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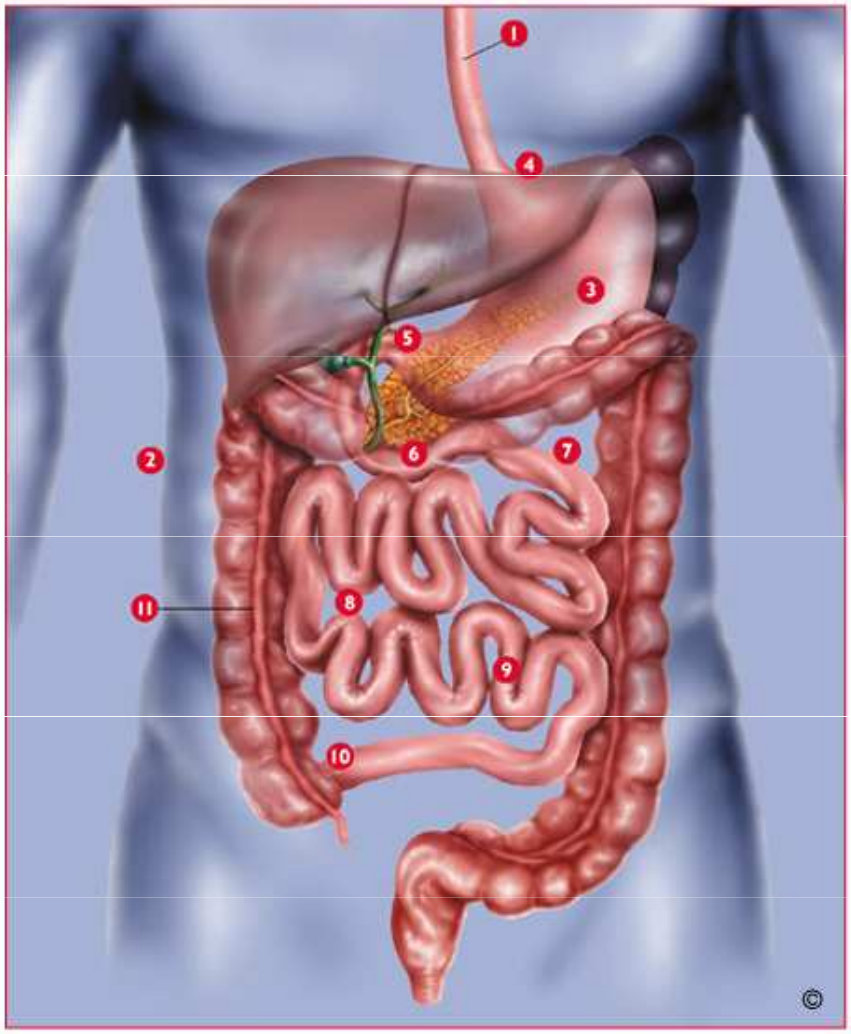
Pathophysiology of gastrointestinal tract

pt. 1, upper GIT

Jaromír Gumulec

The GIT



1- esophagus
2- peritoneal cavity
3- stomach (1.5l)
4- gastroesophageal junction
5- pylorus
6- small intestine (4.5 – 6m)
    7- duodenum
    8- jejunum
    9- ileum
10- ileocoecal valve
11- large intestine
    ascendent
    transversal
    descendent colon
    rectum + anus

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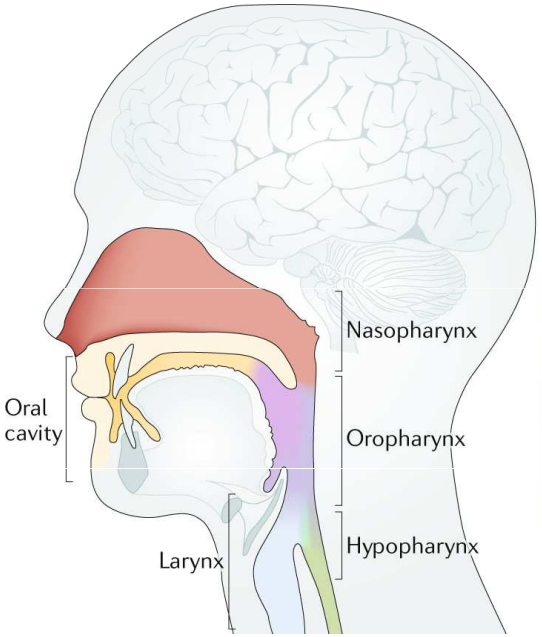
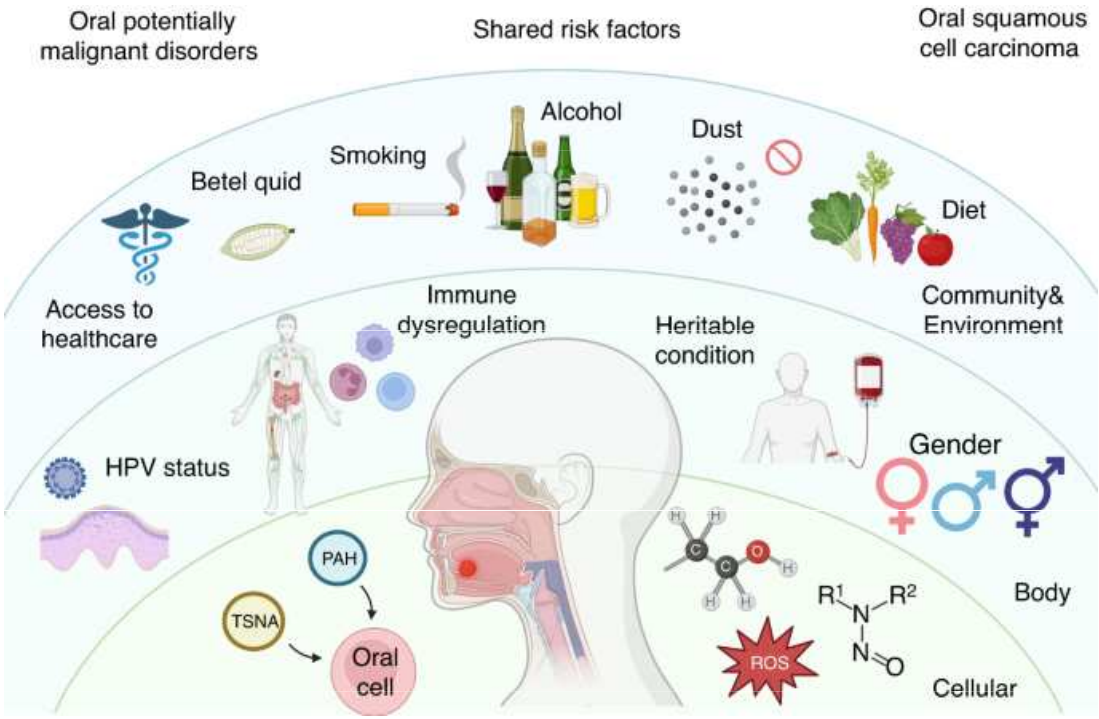
Head and neck squamous cell cancer

- **Etiology**: tombacco, alcohol, HPV, UV light, poor oral hygiene, exposure environmental polutants



Cancer subtype	Annual incidence	
	Worldwide	USA
Oral cavity and lip	358,864	33,950
Laryngeal	177,422	13,150
Nasopharyngeal	129,079	Rare
Oropharyngeal	92,887	NA
Hypopharyngeal	80,608	NA



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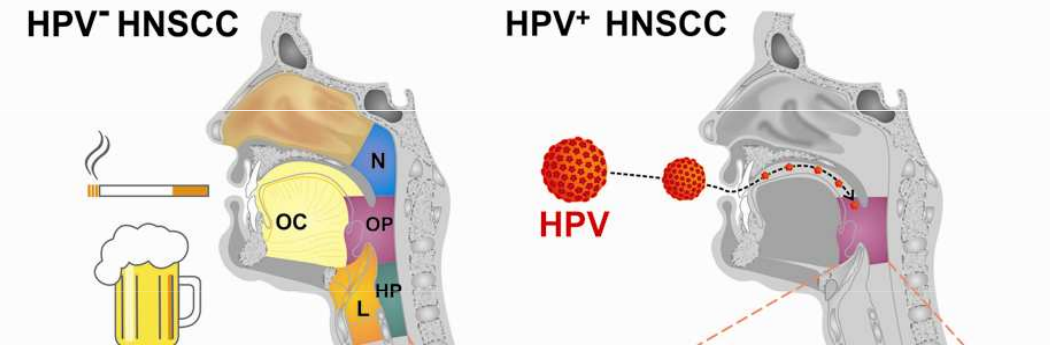
Head and neck squamous cell cancer

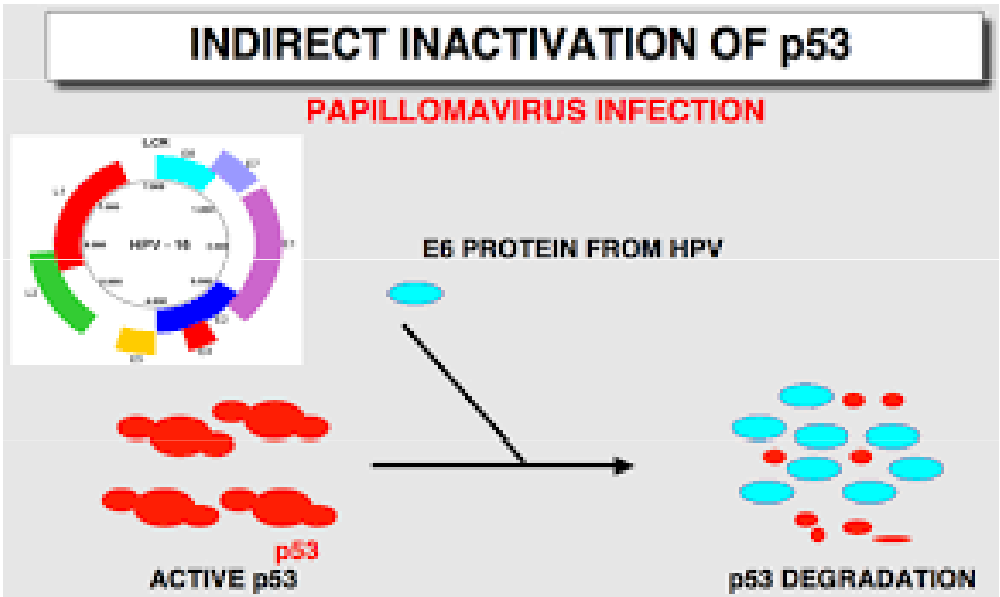
Pathogenesis:

- **Initiation**: Exposure to carcinogens or oncogenic viruses (e.g., HPV) leads to **genetic alterations** (mutations, deletions, amplifications)
- **Promotion**: Proliferation of initiated cells driven by continued exposure of carcinogens.
- **Progression**: additional genetic alterations, leading to **invasive** carcinoma.



Molecular Alterations:

- **TP53** mutations: Commonly observed in HNSCC, associated with resistance to apoptosis and poor prognosis.
- **HPV** infection: Integration of HPV DNA into host genome, leading to overexpression of viral oncoproteins (e.g., E6, E7), inactivation of tumor suppressor genes (e.g., p53, Rb), and promotion of cellular proliferation.
- **EGFR** (epidermal growth factor receptor) overexpression: Associated with tumor proliferation, angiogenesis, and resistance to therapy



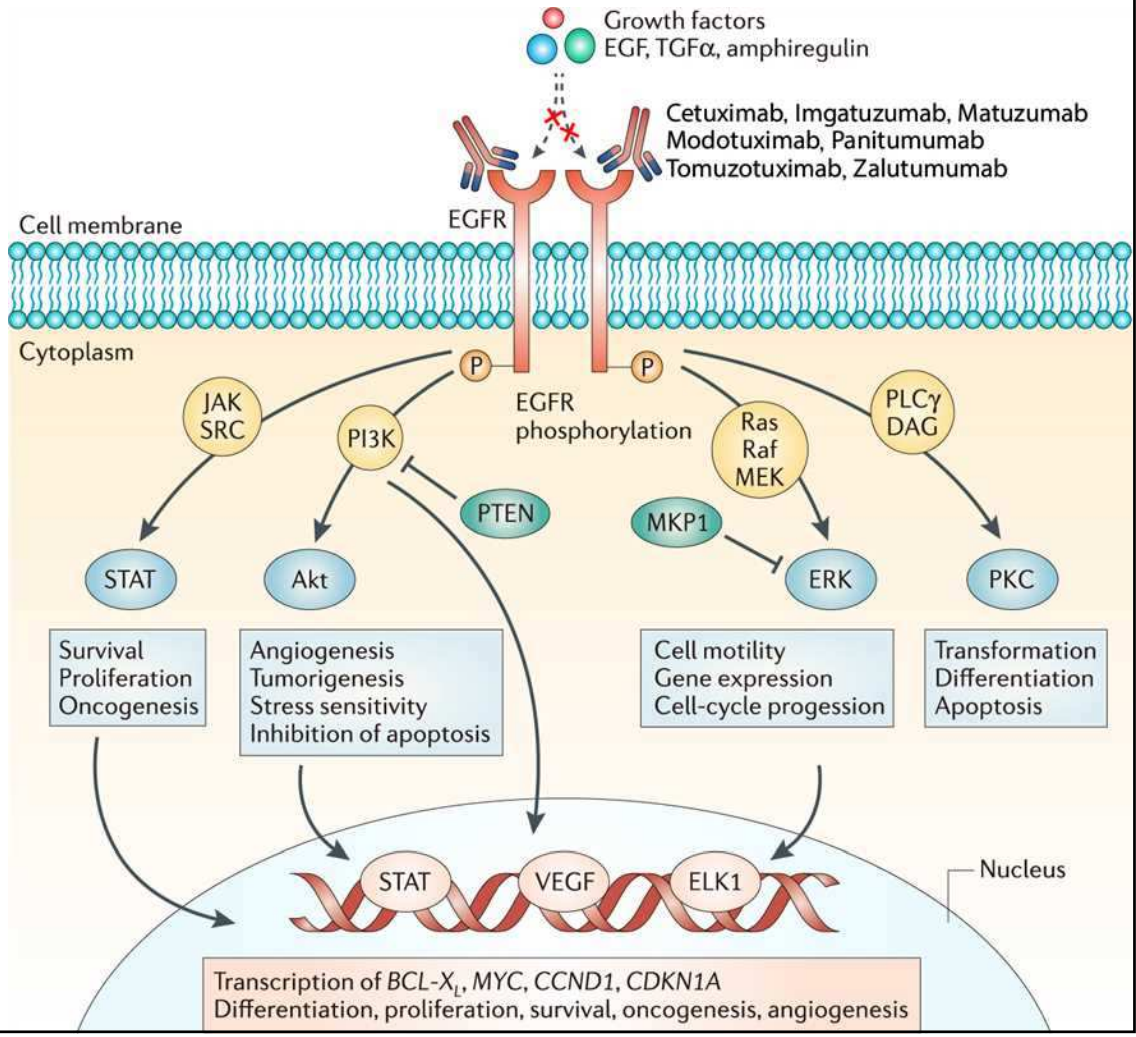
EGFR in head and necjsquamous cell cancer

Impact on Tumor Behavior:

- **Proliferation**: EGFR signaling stimulates cell proliferation and tumor growth.
- **Survival**: Enhances cell survival by inhibiting apoptosis **Invasion and Metastasis**:

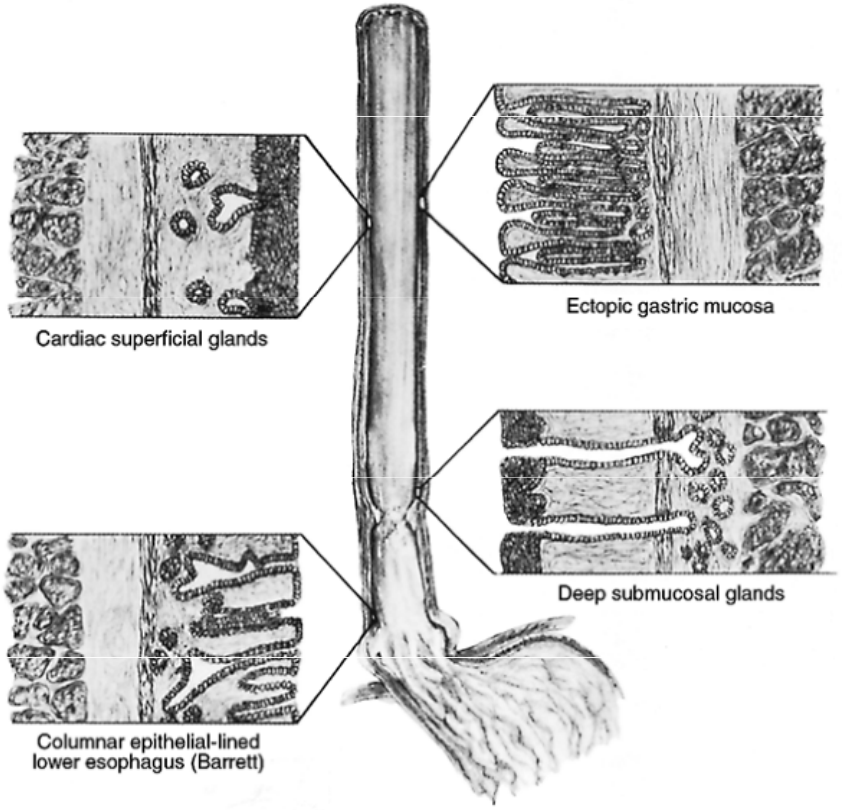
Clinical Implications:

- **Prognostic Marker**: Higher EGFR expression associated with poorer prognosis
- **Therapeutic Target**: EGFR inhibitors (e.g., cetuximab) used in targeted therapy
- **Resistance Mechanisms**: Development of resistance to EGFR inhibitors through HER2, MET or mutations in EGFR itself.



Esophagus - anatomy

- Upper sphincter (cricopharyngeal muscle)
- Upper 2/3 – skeletal muscle, squamous epithelium
- Lower 1/3 – smooth muscle
- Lower sphincter (LES)
- Cylindrical epithelium in the terminal part



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Esophageal diverticula

Weakness in the esophageal wall leading to outpouching formation

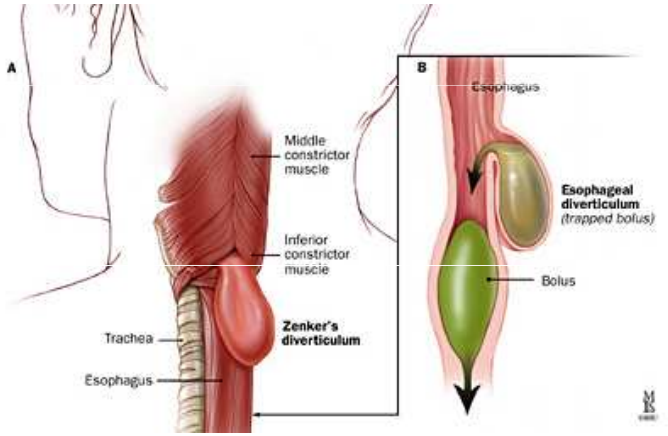
- true diverticula (traction) – include muscular layer
- pseudodiverticula – only mucous layer

Localization

- **Zenker's Diverticulum**: Located in the posterior hypopharyngeal wall, just above the upper esophageal sphincter.
- **Epiphrenic Diverticulum**: Arises in the distal esophagus, typically just above the lower esophageal sphincter.

Factors contributing to the development:

- Zenker's Diverticulum: Dysfunction of the **cricopharyngeal muscle** (upper esophageal sphincter dysfunction) leads to **increased pressure in the hypopharynx during swallowing, causing mucosal herniation**.
- Epiphrenic Diverticulum: Associated with esophageal **motility disorders** such as achalasia or diffuse esophageal spasm, leading to increased intraluminal pressures in the distal esophagus.



pseudodiverticulum true diverticulum

Esophageal diverticula

Factors contributing to the development:

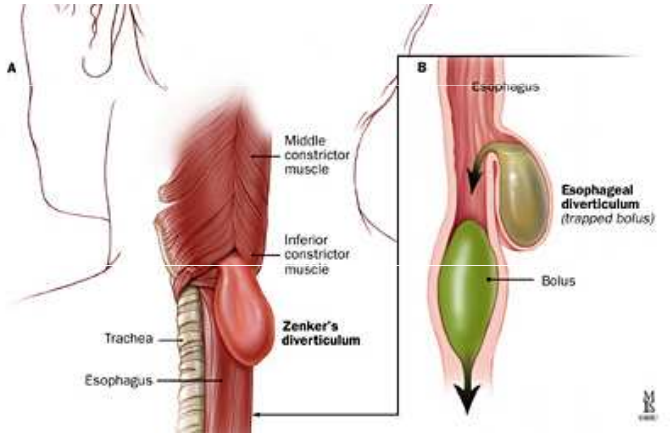
- Increased intraesophageal pressure
- Dysfunction of the esophageal sphincters
- Structural abnormalities
- Motor disorders (e.g., achalasia)

Pathophysiology:

- Result of mediastinal or periesophageal inflammation or fibrosis
- Traction on the esophageal wall leads to outpouching

Clinical features and complications:

- Often asymptomatic
- Dysphagia if large enough to obstruct the esophageal lumen
- Diverticulitis: Inflammation or infection of diverticula, usually resulting from fecal stasis and microperforation of diverticular wall.



pseudodiverticulum true diverticulum

Dysphagia

•Difficulty swallowing, a common symptom in esophageal diverticula
•Mechanisms:
- Mechanical obstruction caused by the diverticulum
- Functional impairment due to associated motility disorders

Functional
- Inflammation in gastroesophageal reflux
- Sclerodermia
- Neuropathy (e.g. in diabetes)
- Amyotrophic lateral sclerosis
- Achalasia

Obstructive
Tumours
Strictures
Peptic ulcers

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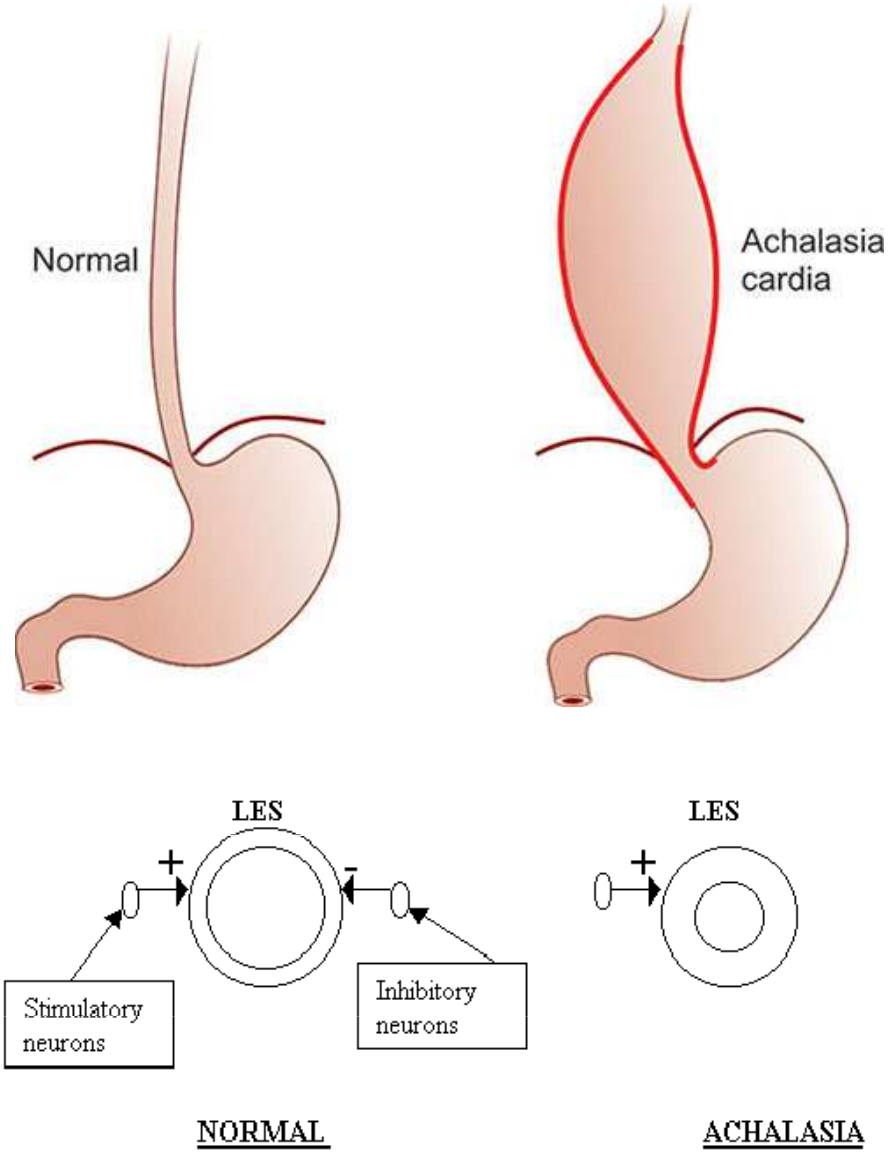
Esophageal achalasia

The lower sphincter is incapable of relaxation
This leads into esophageal **dilatation** and **loss of peristaltic** movements

- The primary cause is the **disorder of myenteric plexus** (plexus Auerbachi), which produces **NO**
- NO acts as a neurotransmitter, leading to relaxation of the LES

Most often, it is caused by **autoimune destruction**

Complications: Esophageal dilation, aspiration pneumonia.



Hiatal hernias

- Weakness in Diaphragmatic Structures:
  - phrenoesophageal ligament and muscular diaphragmatic crura, allowing the stomach to herniate through the esophageal hiatus.
- Increased Intra-abdominal Pressure: (obesity, pregnancy, chronic cough, or heavy lifting)
- Aging: Age-related changes in connective tissue

sliding

Lower esophageal sphincter and upper part of stomach slides into thoracic cavity

Low external pressure in the thoracic cavity leads into the loss of function of LES and gastroesophageal reflux

paraesophageal

Part of stomach‘s fundus is squeezed into thoracic cavity paralelly with esophagus

This can lead into its incarceration or strangulation with necrosis (life-threatening)

Mostly, it manifests by pain and vomiting

Hiatal hernias – risk factors, complications

- Wide hiatus
- Obesity
- High intraabdominal pressure
- Gravidity

Complications:
•Gastroesophageal Reflux Disease
•Esophagitis: Barrett's esophagus
•Bleeding

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Gastroesophageal reflux disease (GERD)

Retrograde movement of gastric juice = Loss of anti-reflux barrier

Pathophysiology:

- Incompetent lower esophageal sphincter (LES) allowing retrograde flow of gastric contents.
- Impaired esophageal clearance mechanisms.
- Factors contributing to LES dysfunction:
  - Hiatal hernia
  - Obesity
  - Smoking
  - Certain medications (e.g., anticholinergics, calcium channel blockers)

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GERD – symptoms and complications

- Clinical Features:
  - Heartburn: Retrosternal burning sensation, often exacerbated by lying down or after meals.
  - Regurgitation: Sour or bitter taste in the mouth due to refluxed gastric contents.
  - Dysphagia: Sensation of difficulty swallowing, especially in severe cases.
- Complications:
  - Esophagitis: Inflammation of the esophageal mucosa.
  - Barrett's esophagus: Metaplastic change in the esophageal epithelium, predisposing to esophageal adenocarcinoma.

Barrett‘s esophagus

metaplastic change in the esophageal epithelium, where normal **squamous epithelium is replaced by columnar epithelium** containing goblet cells.

Causes

- GERD
- Hiathal hernia
- Genetic factors
- Lifestyle (obesity, smoking), age, male gender, NSAID overuse

Barrett‘s esophagus

Mechanism

•Activation of signaling pathways involved **in epithelial cell differentiation and proliferation**

•Wnt/β-catenin, Notch, and Hedgehog signaling, contributes to the **development and maintenance** of metaplasia.

Complications:

•Esophageal Adenocarcinoma (EAC)
(not Esophageal Squamous Cell Carcinoma!)

•Dysplasia:

•Gastroesophageal Reflux Disease (GERD)

Esophageal varices

Definition: dilated, tortuous veins located in the submucosa of the esophagus, typically as a result of portal hypertension.

Pathophysiology

- Portal hypertension from liver cirrhosis.
- Collateral vessels form, causing varices.
- Varices prone to rupture, leading to bleeding.

Causes of Portal Hypertension:

- Liver Cirrhosis: Main cause.
- Portal Vein Thrombosis.
- Budd-Chiari Syndrome (hepatic venous outflow obstruction).

Esophageal varices - complications

Diagnosis:

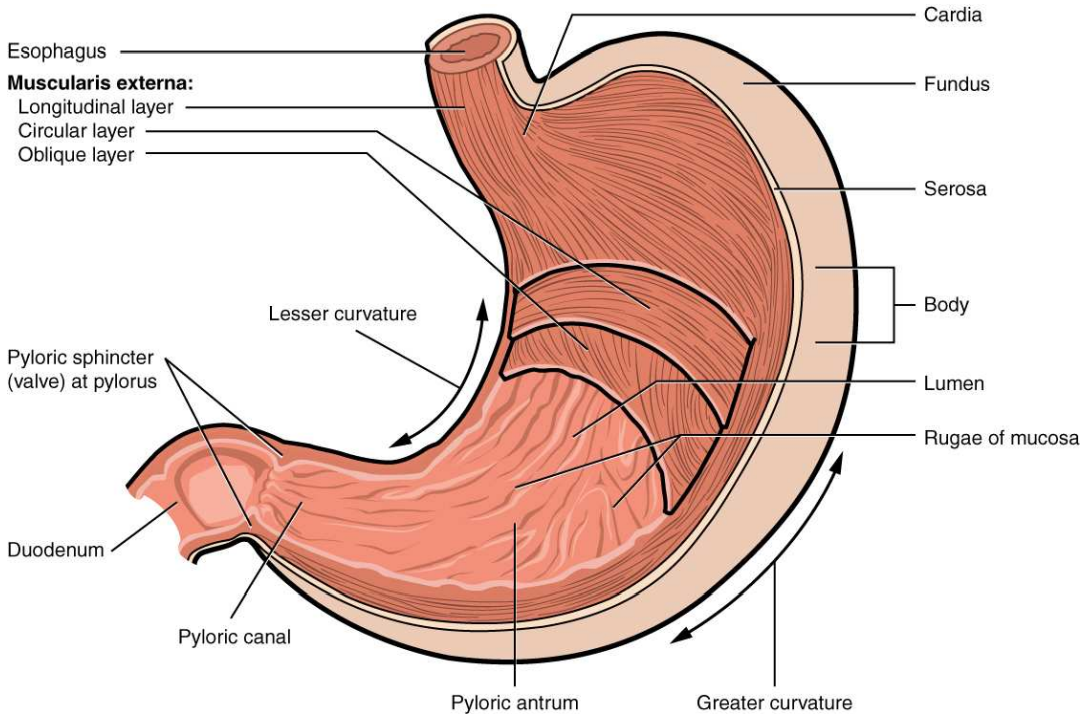
- Upper endoscopy.
- Imaging: Doppler ultrasound, CT, MRI.
- Liver function tests.

Complications:

- Variceal hemorrhage.
- Hypovolemic shock.
- Hepatic encephalopathy.

Stomach physiology

- Motor functions of the stomach
  - storage
  - mixing and propulsion
  - emptying
- Secretions
  - parietal cells - HCl, intrinsic factor
  - chief cells – enzymes (pepsinogen, gastric lipase)
  - surface cells - mucous, sodium bicarbonate



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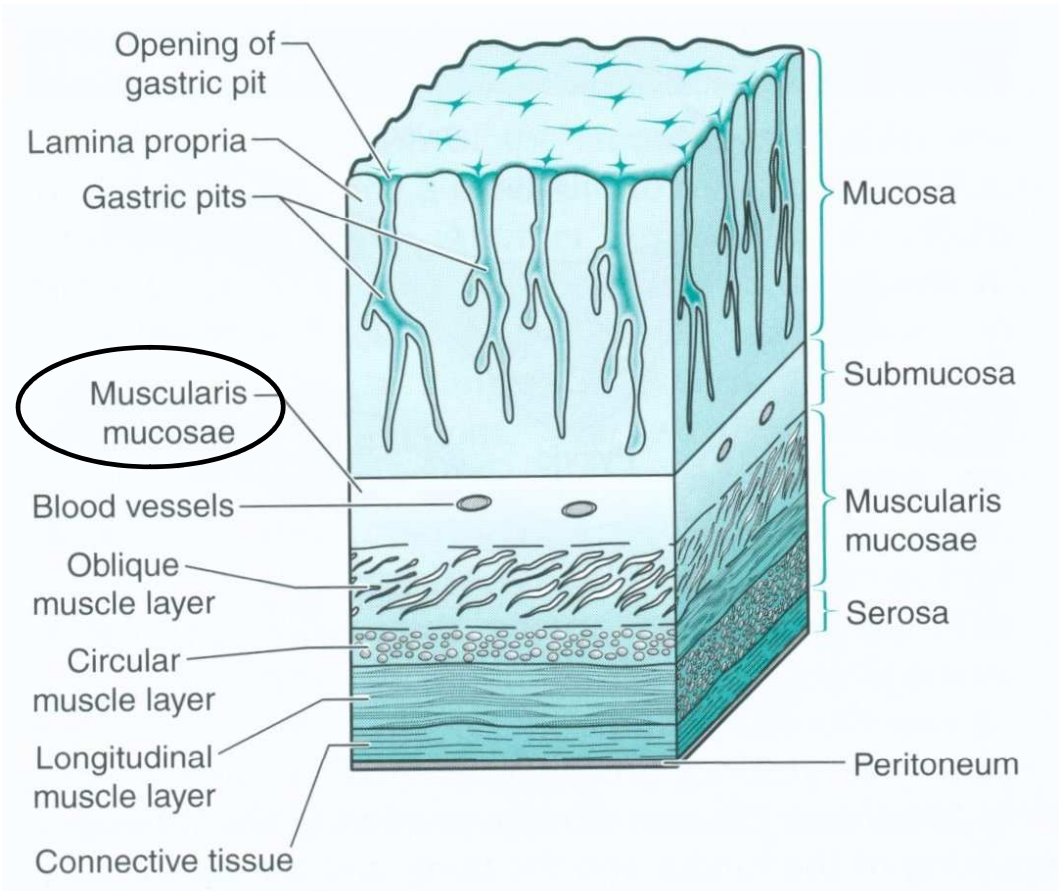
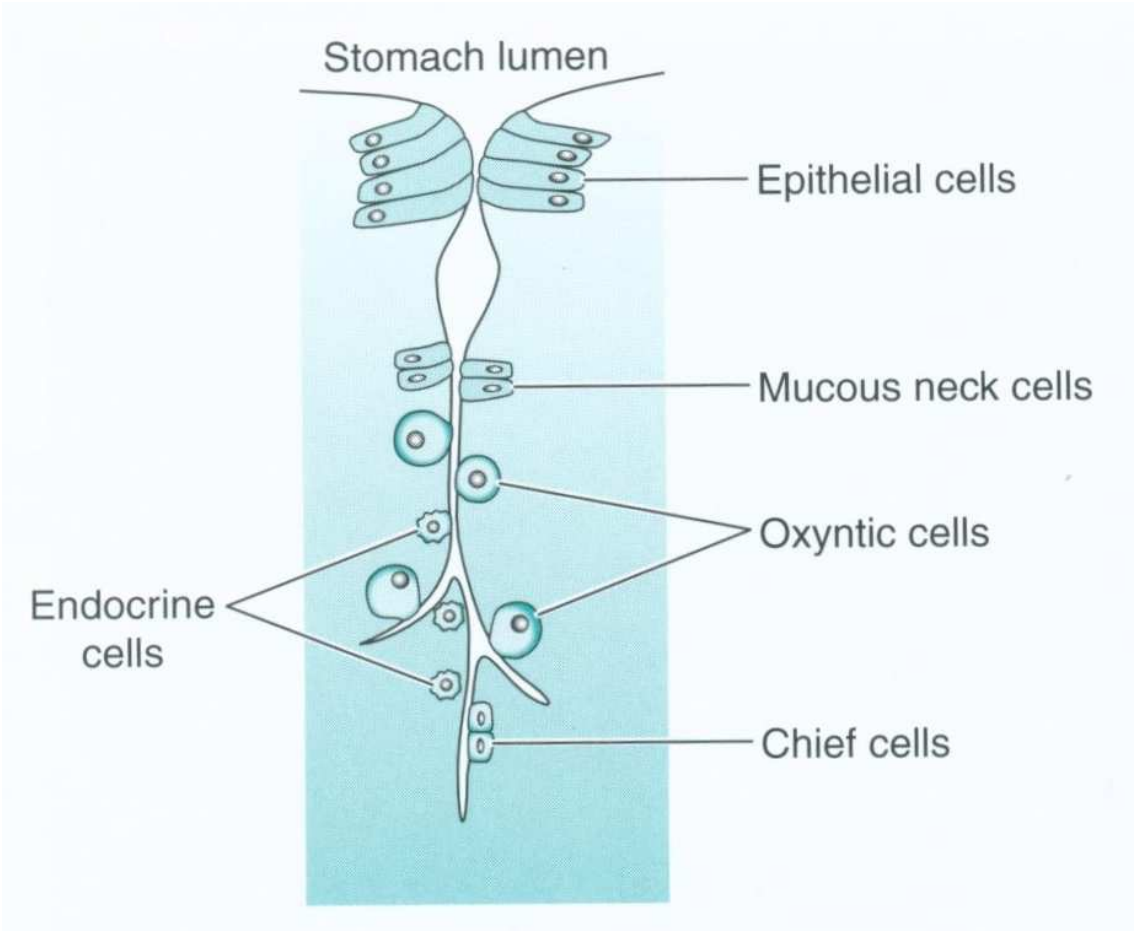
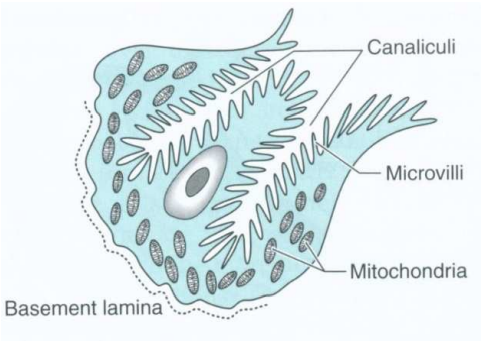

Opening of gastric pit
Lamina propria
Gastric pits
Muscularis mucosae
Blood vessels
Oblique muscle layer
Circular muscle layer
Longitudinal muscle layer
Connective tissue
Mucosa
Submucosa
Muscularis mucosae
Serosa
Peritoneum


Stomach lumen
Epithelial cells
Mucous neck cells
Oxyntic cells
Endocrine cells
Chief cells

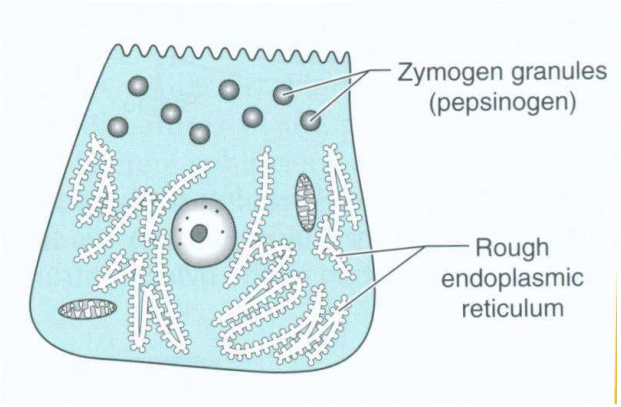
Parietal cell



•Secretion of **Hydrochloric Acid** (HCl):
- Activated by histamine, gastrin, and acetylcholine.
- Lowers pH of gastric contents for optimal enzymatic activity and antimicrobial defense.

•Secretion of **Intrinsic Factor**:
- Essential for absorption of vitamin B12 in the ileum.
- Deficiency leads to pernicious anemia.

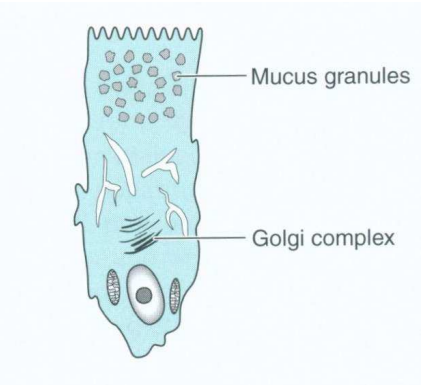
Chief cell



•Secretion of **Pepsinogen**:
- Inactive precursor of pepsin, a proteolytic enzyme.
- Activated to pepsin by low pH in the stomach.

•Contribution to Protein Digestion:
- Breaks down dietary proteins into peptides and amino acids.

Mucous neck cell



•Production of **Mucus and bicarbonate**: Forms protective layer over gastric mucosa.
•Prevents self-digestion by gastric acid and pepsin.
•Facilitates smooth passage of food through stomach.

Other cell types

- Enterochromaffin-like (ECL) Cells:
  - Secretion of Histamine:
    - Acts as a paracrine signaling molecule to stimulate parietal cells.
    - Potentiates secretion of HCl in response to gastrin and acetylcholine.
- G Cells (Gastric Cells):
  - Secretion of Gastrin:
    - Stimulates acid secretion by parietal cells.
    - Promotes gastric motility and emptying.
    - Regulated by luminal pH and presence of food in stomach.
- D Cells:
  - Secretion of Somatostatin:
    - Inhibits acid secretion by parietal cells.
    - Acts as a negative feedback regulator of gastric acid secretion.

Phases of gastric secretion regulation

Phase	Trigger	Mechanism	Contribution to Secretion
Cephalic Phase	Smell, taste, sight, thought of food	**Vagus nerve (ACh)** stimulates parietal cells, G cells	~30% of total secretion
Gastric Phase	Food enters stomach (distension, peptides, pH change)	**Gastrin (G cells), vagus nerve (ACh), histamine (ECL cells)**	~60% of total secretion
Intestinal Phase	Chyme enters duodenum	**Enterogastric reflex (inhibitory), secretin, CCK, GIP**	~10% of secretion, mainly inhibitory

Neural Regulation of Gastric Secretion

- **Vagus nerve (parasympathetic system)** plays a major role:
  - Stimulates **parietal cells** (HCl secretion).
  - Stimulates **G cells** (gastrin release).
  - Stimulates **chief cells** (pepsinogen release).
  - Increases **mucus production**.
- **Local enteric nervous system (ENS)**:
  - Controls **peristalsis**, secretion, and feedback inhibition.

Neurotransmitters Involved

Neurotransmitter	Effect
Acetylcholine (ACh)	Stimulates **parietal cells**, **G cells**, and **ECL cells** (histamine release)
Gastrin-releasing peptide (GRP)	Stimulates **G cells** (gastrin release)
VIP (Vasoactive Intestinal Peptide)	Inhibits gastric secretion, stimulates bicarbonate secretion
Somatostatin (from D cells)	Inhibits **gastrin**, **parietal cells**, and **histamine release**

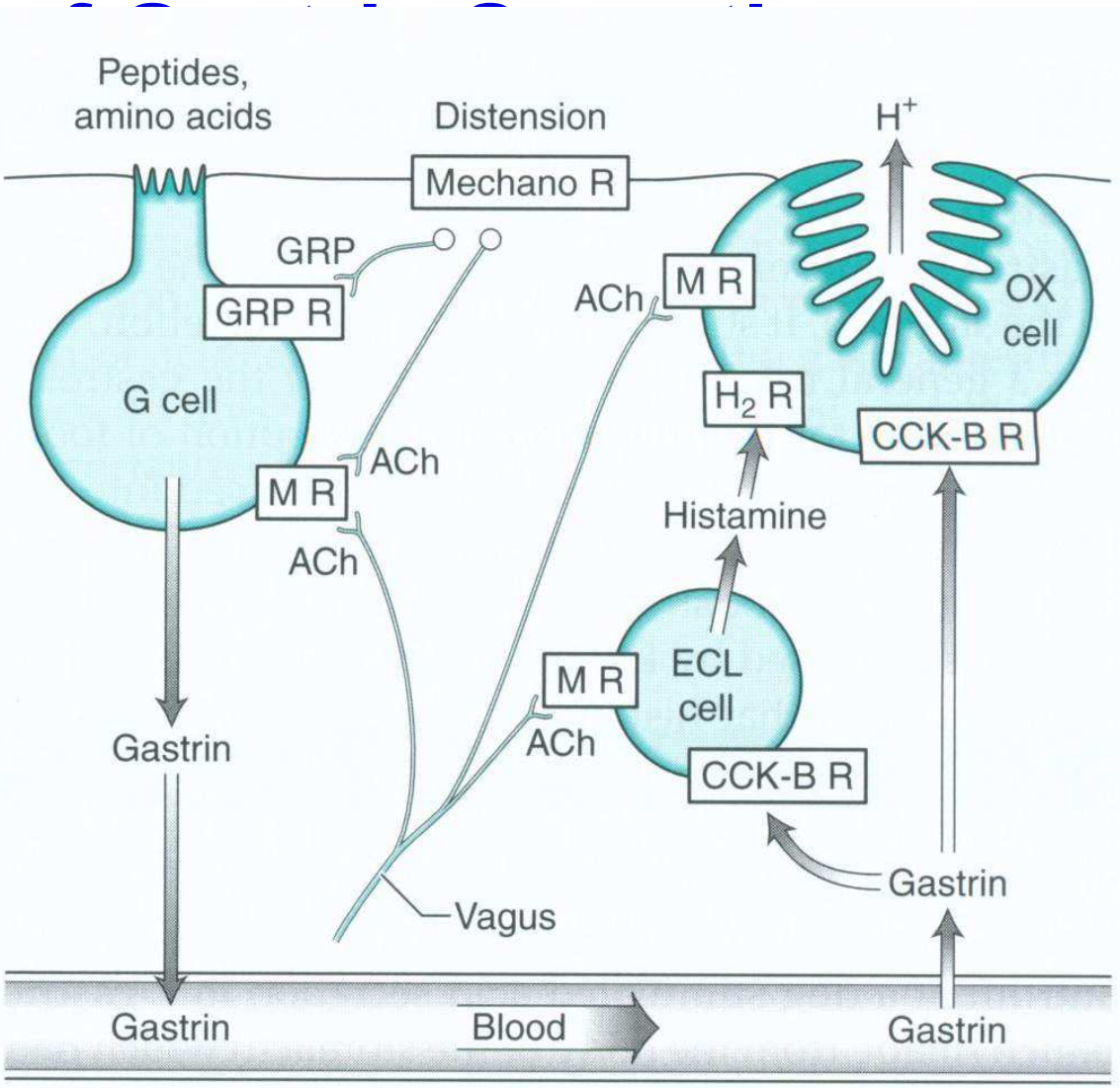
Hormonal Regulation

Gastrin (Key Stimulatory Hormone):

- **Secreted by**: **G cells** (in the antrum of the stomach).
- **Stimulus**:
  - Presence of **peptides/amino acids** in the stomach.
  - Gastric distension.
  - Vagal stimulation (via GRP).
- **Effects**:
  - Stimulates **parietal cells** → ↑ **HCl** secretion.
  - Stimulates **chief cells** → ↑ **pepsinogen** secretion.
  - Stimulates **ECL cells** → ↑ **histamine**, which further stimulates acid secretion.
  - Enhances gastric motility.

Histamine (Paracrine Regulation)

- **Secreted by**: **Enterochromaffin-like (ECL) cells**.
  - **Stimulus**: **Gastrin** and **vagal stimulation**.
  - **Effect**: Binds **H_2 receptors on parietal cells** → **potentiates acid secretion**.
  - **Clinical relevance**: **H_2 blockers** (e.g., ranitidine) reduce acid secretion



Hydrochloric acid secretion in parietal cells

•Stimulation: Triggered by various stimuli including histamine, gastrin, and acetylcholine.
•Activation of H+/K+ ATPase Pump:
- Proton pump located on the apical membrane of parietal cells.
- Exchanges cytoplasmic K+ for luminal H+ ions, generating an electrochemical gradient.

•Secretion of HCl:
- H+ ions are actively pumped into the stomach lumen.
- Cl- ions follow passively via anion channels, forming HCl.

•Acidification of Gastric Contents:
- Lowers pH to around 1-2, creating an acidic environment optimal for digestion and microbial defense.

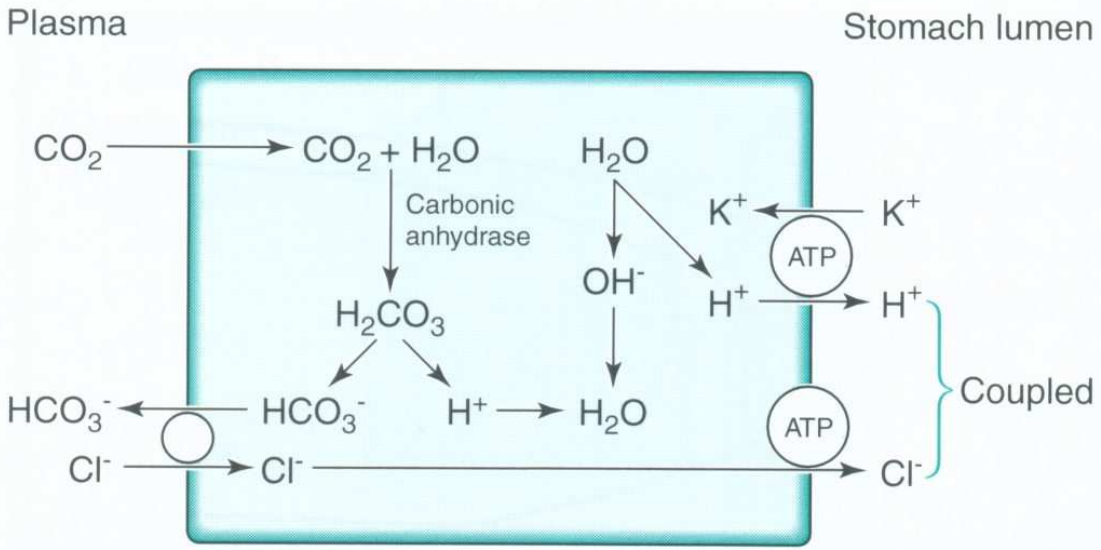


Fig. 3.7
Hydrochloric acid secretion by the oxyntic cell.

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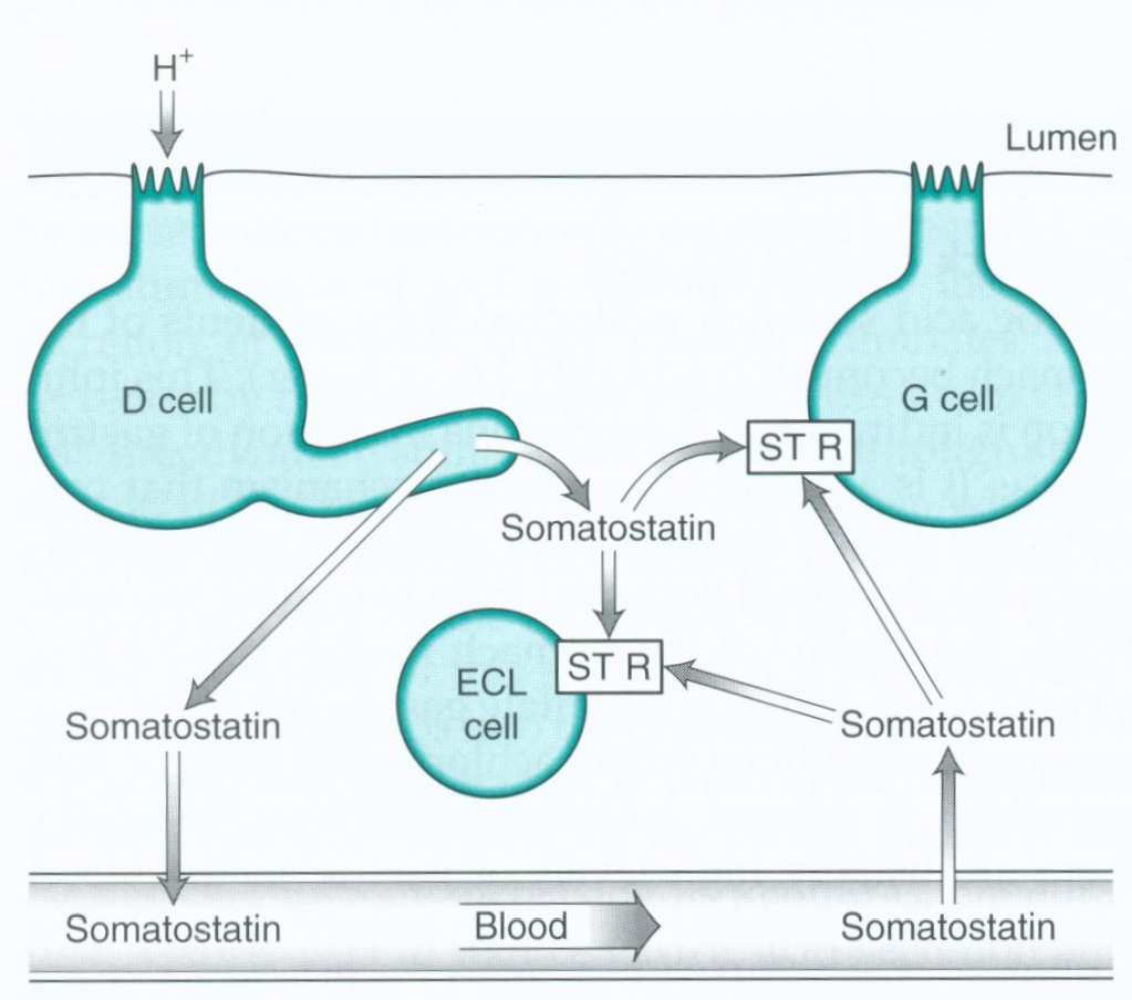
Somatostatin : Negative Regulation of HCl

- **key inhibitory regulator** of gastric acid secretion
- Released by D cells in response to low luminal pH and inhibits acid secretion by parietal cells.

Feedback loop helps maintain gastric pH balance and prevent excessive acid production.

- Release Stimuli:
  - Low pH (acidic conditions, pH <3 in stomach) → Direct stimulation of D cells.
  - Secretin (from S cells in duodenum) → Enhances somatostatin release.
  - CCK (from I cells in duodenum) → Also promotes somatostatin release.
  - Vagal stimulation (ACh, via M3 receptors) inhibits somatostatin (during the cephalic and gastric phases).



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Pathology

- Pathophysiology:
  - **Peptic Ulcer Disease** (PUD): Erosion of gastric or duodenal mucosa due to imbalance between protective factors (mucus, bicarbonate) and damaging factors (acid, pepsin).
  - **Gastritis**: Inflammation of gastric mucosa, often due to infection (Helicobacter pylori), NSAID use, or alcohol abuse.
  - **Gastric Cancer**: Malignant tumor arising from gastric epithelium, often associated with chronic gastritis, H. pylori infection, or genetic predisposition.
  - **Zollinger-Ellison syndrome**
  - **Gastroparesis**
- Common Symptoms:
  - **Dyspepsia**: Epigastric discomfort, bloating, early satiety.
  - **Hematemesis:** Vomiting of blood, indicative of gastrointestinal bleeding.
  - **Melena**: Dark, tarry stools due to digested blood.
  - **Nausea**, vomiting, weight loss.

Gastritis

Inflammation of the gastric mucosa, characterized by mucosal injury and infiltration of inflammatory cells.

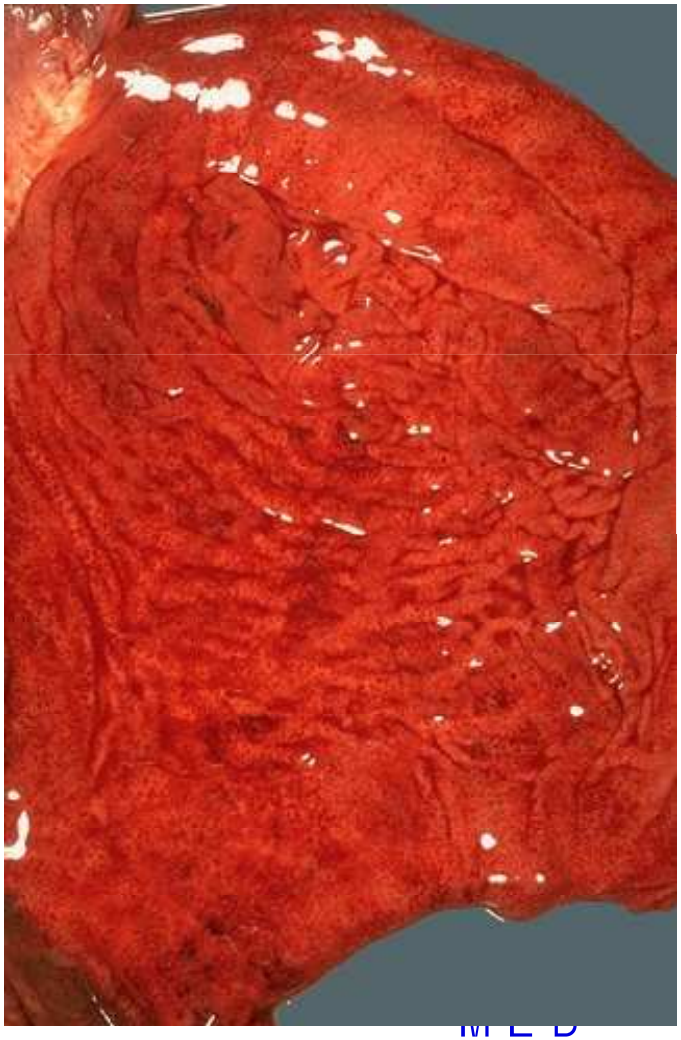
- **Acute Gastritis**:
  - Sudden onset, often due to irritants such as NSAIDs, alcohol, or infectious agents (e.g., H. pylori).
- **Chronic Gastritis**:
  - Persistent inflammation, typically associated with H. pylori infection, autoimmune conditions (e.g., autoimmune gastritis), or long-term use of NSAIDs.
- Etiology:
  - **Helicobacter pylori (H. pylori) infection**: Most common cause of chronic gastritis, implicated in peptic ulcer disease and gastric cancer.
  - **NSAID Use**: Direct mucosal injury leading to erosions and inflammation.
  - **Alcoho**l: Disruption of mucosal barrier and stimulation of acid secretion.
  - **Autoimmune Disorders**: Antibodies target gastric mucosal cells, leading to chronic inflammation (e.g., autoimmune gastritis).
  - Severe inless

Acute Gastritis mechnaism

Etiology:

- **Helicobacter pylori (H. pylori) infection**: Most common cause of chronic gastritis, implicated in peptic ulcer disease and gastric cancer.
- **NSAID Use**: Inhibtion of prostaglandins, Direct mucosal injury leading to erosions and inflammation.
- **Alcoho**l: Disruption of mucosal barrier and stimulation of acid secretion.
- **Severe inless**

- Disruption of **mucosal barrier** → acid-induced injury → inflammation.
- **Symptoms**: Epigastric pain, nausea, vomiting, GI bleeding (if severe).



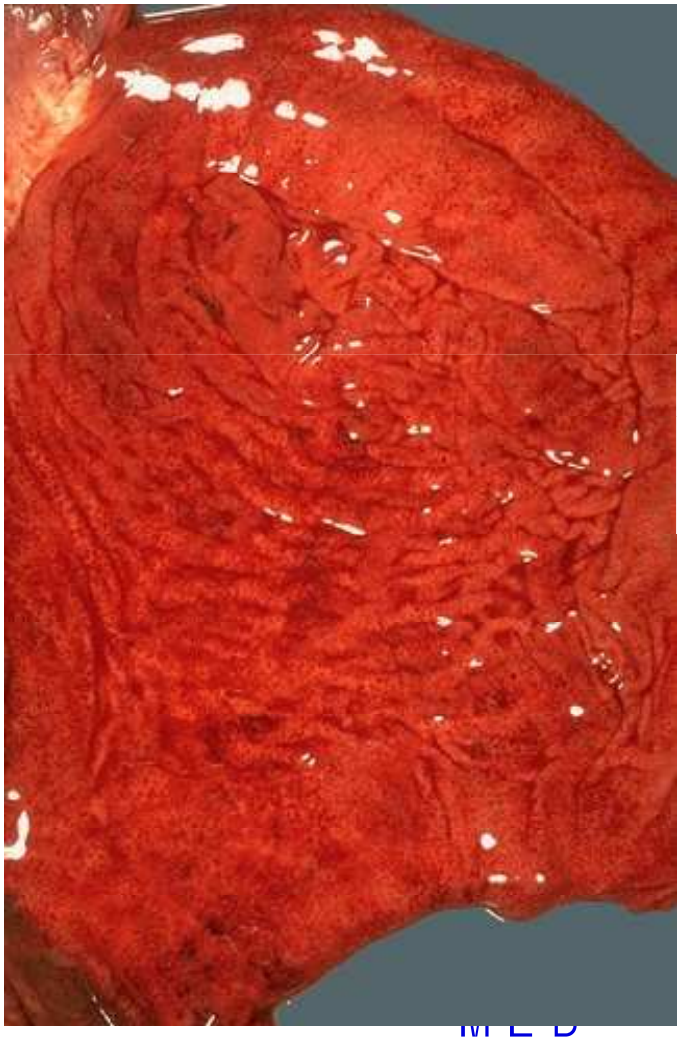
Gastritis mechnaism

•Activation:
- H. pylori: Release of virulence factors (e.g., cytotoxin-associated gene A, CagA) causing mucosal damage.
- NSAIDs/Alcohol: Direct injury to gastric mucosa, disrupting barrier function.

•Inflammatory Response:
- **Recruitment of immune cells** (neutrophils, lymphocytes) to the gastric mucosa.
- **Release of pro-inflammatory cytokines** (e.g., interleukin-1β, tumor necrosis factor-α).

•Mucosal Damage:
- Disruption of epithelial integrity, erosion of gastric mucosa.
- Activation of inflammatory pathways, amplifying tissue injury.

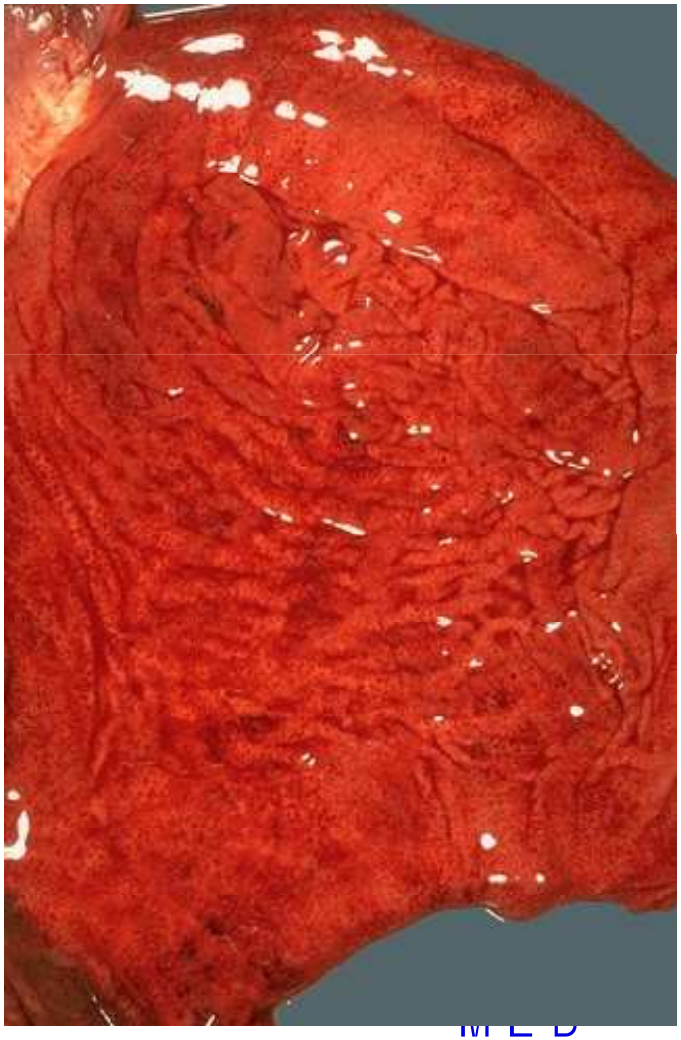
•Consequences:
- Chronic Inflammation: Persistence of inflammatory
- Ulcer Formation
- Carcinogenesis: Chronic inflammation-associated



Gastritis mechnaism

- **Type A (Autoimmune metaplastic atrophic gastritis)**:
  - **Pathophysiology**: Autoantibodies against **parietal cells & intrinsic factor** → **achlorhydria**, **pernicious anemia** (B12 deficiency).
  - **Associations**: Increased risk of **gastric cancer**.

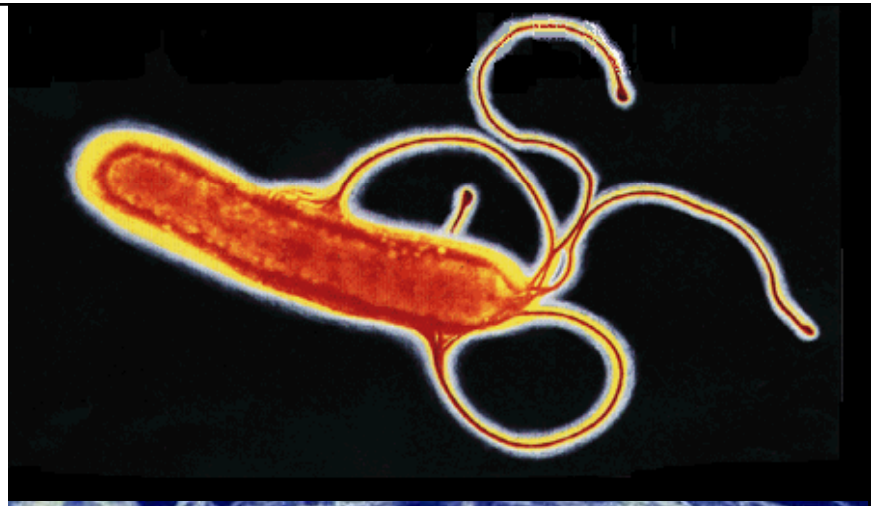
- **Type B (H. pylori-associated gastritis)**:
  - **Pathophysiology**: H. pylori colonizes antrum → **inflammation**, **increased gastrin** → increased acid secretion → risk of **peptic ulcer disease**.
  - **Associations**: Can progress to **MALT lymphoma**, gastric adenocarcinoma.

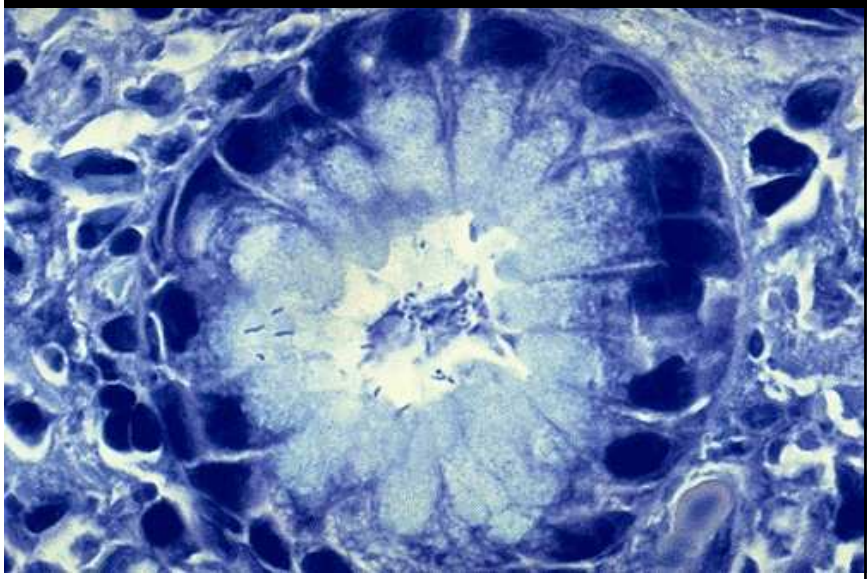


H Pylori

- Gram-negative, spiral-shaped, microaerophilic bacterium
- Resides in the gastric mucosa, primarily in the antrum of the stomach
- 50-60% of the global population infected, but only some develop clinical disease

•Adherence
•Colonization
•Inflammatory Response





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Helicobacter pylori

- **Urease Production:**
  - H. pylori converts urea to NH_3+CO_2, buffering gastric acid.
- Movement:
  - Flagella enable motility, facilitating penetration of mucus layer.
- Adhesins:
  - BabA, SabA, AlpA/B: Bind to gastric epithelial cells, facilitating colonization.
- Cytotoxin-Associated Gene A (**CagA)**:
  - Injected via Type IV Secretion System (T4SS).
  - Phosphorylated CagA alters host cell signaling, contributing to gastric carcinogenesis.
- Vacuolating Cytotoxin A (**VacA**):
  - Forms pores, causing vacuolation and cellular damage.
  - Induces apoptosis and modulates immune response.
- Gamma-Glutamyl Transpeptidase (GGT):
  - Generates reactive oxygen species, promoting oxidative stress.
  - Impairs host immune response and mucosal integrity.
- Outer Inflammatory Protein A (OipA):
  - Induces inflammation and enhances adherence.

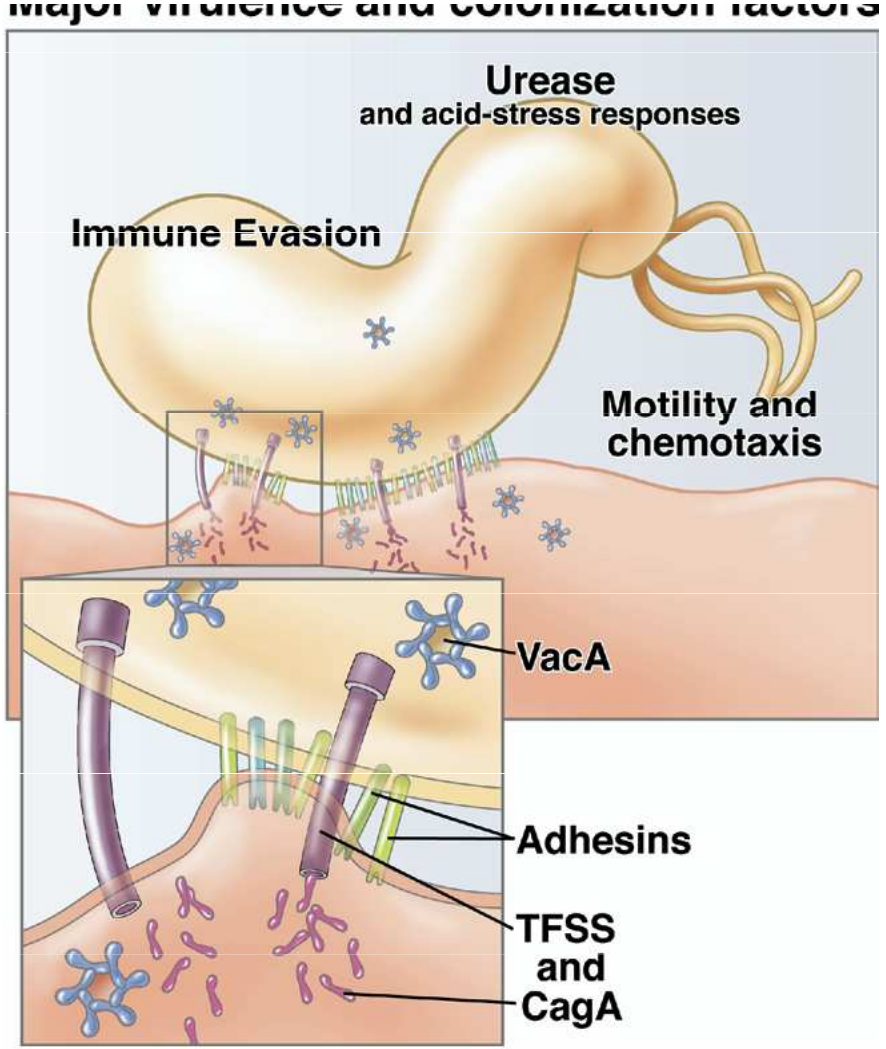


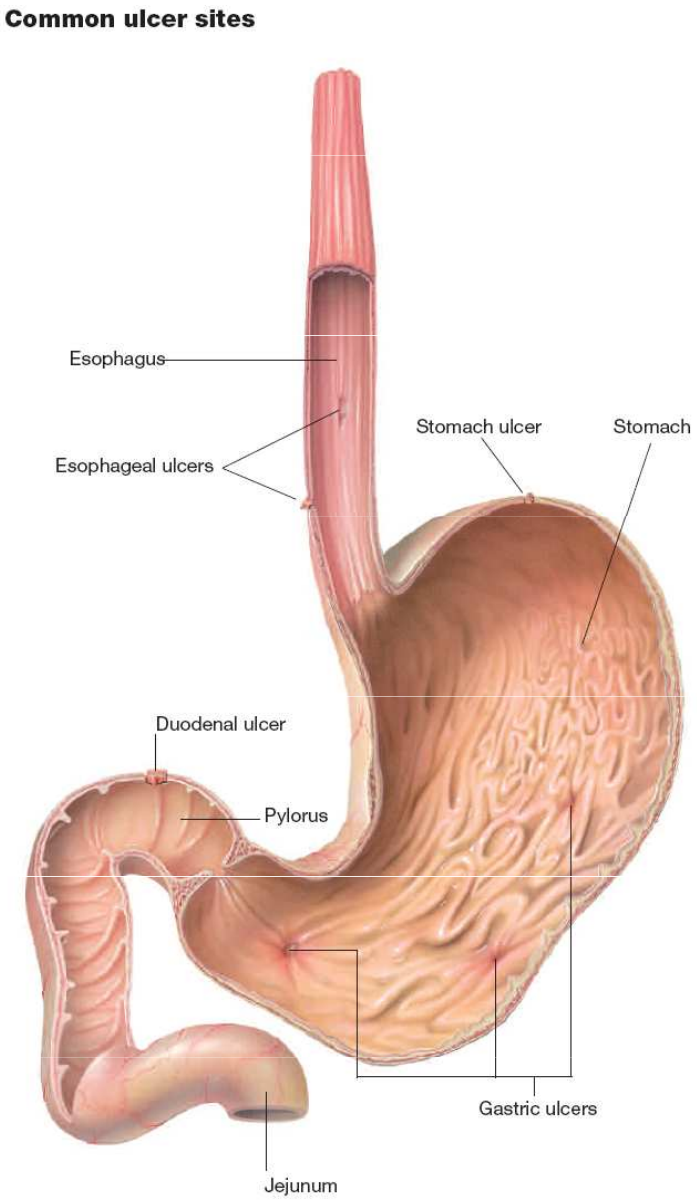
Figure 1 *Helicobacter pylori* major virulence and colonization factors

H Pylori

- **Induction of Chronic Inflammation**
  - **H. pylori triggers an immune response**, but evades clearance.
  - **Inflammation leads to:**
    - Chronic **gastritis** (lymphocyte infiltration, epithelial damage).
    - Increased **gastrin secretion** → **acid hypersecretion** (→ duodenal ulcers).
    - **Metaplasia & dysplasia** → potential progression to **gastric adenocarcinoma**.
  - Diagnostic Tests:
    - Stool antigen test (detects H. pylori antigens).
    - Endoscopic biopsy with histology or urease test.
    - Urea breath test (detects CO_2 from urease activity).

Peptic ulcer

- Mucosal defect reaching deeper than muscularis mucosae layer, localized in areas exposed to acid-pepsin secretions.
- Causes:
  - Helicobacter pylori (H. pylori) infection
  - NSAIDs Disrupt mucosal integrity, inhibit prostaglandin synthesis, increasing susceptibility to injury.
  - Excessive alcohol consumption, smoking, stress, and genetic predisposition.
- Most Common Locations:
  - Gastric ulcers → Lesser curvature of the stomach (near the antrum).
  - Duodenal ulcers → First part of the duodenum.



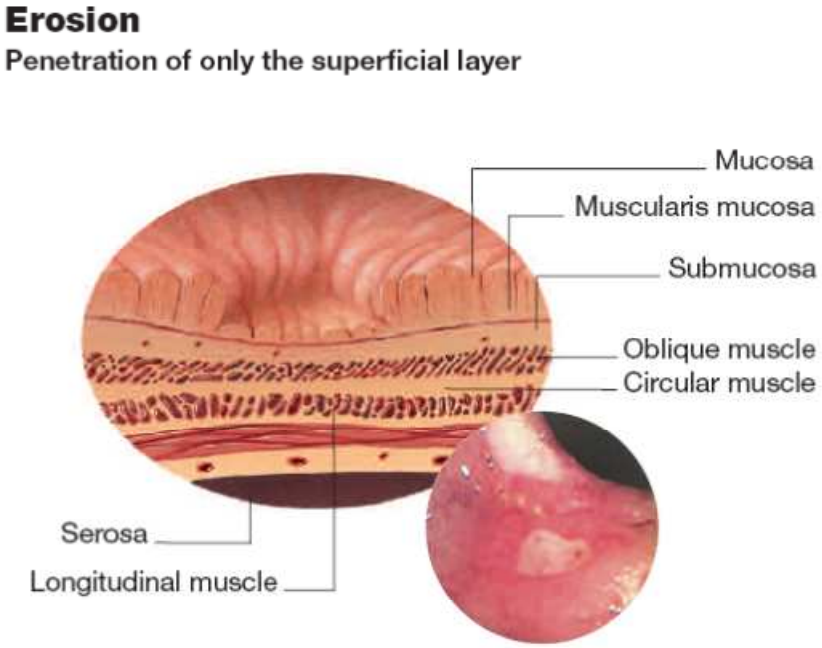
Pathological anatomy

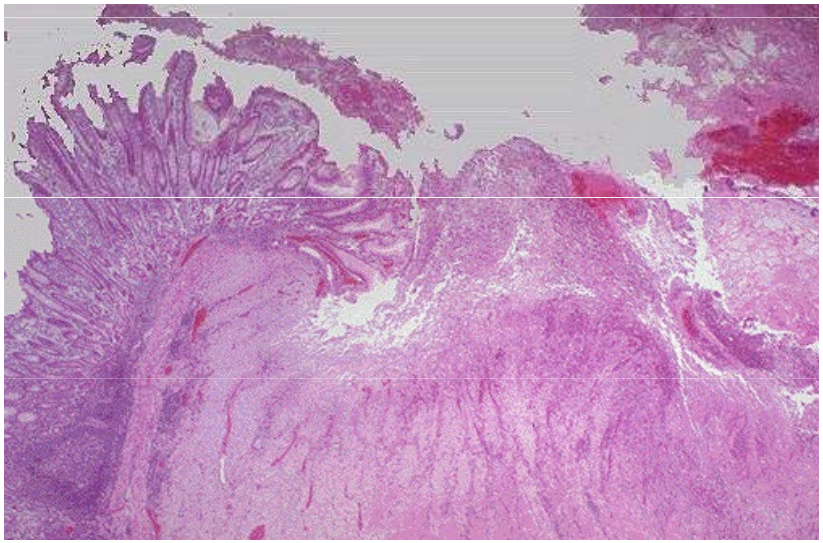
Diagnosis:

•Upper Endoscopy: Direct visualization of ulcers, biopsy for H. pylori testing and histological examination.

•H. pylori Testing: Serology, urea breath test, stool antigen test.

•Imaging Studies: Upper GI series, CT scan, MRI, to assess ulcer size and complications.





Stomach vs. Duodenal Ulcers Differences

Feature	**Gastric Ulcers** (Stomach)	**Duodenal Ulcers**
Location	Lesser curvature of the stomach (antrum)	First portion of the duodenum
Primary Cause	↓ **Mucosal protection** (weakened barrier)	↑ **Acid secretion**
H. pylori association	**~70%** of cases	**>90%** of cases
Gastrin levels	**Normal or decreased**	**Increased** (due to reduced acid inhibition)
Gastric acid secretion	**Normal or low** (mucosal damage is primary issue)	↑ **Increased** (H. pylori affects inhibitory feedback)
Pain Pattern	**Worsens with food** (acid secretion directly irritates ulcer)	**Improves with food** (bicarbonate-rich secretions neutralize acid), worsens 2-3 hours later or at night
Cancer Risk	**Higher (gastric adenocarcinoma risk)**	**Lower risk of malignancy**
Complications	Bleeding (gastric artery erosion), perforation, gastric outlet obstruction	Perforation (into pancreas), bleeding (gastroduodenal artery erosion)

Complications of peptic ulcer

Complications:

- **Bleeding**: Major complication, requires urgent medical attention and may necessitate endoscopic hemostasis or surgery.
- **Perforation**: Ulcer penetration through the gastric wall, leading to peritonitis and requiring emergency surgery.
- **Gastric Outlet Obstruction**: Scar tissue formation or edema may obstruct gastric emptying, requiring endoscopic dilation or surgical intervention.

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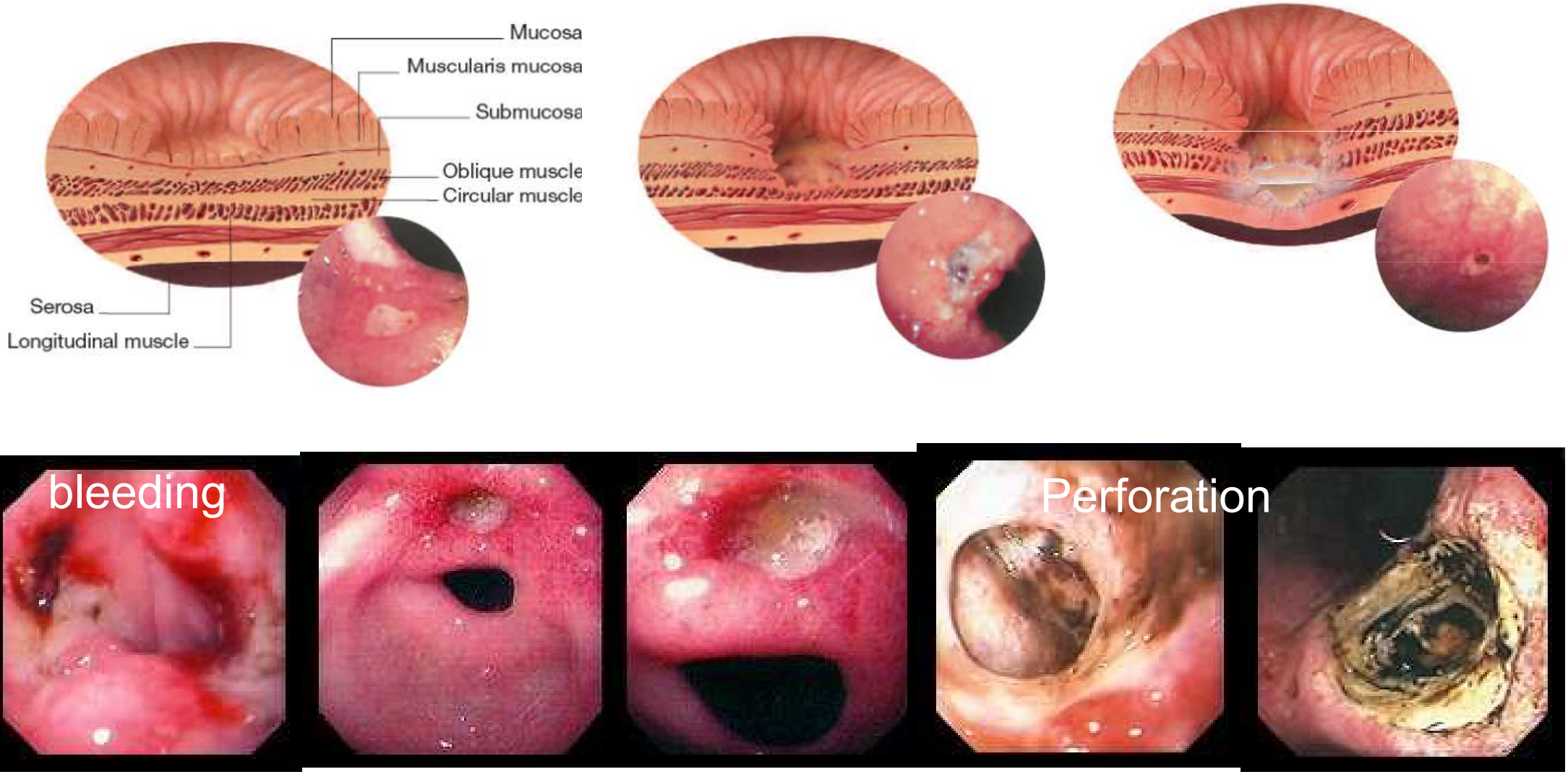
Erosion
Penetration of only the superficial layer

Acute ulcer
Penetration into muscle layer

Perforating ulcer
Penetration of wall



Treatment

- Eradication of H. pylori: Antibiotics (e.g., clarithromycin, amoxicillin) with proton pump inhibitors (PPIs).
- Acid Suppression: PPIs or H2-receptor antagonists to reduce acid secretion and promote ulcer healing.
- NSAID Use: Discontinue or reduce dosage, consider alternative medications or gastroprotective agents.
- Lifestyle Modifications: Smoking cessation, moderation of alcohol intake, stress management.

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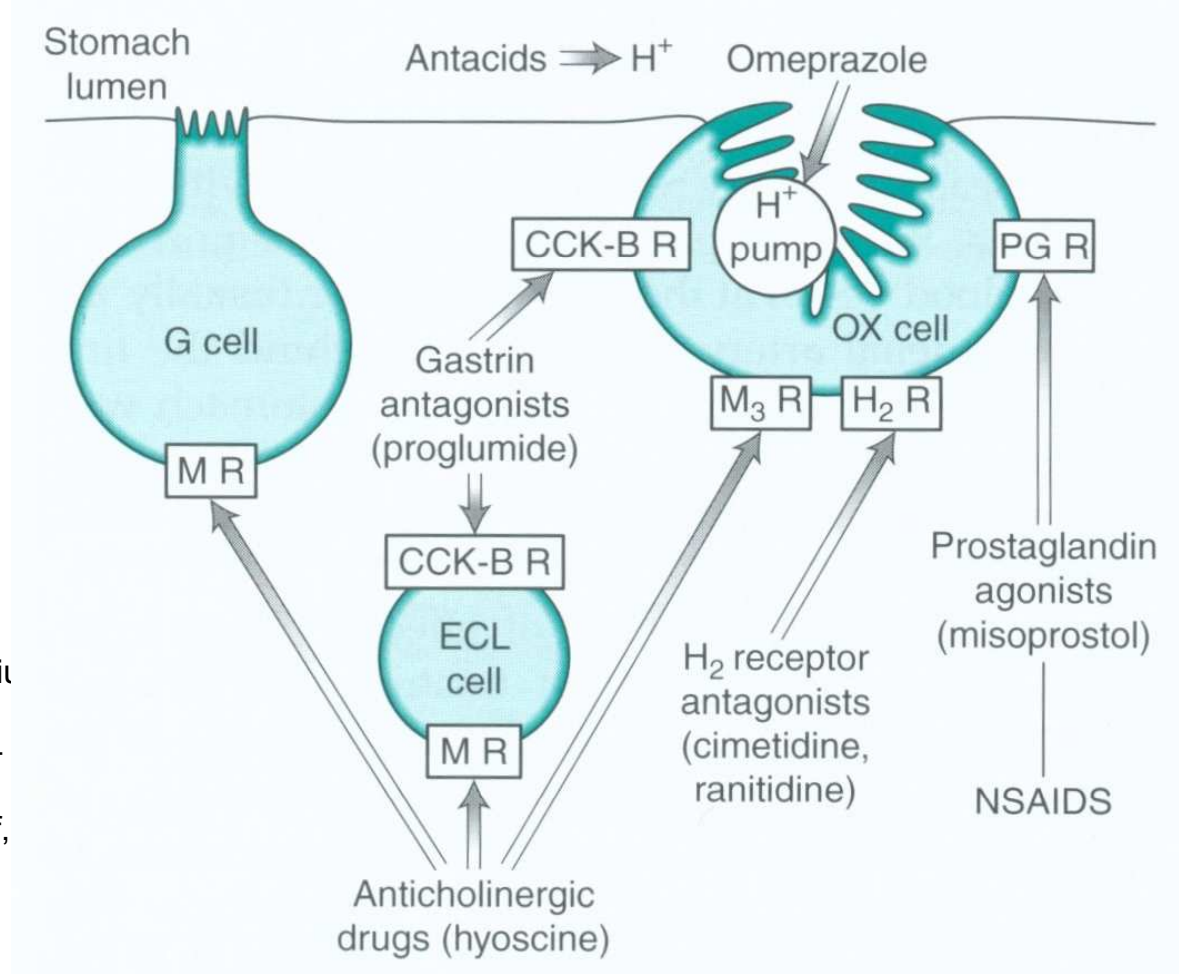
Treatment

- Histamine Receptor Antagonists (H2 Blockers):
  - Examples: Ranitidine, Cimetidine, Famotidine.
  - Mechanism: Block histamine receptors (H2 receptors) on parietal cells, reducing gastric acid secretion.
- Proton Pump Inhibitors (PPIs):
  - Examples: Omeprazole, Esomeprazole, Lansoprazole.
  - Mechanism: Irreversibly inhibit the H+/K+ ATPase pump on parietal cells, preventing acid secretion.
- Antacids:
  - Examples: Aluminum hydroxide, Magnesium hydroxide, Calciu carbonate.
  - Mechanism: Neutralize gastric acid, providing rapid but short-term relief from ulcer symptoms.
  - Result: Temporary reduction in acidity and symptomatic relief, but not effective for long-term ulcer management.



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Stomach vs duodenal ulcers

	Gastric	Duodenum
Causes	H. pylori infection. NSAID use. Excessive alcohol consumption. Smoking.	H. pylori infection NSAID use. Hypersecretory states (e.g., Zollinger-Ellison syndrome).
Clinical presentation	Epigastric pain **worsened by meals.** Nausea and vomiting. Hematemesis or melena.	Epigastric pain **relieved by meals** (hunger pain). Nighttime awakening due to pain. Hematemesis or melena

Gastric Cancer

- **Types**:
  - **Adenocarcinoma** (most common).
  - **MALT lymphoma** (associated with H. pylori).
- **Risk Factors**:
  - H. pylori (chronic inflammation → atrophic gastritis → metaplasia → dysplasia).
  - Diet: High salt, smoked foods, nitrosamines.
  - Chronic gastritis (autoimmune or H. pylori-related).
  - Genetic syndromes (e.g., Lynch syndrome).
- **Clinical Features**:
  - **Weight loss, early satiety, epigastric pain**.
  - **Acanthosis nigricans** (paraneoplastic sign).
  - **Virchow's node (supraclavicular)**,

Gastroparesis

- **Definition**: **Delayed gastric emptying without mechanical obstruction**.
- **Causes**:
  - **Diabetes mellitus** (autonomic neuropathy).
  - **Vagal nerve damage** (post-surgical, idiopathic).
  - **Medications** (e.g., opioids, anticholinergics).
- **Symptoms**:
  - Nausea, bloating, early satiety, vomiting undigested food.
- **Diagnosis**:
  - **Gastric emptying scintigraphy**.
- **Treatment**:
  - Dietary modifications, **prokinetic agents** (metoclopramide, erythromycin).

Zollinger-Ellison Syndrome

- **Pathophysiology**:
  - **Gastrin-secreting tumor (gastrinoma)** → excessive acid production.
  - Leads to **multiple peptic ulcers**, diarrhea, acid-related complications.
- **Diagnosis**:
  - Elevated **serum gastrin** levels.
  - **Secretin stimulation test** (gastrin remains elevated).
- **Treatment**:
  - High-dose **proton pump inhibitors (PPIs)**.
  - Surgical removal if localized.