GI Secretions - Gastric
Learning Objectives

1. List the endocrine and exocrine secretions of the stomach, their cells of origin and their functions.

2. Explain how gastric secretion is stimulated during the cephalic, gastric and intestinal phases.

3. Describe the various mechanisms that inhibit secretion of gastric acid.

4. Describe how pepsinogen secretion is controlled and what factors are important for its conversion to pepsin.

5. Explain what is meant by the “gastric mucosal barrier” and indicate the main agents known to disrupt it.
Gastric Secretion

Gastric Juice:

- Fluid secreted by gastric mucosal cells ~ 2 liters/day (varies considerably)

- Contains 4 major components:
  1. **HCl:** Initiate process of protein digestion
  2. **Pepsinogen:**
  3. **Intrinsic factor:** Required for vitamin B$_{12}$ absorption in ileum → only ESSENTIAL component of juice
  4. **Mucus:** Protects gastric mucosa from corrosive action of HCl and lubricates gastric contents
Gastric Cells

Gastric mucosa contains several cell types that secrete various components of gastric juice

1. Oxvntic (acid secreting) Glands – body of stomach - empty secretory products via ducts into lumen of stomach – openings of duct = pits

a. Surface epithelial cells - line pits – secrete visible, alkaline mucus → protects mucosa from mechanical / chemical damage

b. Mucous neck cells - secrete soluble (clear) mucus; serve as parent cells for replacement of other cell types

c. Parietal (oxyntic) cells - secrete HCl & intrinsic factor (a glycoprotein)

d. Chief (peptic) cells - synthesize & secrete pepsinogen
**Pepsinogen Secretion**

2 Classes:
- **Group I**: secreted by chief and mucous cells in oxyntic glands
- When pH of gastric contents is lowered by $\text{H}^+$ secretion → conversion to pepsin → begin protein digestion
- Secretion increased by vagal stimulation (ACh most potent); $\text{H}^+$ also triggers local reflexes which stimulate chief cells → pepsinogen secretion
- **Group II**: secreted throughout the stomach and by Brunner's glands in duodenum

**Intrinsic Factor Secretion**
- Mucoprotein secreted by parietal cells
- **Essential** for absorption of Vitamin $\text{B}_{12}$ in terminal ileum
- **Pernicious anemia**: absence of intrinsic factor → inability to form mature RBCs; oxyntic cell mass is greatly reduced and acid secretion is very low (achlorhydria)
2. **Pyloric glands:**
   - Antrum of stomach - similar to oxyntic glands but with deeper pits
   - Contain:
     1. **G cells**: Secrete gastrin not into pyloric ducts but into circulation
     2. **Mucous neck cells**: Secrete mucus, $\text{HCO}_3^-$, and pepsinogen ($\text{HCO}_3^-$ and mucus – protective neutralizing effect on gastric mucosa)
Secretory Products of Various Gastric Cells

<table>
<thead>
<tr>
<th>Cell Type</th>
<th>Location</th>
<th>Secretion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parietal cells</td>
<td>Body</td>
<td>HCl, Intrinsic factor</td>
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<tr>
<td>Chief cells</td>
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<td>Pepsinogen</td>
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<td>Antrum</td>
<td>Gastrin</td>
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<td>Mucous cells</td>
<td>Antrum</td>
<td>Mucus, Pepsinogen</td>
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</table>
Parietal Cells and HCl Secretion

- **Function**: Secretion of HCl to acidify gastric contents between pH 1-2 converts inactive pepsinogen to active pepsin for protein digestion

- **HCl**
  1. Converts inactive pepsinogen to pepsin
  2. Provides an acidic pH for pepsin activity
  3. Kills ingested bacteria
1. \( \text{CO}_2 + \text{H}_2\text{O} \rightarrow \text{H}_2\text{CO}_3 \) – catalyzed by carbonic anhydrase (CA) \( \rightarrow \text{H}_2\text{CO}_3 \) dissociates to \( \text{H}^+ + \text{HCO}_3^- \)

2. \( \text{H}^+ \) secreted into lumen via \( \text{H}^+\text{-K}^+ \text{ATPase} \) – \( \text{Cl}^- \) follows \( \text{H}^+ \) through channels

3. Basolaterally – \( \text{HCO}_3^- \) absorbed via \( \text{Cl}^- \) exchanger

4. Overall \( \rightarrow \) net secretion \( \text{HCl} \) and net absorption \( \text{HCO}_3^- \)
Control of HCl Secretion

- 3 substances stimulate H\(^+\) secretion:
  1. ACh (neurocrine)
  2. Histamine (paracrine)
  3. Gastrin (hormone)

- H\(_2\) receptor blockers:
  Cimetidine (Tagamet) & Ranitidine (Zantac) inhibit gastric acid secretion

- Omeprazole inhibits H\(^+\)-K\(^+\) ATPase
Test Question

Which one of the following stimulates $H^+$ secretion from the parietal cell?

A. Omeprazole
B. Cimetidine
C. Histamine
D. Somatostatin
E. Ranitidine
Stimulation of HCl Secretion:

1. Cephalic Phase

- ~30% of total HCl secretion – in response to a meal

- Stimuli for secretion: smelling and tasting, chewing, swallowing and conditioned reflexes in anticipation of food

- 2 mechanisms promote HCl secretion:
  
  1. Direct stimulation of parietal cell by vagus nerve – Ach release
  
  2. Indirect stimulation of parietal cells by gastrin – vagal release of GRP
2. Gastric Phase

~60% of total HCl secretion in response to meal

Stimuli for secretion:
(i) Distension of stomach
(ii) Protein breakdown products – amino acids and small peptides

4 secretory mechanisms:
1. Distension causes direct vagal stimulation of parietal cells
2. Distention causes indirect stimulation of parietal cells by gastrin
3. Distension of antrum involves local reflexes that stimulate gastrin release
4. Direct effect of amino acids and peptides on G cells to stimulate gastrin

FYI - Alcohol and caffeine stimulate HCl secretion
3. Intestinal Phase

- 10% of total HCl secretion

- Chyme in duodenum and products of protein digestion stimulates acid secretion
The Gastric Mucosal Barrier

- Protective mucus gel on luminal surface of stomach with alkaline secretions entrapped within it
- Prevents damage to mucosa by gastric contents
- Mucus gel layer = 0.2 mm thick separates HCO\(_3^-\) rich secretions of surface epithelial cells from acidic gastric contents
- Mucus allows pH of the epithelial cells to be maintained at nearly neutral pH, despite a luminal pH of about 2
- Mucus slows diffusion of acid and pepsins to epithelial cell surface
- Protection of the gastric epithelium depends on mucus and HCO\(_3^-\) secretion; both needed to hold pH at epithelial cell surface near neutral
The Gastric Mucosal Barrier (cont’d)

![Diagram of the gastric mucosal barrier with protective factors and damaging factors listed in a table.]

**Protective factors**
- HCO$_3^-$ and mucus
- Prostaglandins
- Mucosal blood flow
- Growth factors

**Damaging factors**
- H$^+$ and pepsin
- H. pylori
- NSAIDs
- Stress
- Smoking
- Alcohol
Inhibition of HCl Secretion

- **Normal physiological inhibition of gastric acid secretion**: Presence of acid; fat; protein digestion products

- Inhibited when HCl no longer needed to convert pepsinogen – pepsin$\rightarrow$ when chyme moves to small intestine - decreased pH of gastric contents

- Food acts as buffer – when moves to small intestine lose buffering capacity – further H$^+$ secretion reduces pH – inhibits gastrin – decreases H$^+$ secretion

- **Major inhibitory factor**: Somatostatin
  - **Direct**: binds to receptors on parietal cells – reduces cAMP levels- antagonizes histamine effects on H$^+$ secretion
  - **Indirect**: inhibits histamine and gastrin release to reduce stimulatory effects of these peptides

- **Prostaglandins**: Antagonize histamine’s stimulatory action on H$^+$ secretion- inhibit adenylyl cyclase
Inhibition of HCl Secretion (cont’d)

Somatostatin:
Major inhibitory factor

Direct: binds to receptors on parietal cells – reduces cAMP levels- antagonizes histamine effects on H⁺ secretion

Indirect: inhibits histamine and gastrin release to reduce stimulatory effects of these peptides

Prostaglandins: antagonize histamine stimulatory action on H⁺ secretion- inhibit adenylyl cyclase – reduces cAMP levels
Test Question

Tagamet is a drug used to prevent H+ secretion. Which one of the following does Tagamet actively block?

A. CCK receptor
B. H+-K+- ATPase
C. H2 receptor
D. M3 receptor
E. None of the above

The correct answer is C. H2 receptor.
## Summary

### Exocrine Cells

<table>
<thead>
<tr>
<th>Type of Secretory Cell</th>
<th>Product Secreted</th>
<th>Stimuli for Secretion</th>
<th>Function(s) of Secretory Product</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mucous cells</strong></td>
<td>Alkaline mucus</td>
<td>Mechanical stimulation by contents</td>
<td>Protects mucosa against mechanical, pepsin, and acid injury</td>
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<td><strong>Chief cells</strong></td>
<td>Pepsinogen</td>
<td>ACh, gastrin</td>
<td>When activated, begins protein digestion</td>
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<td><strong>Parietal cells</strong></td>
<td>Hydrochloric acid</td>
<td>ACh, gastrin, histamine</td>
<td>Activates pepsinogen, breaks down connective tissue, denatures proteins, kills microorganisms</td>
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<tr>
<td></td>
<td></td>
<td>Intrinsic factor</td>
<td>Facilitates absorption of vitamin B₁₂</td>
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### Endocrine/Paracrine Cells

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<td>Enterochromaffin-like (ECL) cells</td>
<td>Histamine</td>
<td>ACh, gastrin</td>
<td>Stimulates parietal cells</td>
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<td><strong>G cells</strong></td>
<td>Gastrin</td>
<td>Protein products, ACh</td>
<td>Stimulates parietal, chief, and ECL cells</td>
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<tr>
<td><strong>D cells</strong></td>
<td>Somatostatin</td>
<td>Acid</td>
<td>Inhibits parietal, G, and ECL cells</td>
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### Diagram

- **Parietal cells**
- **Chief cells**
- **G cells**
- **Mucous cells**
- **Mucus**
- **Gastrin (to circulation)**
- **HCl**
- **Intrinsic factor**

### Table: Cell Type, Location, and Secretion

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