Gastritis
Definition

- The term *gastritis* is used to denote inflammation associated with mucosal injury.
- Gastritis is mostly a histological term that needs biopsy to be confirmed.
- Gastritis is usually due to infectious agents (such as Helicobacter pylori) and autoimmune and hypersensitivity reactions.
Definition

■ Epithelial cell damage and regeneration without associated inflammation is properly referred to as "gastropathy."

■ Gastropathy may be referred without histological evidence and just according to gross appearance in endoscopy or radiology.

■ Gastropathy is usually caused by irritants such as drugs (eg, nonsteroidal antiinflammatory agents and alcohol), bile reflux, hypovolemia, and chronic congestion.
Gross–histologic correlation?
Among 98 patients with endoscopic mucosal changes attributed to gastritis, 27 percent had a normal endoscopic biopsy specimen; i.e. **PPV of 73 percent** or at least 1 in four false positive diagnosis.
Research evidence

- among 69 patients with a normal endoscopic appearance, 63 percent had histological evidence of gastritis. **NPV equals to 27 percent**
Classification

- Acute vs. chronic
  - Acute refers to short term inflammation
  - Acute referring to neurophilic infiltrate
  - Chronic referring to long standing forms
  - Chronic referring to mononuclear cell infiltrate especially lymphocyte and maccrophages
Non HP gastritis (ICD10)

1. Chemical gastritis (acute • chronic)
   - Alcoholic gastritis
   - Drug induced gastritis (e.g., NSAID)
   - Reflux (due to duodenal juice or bile) gastritis
   - Other chemical gastritis

2. Radiation gastritis

3. Allergic gastritis

4. Autoimmune gastritis

5. Special forms of gastritis

6. Gastritis • NOS

7. Duodenitis
CLASSIFICATION

GASTRITIS

ACUTE
- STRESS
- NSAID

COMMON
- BILE
- HP

CHRONIC
- EMAG
- AMAG
CLASSIFICATION

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Acute hemorrhagic erosive

- hemorrhagic and erosive lesions shortly after exposure of the gastric mucosa to various injurious substances or a substantial reduction in mucosal blood flow
ACUTE GASTRITIS - MORPHOLOGY

Mucosal congestion, oedema, inflammation & ulceration
Acute hemorrhagic erosive

- nonsteroidal antiinflammatory drugs (NSAIDs), alcohol, or bile acids) or to mucosal hypoxia (such as in trauma, burns [Curling's ulcers] or sepsis) or to a combination of factors such as with antineoplastic chemotherapy

- Gastric and duodenal ulceroinflammatory ulcers occurring during severe damage to the central nervous system (Cushing's ulcers) are often considered in this group
Acute hemorrhagic erosive

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Acute hemorrhagic erosive

- specific pathogenetic factor in NSAID-induced acute hemorrhagic and erosive gastropathy is the inhibition of prostaglandin production. Prostaglandins, especially those of the E class, protect against acute mucosal injury due to NSAIDs and other injurious substances by several mechanisms, including the stimulation of mucus and bicarbonate secretion, and maintenance of mucosal blood flow
NSAID GI toxicity risk factor

- Prior history of an adverse GI event (ulcer, hemorrhage) increases risk four to fivefold
- Age >60 increases risk five to sixfold
- High (more than twice normal) dosage of a NSAID increases risk 10-fold
- Concurrent use of glucocorticoids increases risk four to fivefold
- Concurrent use of anticoagulants increases risk 10- to 15-fold
HP and NSAID

- Patients with a history of uncomplicated or complicated peptic ulcers (gastric, duodenal) should be tested for H. pylori prior to beginning a NSAID or low dose aspirin. If present, H. pylori should be treated with appropriate therapy, even if it is believed that the prior ulcer was due to NSAIDs.
Acute hemorrhagic erosive

- Hemorrhagic or erosive gastropathy may be associated with the development of gastric or duodenal ulcers. Acute ulceration is most likely to occur in relation to shock-induced hemodynamic instability (ie, the stress ulcer syndrome).
For patients who are at high risk for NSAID-related gastroduodenal toxicity, primary therapy with a COX-2 selective inhibitor such as rofecoxib is a reasonable option.
NSAID prophylaxis

For high-risk patients taking nonselective NSAIDs, misoprostol (at a dose of 200 µg four times daily) and lansoprazole (15 or 30 mg daily) have received FDA approval for prophylaxis against NSAID-induced ulcer disease and its complications.
Stress ulcer pathophysiology

- Hypersecretion of acid – head trauma.
- Defects in gastric glycoprotein mucus – In critically ill patients, increased concentrations of refluxed bile salts or the presence of uremic toxins can denude the glycoprotein mucous barrier.
- Ischemia – Shock, sepsis, and trauma can lead to impaired perfusion of the gut.
Stress ulcer risk factors

- Risk factors –two major risk factors for clinically significant bleeding due to stress ulcers are: mechanical ventilation for more than 48 hours (odds ratio 15.6); and coagulopathy (odds ratio 4.3). The risk of clinically important bleeding in patients without either of these risk factors was only 0.1 percent.
Stress ulcer risk factors

- Shock
- Sepsis
- Hepatic failure
- Renal failure
- Multiple trauma
- Burns over 35 percent of total body surface area
- Organ transplant recipients
- Head or spinal trauma
- Prior history of peptic ulcer disease or upper GI bleeding
Common type of gastritides
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Helicobacter pylori is a spiral shaped, microaerophilic, gram negative bacterium measuring approximately 3.5 microns in length and 0.5 microns in width.
- Urease forms ammonia and bicarbonate that neutralize gastric acid and form a protective cloud around the organism.
Urease appears to be vital for its survival and colonization; it is produced in abundance, making up more than 5 percent of the organism's total protein weight.
- spiral shape, flagella facilitate its passage through the mucus layer
H. pylori then attaches to gastric epithelial cells by means of specific receptor-mediated adhesion.
Helicobacter pylori is the most common chronic bacterial infection in humans; 50 percent of the world's population is affected.
Therefore, the frequency of H. pylori infection for any age group in any locality reflects that particular cohort's rate of bacterial acquisition during childhood years.
Factors such as density of housing, overcrowding, number of siblings, sharing a bed, and lack of running water have all been linked to a higher acquisition of H. pylori infection.
The route by which infection occurs remains unknown. Person-to-person transmission of H. pylori through either fecal/oral or oral/oral exposure seems most likely.
Humans appear to be the major reservoir of infection; however, bacteria have been isolated from primates in and from domestic cats and in milk and gastric tissue of sheep.
Non GI associated disorders

- Coronary heart disease
- Rosacea
- Iron deficiency
- Anorexia in aging
Platelet aggregation mediated by an H. pylori interaction with von Willebrand factor is speculated to contribute to infection related ulcer disease but also possibly non-GI manifestations of infection such as cardiovascular disease and idiopathic thrombocytopenia.
A B cell response to H. pylori (with production of IgG and IgA antibodies) occurs locally in the gastroduodenal mucosa and systemically. The role of local antibodies in producing tissue injury or modulating inflammation in H. pylori infection remains controversial. Prolonged stimulation of gastric B cells by activated T cells can lead to MALT lymphoma in rare cases.
Vac A & Cag A

- vacuolating cytotoxin (VacA) which causes cell injury in vitro and gastric tissue damage in vivo. All H. pylori contain the gene coding for VacA; however, only those strains with the cytotoxin-associated gene A (cagA)

- Strains producing VacA and CagA cause more intense tissue inflammation and induce cytokine production
Approximately 85 to 100 percent of patients with duodenal ulcers have CagA+ strains, compared to 30 to 60 percent of infected patients who do not develop ulcers.

CagA strains may be associated with a higher frequency of precancerous lesions.
Host polymorphism of IL-1 beta (and possibly IL-10) appears to determine the degree of inflammatory response to infection, resulting alteration in acid secretion (hyper or hypo secretion), and risk for subsequent gastric cancer.
IgA antibodies may modulate mucosal injury by inhibiting antigen uptake, disrupting bacterial adherence and motility, and neutralizing various toxins. IgG presumably augments inflammatory injury by activating complement and facilitating neutrophil activation.
Bile reflux gastropathy

- Bile reflux gastropathy typically results from the regurgitation of bile into the stomach because of an operative stoma, an incompetent pyloric sphincter, or abnormal duodenal motility.
Bile reflux gastropathy

- The effect of bile salts on gastric mucosa is comparable to that seen after chronic NSAID use.
Chronic metaplastic gastritides
CLASSIFICATION

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Metaplasia, especially of the intestinal type, is virtually a universal feature of atrophic gastritis and is often the most dependable defining morphologic feature.

- Metaplasia is highly relevant to the pathogenesis of atrophic gastritis and to its complications (e.g., pernicious anemia, gastric ulcer, and gastric cancer).
The term metaplastic atrophic gastritis makes a sharp distinction between metaplastic and nonmetaplastic forms of gastric atrophy, especially the atrophic change (gastrinopenic type) often noted in the oxyntic mucosa (ie, mucosa of the body and fundus), which remains in place after antrectomy for peptic ulcer.
Endoscopic surveillance in patients from developed countries who do not have dysplasia is probably unnecessary.
AUTOIMMUNE METAPLASTIC ATROPHIC GASTRITIS (AMAG) is an inherited form that is associated with an immune response in the oxyntic mucosa directed against parietal cells and intrinsic factor. AMAG is inherited as an autosomal dominant disorder.
SYNONYMS OF AMAG

- TYPE A GASTRITIS
- AUTOIMMUNE GASTRITIS
- DIFFUSE CORPORAL GASTRITIS
metaplastic atrophic gastritis

- The chronic inflammation, gland atrophy, and epithelial metaplasia of AMAG are closely paralleled by elevated serum antibodies to parietal cells and to intrinsic factor, reflecting its autoimmune origin.
metaplastic atrophic gastritis

- The loss of parietal cell mass leads to profound hypochlorhydria, while the inadequate production of intrinsic factor leads to vitamin B12 malabsorption and pernicious anemia.
Patients with AMAG are at increased risk for the development of gastric carcinoid tumors and adenocarcinoma.
metaplastic atrophic gastritis

surveillance strategy for patients diagnosed with pernicious anemia

• Upper endoscopy soon after diagnosis
• Removal of gastric polyps if possible; most of these polyps will be benign
• Frequent reinvestigation in patients whose polyps are not removed or who have severe mucosal dysplasia; in the remaining patients follow-up endoscopies should be performed at approximately five-year intervals.
Patients with AMAG are less likely to be infected by H. pylori than aged-matched controls. Two possible explanations are that the metaplastic epithelium is unsuitable for H. pylori colonization, and that the associated hypochlorhydria encourages overgrowth by other bacterial species.
metaplastic atrophic gastritis

- Environmental metaplastic atrophic gastritis (EMAG) is due to environmental factors, such as diet and H. pylori infection, on the gastric mucosa.
metaplastic atrophic gastritis

- Unlike AMAG, mucosal changes in patients with EMAG affect both the corpus and antrum in a multifocal distribution, but with heaviest involvement of the antrum.
metaplastic atrophic gastritis

- **EMAG vs AMAG**
  - Gastric acid production does not disappear entirely
  - Serum gastrin is not elevated
  - Parietal cell and intrinsic factor autoantibodies and pernicious anemia are absent
There is an increased risk for gastric ulcer compared to AMAG, presumably due to the accompanying hypochlorhydria the latter disorder
metaplastic atrophic gastritis

- diagnosis of EMAG should **not** be made from biopsy specimens unless **at least 20 percent** of the available antral or transitional mucosa is replaced by metaplastic glands, or there is unequivocal atrophy.
Possible exceptions are nitroso compounds, which may be important in EMAG and in the development of gastric cancer. Nitroso compounds, which are known carcinogens, are generated in the gastric lumen by bacterial metabolism of nitrates.
metaplastic atrophic gastritis

chronic infection  →  
cell injury/ inflammation  →  
susceptibility to mutagenic factors.
Hyperplastic gastropathies

proliferative, inflammatory, and infiltrative conditions are associated with large folds due to excessive number of mucosal epithelial cells
Ménétrier's disease

- Epithelial hyperplasia involving the surface and foveolar mucous cells (ie, foveolar hyperplasia); the oxyntic glands can be normal or atrophic.
Zollinger-Ellison syndrome

Increased numbers of parietal cells with no change in surface and foveolar mucous cells.
Hyperplastic gastropathies

mixed-type in which both mucous and oxyntic glandular cells show hyperplasia, may be seen in as lymphocytic and H. pylori gastritis.
Large gastric folds > 1.0 cm

- Chronic gastritis/lymphoid hyperplasia – 40
- Benign tumors – 16
- Gastric malignancy – 12
- Zollinger-Ellison syndrome – 10
- Menetrier's disease – 8
Ménétrier's

- Epigastric pain – 65 percent
- Asthenia – 60 percent
- Anorexia – 45 percent
- Weight loss – 45 percent
- Edema – 38 percent
- Vomiting – 38 percent

- 80 percent of patients had hypoalbuminemia
Ménétrier's

- Surgery has been advocated for patients with intractable pain, hypoalbuminemia with edema, hemorrhage, pyloric obstruction, and for those in whom a malignancy cannot be excluded.
Ménétrier's

- Gastric atrophy?
- Gastric cancer?
Zollinger-Ellison syndrome

- 0.1 to 1 percent of patients with peptic ulcer disease.
- Underestimation!
  - symptoms similar to typical peptic ulcer.
  - symptoms may be controlled by standard doses of an antisecretory drug.
  - patients may not be tested for hypergastrinemia.
Most patients are diagnosed between the ages of 20 and 50. The male to female ratio ranges between to 2:1.
Gastrinomas can be either sporadic (80 percent) or associated with multiple endocrine neoplasia type 1
Diarrhea in ZES

• The high rate of acid volume load that cannot be absorbed by the intestine
• The excess acid exceeds the neutralizing capacity of pancreatic bicarbonate. The exceptionally low pH of the intestinal contents inactivates pancreatic digestive enzymes, interferes with the emulsification of fat by bile acids, and damages intestinal epithelial cells and villi.
• The extremely high serum gastrin concentrations may inhibit absorption of sodium and water by the small intestine,
Signs of ZES

- Multiple ulcers
- diarrhea
- ulcer in atypical site
- resistant ulcer
- enlarged folds
- severe esophagitis
- FH of MEN1
ZES diagnosis

Exclude hpoacidity!

Check gastrin, if >1000=ZES.

<1000 but abnormal secretin test to be performed, +200 pg/ml is ZES
Localization of gastrinoma

- SPECT imaging with pentetreotide should be the **first test** because of its high sensitivity for both primary tumors and hepatic metastases.

- If no tumor or metastases are found but clinical suspicion remains high, endoscopic ultrasonography (EUS) or dual phase helical CT scan should be performed.
ZES treatment

- Omeprazole effectively controlled acid output in all patients.

- No patients experienced tachyphylaxis, and no hematologic, metabolic, or gastric toxicity was noted.
ZES treatment

- any patient with a sporadic gastrinoma and without evidence of metastatic spread of disease should be offered exploratory laparotomy with curative intent
ZES treatment

- Laparotomy is not routinely recommended for patients with ZES as part of MEN 1 since the multifocal nature of the tumors in this disorder almost uniformly precludes cure of gastrin hypersecretion.
Portal hypertensive gastropathy

- Portal hypertensive gastropathy characteristically appears as a fine white reticular pattern separating areas of pinkish mucosa on endoscopy, giving the gastric mucosa a "snakeskin" appearance.
Portal hypertensive gastropathy