Stomach 1

Parts of stomach

- **Cardia** — mucin secreting foveolar cells
- **Fundus** — parietal cells producing (HCL) chief cells producing (pepsin).
- **Body** — parietal cells producing (HCL) chief cells producing (pepsin).
- **Antrum (pylorus)** — neuroendocrine G cells (gastrin)

Gastric diseases

- **Inflammatory**
  - Acute gastritis.
  - Chronic gastritis.
  - Acute gastric ulcer.
  - Chronic peptic ulcer
- **Neoplastic**
  - Benign
  - Malignant

ACUTE GASTRITIS & gastropathy

Acute gastritis:
Mucosal injury, neutrophils present.
Gastropathy:
regenerative, rare or no inflamm

Causes
- NSAIDs
-alcohol
- bile
-stress-induced

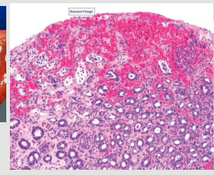
Clinical features:
- Asymptomatic.
- Epigastric pain
- nausea
- vomiting.
- Severe: erosions, ulcers, hematemesis(vomiting of blood)
- melena(presence of blood in feces)

Pathogenesis:- Imbalance between protective and damaging forces

- **Normal State**
  Damaging Forces: Gastric acid + pepsin enzymes.
  Defensive Forces: Mucus layer, bicarbonate, blood flow, rapid cell repair, prostaglandins.
- **Injury Phase**
  Causes:
  Infection: H. pylori (disrupts mucus barrier).
  Drugs: NSAIDs/aspirin (block protective prostaglandins).
  Lifestyle: Alcohol, smoking, stress (reduce defenses).
  Other: Acid hypersecretion, bile reflux.
- **Ulcer Formation**

Main causes of the imbalance :
- NSAIDs (COX1 and COX2 inhibitors)
- Uremic patients (ammonia inhibit bicarbonate transport)
- H pylori (urease produces ammonia)
- Aging (reduced mucin and bicarbonate secretion)
- Hypoxia (high altitudes)
- Harsh chemicals, (acids or bases) (direct epithelial injury)
- Alcohol, NSAIDs, radiation therapy (direct mucosal damage)
-Chemotherapy (inhibit DNA synthesis and cellular renewal)

Morphology :
- Hyperemia (redness).
- Edema and slight vascular congestion
- Neutrophils, lymphocytes, and plasma cells are not prominent.
- Neutrophils : Active inflammation (gastritis) .
- Intact surface epithelium if mild.
- Acute erosive hemorrhagic gastritis (Advanced)



Stress-Related Mucosal Disease

=> Stress ulcers: critically ill patients with shock, sepsis, or severe trauma.
=> Curling ulcers: proximal duodenum , severe burns or trauma.
=> Cushing ulcers: stomach, duodenum, or esophagus due to CNS injury as stroke, high risk of perforation.

Causes
Severe physiologic stress:
- Trauma
- Extensive burns
- Intracranial disease
- Major surgery
- Serious medical disease
- Critically ill patients

Clinical features:
- Nausea, vomiting,
- Melena
- Coffee -ground hematemesis
- Perforation complication.

- Prophylaxis with proton pump inhibitors
- Outcome depends on severity of underlying cause.

Pathogenesis:-

- **Stress related injury:**
  Mostly due to **Local ischemia** caused by.
  - Systemic hypotension.
  - Decreased blood flow (Splanchnic vasoconstriction)
  - Systemic acidosis (lower intracellular PH).
  - COX2 expression is protective.
- **CNS injury and Cushing ulcers:**
  Direct vagal stimulation, acid hypersecretion.

Morphology :
- Spectrum (Shallow to deep).
- Acute ulcers are rounded and typically < 1 cm.
- Ulcer base brown to black.
- Multiple, anywhere in stomach
- Normal adjacent mucosa
- No scarring; because it's acute not chronic
- Healing with complete epithelialization occurs days or weeks after removal of injurious factors

CHRONIC GASTRITIS

=> Stress ulcers: critically ill patients with shock, sepsis, or severe trauma.
=> Curling ulcers: proximal duodenum , severe burns or trauma.
=> Cushing ulcers: stomach, duodenum, or esophagus due to CNS injury as stroke, high risk of perforation.

Causes
- Helicobacter pylori associated gastritis: most common.
- Autoimmune atrophic gastritis: less than 10% of cases.
Less common
- Chronic NSAID
- Radiation injury
- Chronic bile reflux.

Clinical features:
- Nausea, vomiting and upper-abdominal discomfort
- Hematemesis uncommon.
➡️ Less severe but more prolonged symptoms.

Complications of chronic gastritis
- Peptic ulcer.
- Mucosal atrophy.
- Intestinal Metaplasia
- Dysplasia.

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

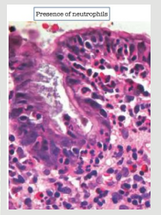
Helicobacter pylori Gastritis

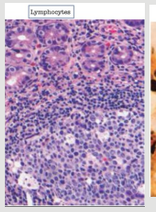
Spiral or curved, G-ve, bacilli.
> In almost **all duodenal ulcers** and **majority of gastric ulcers** or chronic gastritis.
> Epidemiology:
_ Poverty, poor sanitation. Acquired in childhood, persists to adult-life.
_ Acute infection is subclinical.

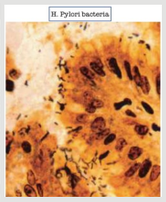
Pathogenesis:
> Non-invasive, adapted to live in the mucus layer due to:
- Flagella: allow motility.
- Urease: split urea to ammonia, protect bacteria from acidic pH.
- Adhesins: bacterial adherence to foveolar cells
- Toxins: (CagA) mucosal damage.

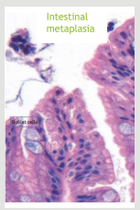
Starts as Antral **gastritis** => stimulate G cells => increased acid production => peptic ulcer =>
If severe: spread to body with **atrophy** (damage Parietal cells). => Intestinal **metaplasia** => increased risk of **gastric cancer**.

MORPHOLOGY
~~ Gastric antral biopsy: H. pylori in mucus layer.
~~Regenerative changes (hyperplastic polyps)
~~ Neutrophils, Plasma cells, lymphocytes & macrophages.
~~ **Lymphoid aggregates** >>> increased risk of MALT lymphoma.
~~ Intestinal **metaplasia** (goblet cells)>>> dysplasia >> increased risk of **adenocarcinoma**









Diagnosis and treatment
- Serologic test: anti-H .pylori antibodies.
- Stool test for H.pylori. - Urea breath test.
- Gastric antral biopsy (rapid urease test during endoscopy). - Bacterial culture.
- PCR test for bacterial DNA.
=> **Treatment**: combinations of 2 antibiotics and PPI (triple therapy).

Autoimmune Gastritis

=> Antibodies to parietal cells and intrinsic factor in serum.
- Reduced serum pepsinogen I levels
- Antral endocrine cell hyperplasia
- Vitamin B12 deficiency >>> pernicious anemia and neurologic changes
- Impaired gastric acid secretion (Hypo acidity) (**achlorhydria**)
- Marked hypergastrinemia
- Spares the antrum.

Pathogenesis:
loss of parietal cells => reductions in acid and intrinsic factor secretion.
Acid reduction => Hyperplasia of antral G cells
=> hypergastrinemia(⬆️gastrin)
Deficient intrinsic factor => deficient ileal Vitamin B12 absorption >> pernicious anemia.

MORPHOLOGY
~~ Damage of the oxyntic (acid-producing) mucosa.
~~ Diffuse atrophy, thinning of wall, loss of gastric folds
~~ Lymphocytes, plasma cells, macrophages, less likely neutrophils.
~~ Intestinal metaplasia >>> dysplasia >> carcinoma.
~~ G- cell hyperplasia >>> **carcinoids**.

Clinical features:
_ 60 years, slight female predominance.
_ Often associated with other autoimmune diseases
_ Dyspepsia. عسر هضم
_ Anemia (VB12 or iron)

Note:-
prostaglandins E2 and I2:
Stimulate nearly all the **defense mechanisms** including
1. Mucus and bicarbonate secretion,
2. mucosal blood flow
3. Epithelial restitution.

Peptic Ulcer Disease

- Main factors: H. pylori infection or NSAID use
- **Imbalance between mucosal defenses and damaging forces.**
- Any portion of the GIT exposed to acidic gastric juices
- Most common in gastric antrum, first part of duodenum.
- Esophagus in (GERD) or ectopic gastric mucosa (Meckel diverticulum)

Pathogenesis of PUD:

> 70% of cases are associated with H. pylori infection worldwide.
Only 5 -10% of H. pylori–infected persons (host factors, bacterial strains).
Gastric acid is fundamental in pathogenesis.
Cofactors: smoking, chronic NSAIDs, high-dose corticosteroids, alcoholic cirrhosis, COPD, CRF, hyperparathyroidism.
Hyperacidity is caused by:
- H. pylori.
- Parietal cell hyperplasia.
- Excessive secretory response (vagal)
- Hypergastrinemia as in Zollinger-Ellison syndrome

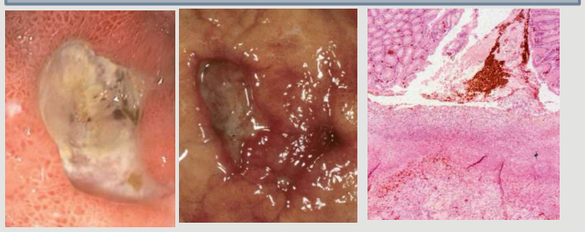
MORPHOLOGY

4:1, proximal duodenum : stomach.
~ Anterior duodenal wall or antrum.
~ >80% solitary.(isolated alone)
~ Round to oval, sharply punched-out
~ Base of ulcers is smooth and clean
~ Granulation tissue.
~ Hemorrhage & Perforation are complications.

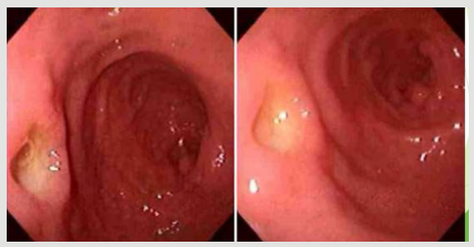
Clinical Features

- Epigastric burning or aching pain
- Complication: Iron deficiency anemia, frank hemorrhage, or perforation.
- Pain 1 to 3 hours after meals at daytime
- Worse at night, relieved by alkali or food
- Nausea, vomiting, bloating, bletching.
- Current therapies are aimed at H.pylori eradication.
- Surgery reserved for complications.

Zollinger-Ellison syndrome
Multiple peptic ulcerations
> Stomach , duodenum, even jejunum
> Caused by uncontrolled release of gastrin by a tumor (gastrinoma) and the resulting massive acid production.



Duodenal ulcer



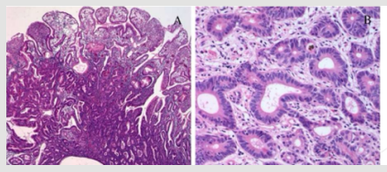
GASTRIC POLYPS AND TUMORS

Gastric polyps

Polyps: masses projecting above the level of adjacent mucosa
- 75% of all polyps.
- Arise in a background of chronic gastritis
- Regress after H.pylori eradication.

- Inflammatory polyps
- Hyperplastic Polyps

Gastric Adenoma:
- 10% of all polyps.
- Increase with age.
- M: F = 3:1
- Background: chronic gastritis, atrophy and intestinal metaplasia.
- **Dysplasia, low- or high-grade.**
- Risk of adenocarcinoma related to the size (greatest if > 2cm).
- Risk of carcinoma higher than colonic adenoma.
- 30% have concurrent CA.



Gastric adenocarcinoma

- 90% of all gastric cancers.
- Early symptoms mimic gastritis => late diagnosis.
- Marked geographic variation (Japan, Costa Rica, Chile).
- Screening >> early detection.
- Background of mucosal atrophy and intestinal metaplasia.
- PUD does not increase risk, except after surgery
- In USA rates dropped > 85%, BUT increased rate of cardia cancer due to GERD & obesity.

Pathogenesis
~ Genetic alterations (H.Pylori associated chronic gastritis , lesser extent EBV (10%).
~ Most cases are sporadic.

Lauren classification: separates gastric cancers into

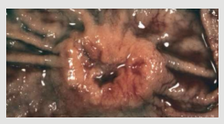
Intestinal

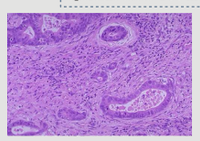
-Bulky.
- Exophytic mass or ulcer.
- Form glands.

Familial intestinal type cancer: FAP, APC gene mutation.

Sporadic intestinal-type Ca: B catenin mutation

Sporadic cases: P53 mutation + HER2 amplification





Clinical Features

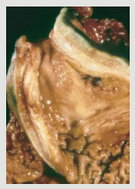
~ High-risk areas
~ Develops from precursor (adenoma, dysplasia associated w/ intestinal metaplasia)
~ Mean age 55 yrs.
~ M:F 2:1

Diffuse

-Infiltrative growth pattern
- Discohesive cells (signet ring cells)
- Desmoplastic reaction (stiffens wall, flat ruge, linitis plastica).

Sporadic diffuse type: somatic CDH1 mutation in 50%.

Familial diffuse type: germline mutations in CDH1 (E-cadherin).

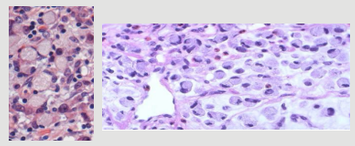


Clinical Features

~ Incidence uniform across countries.
~ No precursor lesion.
~ M:F 1:1
~ Younger age.

Most powerful prognostic factors: depth of invasion & extent of nodal and distant metastasis at the time of diagnosis

Signet ring cells:
large mucin vacuoles that expand the cytoplasm and push the nucleus to the periphery



Lymphoma

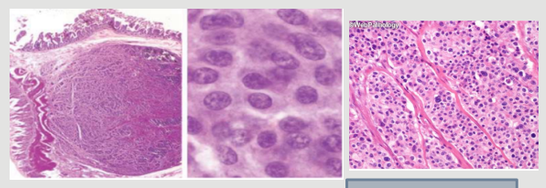
- Stomach is the most common site of extranodal lymphoma.
- 5% of all gastric malignancies.

Most common type : extranodal marginal zone B-cell lymphomas (MALToma)=> (indolent)

Second most common lymphoma: diffuse large B cell lymphoma (aggressive)

Neuroendocrine (Carcinoid) Tumor

- Tumors arising from neuroendocrine-differentiated gastrointestinal epithelia (e.g., G cells).
- > 40% occur in the small intestine.
- Associated with endocrine cell hyperplasia, chronic atrophic gastritis, and Zollinger- Ellison syndrome
- Slower growing than carcinomas.



Nest pattern
Salt and pepper nuclei

carcinoid syndrome
> Due to vasoactive substances
> Seen in 10% of cases.
> strongly associated with metastatic disease.
> manifest as Cutaneous flushing, sweating, bronchospasm,
colicky abdominal pain, diarrhea, and right- sided cardiac valvular fibrosis

Gastrointestinal Stromal Tumor

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