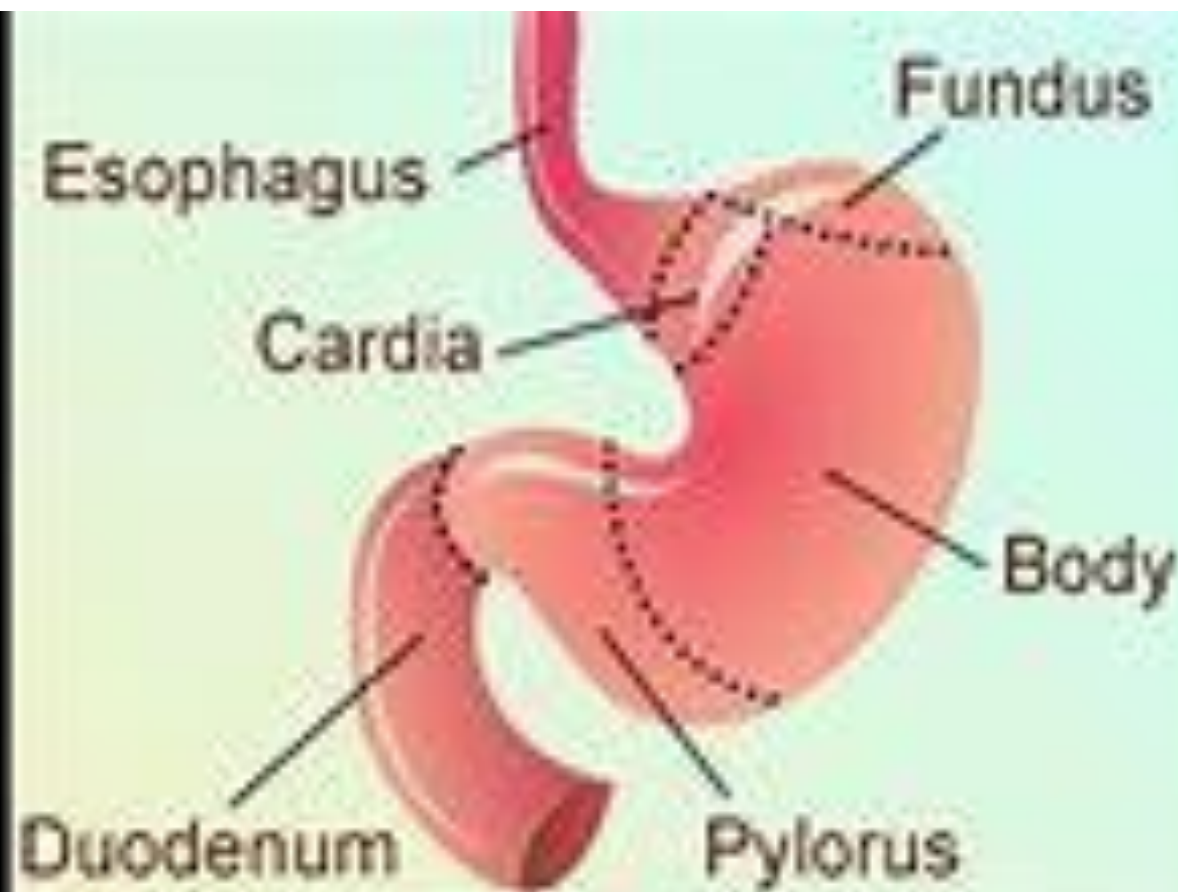


# Gastritis



PhD, assoc. prof. Rodica Bugai



After receiving ingested food from the esophagus, the stomach breaks it down into chyme, and empties it into the duodenum.

# Gastritis definition

**Gastritis** can be an acute or chronic gastric disease, characterized by inflammatory lesions produced by various etiologic and pathogenic factors.



# Gastritis classification

Gastritis classification is as follows:

## **1. Clinical evolution**

A. Acute.

B. Chronic.

# Gastritis classification

## 2. Etiology

### A. Infectious:

-Bacterial: H. Pylori (mostly), Helicobacter Heilmannii, alpha hemolytic Streptococcus, Staphylococcus etc.

-Viral: Cytomegalovirus, Herpes-virus

-Fungal: Candida

-Parasites: Strongiloides, Toxoplasma etc

B. Autoimmune : Atrophic gastritis with Biermer anemia.

C. Drug-induced : NSAIDS(nonsteroid anti-inflammatory) etc.

D. Specific: Crohn's disease, eosinophilic gastritis, lymphocytar gastritis.

# Gastritis classification

- *Type- A* (autoimmune)
- *Type B* (produced by H. Pylori infection)
- *Type C* (chemical - usually related to chronic bile reflux or NSAID and aspirin intake)

# Gastritis classification

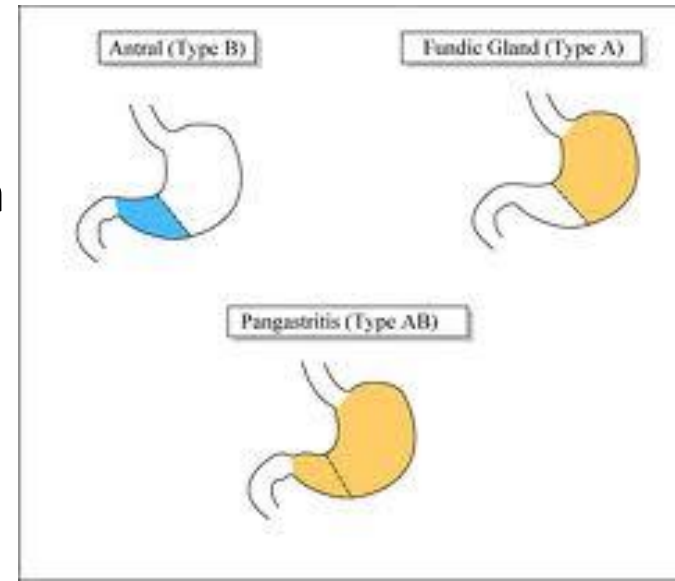
## 3. Endoscopic

### A. *Endoscopic forms of gastritis:*

- erythematous exudative
- maculo-erosive
- papulo-erosive
- atrophic
- hypertrophic
- hemorrhagic
- phlegmonous

### B. *Classification by extension:*

- antral-type B-produced by H. Pylori infection
- fundic-Type A-autoimmune (generating Biermer anemia)
- pangastritis.



# Gastritis classification

- **4. Histologic**

**A. Acute gastritis** - numerous neutrophils localized intraepithelial, in the lamina propria or aggregated in the glandular lumens (cryptic abscesses).

**B. Chronic gastritis** - immuno-competent lymphocytes and plasmocytes. It evolves in some decades to atrophic gastritis. The activity degrees depend on the presence of neutrophils and the degree of infiltration in the profound layers. Low activity is characterized by presence of neutrophils only in the lamina propria. In the moderate activity, the neutrophils are present in high density in the gastric foveoles. The degree of activity is severe when the neutrophils are present intraepithelial. Chronic gastritis is inactive when neutrophils are absent.

**C. Atrophic gastritis** represents the final stage of chronic gastritis evolution, and is characterized by the disappearance of the oxyntic glandular structure, with a distortion of the reticulin net. The inflammatory process invades the whole wall thickness; the histopathologic examination should mention the presence or absence of intestinal metaplasia.



# Epidemiology

## Mortality/Morbidity

The mortality/morbidity is dependent on the etiology of the gastritis. Generally, most cases of gastritis are treatable once the etiology is determined. The exception to this is phlegmonous gastritis, which has a mortality rate of 65%, even with treatment.

## Sex

No sexual predilection exists.

## Age

Gastritis affects all age groups. The incidence of *H pylori* infection increases with age.



# Acute Gastritis

Acute gastritis is a term covering a broad spectrum of entities that induce inflammatory changes in the gastric mucosa.

# Etiology of acute gastritis

Acute gastritis has a number of causes, including:

- **Drugs** - NSAIDs, such as aspirin, ibuprofen, and naproxen; cocaine; iron; colchicine, when at toxic levels, as in patients with failing renal or hepatic function; kayexalate; chemotherapeutic agents, such as mitomycin C, 5-fluoro-2-deoxyuridine, and floxuridine
- Potent **alcoholic** beverages, such as whisky, vodka, and gin
- **Bacterial infections** - *H pylori* (most frequent), *H heilmanii* (rare), streptococci (rare), staphylococci (rare), *Proteus* species (rare), *Clostridium* species (rare), *E coli* (rare), tuberculosis (rare), secondary syphilis (rare)
- **Viral infections** (eg, CMV)
- **Fungal infections** - Candidiasis, histoplasmosis, phycomycosis
- **Parasitic infection** (eg, anisakidosis)
- **Acute stress** (shock)
- **Radiation**
- **Allergy and food poisoning**
- **Bile:** The reflux of bile (an alkaline medium important for the activation of digestive enzymes in the small intestine) from the small intestine to the stomach can induce gastritis.
- **Ischemia:** This term is used to refer to damage induced by decreased blood supply to the stomach. This rare etiology is due to the rich blood supply to the stomach.
- **Direct trauma**

# Acute Gastritis

- The different etiologies share the same general clinical presentation.
- However, they differ in their unique histologic characteristics.
- The inflammation may involve the entire stomach (eg, pangastritis) or a region of the stomach (eg, antral gastritis).
- Acute gastritis** can be broken down into 2 categories: **erosive** (eg, superficial erosions, deep erosions, hemorrhagic erosions) and **nonerosive** (generally caused by *Helicobacter pylori*).

# Acute Gastritis

- **Acute gastritis** can be broken down into 2 categories: **erosive** (eg, superficial erosions, deep erosions, hemorrhagic erosions) and **nonerosive**

# Pathophysiology

The common mechanism of injury is an imbalance between the **aggressive** and the **defensive factors** that maintain the integrity of the gastric lining (mucosa).

# Acute erosive gastritis

**can result from the exposure to a variety of agents or factors.**

These agents/factors include **nonsteroidal anti-inflammatory medications (NSAIDs), alcohol, cocaine, stress, radiation, bile reflux, and ischemia.**

The gastric mucosa **exhibits hemorrhages, erosions, and ulcers.**

NSAIDs, such as aspirin, ibuprofen, and naproxen, are the most common agents. This results from oral or systemic administration of these agents either in therapeutic doses or in supratherapeutic doses.

Because of gravity, the inciting agents lie on the greater curvature of the stomach. This partly explains the development of acute gastritis *distally* on or *near the greater curvature* of the stomach in the case of orally administered NSAIDs.

However, the major mechanism of injury is `the reduction in prostaglandin synthesis. Prostaglandins are chemicals responsible for maintaining mechanisms that result in the protection of the mucosa from the injurious effects of the gastric acid. Long-term effects of such ingestions can include fibrosis and stricture.

# ***Gastritis associated with H pylori***

- *H pylori* are gram-negative rods that have the ability to colonize and infect the stomach
- The corkscrew-shaped bacterium called *H pylori* is the most common cause of gastritis.
- The prevalence of *H pylori* in otherwise healthy individuals varies depending on age, socioeconomic class, and country of origin.
- The infection is usually acquired in childhood, the number of people infected with *H pylori* increases with age.
- Evidence of *H pylori* infection can be found in 20% of individuals younger than 40 years and in 50% of individuals older than 60 years.





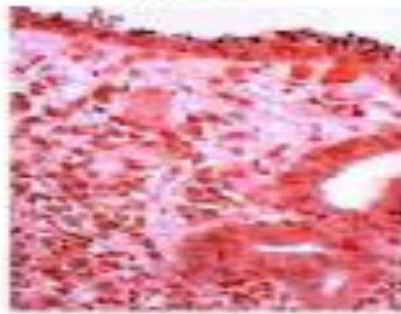
# ***Gastritis associated with H pylori***

Transmission is likely from person to person through the oral-fecal route or through the ingestion of contaminated water or food. This is why the prevalence is higher in lower socioeconomic classes and in developing countries.

*H pylori* is associated with 60% of *H pylori* gastritis typically starts as an acute gastritis in the antrum, causing intense inflammation, and over time, it may extend to involve the entire gastric mucosa resulting in chronic gastritis.

Gastric Mucosal Lesions During Chronic *Helicobacter pylori* Infection

Chronic Active Gastritis



Gastric Atrophy With Intestinal Metaplasia



# ***Gastritis associated with H pylori***

The bacterium imbeds itself in the mucous layer, a protective layer that coats the gastric mucosa.

It protects itself from the acidity of the stomach through the production of large amounts of urease, an enzyme that catalyzes the breakdown of urea to the alkaline ammonia and carbon dioxide.

The alkaline ammonia neutralizes the gastric acid in the immediate vicinity of the bacterium conferring protection.

# ***Gastritis associated with H pylori***

*H pylori* also has flagella that enable it to move and help it to penetrate the mucous layer so that it comes into contact with gastric epithelial cells. It also has several adhesions that help it to adhere to these cells.

It produces inflammation by activating a number of toxins and enzymes that activate IL-8, which eventually attracts polymorphs and monocytes that cause *acute gastritis*.

Antigen-presenting cells activate lymphocytes and other mononuclear cells that lead to *chronic superficial gastritis*. The infection is established within a few weeks after the primary exposure to *H pylori*.

# *Gastritis associated with *H pylori**

The intense inflammation can result in the loss of gastric glands responsible for the production of acid. This is referred to as [atrophic gastritis](#). Consequently, gastric acid production drops.



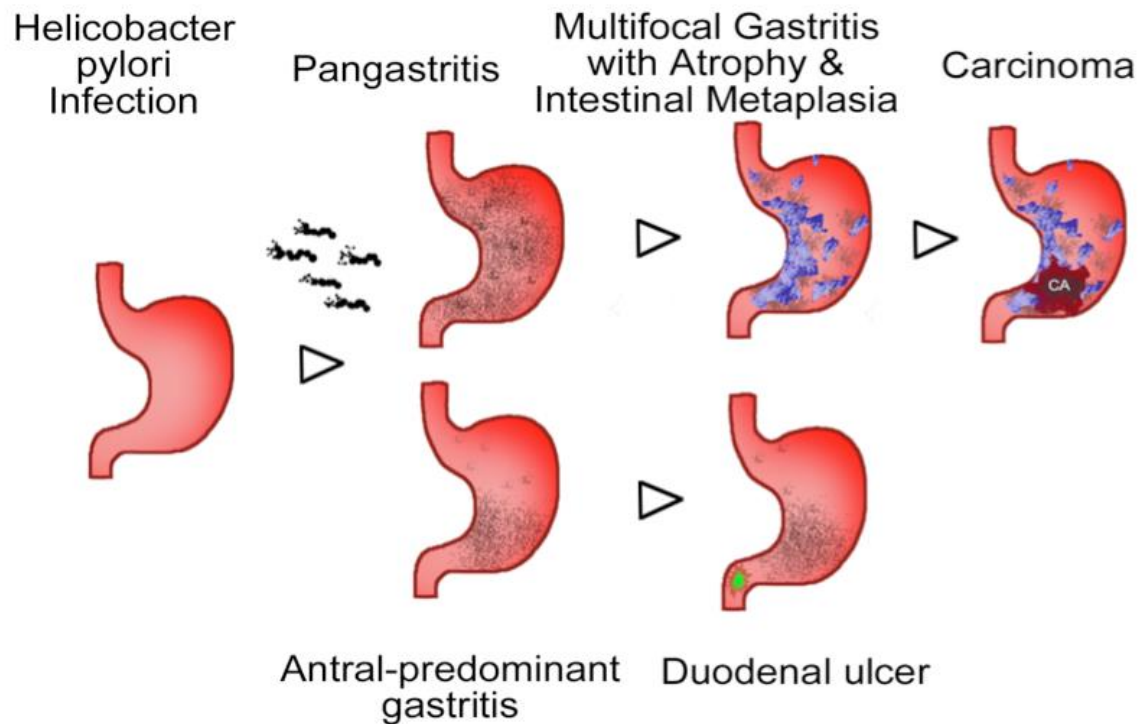
Healthy stomach



Stomach suffering from atrophic gastritis

# Gastritis associated with *H pylori*

The virulence genotype of the microbe is an important determinant for the severity of the gastritis and the formation of intestinal metaplasia, the transformation of gastric epithelium. This transformation can lead **gastric cancer**



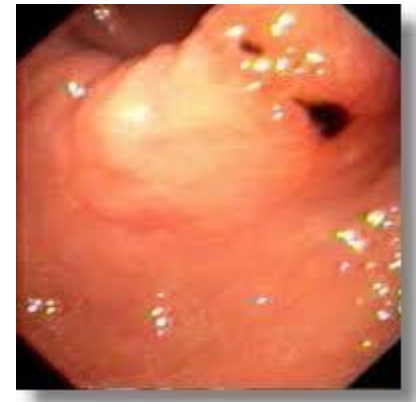
# *Gastritis associated with *H pylori**

The **macroscopic** aspect is of diffuse or patchy congestion, mostly antral with acute or chronic erosions.

In 25% of cases a nodular gastritis appears.



Nodular **Gastritis** seen in the stomach



Erosive **gastritis**

# Phlegmonous gastritis

is an uncommon form of gastritis caused by numerous bacterial agents, including streptococci, staphylococci, *Proteus* species, *Clostridium* species, and *Escherichia coli*.

Phlegmonous gastritis usually occurs in individuals who are debilitated. It is associated with a recent large intake of alcohol, a concomitant upper respiratory tract infection, and AIDS.

Phlegmonous means a diffuse spreading inflammation of or within connective tissue. In the stomach, it implies infection of the deeper layers of the stomach (submucosa and muscularis).

As a result, purulent bacterial infection may lead to gangrene.

Phlegmonous gastritis is rare.

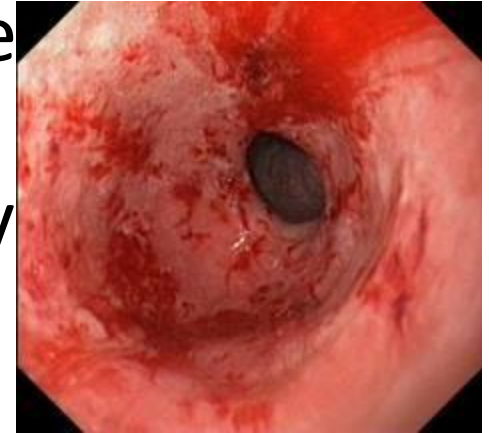
The clinical diagnosis is usually established in the operating room, as these patients present with an acute abdominal emergency requiring immediate surgical exploration.

Without appropriate therapy, it progresses to peritonitis and death.



# Ulcerohemorrhagic gastritis

Ulcerohemorrhagic gastritis is most commonly seen in patients who are critically ill. Ulcerohemorrhagic gastritis is believed to be secondary to ischemia related to hypotension and shock or to the release of vasoconstrictive substances, but the etiology is often unknown. The gastric mucosa reveals multiple petechiae, mostly in the fundus and body, or exhibits a diffusely hemorrhagic pattern.

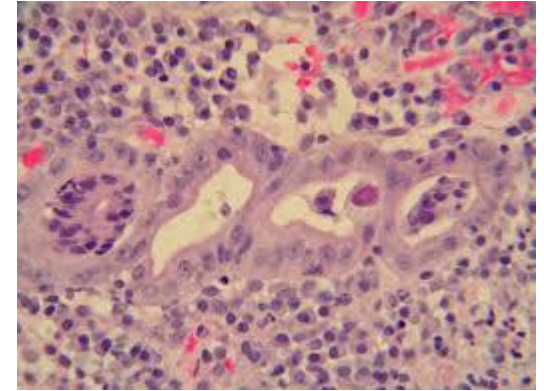


Haemorrhagic  
Gastritis



# Viral gastritis

Viral infections can cause gastritis. **Cytomegalovirus (CMV)** is a common viral cause of gastritis. It is usually encountered in individuals who are immunocompromised, including those with cancer, immunosuppression, transplants, and AIDS. Gastric involvement can be localized or diffuse.



Cytomegalovirus Gastritis

# Fungal gastritis

**Fungal infections** that cause gastritis include *Candida albicans* and histoplasmosis.

Gastric phycomycosis is another rare lethal fungal infection.

The common predisposing factor is immunosuppression.

*C albicans* rarely involves the gastric mucosa. When isolated in the stomach, the most common locations tend to be within a gastric ulcer or an erosion bed. It is generally of little consequence.

*Disseminated histoplasmosis* can involve the stomach. The usual presenting clinical feature is bleeding from gastric ulcers or erosions on giant gastric folds.

# **Parasitic causes of gastritis**

**Parasitic infections** are rare causes of gastritis. Anisakidosis is caused by a nematode that embeds itself in the gastric mucosa along the greater curvature. Anisakidosis is acquired by eating contaminated sushi and other types of contaminated raw fish.

It often causes severe abdominal pain that subsides within a few days.

This nematode infection is associated with gastric fold swelling, erosions, and ulcers.

# Eosinophilic gastritis

is often seen in conjunction with [eosinophilic gastroenteritis](#) but can be associated with various disorders, including food allergies (eg, cow milk, soy protein), collagen vascular diseases, parasitic infections, gastric cancer, lymphoma, Crohn disease, vasculitis, drug allergies, and *H pylori* infections.

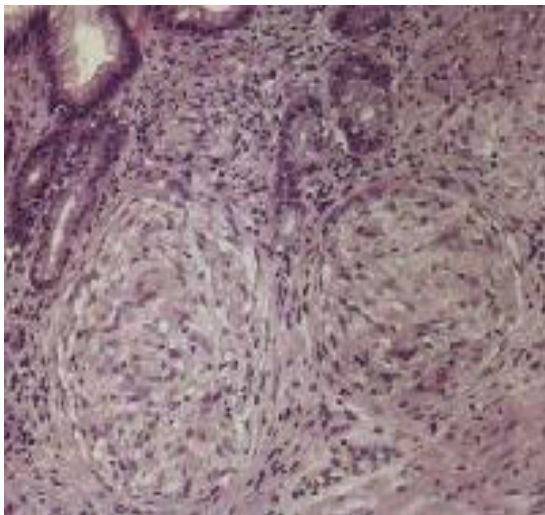
An eosinophilic infiltrate is seen involving the gastric wall or epithelium.



Eosinophilic gastritis.

# Infectious granulomatous gastritis

- **Granulomatous gastritis** is a rare entity. Tuberculosis may affect the stomach and cause caseating granulomas. Fungi can also cause caseating granulomas and necrosis, a finding that is usually observed in patients who are immunosuppressed.



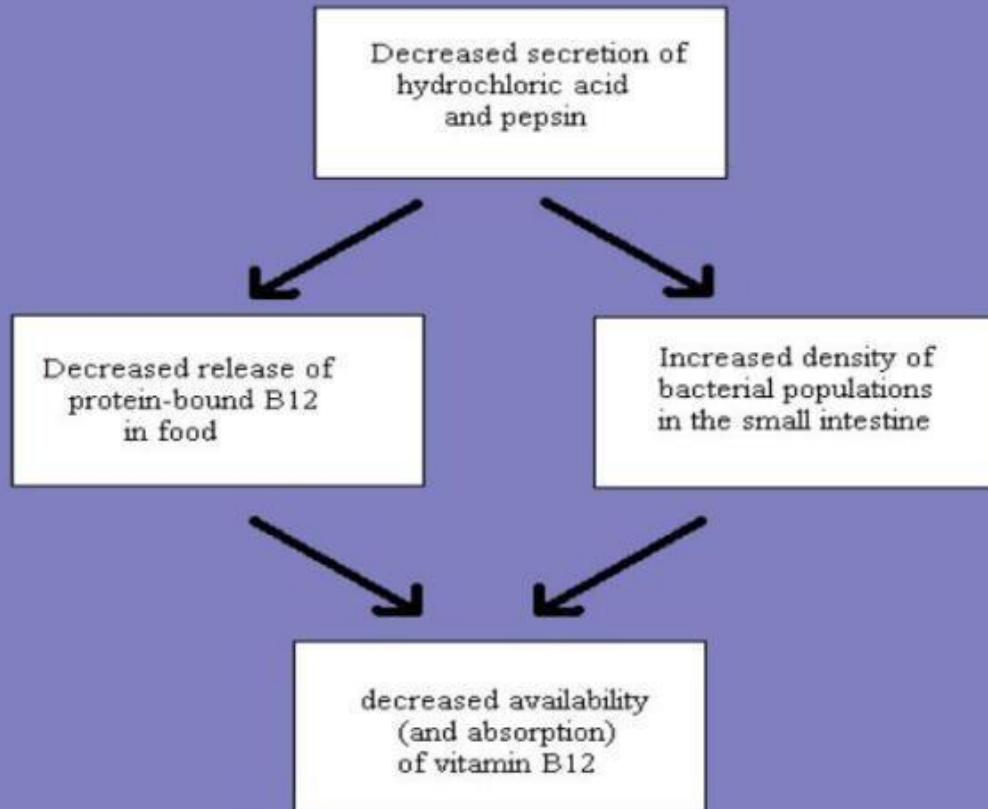
Granulomatous chronic gastritis

# Autoimmune gastritis

- This type of gastritis is associated with serum antiparietal and anti-intrinsic factor (IF) antibodies.
- The gastric corpus undergoes progressive atrophy, IF deficiency occurs, and patients may develop [pernicious anemia](#).
- The development of chronic [atrophic gastritis](#) limited to corpus-fundus mucosa and marked diffuse atrophy of parietal and chief cells characterize autoimmune atrophic gastritis. Autoimmune gastritis is associated with serum antiparietal and anti-IF antibodies that cause IF deficiency, which, in turn, causes decreased availability of cobalamin and, eventually, pernicious anemia in some patients.

# Autoimmune gastritis

## Consequences of Atrophic Gastritis: Vit B<sub>12</sub>



# Chronic noninfectious granulomatous gastritis

- Noninfectious diseases are the usual cause of gastric granulomas and include [Crohn disease](#), [sarcoidosis](#), and isolated granulomatous gastritis. Crohn disease demonstrates gastric involvement in approximately 33% of the cases. Granulomas have also been described in association with gastric malignancies, including carcinoma and malignant lymphoma. Sarcoidlike granulomas may be observed in people who use cocaine, and foreign material is occasionally observed in the granuloma.

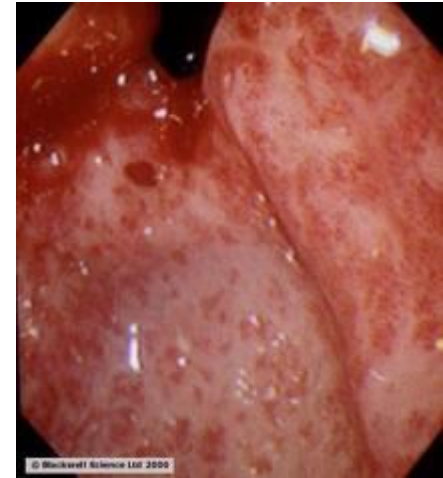


# Lymphocytic gastritis

- This is a type of chronic gastritis with dense infiltration of the surface and foveolar epithelium by T lymphocytes and associated chronic infiltrates in the lamina propria.
- Because of similar histopathology relative to [celiac disease](#), lymphocytic gastritis has been proposed to result from intraluminal antigens.
- High anti-*H pylori* antibody titers have been found in patients with lymphocytic gastritis, and, in limited studies, the inflammation disappeared after *H pylori* eradication.
- However, many patients with lymphocytic gastritis are serologically negative for *H pylori*.
- A number of cases may develop secondary to intolerance to gluten and drugs such as ticlopidine.

# Radiation gastritis

- Small doses of radiation (up to 1500 R) cause reversible mucosal damage, whereas higher radiation doses cause irreversible damage with atrophy and ischemic-related ulceration.
- Reversible changes consist of degenerative changes in epithelial cells and nonspecific chronic inflammatory infiltrate in the lamina propria.
- Higher amounts of radiation cause permanent mucosal damage, with atrophy of fundic glands, mucosal erosions, and capillary hemorrhage.
- Associated submucosal endarteritis results in mucosal ischemia and secondary ulcer development.



Conspicuous swelling and erythema due to radiation

# Symptoms of gastritis

*No correlation exists between microscopic inflammation (histologic gastritis) and the presence of gastric symptoms (eg, abdominal pain, nausea, vomiting).*

In fact, most patients with histologic evidence of acute gastritis (inflammation) are **asymptomatic**. The diagnosis is usually obtained during endoscopy performed for other reasons.

Acute gastritis may present with an array of symptoms, the most common being **nondescript epigastric discomfort**.

Other symptoms include **nausea, vomiting, loss of appetite, belching, and bloating**.

Occasionally, **acute abdominal pain** can be a presenting symptom (in *phlegmonous gastritis*) where severe abdominal pain accompanied by nausea and vomiting of potentially purulent gastric contents can be the presenting symptoms. **Fever, chills, and hiccups** also may be present.

# Diagnosis of gastritis

The diagnosis of gastritis may be suspected from the patient's history and can be confirmed histologically by biopsy specimens taken at endoscopy.



# History of disease

- Gnawing or burning epigastric distress, occasionally accompanied by nausea and/or vomiting. The pain may improve or worsen with eating.
- Previous mucosal injury (eg, gastritis, peptic ulcer disease, endoscopic injury caused by polypectomy, injury caused by any surgery)
- History of eating raw fish
- Exposure to potentially noxious drugs or chemical agents. This includes corticosteroids or other prescription medications that can cause gastritis.
- Routine use of aspirin or NSAIDs, especially at high doses

# The physical examination

findings are often normal with occasional mild epigastric tenderness.

The examination tends to exhibit more abnormalities as the patient develops complications in relation to gastritis.

# Imaging Studies

- Four **radiologic** signs of acute gastritis are fairly consistent regardless of the etiology. These signs include *thick folds, inflammatory nodules, coarse area gastrica, and erosions*.
- **Tomography scan** and **plain films** of the abdomen can demonstrate *thickening* of the gastric wall in the case of phlegmonous gastritis.
- **Double-contrast barium radiography** can demonstrate the nematodes that cause anisakidosis.

# *H pylori* tests

Three nonendoscopy-based *H pylori* tests are available:

1. ***H pylori* stool antigen test (HpSA).** It has sensitivity and specificity of greater than 90%. It can be used for both the diagnosis of *H pylori* and the confirmation of eradication after therapy.
2. **An urea breath test.** It uses <sup>13</sup>C- or <sup>14</sup>C-labeled urea taken orally. *H pylori* metabolizes the urea and liberates labeled carbon dioxide that is exhaled. This, in turn, can be quantified in breath samples. The sensitivity and specificity of the urea breath test is greater than 90%. This is considered the noninvasive diagnostic method of choice in situations where endoscopy is not indicated. It can also be used to confirm eradication after therapy
3. The third test depends on the presence of **antibodies to *H pylori* in the serum.** The major drawback to this test is that serologic assays may remain positive for as long as 3 years after eradication of the bacteria. Therefore, serologic assays are often unreliable to document eradication of *H pylori*. This test can be used for the diagnosis of *H pylori*, provided that the patient has not received any prior therapy for it.



# *H pylori* tests

Three endoscopy-based *H pylori* tests are available:

1. **Rapid urease test (RUT).** It is performed by placing a gastric biopsy specimen, obtained on endoscopy, onto a gel- or membrane-containing urea and a pH-sensitive indicator. If *H pylori* is present, the bacterial urease hydrolyzes urea and changes the color of the media. The sensitivity and specificity of this test is greater than 90%.
2. **A bacterial culture *H pylori*.** It is highly specific but is not widely used because of the degree of expertise required. It is used when antibiotic susceptibilities are necessary.
3. **Histologic detection of *H pylori* in the biopsy specimen** is another endoscopy-based test. Appropriate staining is achieved using such stains as hematoxylin and eosin, Warthin-Starry, Giemsa, or Genta.

# Endoscopy

Endoscopy may reveal a **thickened, edematous, nonpliable wall with erosions and reddened gastric folds**. The **edema** can be severe resulting in gastric outlet obstruction. **Ulcers** and **frank bleeding** might be present.

The nematodes that cause **anisakidosis** can be seen on endoscopy.

Endoscopy can be used to help diagnose gastric **syphilis** and **tuberculosis**.

# Histologic Findings

**Histologic examination of a biopsy specimen can help in establishing the etiologic agent of gastritis.**

- *H. pylori* can be found by histologic staining of a gastric mucosal biopsy specimen.
- The main histologic feature of **CMV infection** is cytomegalic cells with intranuclear inclusions
- 
- The main histologic feature of *C albicans* infection is yeast forms in a biopsy specimen.
- The main histologic feature of **tuberculosis** is necrotizing granulomas.
- The main histologic feature of **histoplasmosis** is nonnecrotizing granulomas containing the organisms.
- In ulcero-hemorrhagic gastritis, the epithelium appears eroded with edema and hemorrhage with typically little inflammation. In severe cases, the lumen of the stomach may be coated with fibropurulent exudates and the lamina propria may be replaced by eosinophilic hyaline material.
- In iron-induced gastritis, erosions, foveolar hyperplasia, or even hyperplastic-type polyps can be detected. Iron has been associated with infarctlike necrosis given its corrosive properties. Iron stains can highlight the golden brown pigments in tissue samples, but these are often easily visible. Of note, such findings should be differentiated from glandular **siderosis seen in systemic iron overload or hemochromatosis**.

# Histologic Findings

Histologic features of **chemotherapy-induced gastritis** may include atypical epithelial cells with bizarre features at the base of the glands, limited mitoses, and pleomorphic nuclei. These characteristics may make it difficult to differentiate from an adenocarcinoma.

The histology of **radiation-induced gastritis** include nuclear karyorrhexis and cytoplasmic eosinophilia of the gastric pit epithelium in the first 10 days following treatment, followed by mucosal edema, congestion, submucosal collagen bundle swelling, fibrin deposition, and telangiectasia. If extensive, hemorrhage and ulceration may be evident.

In **eosinophilic gastritis**, a prominent eosinophilic infiltrate is present in the gastric wall or epithelium. Distribution can be patchy, so multiple biopsy specimens should be obtained during endoscopy.

# Differentials

- Cholecystitis
- Cholelithiasis
- Crohn Disease
- Gastric Cancer
- Gastroenteritis, Viral
- Lymphoma, B-Cell
- Peptic Ulcer Disease
- Sarcoidosis

# The treatment



## The diet:

A diet with avoidance of acid, hot or seasoned food might still be recommended. The exclusion of coffee during the acute period may be recommended.

Aspirin intake, as well as NSAIDS and corticoids should be forbidden.

# Medical therapy

***Administer medical therapy as needed, depending on the cause and the pathological findings.***

- No specific therapy exists for gastritis, except for cases caused by *H pylori*.
- Administer fluids and electrolytes as required, particularly if the patient is vomiting.

# Medical therapy

## A) Antisecretory drugs

### - *H2 histaminic receptor blockers:*

- Cimetidine 1000mg/day
- Ranitidine 300 mg/day
- Nizatidine(Axid) 300 mg/day
- Famotidine (Quamatel) 40mg/day
- 

Famotidine will be preferred, given once or twice a day and without drug interferences of Cimetidine(cytochrome P450).

### - *HK ATP-ase pump blockers:*

- Esomeprazole (Nexium) 40mg/day
- Omeprazole (Losec, Antra, Ultop) 40 mg/day
- Pantoprazole (Controloc) 40 mg/day
- Lanzoprazole (Lanzap) 30mg/day
- Rabeprazole (Pariet) 20mg/day
- The duration of antisecretory therapy will be for 6-8 weeks.

## B) Gastric mucosal protectives

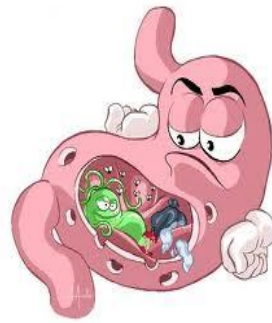
-sucralfate 4g/day (qid)might be associated.

## C) Antacids

To neutralize the acid excess and reduce the painful symptoms, symptomatic medication such as Maalox, Almagel, Alfogel etc. are used.



# The eradication of *Helicobacter Pylori* infection



- **The schemes** including proton pump blockers (zomeprazole, lansoprazole or pantoprazole), associated with two antibiotic indicated, triple or even quadruple schemes are used.

**The triple therapy** includes

OAM=Omeprazole(40mg/day)+Amoxicillin(2g/day)+Metronidazole(1500mg/day); or the ideal association is

OAC=Omeprazole+Amoxicilline+Claritromicine(macrolide in dose of 1000mg/day).

**The quadruple therapy** is composed of Omeprazole+Subcitric bismuth (De-Nol)+Tetracycline+Metronidazole.

- The most widely used efficient therapies to eradicate *H pylori* are triple therapies, and they are recommended as first-line treatments; quadruple therapies are recommended as second-line treatment when triple therapies fail to eradicate *H pylori*.

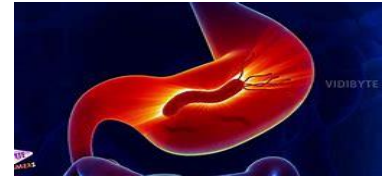
**The anti HP therapy** duration is for 10-14 days.

# Surgical Care

- Surgical intervention is not necessary, except in the case of phlegmonous gastritis. With this entity, surgical intervention with resection of the affected area may be the most effective form of treatment.

# Guidelines

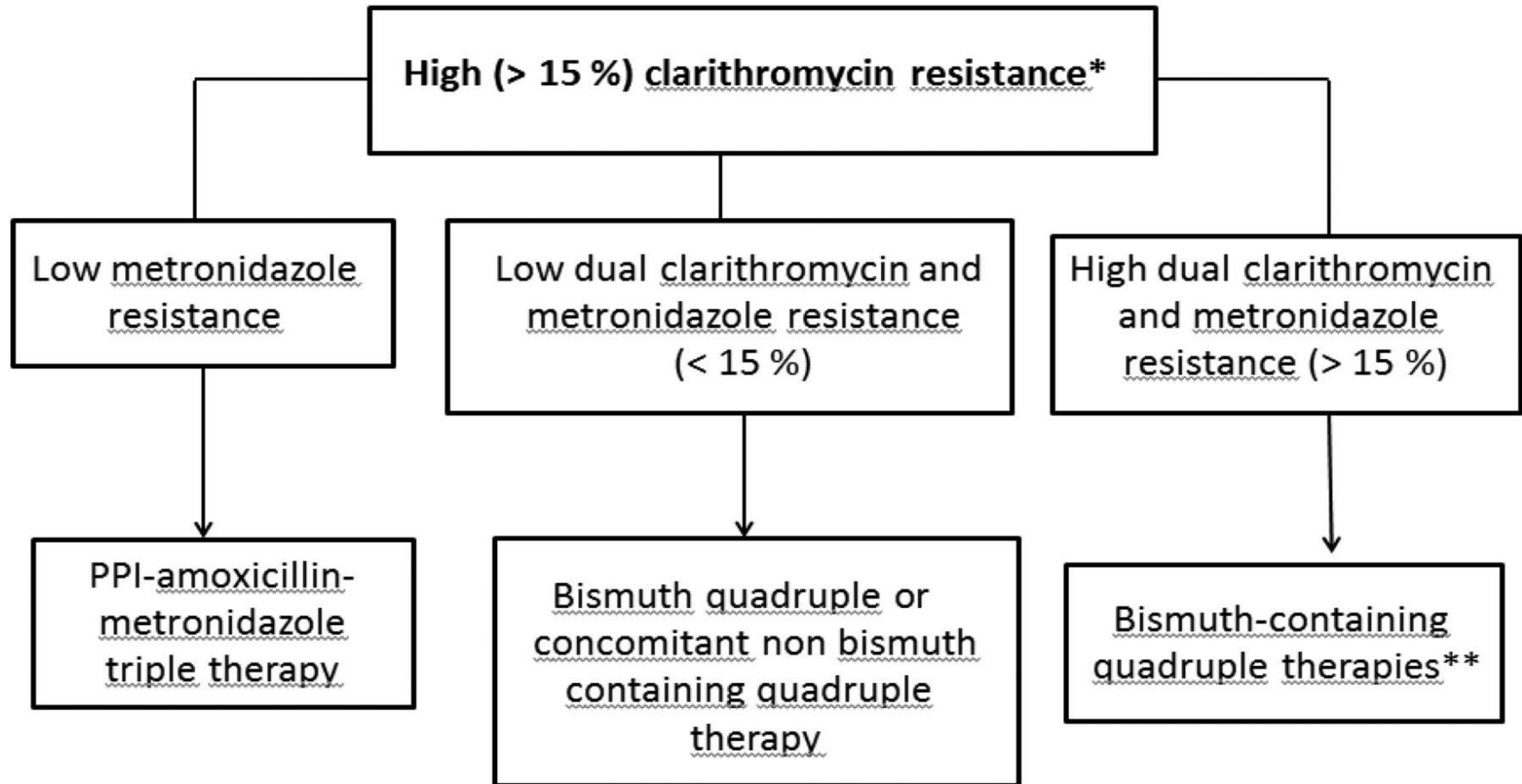
## Management of *Helicobacter pylori* infection—the Maastricht V/Florence Consensus Report



- *H. pylori* resistance rates to antibiotics are increasing in most parts of the world.
- In areas of high (>15%) clarithromycin resistance, bismuth quadruple or non-bismuth quadruple, concomitant (PPI, amoxicillin, clarithromycin and a nitroimidazole) therapies are recommended.  
In areas of high dual clarithromycin and metronidazole resistance, bismuth quadruple therapy (BQT) is the recommended first-line treatment.
- Currently, concomitant therapy (PPI, amoxicillin, clarithromycin, and a nitroimidazole administered concurrently) should be the preferred non-bismuth quadruple therapy, as it has shown to be the most effective to overcome antibiotic resistance.
- In areas of low clarithromycin resistance, triple therapy is recommended as first-line empirical treatment. Bismuth-containing quadruple therapy is an alternative.
- The treatment duration of PPI-clarithromycin based triple therapy should be extended to 14 days, unless shorter therapies are proven effective locally.

# Guidelines

## Management of *Helicobacter pylori* infection—the Maastricht V/Florence Consensus Report



\* Regardless of their population expectations, individuals who have previously taken clarithromycin and/or metronidazole should be considered high risk patients for dual resistance.

\*\* If bismuth is not available, levofloxacin, rifabutin and high dose dual (PPI + amoxicillin) therapies might be considered. If tetracycline is not available, bismuth-containing quadruple therapy combining furazolidone-metronidazole or amoxicillin-metronidazole can be considered.

Thank you

