Pathology

● Sheet ○ Slide

number 3

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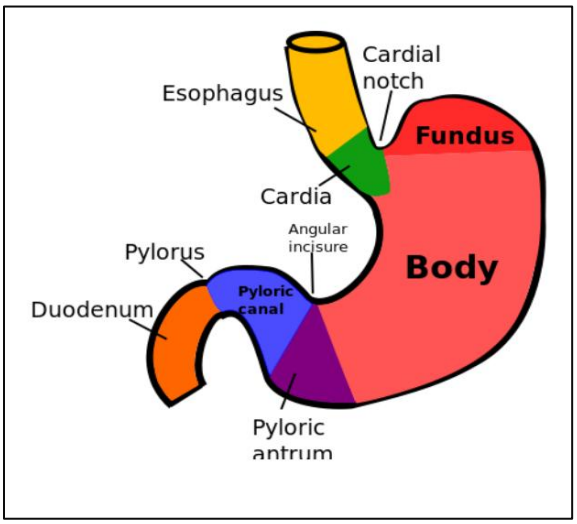
We are done with the diseases of esophagus in the last lecture, now in this one we are going to talk about **diseases of stomach**.

The stomach is divided into four main regions:
1- cardia
2- fundus
3- body
4- pylorus



Cardia is the main source of mucus secretion (from foveolar cells) which protects mucosa.
Gastrin is secreted from the G cells in the antrum, it stimulates acid secretion from the parietal cells in body and fundus.
The chief cells secrete pepsinogen for digestion.

Main diseases affecting the stomach

1- **Inflammations**: acute gastritis, acute peptic ulcer, chronic gastritis, peptic ulcer disease (chronic ulcer).
2- **Neoplasms**: gastric polyps and gastric malignancies.

Inflammation

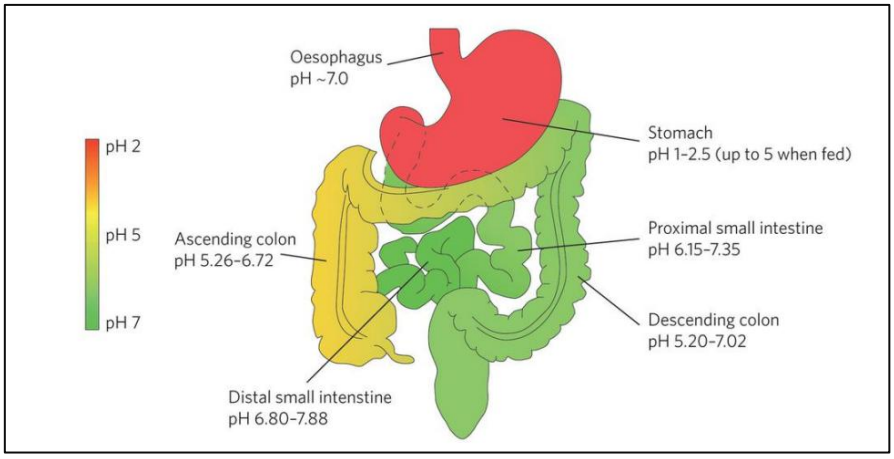
In order to understand inflammation we need to know about the acidity of the stomach.
The stomach needs large amounts of acid for digestion.
The acidity of the stomach is 1-2 and this is very acidic compared to the things we eat, it is even more acidic than the things that can burn our stomach.
Lemon juice ph is 2, for example.

However, this acidity does not harm the stomach normally, due to protective mechanisms which include:
1- Thick mucus layer from the foveolar cells in the cardia.
2- Bicarbonate which is secreted from the epithelial cells, the bicarbonate acts as a buffer. So in the lumen, the Ph is 1-2, but closer to the epithelial cells,

neutralization happens, the Ph becomes 7, which is neutral.

Inflammatory mediators, mainly prostaglandin E, are responsible for mucus and bicarbonate secretion. When prostaglandins decrease, problems in the protective mechanisms occur.

The idea is that the stomach has a balance between high acidity and protective mechanisms, whenever this balance is disturbed (protection mechanisms decrease or acid secretion increases or both), inflammation will occur.
So in all the diseases that cause inflammation, the main problem is imbalance between the protective mechanisms and the acidity.



Inflammation in the stomach could be :
a- Acute gastritis.
b- Chronic gastritis.

Acute gastritis

What causes acute inflammation?

NSAIDs disrupt the protection by decreasing prostaglandins, therefore decrease bicarbonate and mucus secretion. **Bacteria** can also be a cause of acute gastritis. **Chemicals** like alcohol, strong acids and strong alkali. **Radiotherapy** and **chemotherapy**. These causes can make direct damage to the mucosa and if mucosa is damaged, inflammation occurs.

Note: elderly people are more susceptible to develop acute gastritis, because with aging the mucus production decreases. So there will decreased mucus secretion versus acid secretion.

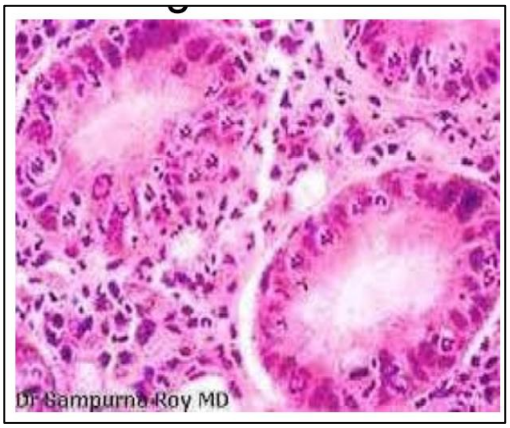
Signs and symptoms of acute gastritis:

1-Nausea

2-Vomiting

3- Epigastric pain.

Morphology of acute gastritis, the main cells are neutrophils, loads of neutrophils are seen attacking the stomach and the glands. So neutrophils are the morphologic evidence of acute inflammation.



Sometimes acute inflammation can be very severe and causes **ulceration**. Ulcer is a defect in the mucosa.

00:00-10:00

What are the causes of acute ulcer in the stomach?

Anything that causes inflammation if severe enough can cause acute ulcer, the most common cause is **NSAID**, high dose of NSAID can cause acute ulcer instead of acute gastritis. Caustic injury can also cause acute ulcer.

One of the most important causes of acute ulcer is **stress ulcer,** the word stress here does not mean psychological stress, it means physiological stress. However, psychological stress can cause problems in stomach but this is not common or severe as physiological stress. Physiological stress happens to critically ill patients (in the ICU), these patients suffer from shock, severe hypovolemia, organ system failure, cardiac failure, sepsis, trauma and burns.

Subtypes of stress ulcers:

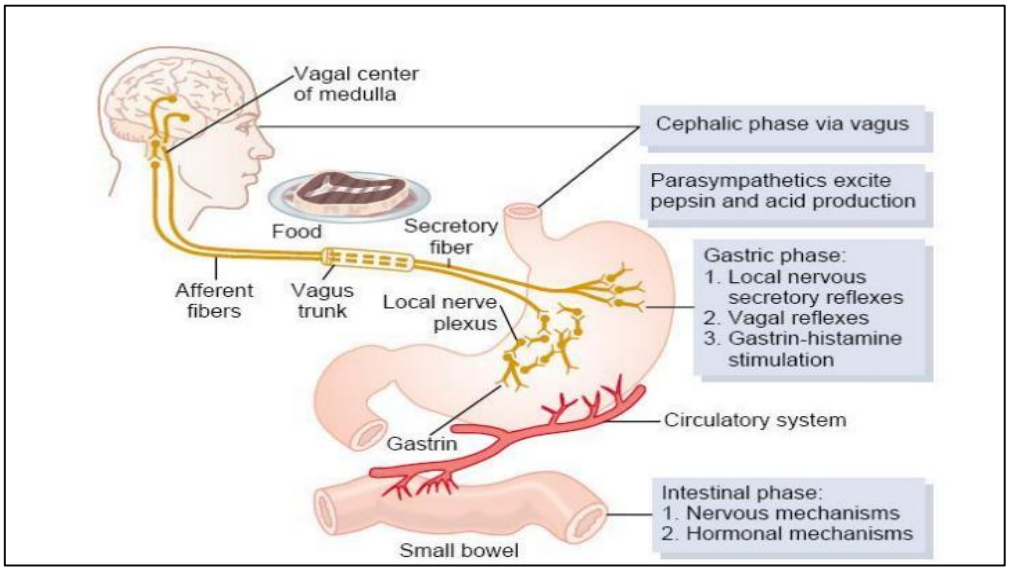
1- **Curling ulcer** for those who have severe burns or severe trauma and they will lose too much fluids and hypovolemia predisposes to the curling ulcer. This is usually seen in the duodenum.

Pathogenesis: when a patient suffers from shock and hypovolemia, there won't be enough blood supply for all the organs, so the body tries to protect itself and shifts the blood to the main organs like heart, kidney and brain. As a result, vasoconstriction occurs in the stomach, blood supply decreases and this leads to hypoxia, hypoxia damages epithelial cells which predisposes to ulcer.

10:00-20:00

Due to hypoxia and lack of oxygen supply, oxidative phosphorylation decreases, anaerobic glycolysis occurs and leads to increased lactic acid production, acidosis and epithelial cell damage.
To sum up, acute stress ulcer is caused mainly by hypoxia and acidosis which are caused by severe hypovolemia.

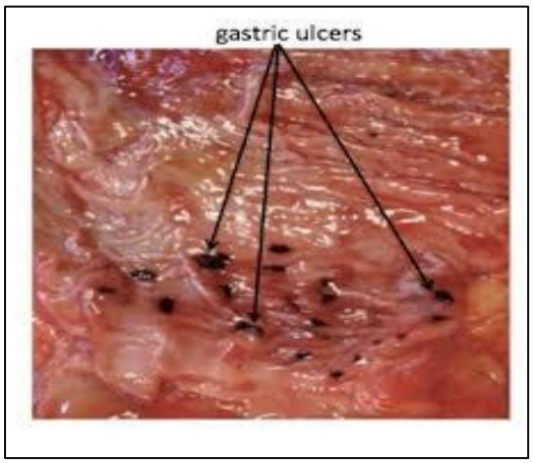
2- **Cushing ulcer** which happens due to increased intracranial pressure.
Pathogenesis: the mechanism of cushing ulcer is different from the other hypovolemic associated ulcers. Intracranial pressure increases due to hemorrhage, infarction, hydrocephalus or tumor. When the intracranial pressure increases, it causes stimulation of the vagus nerve which leads to increased acid production.

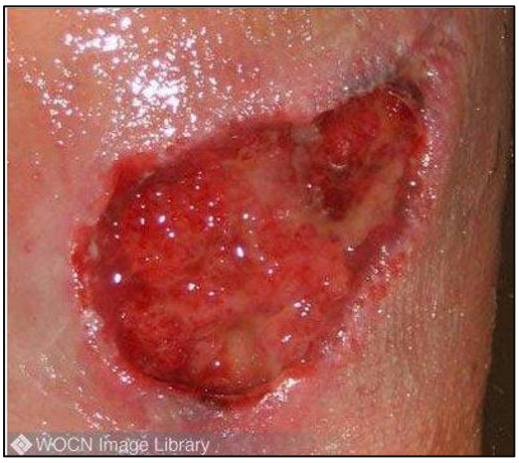


Treatment: we try to protect first, but if ulceration happens, we treat the underlying conditions and the ulcer will heal gradually.

To sum up, when there is a severe physiological stress it can cause acute stress ulcer. The two main subtypes are ; cushing ulcer which is due to increased intracranial pressure and curling ulcer which is due to severe burns and trauma.
This is important when having a patient in the ICU, the stomach must be monitored because acute ulcer could happen and lead to life-threatening hemorrhage and bleeding, in this case the patient is given proton pump inhibitors to protect the stomach.

Morphology of acute ulcer, defect in mucosa, base of ulcer is inflamed, hyperemia, edema, and the
surrounding mucosa is normal, while
it is affected in the chronic ulcer.





Note: cushing ulcer usually causes multiple ulceration, as in the picture to the left.

Signs and Symptoms
1-nausea
2-vomiting
3- coffee ground hematemesis
Note: hematemesis is vomiting blood, it could be either fresh red blood as seen in mucosal tears especially in the esophagus, or coffee ground (brown) blood as seen in stomach ulcer, where it is mixed with acids and becomes brown.

Complications

Bleeding and perforation and these are emergency situations .
The outcome is mainly determined by the severity of the underlying conditions.
Note : acute ulcers heal after treating the underlying cause.

Chronic gastritis

The difference between acute and chronic inflammation is the duration. Acute inflammations last for days while the chronic inflammations last for weeks, months or even more.

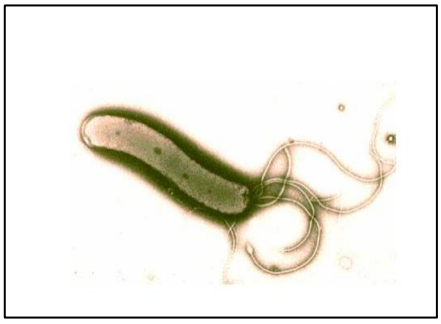
Smptoms

nausea ,vomiting , abdominal discomfort. Hematemesis is rare because chronic gastritis takes time so healing and fibrosis occur, therefore, less tissue damage and bleeding.

Causes of chronic gastritis

1- **Autoimmune gastritis** (type A), 10% of cases.
2- **Helicobacter Pylori associated** gastritis (type B), majority of cases (90%)

H-Pylori is a gram negative bacillus and has flagella which is important for its mobility.
H Pylori is found in duodenal ulcer, gastric ulcer, chronic gastritis and it also associated with gastric adenocarcinoma and lymphoma, so it is a cause of many diseases in the stomach.



H Pylori was discovered by two Australian pathologists, one of them was called Marshall. Marshall stated that gastric ulcer is related to infection, then he decided to drink a beaker full of H Pylori culture to prove that. He expected to have ulcer after a month or more, however, after 3 days he had nausea, 5 days later he started vomiting, after doing endoscopy it was discovered that he suffered from severe gastritis.

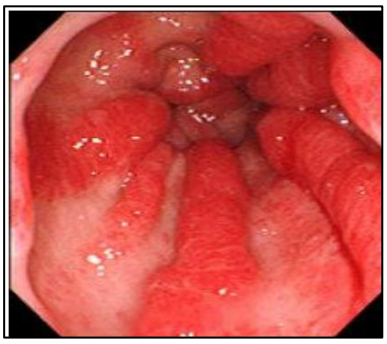
20:00-30:00

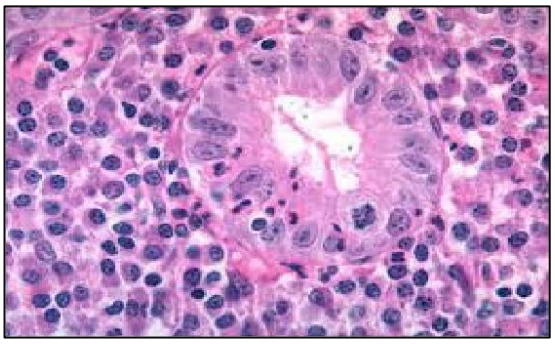
Marshall wanted to prove that H pylori is related to ulcer, but what happened was he proved that it is related to gastritis. However, after several evidences it

was proved that H pylori is related to chronic ulcer.

H Pylori infection is more common in areas of poverty, crowding and poor sanitation. It exists in lots of people but does not cause gastritis in all of them because it depends on the host factors. There are also some virulence factors that help H pylori to cause infection, these include:
1- Flagella helps it moving through the thick viscous mucus layer to reach the epithelium and cause the damage.
2- The enzyme urease which converts urea to ammonia. Ammonia is basic and makes the environment in the stomach less acidic so H Pylori protects itself from the acidity.
3- It can attach to the epithelium.
4- CAG A toxin is thought to be important in gastritis and gastric carcinoma (by mechanisms which are not fully understood).
Notice that not all strains have all these virulence factors, and this contributes to different outcomes of H pylori infection.

Morphology
Chronic inflammation with redness and edema.
Under the microscope we see chronic
inflammatory cells mainly lymphocytes,
and plasma cells, we can also find macrophages, and neutrophils.

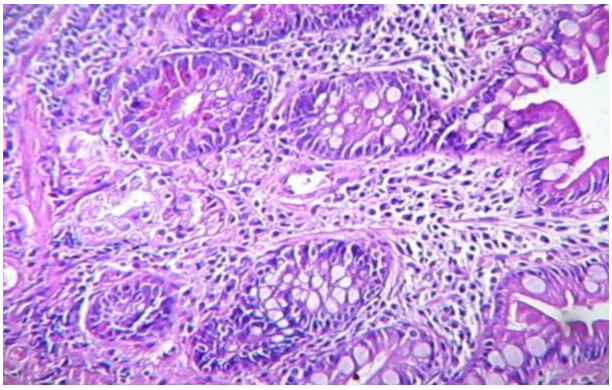


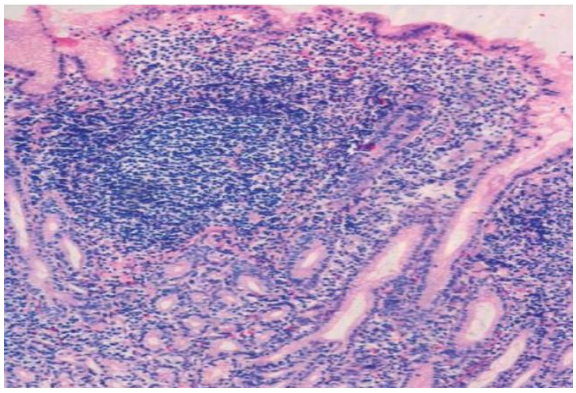


Complications

- Intestinal metaplasia, secretory goblet cells are seen under the microscope, so the epithelium of the stomach changes and is replaced by intestinal mucosa. This could cause adenocarcinoma.

- Lymphoid aggregates might also be seen under the microscope, and this is a precursor for lymphoma.





Left; intestinal metaplasia. Right; lymphoid aggregates.

H Pylori can cause chronic gastritis which predisposes to lymphoid aggregates (leads to lymphoma) and intestinal metaplasia(leads to adenocarcinoma).

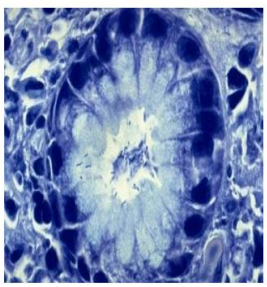
How to diagnose H Pylori?

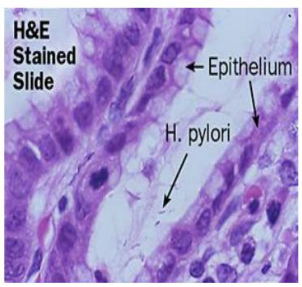
1- Serology to detect anti H pylori antibodies

2- Fecal bacterial detection

3- Urea breath test, H pylori has urease which converts urea to ammonia and carbon dioxide. In this test, the patient is administered with urea containing labeled carbon in it, if the patient has H pylori infection this labeled urea will be converted into labeled carbon dioxide which will be breathed out.

4- Gastric biopsy (curved lines or spiral)





30:00-40:00

5- PCR

6- Culture (stool culture is good, it is not invasive test).

Autoimmune gastritis

It is less common (10%). Autoimmune gastritis does not affect the antrum , while H Pylori mainly affects the antrum. (important for the exam)
It Induces hypergastrinemia (G cells hyperplasia and increased gastrin secretion)

The patient has antibodies against:
1- **Parietal cells**; destruction of parietal cells means no acid secretion and this leads to achlorohydria or hypochlorohydria. With time chief cells are also lost because of atrophy in body type mucosa, this means decreased pepsinogen secretion.
2- **Intrinsic factor** which is important for B12 absorption, absence of the intrinsic factor means low B12 level and pernicious anemia occurs.

Autoimmune gastritis patients have:
1- Hypergastrinemia, gastrin increases.
2- Achlorhydria
3- Pepsinogen decreases
4- Pernicious anemia
5- Atrophy in mucosa, loss of chief cells in the body of stomach

6- Intestinal metaplasia, which predisposes to adenocarcinoma
7-Production of acids decrease .

40:00-44:53

Table; comparison between H pylori and autoimmune chronic gastritis.

	H pylori gastritis	Autoimmune gastritis
site	Mainly antrum	Body.. Spares antrum
Acid production	Usually increased	decreased
gastrin	Normal or decreased	increased
serology	H pylori antibodies	Antibodies to parietal cells and intrinsic factor
complications	Peptic ulcer, adenocarcinoma, lymphoma	Atrophy, pernicious anemia, adenocarcinoma, carcinoid tumor
associations	Poverty, low socioeconomic class	Other autoimmune diseases: thyroiditis, diabetes,

*important for the exam.

Good Luck