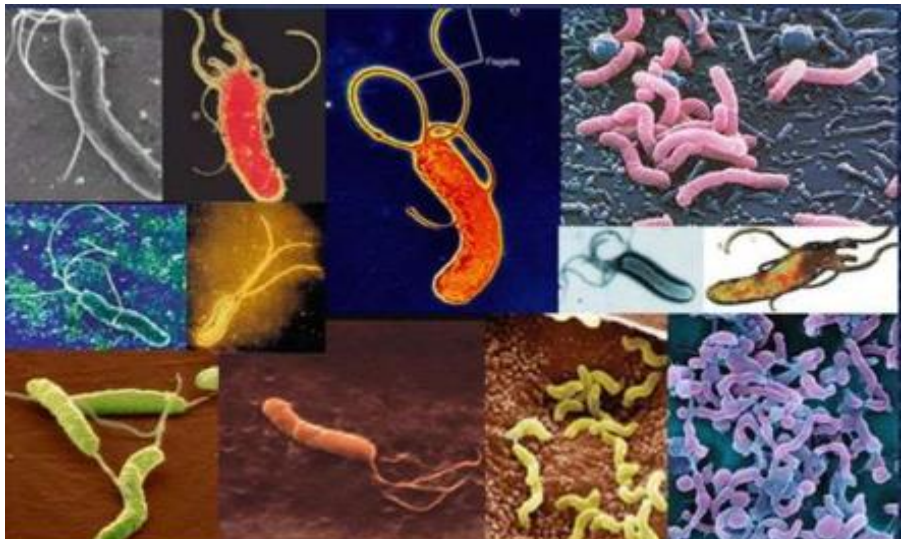
- In normal acid/pepsin attack is balanced by mucosal defences
- Increased attack by hyperacidity Weakened mucosal defence – the major factor *(H. pylori Related)*



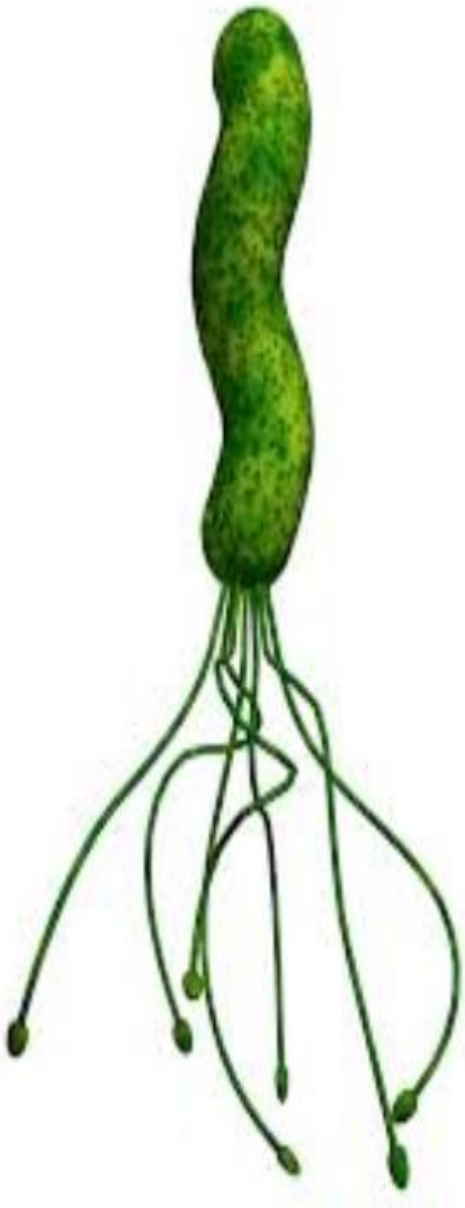
Helicobacter pylori

- Gram -ve Comma Shaped Bacteria Micro Aerophilic with 4-6 Flagella .
- Is most common cause of PUD.
- Transmission is Feco - Oral.
- Secrete urease convert Urea to Ammonia.
- Produce alkaline environment to survive in stomach.
- Higher prevalence in low socio economic.
- Almost all patient with DU and 2/3 of GU are HLO +.

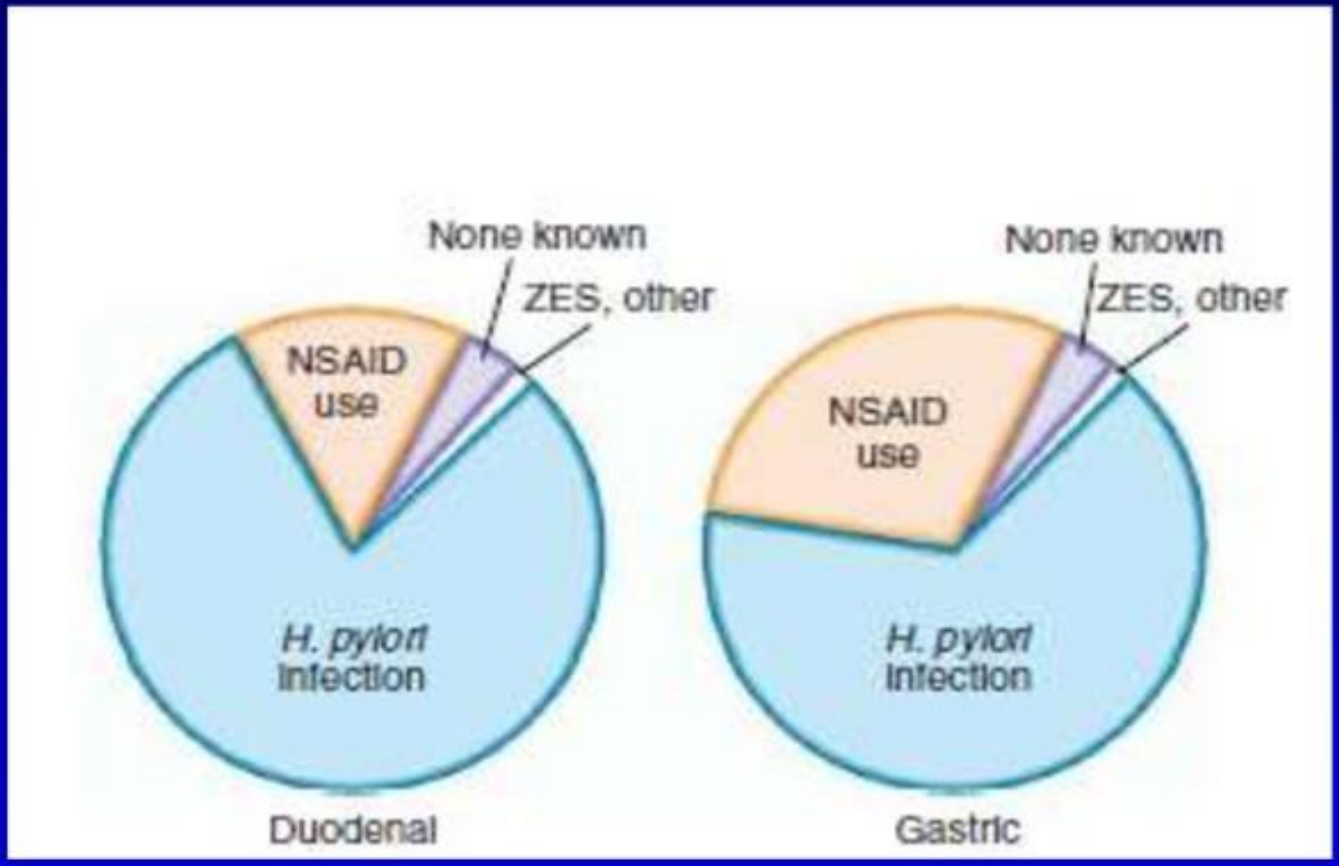




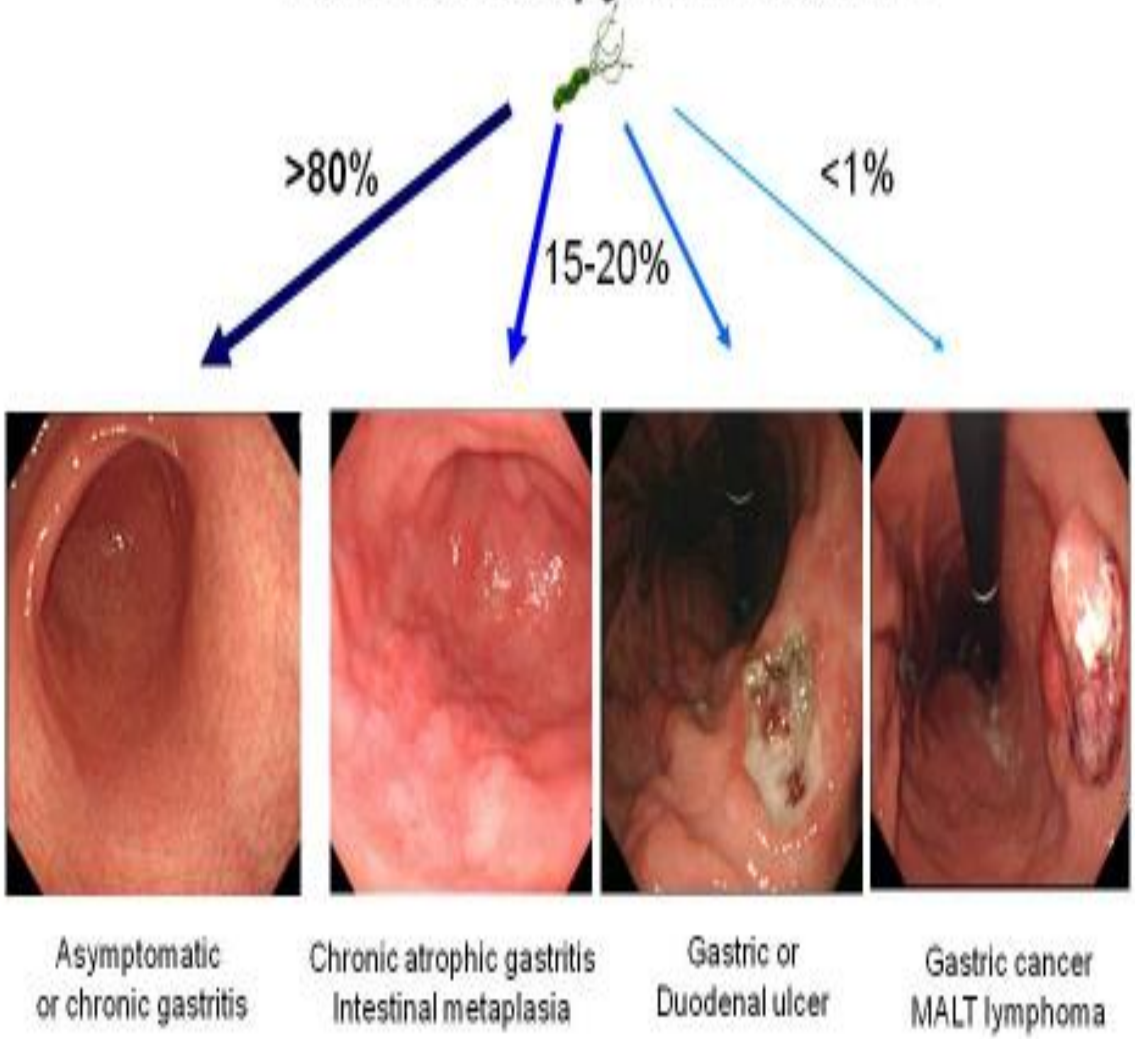
- **Bacterial Infection by *Helicobacter pylori* Breaks Down the Gastro duodenal Mucosal Barrier and Stimulates Gastric Acid Secretion.**
- **At least 75 percent of peptic ulcer patients have been found to have chronic infection of the terminal portions of the gastric mucosa and initial portions of the duodenal mucosa, most often caused by the bacterium *Helicobacter pylori***
- **In *DU*, the rate of gastric acid secretion is greater than normal, sometimes as much as twice normal.**
- **Excess secretion of gastric juices for any reason may cause peptic ulceration.**

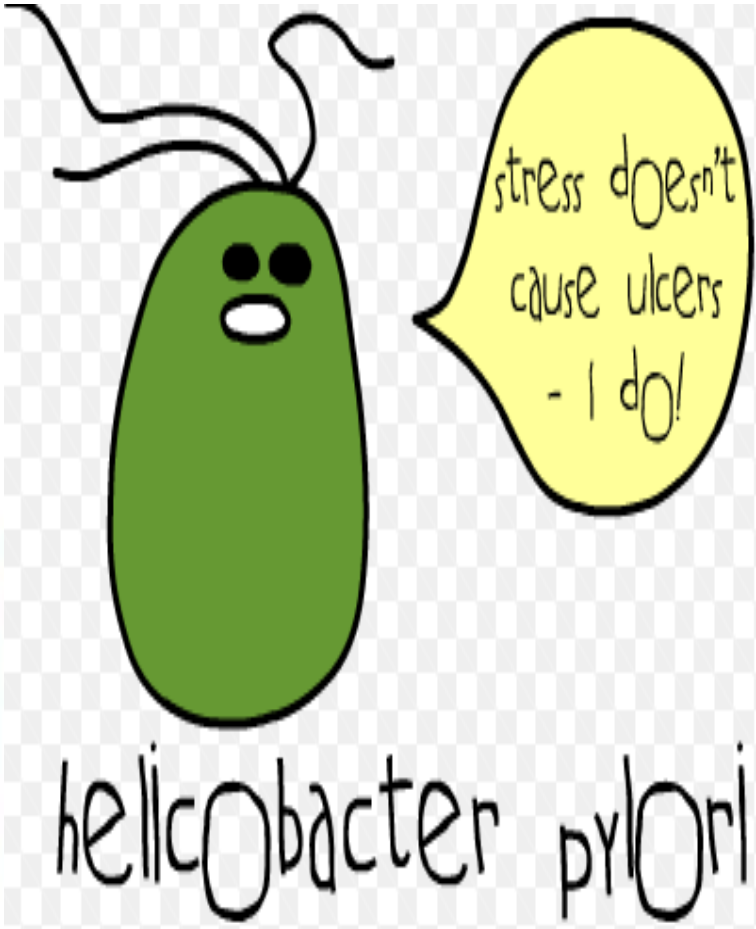


Conditions associated with PUD

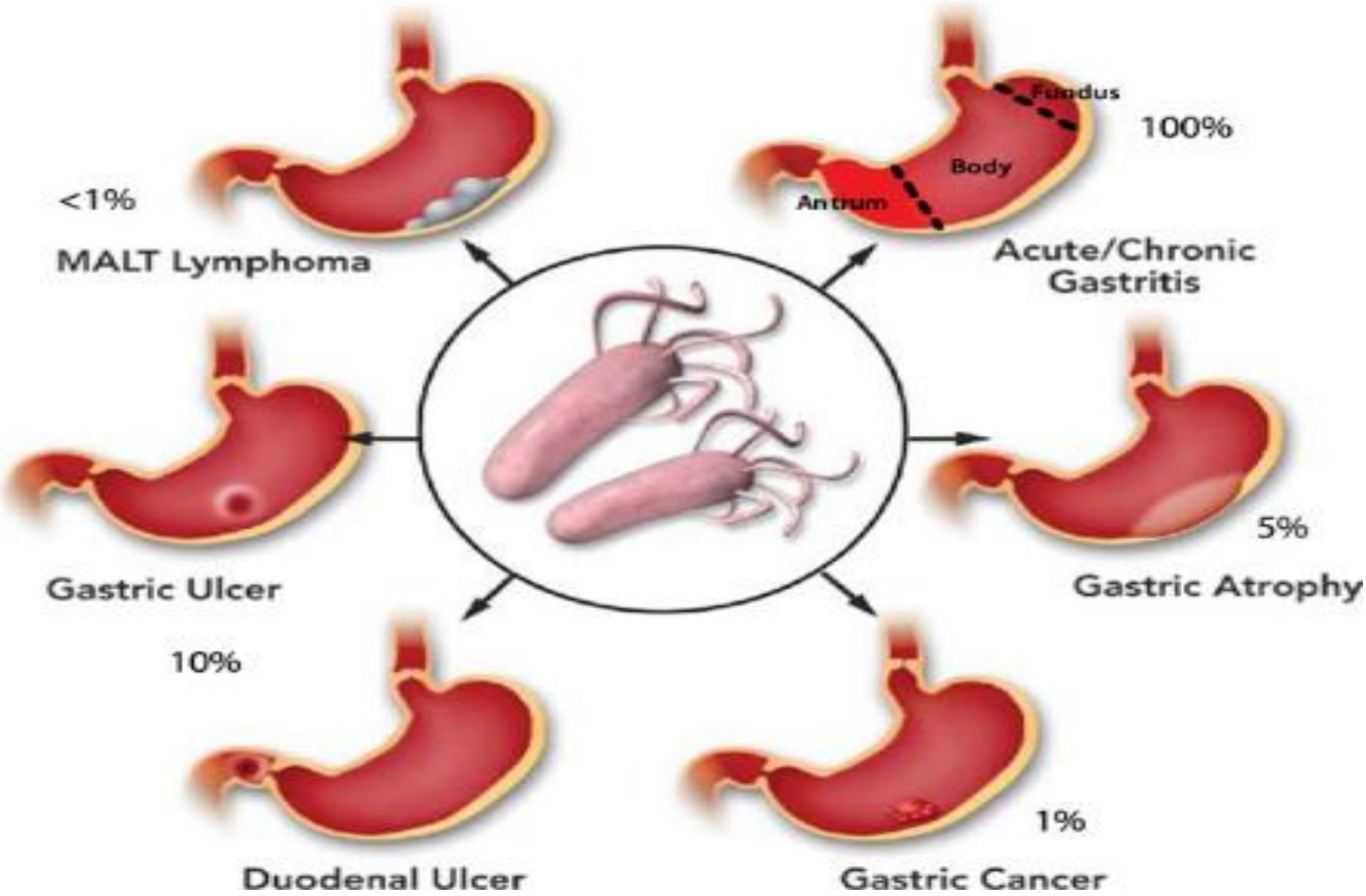


The Clinical Outcomes of *Helicobacter pylori* Infections





HLO OUTCOME


<1%
MALT Lymphoma
Fundus
Body
Antrum
100%
Acute/Chronic Gastritis
Gastric Ulcer
10%
5%
Gastric Atrophy
Duodenal Ulcer
1%
Gastric Cancer

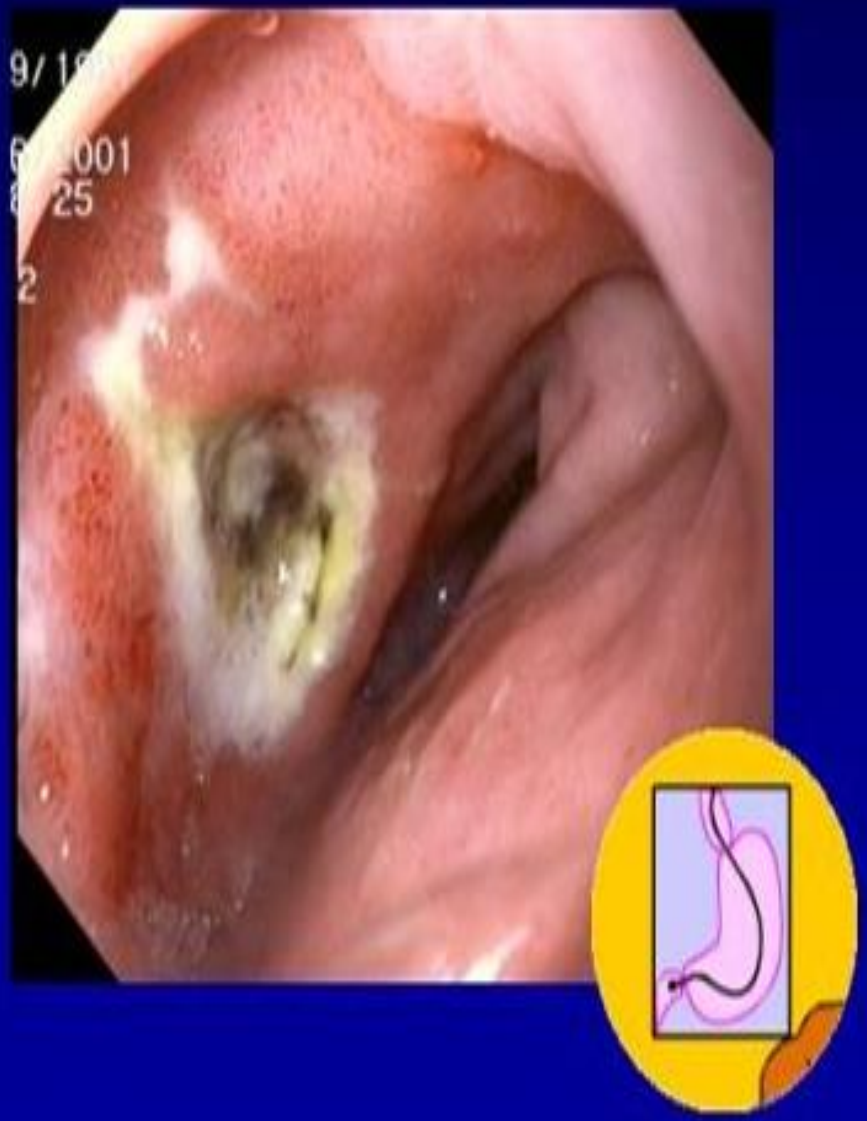
Other factors that predispose to ulcers include

- ***Smoking:*** **presumably because of increased nervous stimulation of the stomach Secretory glands.**
- ***Alcohol:*** **because it tends to break down the mucosal barrier.**
- ***Aspirin and other NSAIDS:*** **drugs that also have a strong propensity for breaking down this barrier.**

Physiology of Treatment

- **Use of Antibiotics along with other agents to kill infectious bacteria.**
- **Proton pump inhibitors (PPI)are used now as their antacid effect is better and duration of action is longer e.g. *Omeprazole.***
- **Administration of an acid-suppressant drug, especially *ranitidine*, an antihistaminic that blocks the stimulatory effect of histamine on gastric gland histamine$_2$ *(H_2) receptors antagonist,* thus reducing gastric acid secretion by 70 to 80 per cent.**
- **Triple Therapy is the recent approach in treatment of peptic ulcer. It includes 2 antibiotics (Clarithromycin + Amoxicillin or metronidazole) and an acid-suppressant (Omeprazole).**

Duodenal Ulcer (DU)



Gastric Ulcer (GU)