Pathology

Sheet Slide

number 5

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Topics to be covered in this lecture:

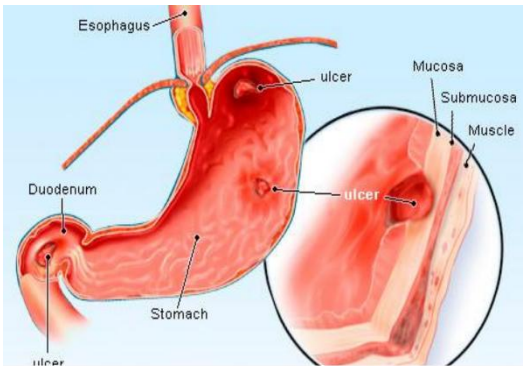
- Peptic ulcer disease.
- Hiatal hernia.
- Gastric neoplasms.

- **Peptic ulcer disease:**
- We have two types of ulcer in the stomach (as we mentioned in the previous lecture): 1- Acute ulcer. 2- chronic ulcer.
- The chronic ulcer in the stomach is what called peptic ulcer disease .
- Causes:
  1-H. pylori. 2-NSAIDS.

Which is commoner?

It depends on the geographic area; for example, in Japan and Jordan H. Pylori is the most common cause of peptic ulcer since this bacteria is common in these regions (almost world wild) , whereas in USA NSAIDS is the most common cause and this is due to:

- ✓ Good control of H. Pylori; as H. Pylori lives in poverty and bad sanitation which they got over it in USA but not in Jordan.
- ✓ Increased aspirin use in aging populations (as a protection of thrombosis).



- Only 5-10% of people having H. Pylori will develop peptic ulcer and that depends on:
  - ✓ The Host factors: The response of the stomach differs from one individual to another.
  - ✓ The pathogenicity of H. Pylori strains , since not all strains are pathogenic .

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- **Can occur in :**
- 1-Duodenum.
- 2-Stomach (between the body and the antrum mainly "antrum")
- 3-Esophagus (reflux esophagitis).
- Duodenum is the most common site of peptic ulcer disease.

(Duodenum : Stomach , 4 : 1).

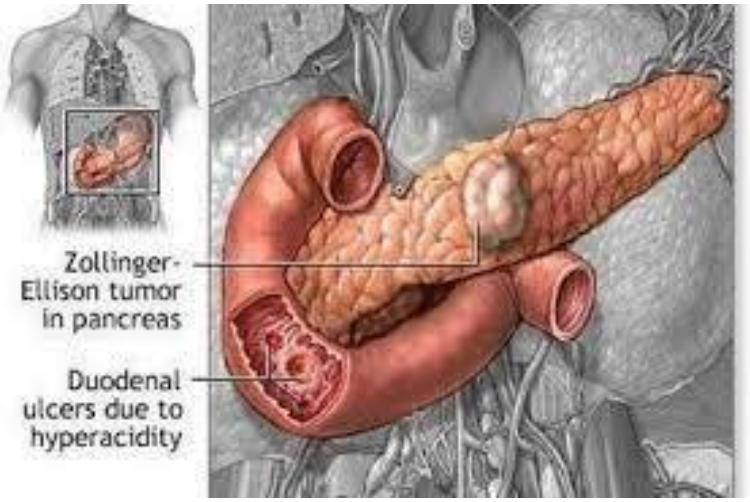
- 10% of males and 4% females develop peptic ulcer in their lifetime.

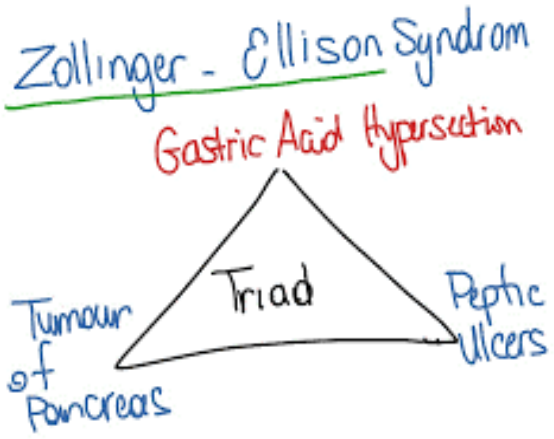
Pathogenesis of peptic ulcer disease:

- Hyperacidity in the stomach is **essential**all types of ulcer.
- Any disruption between the protective mechanism of the stomach and the damaging one will result in ulcer (as mentioned in the previous lecture)

What increases acidity in the stomach?

1- H. Pylori infection
2- Cancer in G-cells which secrete gastrin
   Tumor affecting G-cells in the stomach, duodenum or pancreas (most common)→ increase gastrin production → increase acidity since acid secretion is under the influence of gastrin →resulting in peptic ulcer.
   (point "2" happens in what we call **(Zollinger Ellison Syndrome).**
3- Smoking.
4- NSAIDS : by decreasing the protection of the stomach
5- Alcohol consumption.
6- Psychologic stress.
7- Hypercalcemia: increase gastrin.





Symptoms of peptic ulcer disease:

- Epigastric pain occurring 1-3 hours after meals, is worse at night because when stomach is empty there will be nothing contribute in decreasing its acidity, and relieved by food or alkali .
- Nausea and vomiting.
- Hemorrhage and anemia may occur.

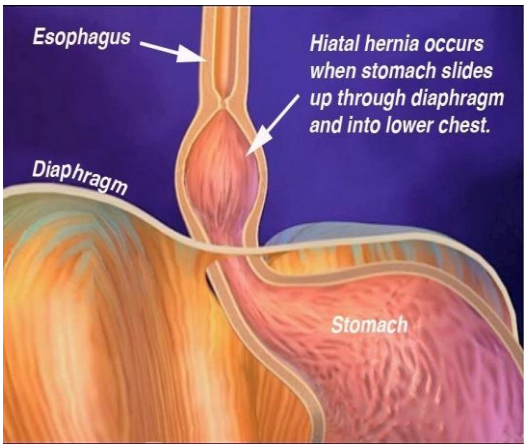
Complications of gastric ulcer:

- Perforation and bleeding: both are very dangerous as you might lose your patient, so surgical intervention is needed in this case.

Treatment of gastric ulcer:

- Surgery was the only treatment for gastric ulcer.
- Nowadays, eradication of H. Pylori and decreasing its load in the body will result in decreasing gastric acidity made surgery unnecessary except in complicated cases (hemorrhage and perforation).

➢ Hiatal hernia:



- Definition: separationofthe diaphragmaticcruraandprotrusion of the stomach into the thorax through the resulting gap.
- Can be congenital or acquired(most common).
- Asymptomatic in 90% of adult cases.
- Fibrosis in the lungs and symptoms similar to GERD may occur.

➢ Gastric neoplasms: (most imp. Topic in this lecture)

- Benign tumors → Polyps
  → Polyp: a mass raised above the mucosa with have smooth surface.
- Malignant tumors → Adenocarcinoma (most imp. one).

Gastric polyps:

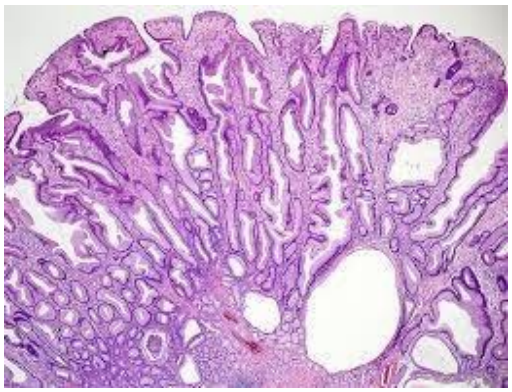
We have two main types of polyps in the GI tract (we have other types but those are the most common):

- 1- Inflammatory and hyperplastic polyps →Hyperplasia alone (division of cells) in the mucosa, so it's usually benign (general rule that they don't transform into malignant tumor)

This is the general rule in the GI tract regarding polyps, <u>except in the stomach</u> as it's mentioned below.

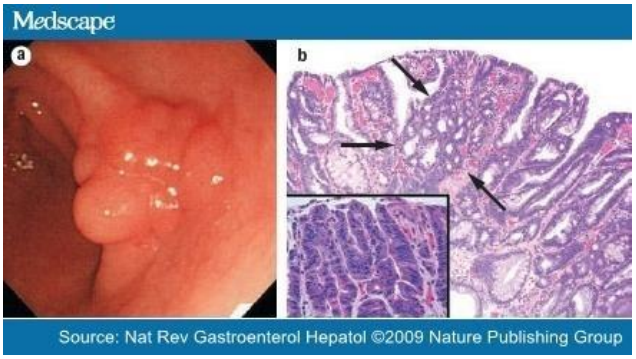
- 2- Adenomatous polyps →Adenomatous polyps **must** have dysplasia, so they might develop adenocarcinoma.

Inflammatory and hyperplastic polyps:



- Hyperplasic polyps in the **stomach**might develop dysplasia (if it gets larger) and eventually adenocarcinoma. **'exception'**
- The risk of developing dysplasia increases in larger polyps; if the polypsbecome larger than 1.5 cm.
- 75% of overall polyps in the stomach.
- Occur in people around 50-60 years.*This picture represent increasing and dilated glands*
- Arise in the background of chronic gastritis that initiates the injury and reactive hyperplasia.
  - ✓ Gastritis (inflammation) → Repair →predisposes to hyperplasia →Hyperplasic polyps.
- If associated with H. Pylori gastritis, polyps may regress after bacterial eradication.

Adenomatous polyps (Gastric adenoma):



- 50-60 years of age.
- Male: Female 3:1.
- Almost always occur in the background of chronic gastritis with atrophy and intestinal metaplasia.
- Risk of developing adenocarcinoma because of dysplasia increases by:
  - ✓ Increasing the size of the polyp to more than 2 cm.
  - ✓ Increasing dysplasia; high grade dysplasia predisposes to cancer more than low grade dysplasia.

Gastric adenocarcinoma:

- The most common cancer in the stomach (90% of stomach tumors), because of its glandular epithelium.
- Most common in Japan, Costa Rica and Eastern Europe(even though the incidence of esophageal cancer is very rare in Japan).

Signs and sypmptoms of adenocarcimoma:

Pain , vomiting and nausea; which are very common symptoms that mimics benign conditions (such as the inflammatory symptoms), so unfortunately we discover adenocarcinomas at very late stage and as a result we lose the ability to cure these patients.

Notes:

- Gastric malignancies are decreasing due to better control of H. Pylori (at least in western countries) , and earlier detection of these polyps , fruits and vegs (protection) .
- Countries that have high incidence of gastric carcinoma(Japan ,Costa Rica) have tried screening through endoscopy and it turns out to be effective as it decreases the overall percentage of cancer However, it is not cost effective in countries that have low incidence o gastric cancer.

Pathogenesis of gastric adenocarcinoma:

- Most important mutations:

✓ Loss of E cadherin (The function of E cadherin → Adhesion)

✓ B catenin mutation

- The main two infections predisposed to gastric adenocarcinoma:

✓ H. Pylori.(the most important)

✓ EBV virus.

Morphology of adenocarcinoma:

- We have two types of gastric adenocarcinoma(Lauren classification):
  - ✓ Intestinal type.

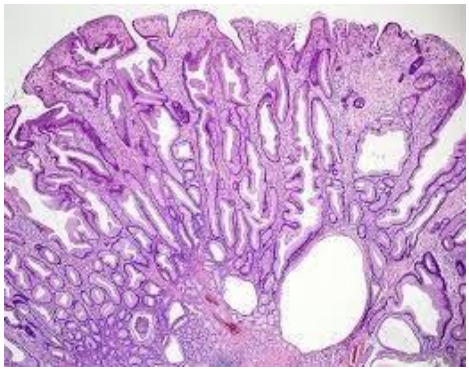
- ✓ Diffuse type.

Type	Intestinal	Diffuse
Morphology	Looks like the glands of the intestine.	Individual cells (no gland appears)
Presence of mass	Comes with a mass and histologically has glands	No mass The wall of the stomach become very thick, white and solid **(linits plastica)***
Incidence	Occurs mainly in high risk areas, so it is the one ***related to chronic gastritis,dysplasia and adenoma*** and ***the one decreasing in incidence as well.***	Incidence is uniform across countries.
Male : Female	2:1	1:1

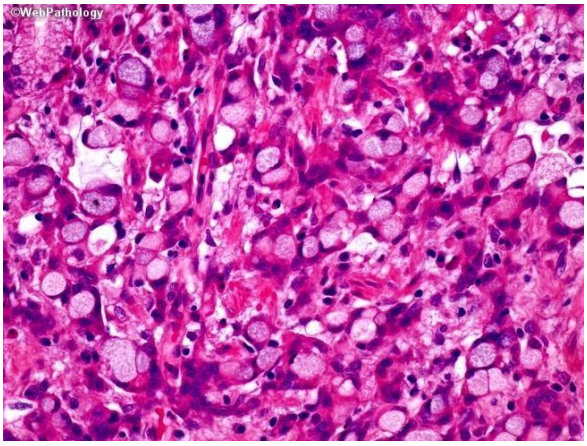
Notes:

- In the diffuse type, there is production of mucus by the tumor cells which will eventually pull the nucleus to the periphery, and this gives it the shape of a ring (signet ring cell), mainly in the cardia, there is no known pre-cancer lesions in this type .
- The intestinal type occurs in people between 50-60 in age , mainly in the body and the antrum of the stomach
- Linitis plastica : thickening in the wall of the stomach due to adenocarcinoma in the stomach (diffused type)

Intestinal type

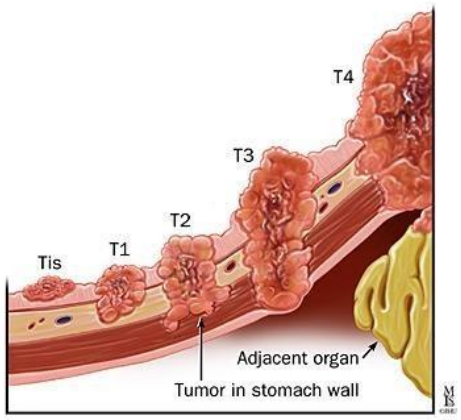


Diffuse type



Prognosis:

- Depends on the TNM stage:
  - ✓ Tstage: describes the size of the original (primary) tumor, and whether it's superficial or has invaded nearby tissues. (more invasion , T increase , prognosis worse)
  - ✓ N stage: describes whether there is lymph nodes involvement or not and the number of lymph nodes that are involved.
  - ✓ M stage: describes distant metastasis.



- As T increases → N increases → M increases → worsens prognosis

Outcome:

• 5 year survival for early lesions: 90% even if there is lymph node metastasis.

Which means: if we have 100 treated patients, after 5 years, 90 out of 100 will stay alive. (5 years survival= how many patient survive after 5 years)

• 5 year survival for advanced stage: 20%

• Overall 5 year survival 30%(late detection, because of the common symptoms that we've already talked about).

Other malignant tumors:

- ## Lymphoma:
- Because of lymphoid aggregate that result from H-pylori which called :mucosa associated lymphoid tissue
- MALTOMA = mucosa associated lymphoid tissue lymphoma
- It's an indolent , slow growing (low grade) lymphoma arising from the lymphocytes within the gastric mucosa

- Usually treated only by H. Pylori eradication , sometimes by chemotherapy
- Other types of lymphoma can arise in the stomach.
- Maltoma is the main lymphoma arising in the stomach, we'll be talking about other types of lymphomas in hematology.

Carcinoid tumor:

• Neuroendocrine tumors arising from neuroendocrine cells like the G cells.

• Can be associated with endocrine cell hyperplasia, chronic atrophic gastritis and Zollinger Ellison syndrome. (precursor

• Symptoms depend on the hormone produced by the tumor cells.

• Gastric and esophageal carcinoids have better prognosis than those in the jejunum.

GEST:

- Mesenchymal tumor of the stomach and other parts of the GIT.
- Peak at 60 years of age.
- Males more than females.
- Cell of origin: interstitial cell of Cajal.
- Majority have c-kit mutation (a tyrosine kinase)
- We can treat patients by targeted therapy against the c-kit, by a drug called imatinib.

It's the possibility of having a dream come true that makes life interesting!

GOOD LUCK