

# GI PHYS RESUMED

DH

# GI Peptides

---

- Includes hormones, neurocrines, and paracrines
- Regulate functions of GI tract
  - ▣ Contraction and relaxation of smooth muscle wall and sphincters
  - ▣ Secretion of enzymes for digestion
  - ▣ Secretion of fluid and electrolytes
  - ▣ Trophic (growth) effects
  - ▣ Some regulate secretion of *other* GI peptides

# GI Peptides

## □ Hormones

- Peptides released from endocrine cells of GI tract
- Secreted into portal circulation and enter systemic circulation
- Target cells may be in GI tract or may be located elsewhere in body
  - Gastrin, Cholecystokinin, Secretin, and Gastric Inhibitory Peptide

## □ Paracrines

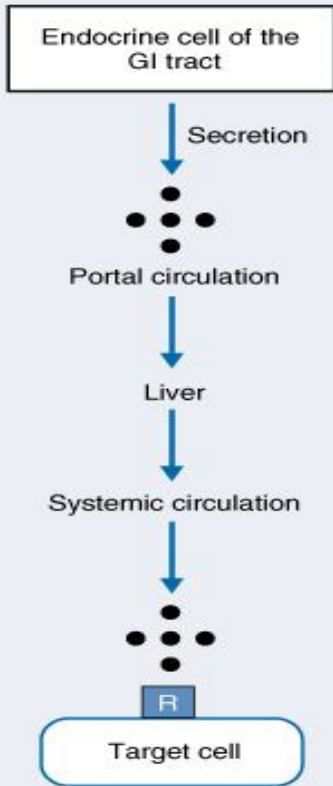
- Secreted by endocrine cells of GI tract
- Act *locally* within same tissue that secretes them
  - Somatostatin (inhibitory actions)

## □ Neurocrines

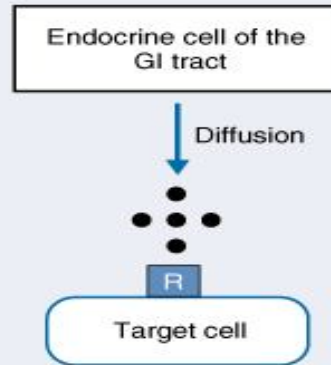
- Released by neurons of GI tract following an AP
  - ACh, norepinephrine, Vasoactive Intestinal Peptide (VIP), Gastrin-Releasing Peptide (GRP), Neuropeptide Y, and Substance P

## GASTROINTESTINAL PEPTIDES

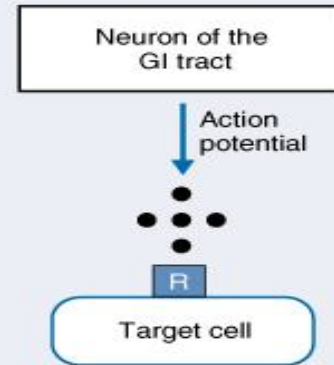
### Hormones



### Paracrines



### Neurocrines



# GI Hormones

## □ Gastrin

- Secreted by G cells in stomach in response to eating
  - Stimuli include proteins, distention of stomach, and vagal stimulation
    - **Gastrin-releasing peptide (GRP)** is released from vagal nerve endings onto G cells
  - Secretion is *inhibited* by low pH in stomach
- Promotes **H<sup>+</sup> secretion** by gastric parietal cells
- Stimulates **growth of gastric mucosa**

# GI Hormones

## □ Cholecystokinin

- Secreted by I cells of small intestine in response to fatty acids and small peptides

5 Actions:

### 1. **Contraction of gallbladder**

- Eject bile from gallbladder into small intestine necessary for emulsification lipids

### 2. **Secretion of pancreatic enzymes**

- Digest lipids, carbohydrates, and proteins

### 3. **Secretion of bicarbonate ( $\text{HCO}_3^-$ ) from pancreas**

### 4. **Growth of exocrine pancreas and gallbladder**

### 5. **Inhibition of gastric emptying**

- Ensures adequate time for digestive and absorptive

# GI Hormones

## □ Secretin

- Secreted by **S cells** of duodenum in response to  $H^+$  and fatty acids
- Promotes **secretion of pancreatic  $HCO_3^-$** 
  - Neutralizing  $H^+$  allows for pancreatic enzymes to digest fats
- Inhibits effects of gastrin on parietal cells ( $H^+$  secretion and growth)

## □ Gastric Inhibitory Peptide (GIP)

- Secreted by small intestine in response to all 3 types of nutrients
- **Stimulates insulin secretion** by pancreas
- **Inhibits gastric  $H^+$  secretion**

# GI Paracrines

---

## □ **Somatostatin**

- Secreted by endocrine cells in response to decreased luminal pH
- *Inhibits* secretion of other GI hormones
- *Inhibits* gastric H<sup>+</sup> secretion

## □ **Histamine**

- Secreted in H<sup>+</sup>-secreting region of stomach
- Stimulates H<sup>+</sup> secretion by gastric parietal cells (along with gastrin and ACh)



# GI Neurocrines

---

- Synthesized in cell bodies of GI neurons
- AP causes release of neurocrine which interacts with receptors on postsynaptic cell
  - ACh (released from cholinergic neurons)
  - Norepinephrine (released from adrenergic neurons)

# Secretion

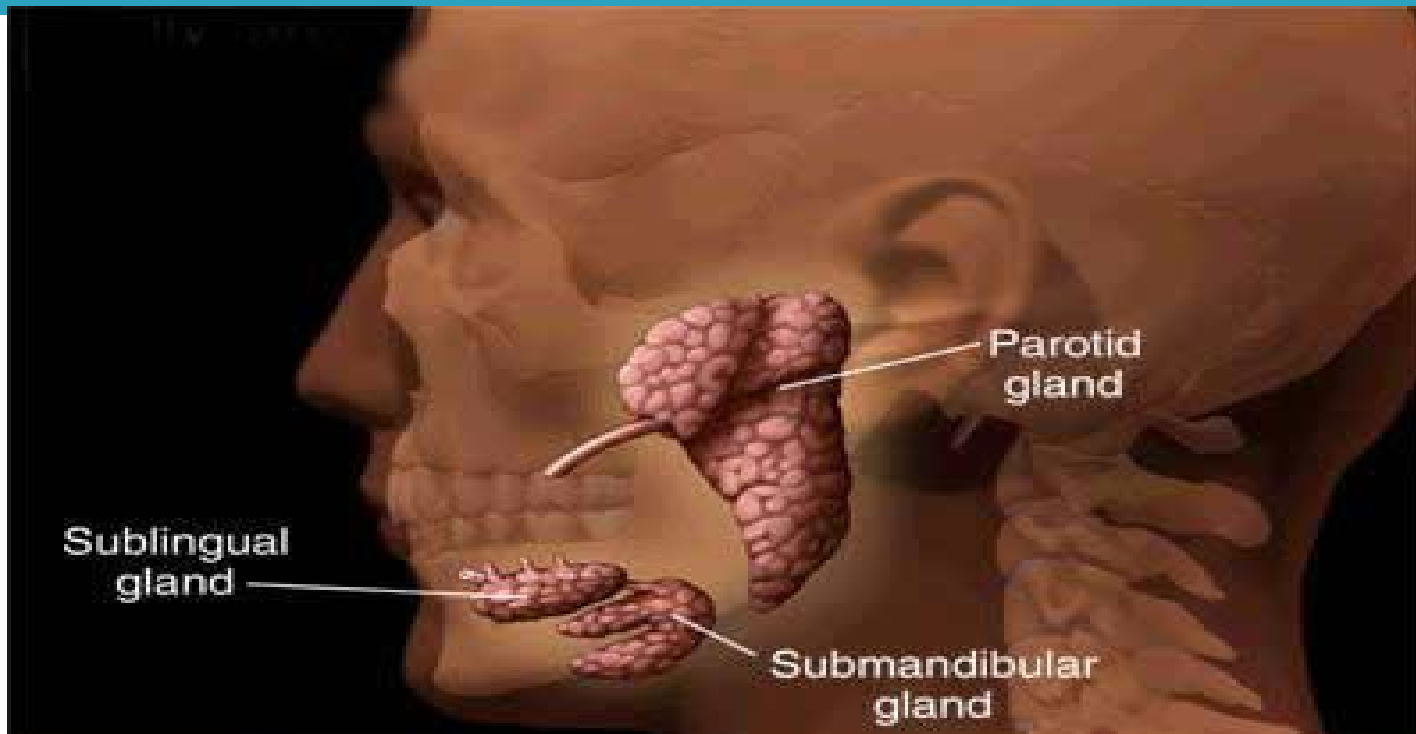
---

- Addition of fluids, enzymes, and mucus to lumen of GI tract
- Secretions produced by
  - ▣ Salivary glands (saliva)
  - ▣ Gastric mucosal cells (gastric secretion)
  - ▣ Pancreatic exocrine cells (pancreatic secretion)
  - ▣ Liver (bile)

# Salivary Secretion

- Salivary glands produce 1 L/day of saliva
- **Functions of saliva**
  - ▣ Initial digestion of starches and lipids by salivary enzymes
  - ▣ Dilution and buffering of ingested foods
  - ▣ Lubrication of ingested food to aid its movement
- **Structure of Salivary Glands**
  - ▣ Parotid glands, submandibular glands, and sublingual glands
  - ▣ Each gland delivers saliva to mouth through a duct

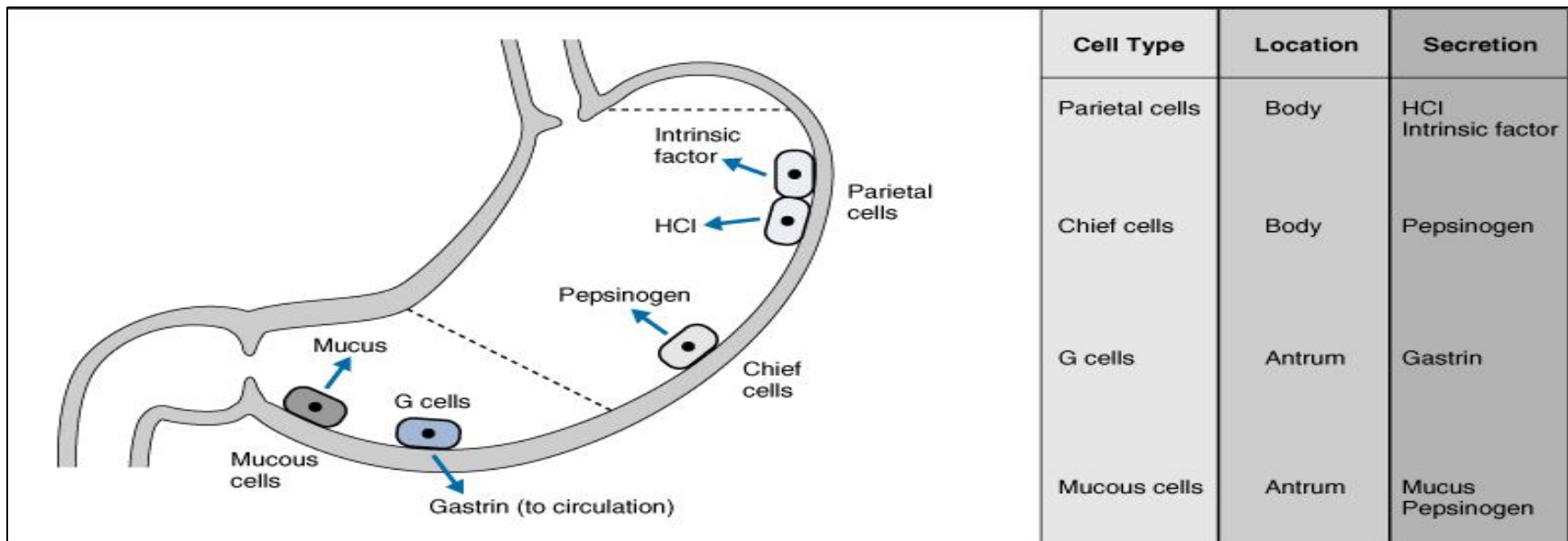
# Salivary Glands



# Gastric Secretion

- Gastric mucosal cells secrete **gastric juice**
  - **HCl** and **pepsinogen** initiate protein digestion
  - **Intrinsic factor** required for absorption of vitamin B<sub>12</sub>
  - **Mucus** protects gastric mucosa from HCl
- **Cell Types of Gastric Mucosa**
  - **Body** of stomach contains oxyntic glands
    - **Parietal cells** → HCl and Intrinsic Factor
    - **Chief cells** → Pepsinogen
  - **Antrum** of stomach contains pyloric glands
    - **G cells** → Gastrin *into the circulation*
    - **Mucous neck cells** → Mucus, HCO<sub>3</sub><sup>-</sup>, and Pepsinogen

# Gastric Secretion



Cell Type	Location	Secretion
Parietal cells	Body	HCl Intrinsic factor
Chief cells	Body	Pepsinogen
G cells	Antrum	Gastrin
Mucous cells	Antrum	Mucus Pepsinogen

**TABLE 8–2. Summary of Gastrointestinal Hormones**

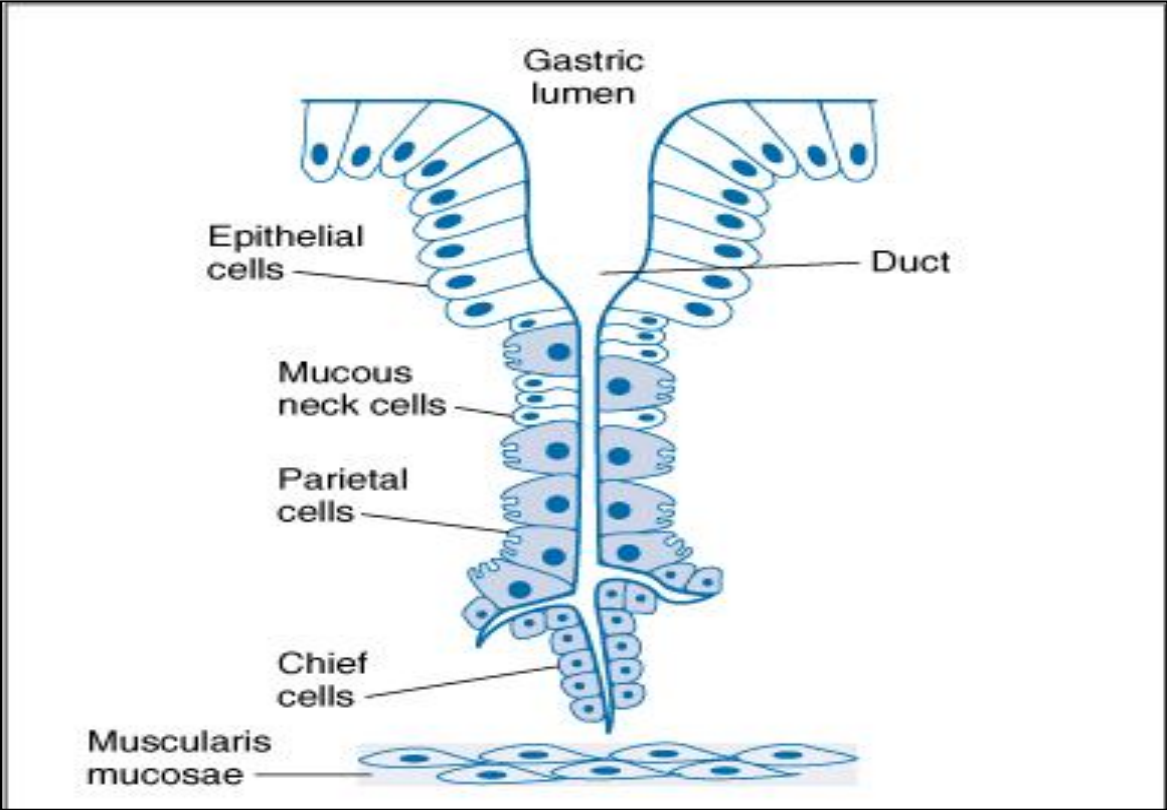
<b>Hormone</b>	<b>Hormone Family</b>	<b>Site of Secretion</b>	<b>Stimuli for Secretion</b>	<b>Actions</b>
<b>Gastrin</b>	Gastrin-CCK	G cells of the stomach	Small peptides and amino acids Distention of the stomach Vagal stimulation (GRP)	↑ Gastric H <sup>+</sup> secretion Stimulates growth of gastric mucosa
<b>Cholecystokinin (CCK)</b>	Gastrin-CCK	I cells of the duodenum and jejunum	Small peptides and amino acids Fatty acids	↑ Pancreatic enzyme secretion ↑ Pancreatic HCO <sub>3</sub> <sup>-</sup> secretion Stimulates contraction of the gallbladder and relaxation of the sphincter of Oddi Stimulates growth of the exocrine pancreas and gallbladder Inhibits gastric emptying
<b>Secretin</b>	Secretin-glucagon	S cells of the duodenum	H <sup>+</sup> in the duodenum Fatty acids in the duodenum	↑ Pancreatic HCO <sub>3</sub> <sup>-</sup> secretion ↑ Biliary HCO <sub>3</sub> <sup>-</sup> secretion ↓ Gastric H <sup>+</sup> secretion Inhibits trophic effect of gastrin on gastric mucosa
<b>Gastric inhibitory peptide (GIP)</b>	Secretin-glucagon	Duodenum and jejunum	Fatty acids Amino acids Oral glucose	↑ Insulin secretion from pancreatic β cells ↓ Gastric H <sup>+</sup> secretion

**TABLE 8-1. Neurotransmitters and Neuromodulators in the Enteric Nervous System**

Substance	Source	Actions
Acetylcholine (ACh)	Cholinergic neurons	Contraction of smooth muscle in wall Relaxation of sphincters ↑ Salivary secretion ↑ Gastric secretion ↑ Pancreatic secretion
Norepinephrine (NE)	Adrenergic neurons	Relaxation of smooth muscle in wall Contraction of sphincters ↑ Salivary secretion
Vasoactive intestinal peptide (VIP)	Neurons of mucosa and smooth muscle	Relaxation of smooth muscle ↑ Intestinal secretion ↑ Pancreatic secretion
Gastrin-releasing peptide (GRP) or bombesin	Neurons of gastric mucosa	↑ Gastrin secretion
Enkephalins (opiates)	Neurons of mucosa and smooth muscle	Contraction of smooth muscle ↓ Intestinal secretion
Neuropeptide Y	Neurons of mucosa and smooth muscle	Relaxation of smooth muscle ↓ Intestinal secretion
Substance P	Cosecreted with ACh	Contraction of smooth muscle ↑ Salivary secretion



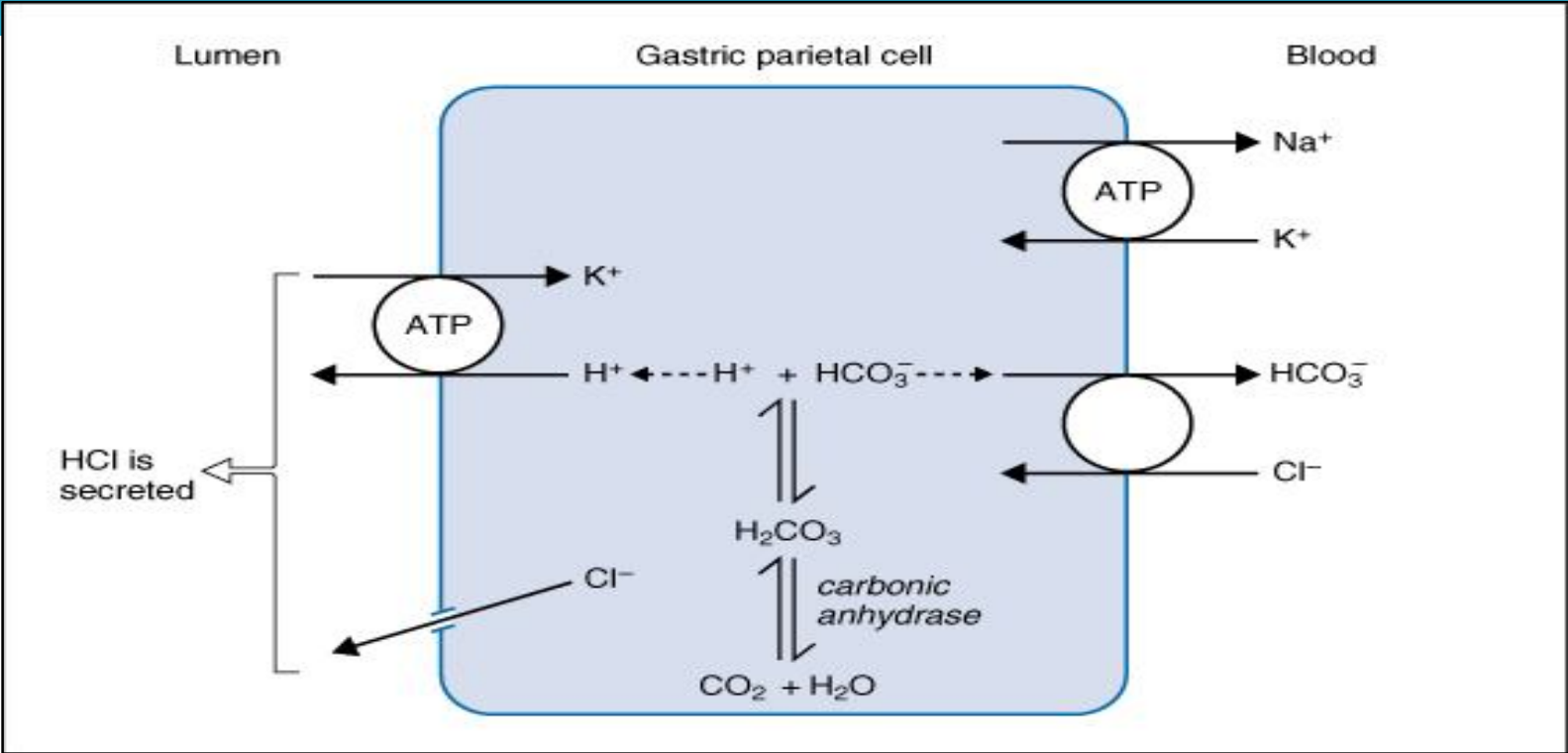
# Gastric Gland



# HCl Secretion

- **Parietal cells** secrete **HCl** which converts *inactive* pepsinogen to pepsin
  
- 1. Within cell,  $\text{CO}_2$  combines with  $\text{H}_2\text{O}$  to form  $\text{H}^+$  and  $\text{HCO}_3^-$
- 2. At **apical membrane**,  $\text{H}^+$  secreted into lumen of stomach via  **$\text{H}^+\text{-K}^+$  ATPase**
  - $\text{Cl}^-$  follows  $\text{H}^+$  into the lumen by diffusing through  **$\text{Cl}^-$  channels**
- 3. At **basolateral membrane**,  $\text{HCO}_3^-$  absorbed into blood via a  **$\text{Cl}^-$ - $\text{HCO}_3^-$  exchanger**
  - Eventually  $\text{HCO}_3^-$  secreted back into GI tract by pancreas

# HCl Secretion



# Regulation of HCl Secretion

## □ ACh

- Released from vagus nerve
- Binds to receptors on parietal cells
- Produces H<sup>+</sup> secretion by parietal cells
- **Atropine** blocks muscarinic receptors on parietal cells

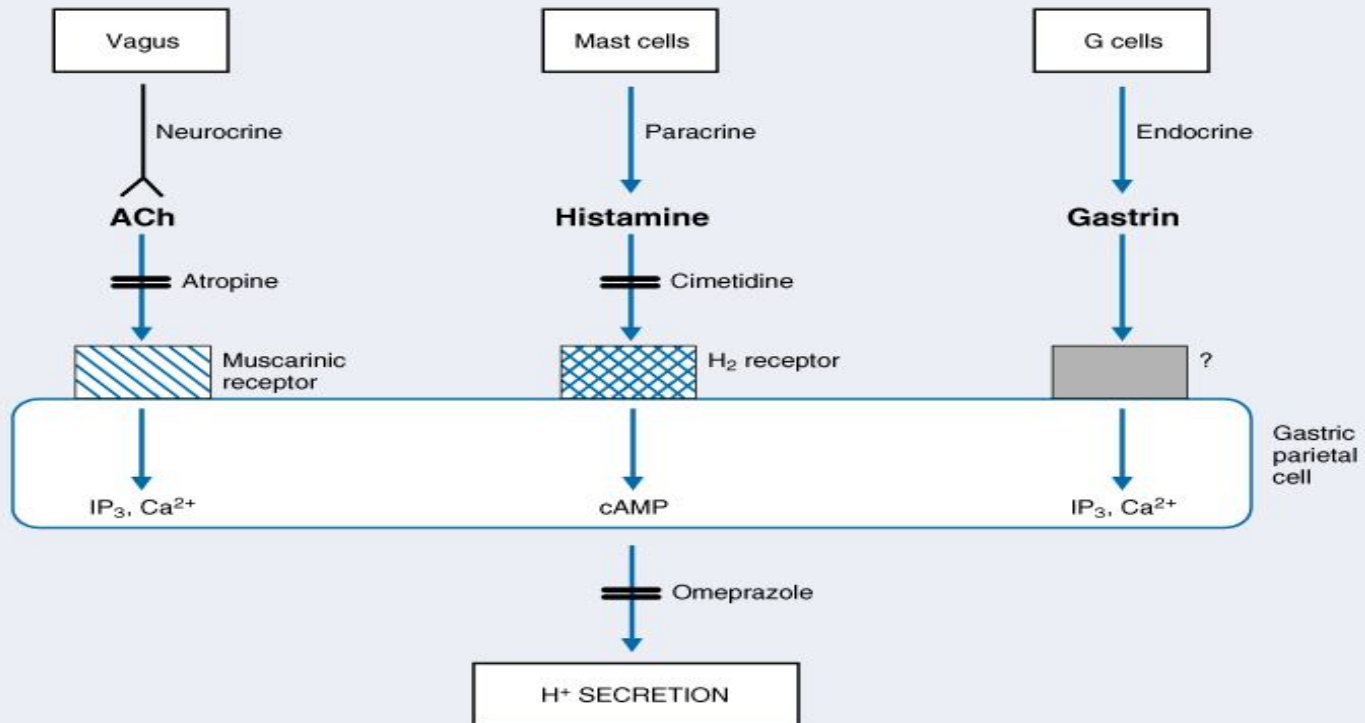
## □ Histamine

- Released from mastlike cells in gastric mucosa
- Binds to **H<sub>2</sub> receptors** on parietal cells
- Produces H<sup>+</sup> secretion by parietal cells
- **Cimetidine** blocks H<sub>2</sub> receptors

## □ Gastrin

- Released into circulation by **G cells** of stomach antrum
- Binds to receptors on parietal cells
- Stimulates H<sup>+</sup> secretion

### REGULATION OF H<sup>+</sup> SECRETION



# Ulcers

## □ Gastric Ulcers

- Mucosal barrier is defective allowing  $H^+$  and pepsin to digest portion of mucosa
- *Helicobacter pylori* produces  $NH_4^+$  from urea
  - $NH_4^+$  breaks down mucosal barrier to  $H^+$

## □ Duodenal Ulcers

- More common
- $H^+$  secretory rates are higher than normal
  - Excess  $H^+$  damages duodenal mucosa

# Pancreatic Secretion

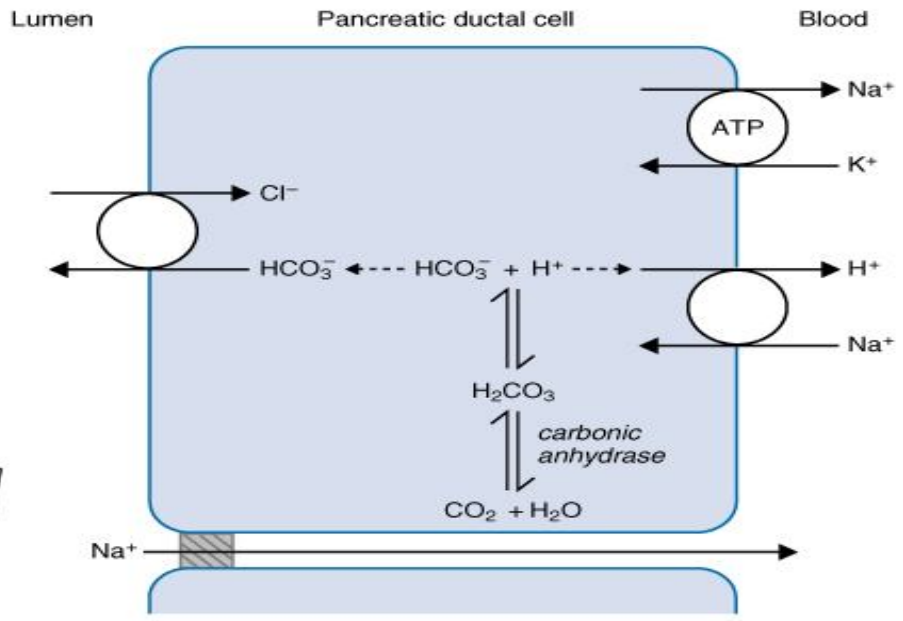
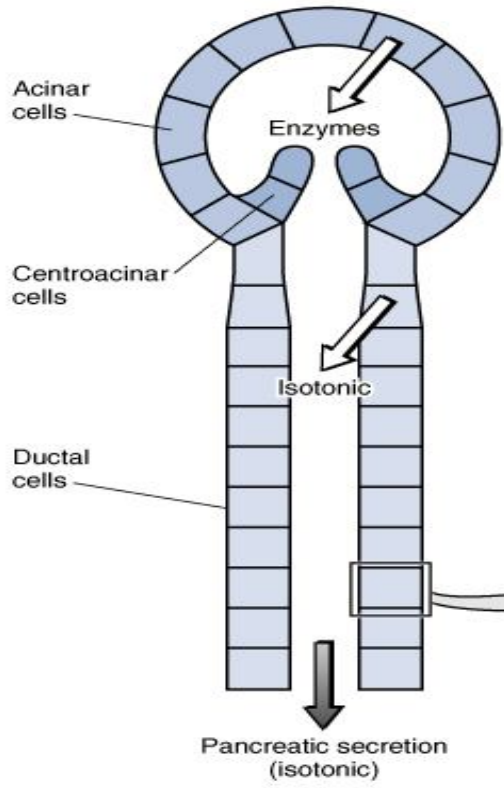
- Exocrine pancreas secretes ~1 L/day into duodenum
  - Fluid consists of  $\text{HCO}_3^-$  and enzymes
    - $\text{HCO}_3^-$  neutralizes  $\text{H}^+$  delivered to duodenum from stomach
    - **Enzymatic portion** digests carbohydrates, proteins, and lipids into absorbable molecules
- **Structure of Pancreatic Exocrine Glands**
  - Comprises ~90% of pancreas
    - Rest of pancreatic tissue is endocrine pancreas and blood vessels
  - **Acinar Cells**
    - Line blind end of branching duct system
    - Secrete enzymatic portion
  - **Ductal Cells**
    - Line the ducts
    - Secrete aqueous  $\text{HCO}_3^-$  component

# HCO<sub>3</sub><sup>-</sup> Secretion

- Apical membrane of ductal cells contains a Cl<sup>-</sup>-HCO<sub>3</sub><sup>-</sup> exchanger
- Basolateral membrane contains Na<sup>+</sup>-K<sup>+</sup> ATPase and a Na<sup>+</sup>-H<sup>+</sup> exchanger
- 1. CO<sub>2</sub> and H<sub>2</sub>O combine in cells to form H<sup>+</sup> and HCO<sub>3</sub><sup>-</sup>
- 2. HCO<sub>3</sub><sup>-</sup> is secreted into pancreatic juice by Cl<sup>-</sup>-HCO<sub>3</sub><sup>-</sup> exchanger
- 3. H<sup>+</sup> is transported into blood by Na<sup>+</sup>-H<sup>+</sup> exchanger
  - Absorption of H<sup>+</sup> causes acidification of pancreatic venous blood



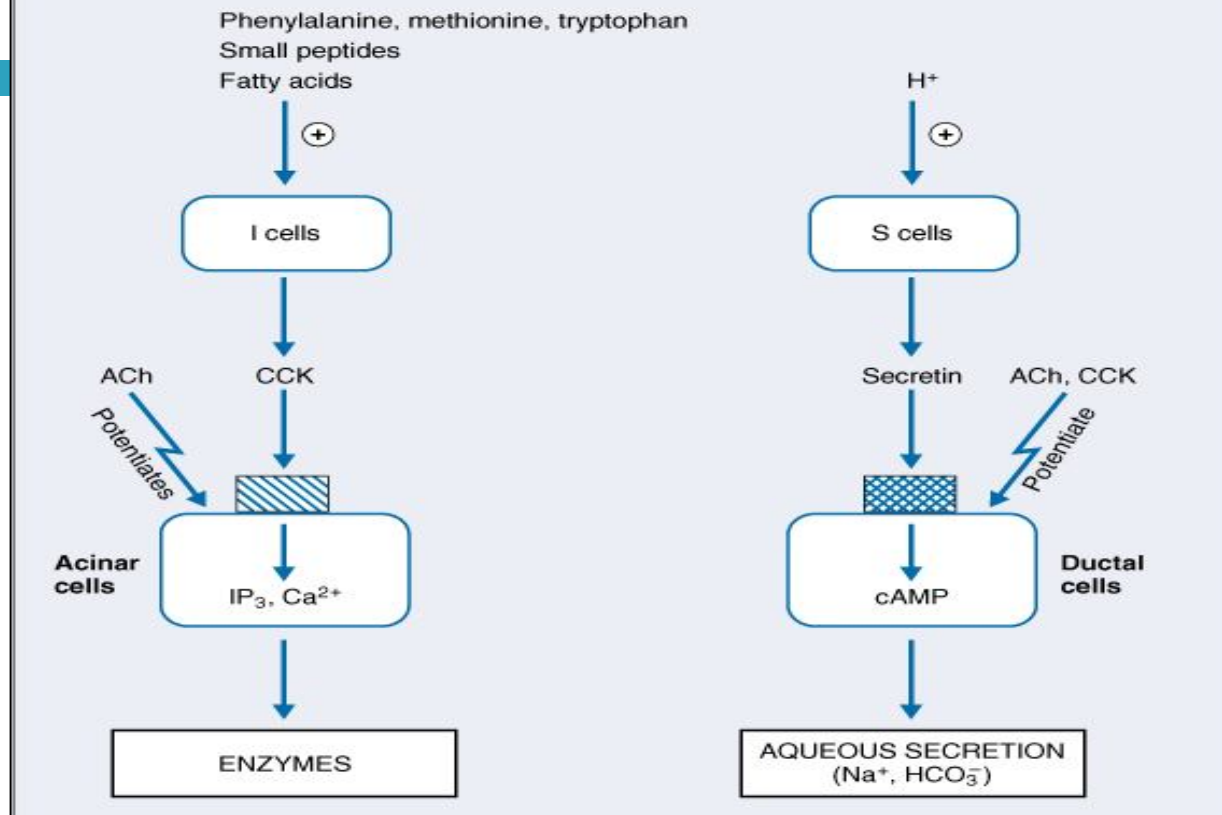
# PANCREATIC SECRETION



# Regulation of Pancreatic Secretion

- **Acinar cells (enzymatic secretion)**
  - Receptors for CCK and muscarinic receptors for ACh
  - **CCK** is most important stimulant
    - I cells secrete CCK in presence of amino acids and fatty acids in intestinal lumen
  - **ACh** also stimulates enzyme secretion
- **Ductal cells (aqueous secretion of  $\text{HCO}_3^-$ )**
  - Receptors for CCK, ACh, and secretin
  - **Secretin** (from S cells of duodenum) is major stimulant
    - Secreted in response to  $\text{H}^+$  in intestine

### REGULATION OF PANCREATIC SECRETION



# Bile Secretion

---

- ❑ Necessary for **digestion and absorption of lipids** in small intestine
- ❑ Mixture of bile salts, bile pigments, and cholesterol
- ❑ Bile salts emulsify lipids to prepare them for digestion
- ❑ Solubilize products of lipid digestion in packets called **micelles**

# Bile Secretion and Recycling

---

1. Produced and secreted by liver
2. Stored in gallbladder
3. Ejected into small intestine when gallbladder contracts
4. After lipids absorbed, bile salts are recirculated to liver via **enterohepatic circulation**
  - ▣ Absorption of bile salts from ileum into portal circulation
  - ▣ Delivery back to liver

# Bile Secretion and Recycling

