Pathology

Doctor 2017 | Medicine | JU | GI

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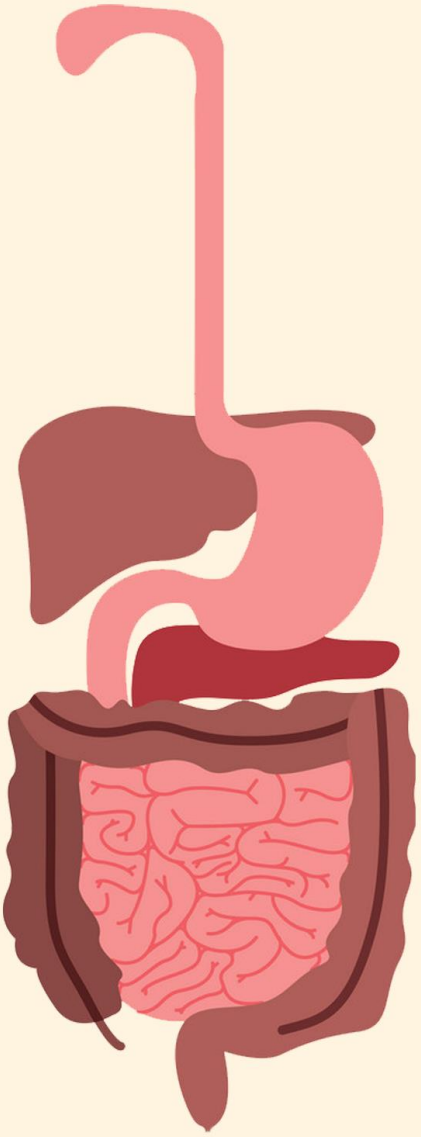


2nd system - GI

pathology of stomach

*before we start discussing the pathology of the stomach we should look at the normal anatomy and histology of the stomach :

-the stomach parts are : first the gastroesophageal junction -> cardia -> fundus & body which represent most of the surface are of the stomach -> antrum -> pylorus (pyloric canal for communication of the stomach with the duodenum through gastroduodenal junction/sphincter.

-the normal histology : different areas of the stomach have different cellular population and different functions for the cell present at each part

Part of stomach	cardia	Body & fundus	Antrum
Type of cells	Mucin secreting foveolar cells	Parietal cells and chief cells	Neuroendocrine G cells and Antral glands
Function of cells	Secretes mucin -_-	Parietal cells : secrete HCL acid Chief cells : Secrete pepsin (the digestive enzyme of stomach)	produce gastrin
Thickness of mucosa	Less than other parts	Thicker than cardia	**She didn't say anything :/**

Side notes about the schedule above :

-the parietal cells have abundant pink eosinophilic cytoplasm while the chief cells have bluish cytoplasm when staining by H&E (hematoxylin and eosin)

- sometimes it's difficult to view G cells by H&E stain so we use certain immunohistochemical stains to see them

In addition regarding histology we have 4 layers of the wall of the stomach :

1)Mucosa which we have discussed already

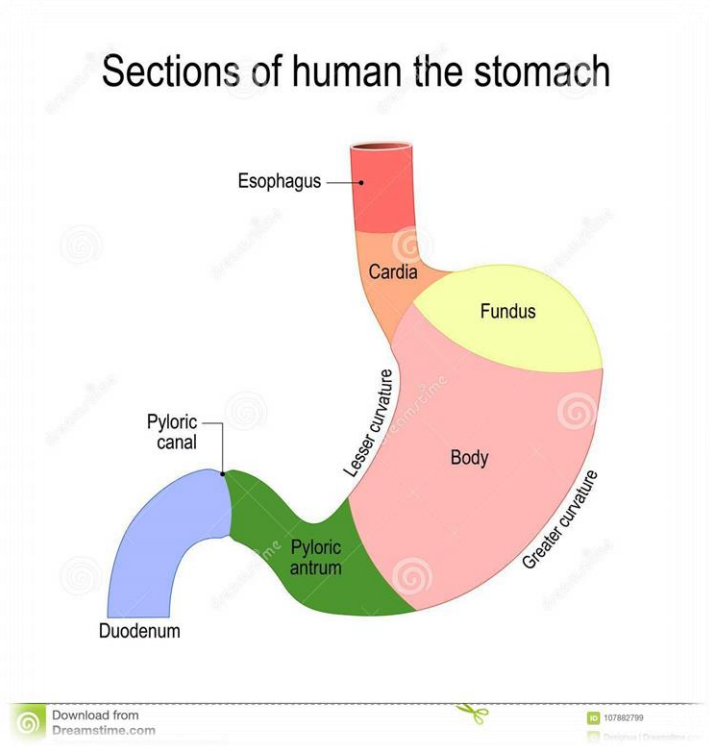
2)muscularis mucosa , that separates the mucosa from the submucosa

3)submucosa

4) the muscularis propria then adventitia and serosa of the stomach

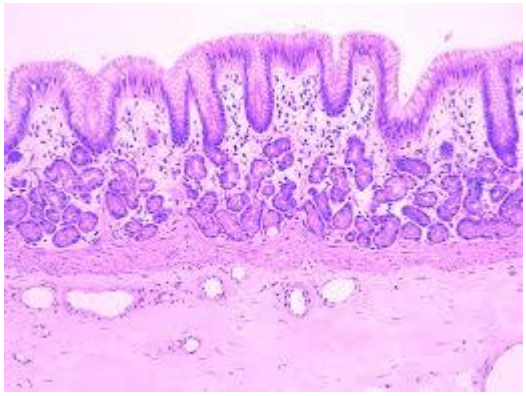
[these 4 layers are constant throughout the stomach however the cellular content are different]

In the drawing below u can see the different parts of the stomach and u can see that it is connected proximally to esophagus by the gastroesophageal junction and at the distal part of the stomach it opens to the duodenum through the pyloric canal or pyloric sphincter . also note that the cardia it's just below the esophagus and the fundus is the upper part of the stomach and , the lesser curvature at the area connecting the esophagus and duodenum from the right side and the to the left side we have the greater curvature



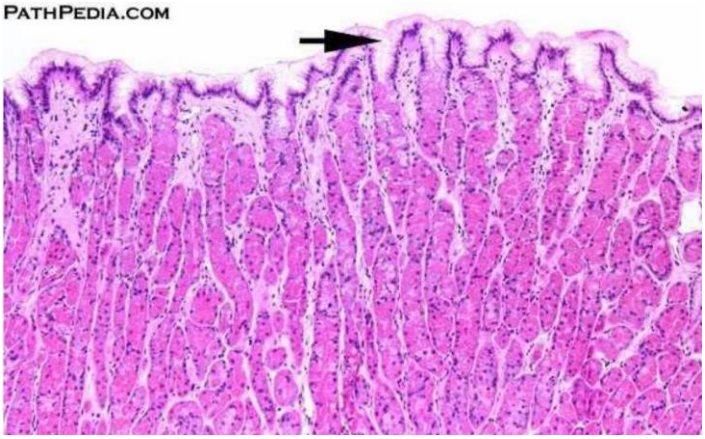
Now in the 3 pictures above a review of the normal histology appearance of each part of the stomach using H&E:

1)Cardia:



Note that surface epithelium is highly mucinous and contains cytoplasmic mucin secreting foveolar cells. Also note the thickness of the mucosa

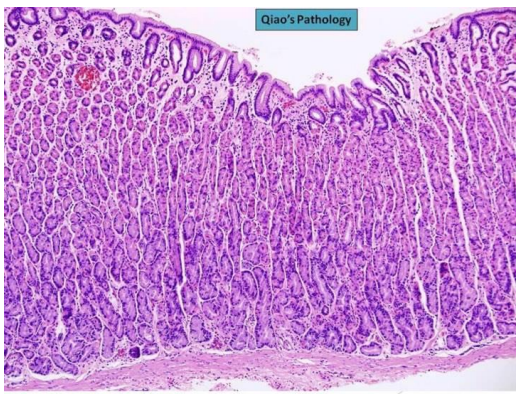
2)Body and fundus:



Note the eosinophilic parietal cells and the bluish chief cells

Clinical note: in GASTRITIS of both the Body and the Cardia, parietal cells will be lost and won't be seen under the microscope, this is a hint for this disease

3) Antrum:



in the antrum you
can see a lot of antro glands(which secrete mucuos),BUT NO parietal(acid secreting cells)

Just note the G-cells

Now we are going to talk about pathology of the stomach which is subdivided into: 1) Inflammatory conditions & 2) neoplastic conditions

1)Inflammatory conditions are very common and they are subdivided into 4 categories those that are acute and those that are chronic:

A)Acute Gastritis B) Chronic Gastritis

C)Acute peptic ulcer D) Chronic peptic ulcer

Acute conditions **chronic conditions**

-peptic: any area that is exposed to the acid and pepsin of the stomach and it could be in the stomach or the lower part of esophagus or the first part of the duodenum or other parts of the GI-tract where u find ectopic gastric tissue the produce acid (HCL) and pepsin so the word peptic is not necessary a disease related to the stomach

ACUTE GASTRITIS AND GASTROPATHY :

These 2 terms are related to similar conditions ,however the main difference between acute gastritis and gastropathy in the morphology under the microscope when we take a gastric biopsy : (see the table in the next page)

Clinical condition	Acute gastritis	Gastropathy
Morphology under microscope	U might see neutrophils indicating inflammation	u only see regenerative changes in the mucosa due to the damage but u don't see inflammatory cells
Causes	1)use of NSAIDS which disrupt the protection of the mucosa 2)alcohol 3)reflex of bile content from duodenum to the stomach either: a) after certain procedures. b) due to physiological stress.	**SAME:D**
Clinical features	Variable , some are Asymptomatic but the others express : nausea and vomiting and epigastric abdominal pain depending on the severity of condition	**SAME:D**

PATHOGENESIS for acute gastritis and gastropathy and even for chronic gastritis and peptic ulcer disease , all these diseases are interrelated in a way or another because the underlying mechanisms are almost the same :

In the stomach we have a very low PH and the media in the stomach and gastric juices are highly acidic and this is a damaging factor by it's nature and can cause damage to the gastric mucosa if it comes in direct contact with it, so the acidity and the pepsin that is present in the juice are NORMAL damaging factors for the mucosa however the mucosa has developed many defensive forces. Usually the development of acute or chronic gastritis develops as a result of imbalance between these protective factors and between the injurious stimuli that we talked about them in the table previously

-the protective factors are variable:

1)surface mucous secretion by the surface epithelial cells which forms a layer of slippery mucous over the epithelial cells protecting them from damage by acid and pepsin

2)bicarbonate ion produced by epithelial cells which will buffer the solution (near the mucous layer) because it gives a slightly alkaline medium near the epithelium

3)very good mucosal blood flow to the whole GI-tract. This will give a high regenerative capacity of the GI-tract in all of it's parts

4)prostaglandin synthesis from arachidonic acid (AA) by cyclooxygenase enzymes (COX)prostaglandin provides protection by increasing mucous secretion and bicarbonate production and increasing the blood mucosa. so any interference with prostaglandin secretion (mainly due to non-selective NSAIDS) will cause an imbalance between protective and injurious factors.

***The injurious factors** are also variable and they are represented by :
1)H.pylori infection , they produce urease enzyme that splits urea → ammonia and the presence of ammonia interferes with the transport of bicarbonate ions to the mucous layer thereby decreasing bicarbonate concentration in the mucous thus decreasing the protection by giving a higher acidic environment
2)NSAIDs since they inhibit cyclooxygenase enzyme -> inhibit PGE2 synthesis and we need them. Both selective COX2 and non-selective cause damage but the non-selective do so more powerfully while selective cox2 milder effect so NSAIDs work by 2 ways (inhibiting PG and directly damaging the epithelial cells)
3)Tobacco
4)gastric hyperacidity whatever the cause of it
5)reflex of bile
6) ischemia due to any cause (decreased blood flow, altitude, etc…) to the GI-tract can alter the defensive and regenrative mechanisms.
7)uremic patients (patients with renal failure)
8) old age also plays a role because mucuous and bicarbonate secretions both decrease with older age
9)Harsh chemicals can cause DIRECT epithelial cell injuy like in consumption of acid or alkaline materials.
10)chemotherapy when taking drugs that interfere with DNA synthesis and mitotic capacity can affect the GI-tract by decreasing proliferation of the cells
-All of these damaging factors do their effect either by directly damaging the cells or by decreasing the protective mechanisms
So in general as a rule [for acute or chronic gastritis or for peptic ulcer disease to develop we should have an imbalance between the protective factors of the stomach and the damaging factors] “reduction of protection or increase in damaging “

***Morphologic features** of acute gastritis and gastropathy are non-specific or even minor and the only change that can be seen in

- endoscopy: is just mild hyperemia and edematous mucosa with prominent vasculature

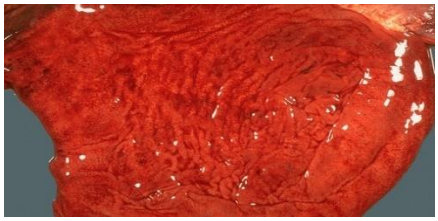
-With gastric biopsy we can see: hyperemia , congestion of the vessels and edema in the lamina propria. we can also see inflammatory cells like neutrophils , lymphocytes and plasma cells but they are not very prominent

-Keep in mind that the presence is not a requisite for diagnosis of acute gastritis , it's mainly the erythema , hyperemia and congestion

-Presence of neutrohpils doesn't mean it's acute , it means that there Is an active inflammation and it can be seen in acute gastritis also in chronic gastritis

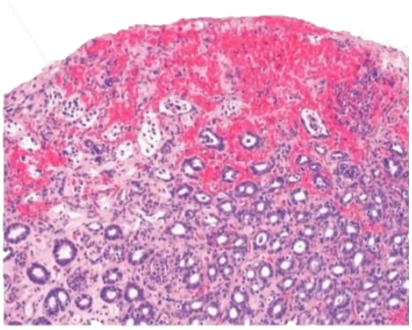
Intact surface epithelium is seen but in more severe cases we can see erosions and hemorrhage and If we see them we call it (acute erosive hemorrhagic gastritis)

The picture below is what the doctor sees when he does an endoscopy of acute gastritis and note that the only clue during endoscopy is hyperemia and redness :



While when u take a biopsy you will see the histologic appearance shown below and u should note the edema in the lamina propria and the congestion of blood vessels and in this slide u can see the erosion at the surface and the mild hemorrhage indicating that it's an (Acute erosive hemorrhagic gastritis stage):

You can also immune cells attacking the glands.



***CHRONIC GASTRITIS**:

-very common disease in outpatient clinics and in gastroenterology clinics and it's the major cause of upper endoscopic procedures performed for patients

-it's different from acute gastritis in which the symptoms are less severe but more prolonged so the main difference between acute and chronic gastritis is the duration & severity of the symptoms

-CAUSES :

1)helicobacter pylori associated gastritis (gram negative bacillus bacteria).It's the MOST COMMON CAUSE of chronic gastritis (accounts for almost 75-80% of cases)

2) autoimmune atrophic gastritis , less than 10% of cases

3) **chronic** use of NSAIDs

4)radiation injury

5) chronic bile reflux

From 3) to 5) are less common causes

-CLINICAL FEAUTRES :

Symptoms of chronic gastritis are somewhat similar to those of acute gastirits but they are less severe and more prolonged and they are :

1)nausea

2)upper-abdominal discomfort

3)vomiting

4)hematemesis (uncommon)

(1-3 are the main symptoms)

-HELICOBACTER PYLORI GASTRITIS (most common cause of chronic gastritis)

Caused a revolution in medicine after the discovery of the association between H.pylori and peptic ulcer disease because before that it was never thought that chronic gastritis may be caused by a pathogen.

-it's spiral shaped or curved and it's Gram negative bacillus

-they can be seen under the light microscope on gastric biopsy specimen on the mucous layer that is present over the mucosa and they have developed many virulent factors in addition to protective factors to withstand gastric juices

-they can be demonstrated by H&E and other special stains like Giemsa stain

-it's present in almost all duodenal ulcers and it's present in the stomach of patients with duodenal ulcers and the majority of gastric ulcers or chronic gastritis so this will leads us to the fact that ALL duodenal ulcers are caused by H.pylori but Gastric ulcers and chronic gastritis MOST of them are caused by H.pylori but they have other causes

-the H.pylori acute infection is usually subclinical (silent) and it passes without any symptoms however the chronic gastritis is the disease that is responsible for most symptoms.

This bacteria is usually acquired during childhood through drinking contaminated water or ingesting contaminated food it can colonize the stomach for years before causing any symptoms. The rate of colonization varies among different populations(from as little as 10% of the population to as much as 80%) according to the geographic location. It is more common in areas with poor sanitation, crowding and poverty (epidemiology of chronic gastritis by H.pylori)

-loves to live in the antrum of the stomach causing antral gastritis and the antral gastritis will lead to the stimulation of G-cells in the antrum →increased gastrin hormone production → stimulate parietal cells to produce HCL acid → Acid over production (**hypersecretion**) and on the long run will cause peptic ulceration

-in severe cases the inflammation can extend all over the stomach affecting the body or the fundus causing pan gastritis and damage to the parietal cell so in these severe cases the bacteria can cause **hyposecretion** of the acid which we call it Achlorhydria , In these severe cases there will be intestinal metaplasia and high risk of gastric cancer. Most cases of gastric cancer are associated with a background of chronic gastritis and intestinal metaplasia

Note : many of us may harbor the H.pylori in their stomach without causing a disease but in some patients it may cause a disease :/

-pathogenesis of H.pylori :

It usually lives **in the mucus layer**. it's usually non-invaisve and even if it invades the mucosa this is not the mechanism by which it cause the disease instead it cause the disease when it's in the mucous layer and it has developed many mechanisms to protect itself from acidic gastric mucosa (the gastric acidity is an important defense mechanism by the stomach against pathogens so most pathogens or bacteria cannot withstand this acidic environment)

-H.pylori virulent factors (how it protects itself from gastric mucosa):

1)presence of flagella that allow motility which helps them to move within the mucous layer

2)presence of urease enzyme that splits urea to ammonia and ammonia alkaline with high PH so it surround itself with a localized alkaline media to protect itself from the acidic environment

3)the presence of Adhesins that helps the bacteria to adhere to the foveolar epithelial cells of the stomach

4)production of toxin and the main toxin that is produced is the Cyto-toxin associated gene A that encodes the CagA which is very important for cancer development because it damages the epithelial cells

-MORPHOLOGY :

When the patient comes with the symptoms of chronic gastritis (epigastric pain,nausea and vomiting) the gastroenterologist offers an endoscopic procedure to visualize the gastric mucosa, or he can take a biopsy and visualize it.

Endoscopy : the most important feature is the redness (**hyperemia**)

Biopsy : the **preferred site is the antrum** because H.pylori loves to live in the **antrum** and it doesn't produce any presence in the acid producing mucosa like in the fundus or the body EXCEPT in very severe cases and remember that when it causes duodenal ulcers it's still present in the stomach but the hyperacidity is the thing that cause duodenal ulcers and we see inflammatory response in the mucosa predominated by plasma cells , lymphocytes , macrophages in the lamina propria and the amount of these cells differ according to the severity of gastritis.

In addition **in active disease** we can see NEUTROPHILS either in lamina propria or attacking the glands of the antrum and sometimes causing small abscess. the H.pylori can be seen within the mucous layer

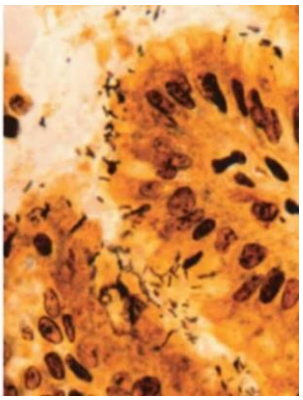
In more severe cases we can see lymphoid aggregates (lymphoid follicles with reactive germinal center as part of the mucosa associated lymphoid the presence of these aggregates increase the risk of MALT lymphoma (mucosa associated lymphoid tissue = MALT)

In long standing and complicated disease we can see intestinal metaplasia in which we can see intestinal type epithelium with Goblet cells. this metaplasia can progress to dysplasia and then to invasive adenocarcinoma

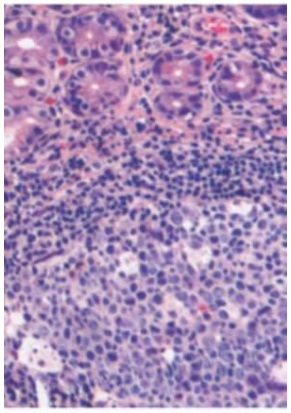
So H.pylori can increase the risk for : 1) MALT Lymphoma

2) gastric adenocarcinoma

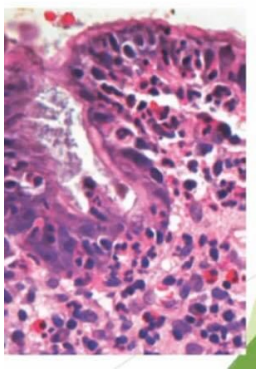
In the picture below the stain is warthin silver stain and u can see the curved H.pylori in black



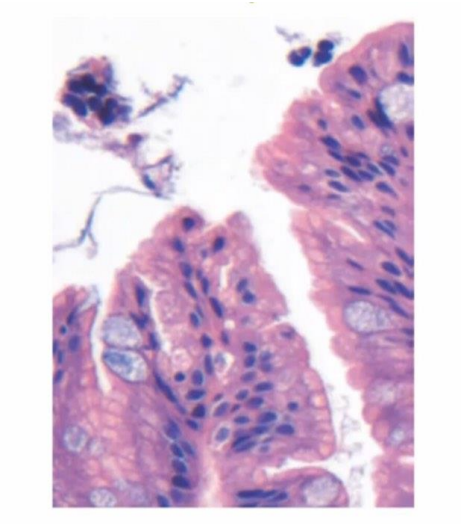
While in this picture u can notice the lymphoid follicles with reactive germinal center and a lot of lymphocytes between the gastric glands, this indicates chronic gastritis because we have a lot of chronic inflammatory cells



In this picture you can see a lot of neutrophils which means that this section is taken from a patient with chronic ACTIVE gastritis:



This picture will show the feared complication of long standing chronic gastritis illustrated with H.pylori infection. As you can see intestinal metaplasia is marked by the presence of Goblet cells characterized by abundant cytoplasm filled with mucin (grey discoloration). The presence of such cells increases the risk of dysplasia and gastric adenocarcinoma. Any patient with such developed intestinal metaplasia should be followed with multiple-regular biopsies to detect any dysplastic events ealry before the transformation into invasive malignancies :



-How to diagnose a patient with H.pylori chronic gastritis :

1st the patient presents with the symptoms (epigastric pain , nausea and vomiting) and the **long duration** of these symptoms the then the doctor offers some investigations that are non-invasive then some invasive investigations

The non-invasive investigations : -blood test (serologic test) for Anti-H.pylori antibodies which are the IgA and IgG antibodies. The problem with this test is that it doesn't always mean that the patient is currently having an active disease because if the patient had a previous infection with H.pylori he would have already developed an immune reaction and igG antibodies would be found in the blood sample.

-The other non-invasive method is stool test for H.pylori microorganism.

-Finally the last noninvasive test is the Urea breath test

Urea breath test : the main idea about it is that we detect the products of the urease enzyme produced by the bacteria. The patient will consume (drink) a solution that contains urea material that contain radio-labeled carbon and then

the patient is left for 20 mins and then we detect the presence of the radio-labeled carbon by giving the patient a bag to breath in
The urease that the bacteria produce will break urea into ammonia and Co2 and this Co2 contain the radio-labeled carbon so it's presence in exhaled air = positive bacterial infection
The invasive investigations are : upper endoscopy for these patients in order to visualize the stomach first and then taking gastric biopsy which is considered the **best way to detect the presence of chronic gastritis** and inflammatory reaction and visualizing the H.pylori bacteria in the mucous layer and remember that the best site for the biopsy is the antrum of the stomach then this biopsy can be used for bacterial culture (colonizing bacteria) or PCR test for bacterial DNA (polymerize chain reaction)

-Treatment : eradication therapy for H.pylori which is formed of at least 2 antibiotics In addition to the proton bump inhibitors to decrease the gastric acidity . the treatment may need a long period of time and the patient should complete the medications in order to eradicate the bacteria.
Sometimes when patients don't complete the medications the may have a recurrence of h.pylori which means that the bacteria wasn't eradicated form the first treatment

***AUTOIMMUNE ATROPHIC GASTRITIS**
This type of gastritis is characterized by antibodies produced by the body against the parietal cells(acid and intrinsic factor producing cells) so it's an immune mediated disease directed against the parietal cells(in the body and fundus). The damage to these cells by this immune reaction will lead to the loss of acid production and the loss of intrinsic factors production. the antibodies can even be directed to the intrinsic factor themselves causing their inactivation. These intrinsic factors normally bind to vitamin B12 and aid in it's absorption in the distal part of ilium, so the inactivation of these factors or the lack of their production will lead to → vitamin B12 deficiency and pernicious anemia which has many neurological manifestations .
Another feature of autoimmune gastritis is the reduced serum level of pepsinogen 1 which is produced by cells of the body and fundus of the stomach. and since the damage in autoimmune gastritis is to this part of the stomach we will have reduced levels of pepsinogen 1 in the serum.

As a response to the loss of acid production, we will have a reflex G-cell hyperplasia In the antrum.
Autoimmune gastritis Typically spares the antrum unlike H.pylori gastritis which typically affects the antrum. Also autoimmune gastritis is usually remarked by Achlorhydria unlike H.yplori infection which is remarked by an increased acid production.

PATHOGENESIS OF AUTOIMMUNE GASTRITS :

(It's immune mediated) antibodies produced by the body are directed against the parietal cells of the body and the fundus of the stomach → loss of these cells → reduction of acid and intrinsic factor secretion , the reduced acid production → reflex hypergastrenemia and hyperplasia of antral gastrin producing cells (G-cells of the antrum)
Deficient intrinsic factors → vitamin B12 deficient absorption in the ilium and to megaloblastic anemia which have many neurological manifestations. A minority of patients will develop megaloblastic anemia.
We also have some chief cell damage in the body of the stomach resulting in reduced pepsingogen1 production
With the progression of the disease there will be total loss of the parietal cells in the body and the fundus with thinning and atrophy of the mucosa and loss of the folds of the stomach at these sites

-MORPHOLOGY IN AUTOIMMUNE GASTRITIS

The H.pylori organisms are **absent** and the preferred biopsy site is the body or the fundus of the stomach not the antrum of the stomach because if you take an antrum biopsy it will be normal especially if taken during early stages of the disease
The body and fundus of the stomach will have a loss of parietal cells,with time there will be diffuse atrophy and thinning of the wall of the body and fundus and loss of folds due to loss of acid producing cells
Main inflammatory infiltrate : lymphocyte , plasma cells and macrophages (chronic inflammatory cells) and less likely you find the neutrophils like those which we mentioned in H.pylori gastritis
On the long run the patient might develop intestinal metaplasia due to the Achlorhydria and it could progress to dysplasia and then to invasive adenocarcinoma so **in BOTH H.PYLORI GASTRITIS AND AUTOIMMUNE GASTRITIS THERE IS A RISK FOR DEVELOPMENT OF GASTRIC ADENOCARCINOMA** but here also in autoimmune gastritis we have G-cell hyperplasia in the antrum as

response for the loss of acidity which can progress to NEUROENDOCRINE TUMORS

Autoimmune gastritis may increase the risk for : 1) Gastric adenocarcinoma
2) neuroendocrine tumors

While H.pylori gastritis increase the risk for : 1) Gastric adenocarcinoma
2) MALT lymphoma

So we consider it Auto-immune disease

-CLINICAL FEATURES :

This type of gastritis mainly affect female patients so there is a slight female predominance and patients are in their 60's (slightly higher age than patients for H.pylori gastritis)

-it's often associated with other autoimmune diseases (autoimmune diseases tend to cluster with each other)

This table is very important

Feature	*H. pylori*–Associated	Autoimmune
Location	Antrum	Body
Inflammatory infiltrate	Neutrophils, subepithelial plasma cells	Lymphocytes, macrophages
Acid production	Increased to slightly decreased	Decreased
Gastrin	Normal to markedly increased	Markedly increased
Other lesions	Hyperplastic/inflammatory polyps	Neuroendocrine hyperplasia
Serology	Antibodies to *H. pylori*	Antibodies to parietal cells (H^+,K^+-ATPase, intrinsic factor)
Sequelae	Peptic ulcer, adenocarcinoma, lymphoma	Atrophy, pernicious anemia, adenocarcinoma, carcinoid tumor
Associations	Low socioeconomic status, poverty, residence in rural areas	Autoimmune disease; thyroiditis, diabetes mellitus, Graves disease

***ACUTE GASTRIC ULCER (STRESS ASSOCIATED GASTRIC DISEASE)** because most often it will develop as a result of physiological stress.

-examples on severe physiological stress:

1)trauma

2)extensive burns in which a large surface area of the skin is involved

3)increased intracranial pressure

4) patients undergoing major surgeries

5)patients with severe medical illness (like critically ill patients/ ICU patients)

*acute gastric ulcer are divided into several types according to the underlying cause and according to their location within the stomach

Type	Stress ulcer	Curling ulcers	Cushing ulcers
Cause	Critically ill patient like patients with shock , sepsis ,trauma	Severe burns or trauma	Elevated Intracranial disease
Location	☹	Proximal duodenum	Stomach , duodenum , esophagus

Note: cushing ulcer have high risk of perforation (rupture to peritoneum and cause peritonitis)

***PATHOGENESIS of stress ulcers** , involves several mechanisms which usually result in local ischemia (reduced blood flow to the stomach) ,this can occur as a part of :

1)systemic hypotension

2) heart failure

3)splanchnic vasoconstriction (vasoconstriction of blood vessels supplying the GI-tract only)

4) systemic acidosis → lowering the PH and increasing acidity →hence damaging the cells.

-Note : the COX2 expression in the gastric mucosa is considered a protective Factor against stress ulcers.

-The pathogenesis of Cushing ulcer involves direct vagal nerve stimulation. As we know, the vagus nerve supplies the stomach and is responsible for the acid hypersecretion, so when we have a direct stimulation of the vagus nerve(as a result of increased intracranial pressure) acid hypersecretion will take place causing damage to the cells. This is the mechanism by which cushing ulcers occur.

so to summarize the pathogenesis :

Stress ulcer → local ischemia

Cushing ulcer → Acid hypersecretion due to vagal nerve stimulation

***MORPHOLOGY**

Acute gastric ulcers are usually diagnosed during endoscopy or depending on the clinical manifestations patients present with (**NOT BIOPSY**).

Upon endoscopy, acute gastric ulcers are usually seen as multiple lesions unlike chronic ulcers which are seen as a single ulcer.

Acute gastric ulcers can be shallow to deep so they are variable, but the important feature is that the surrounding mucosa around the ulcer Is unremarkable (**normal**) unlike cases of chronic peptic ulcers in which the surrounding muosa is seen to be **abnormal.**

In acute gastric ulcer the ulcers are variable in size and are usually less than 1cm in diameter and can occur anywhere in the stomach. The base of the ulcer can have a brown to black discoloration due to the effect of the acidic gastric juices on the blood that result from the bleeding gastric ulcer (the red blood -> black or brown) also they have NO Scarring unlike chronic peptic ulcers.

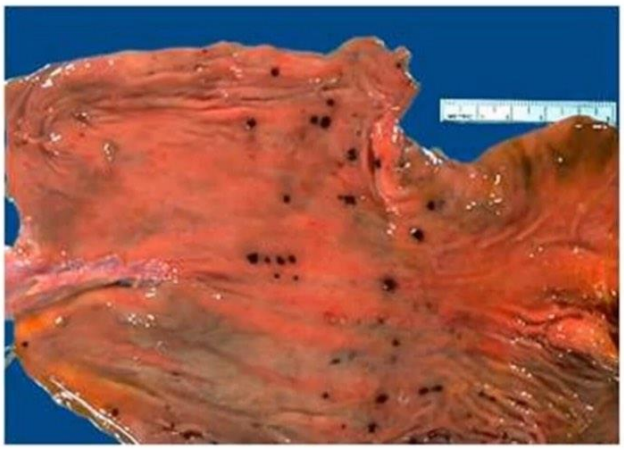
So the main differences between the acute peptic ulcer and the chronic peptic ulcer are : 1) the surrounding mucosa : in acute → normal , chronic → abnormal

2) Acute → no scarring , chronic → scarring

3) Acute → multiple , Chronic → single ulcer

Acute gastric ulcers can heal with complete re-epithelization which occurs days or weeks after the removal of the injurious factors. So when the underlying causes are managed ,ulcers will disappear.

-in the picture below you can see all features of acute peptic ulcers that we have discussed before :



So if the gastric endoscopy of a critically ill patient shows multiple small black ulcers with normal surrounding mucosa distributed all over the stomach you should think of **ACUTE** GASTRIC ULCER

***CLINICAL FEATURES :**

Severely ill patient that started complaining from :

1)nausea and vomiting, sometimes the vomit is bloody stained (**coffee-ground hematemesis**) , the coffee ground appearance is because of the action of gastric juices of the stomach on the fresh blood.

A minority of cases may present with higher degrees of hemorrhage being in need of blood transfusion.

2)melena , indicating upper GI bleeding

3) perforation complication (serious complication)

PREVENTION: the most important thing is prophylaxis, so any patient who is critically ill or is suffering from physiological stress should be offered prophylaxis by proton bump inhibitors. these inhibitors decrease the acidity of the stomack protecting the mucosa from ulceration.

-note : the outcome depends on the severity of the underlying causes, so we treat the underlying causes for complete healing and complete re-epithelization of the mucosa.

((مدام وصلت هون و خلصت هاي المحاضرة المقرفة كافئ نفسك ب أي اشي بالحياة))

U DESERVE IT

I'm so proud of anyone who is reading this since u finished it

أي حد وصل هون لأنو عم بيعد صفحات و يشوف كم ضايلو لا عزاء له

THIS SHEET IS ESPICALLY WRITTEN ON THE HONOR OF : Rawand<3

Good luck all <3

FINALLY THE END

:DDDDDDD