

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

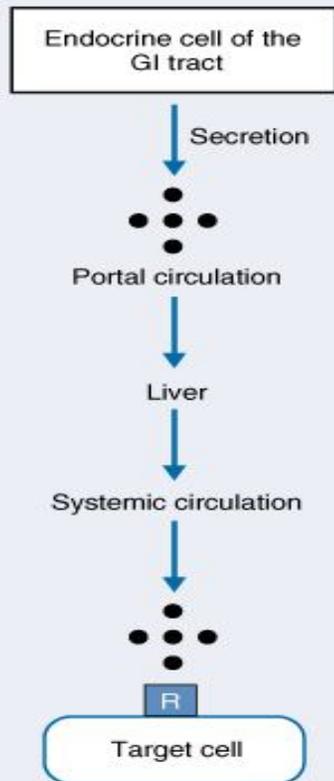
- Secreted by endocrine cells of GI tract
- Act *locally* within same tissue that secretes them
 - Somatostatin (inhibitory actions)

□ Neurocrines

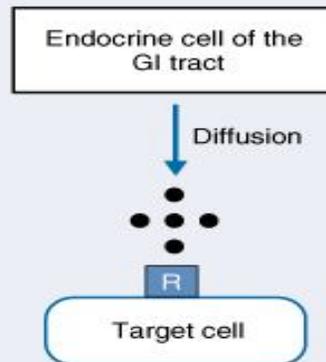
- Released by neurons of GI tract following an AP
 - ACh, norepinephrine, Vasoactive Intestinal Peptide (VIP), Gastrin-Releasing Peptide (GRP), Neuropeptide Y, and Substance P

GASTROINTESTINAL PEPTIDES

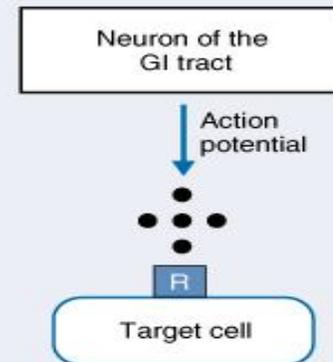
Hormones



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⁺ 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 (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⁺ secretion

□ **Histamine**

- Secreted in H⁺-secreting region of stomach
- Stimulates H⁺ 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)

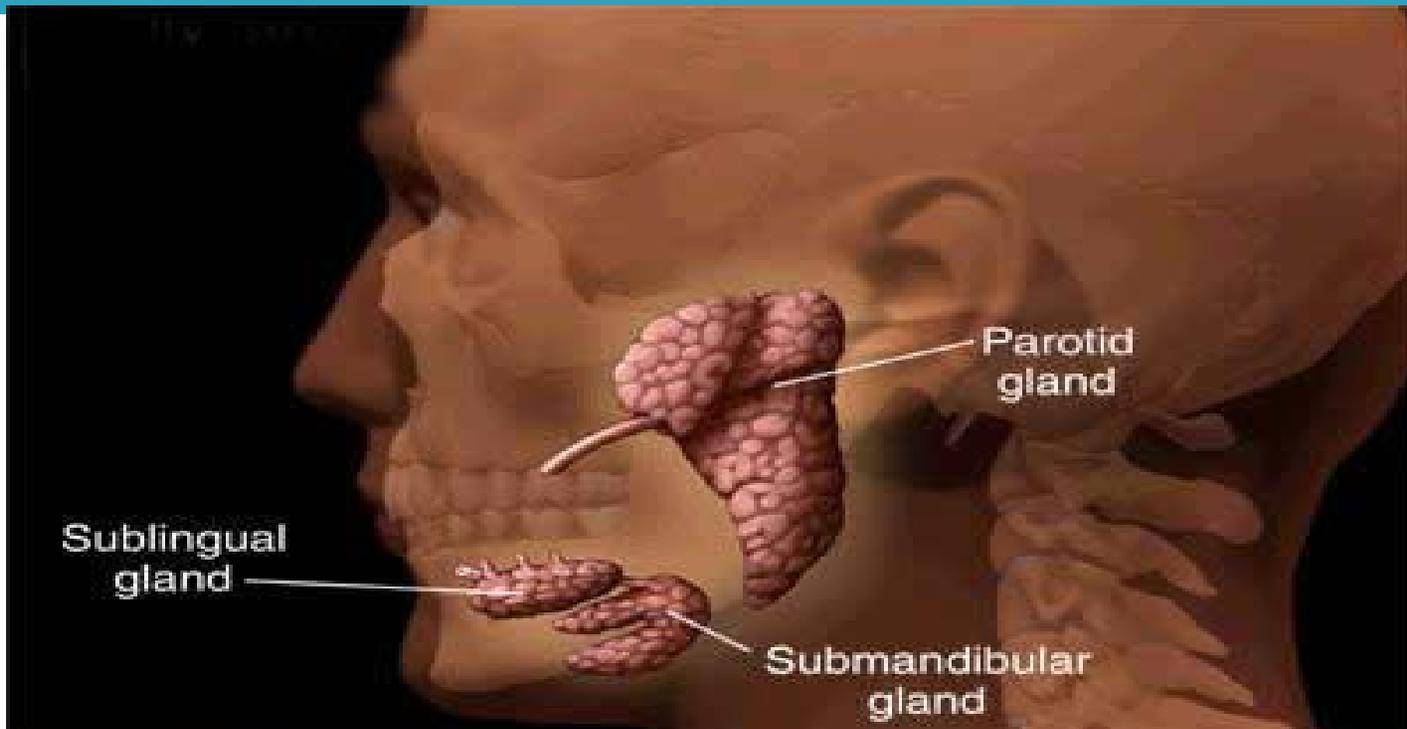
Secretion

- 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 B₁₂
 - **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, HCO₃⁻, and Pepsinogen

Gastric Secretion

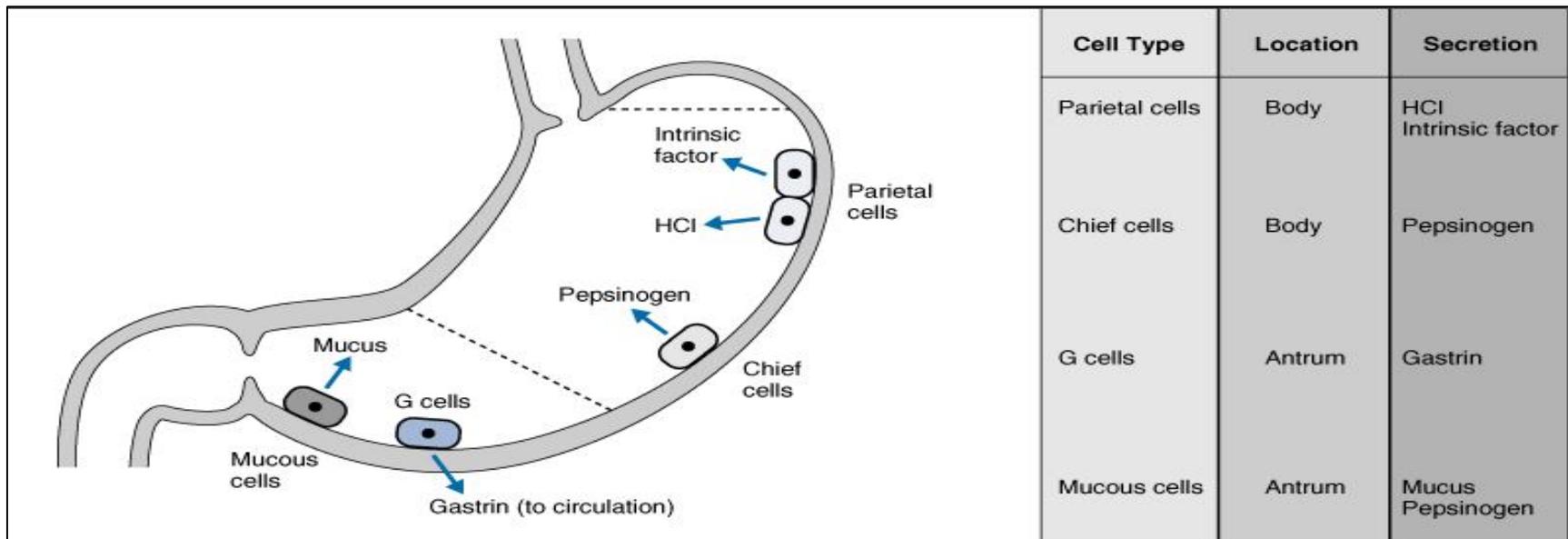


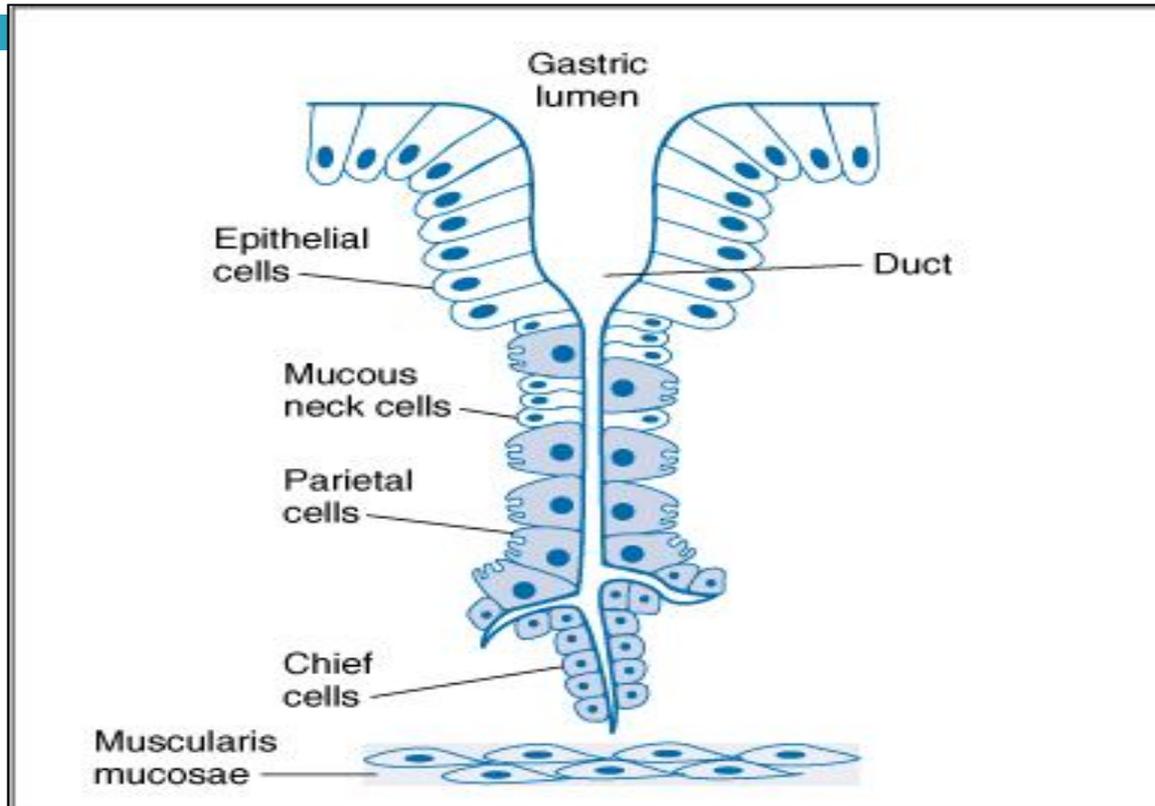
TABLE 8–2. Summary of Gastrointestinal Hormones

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

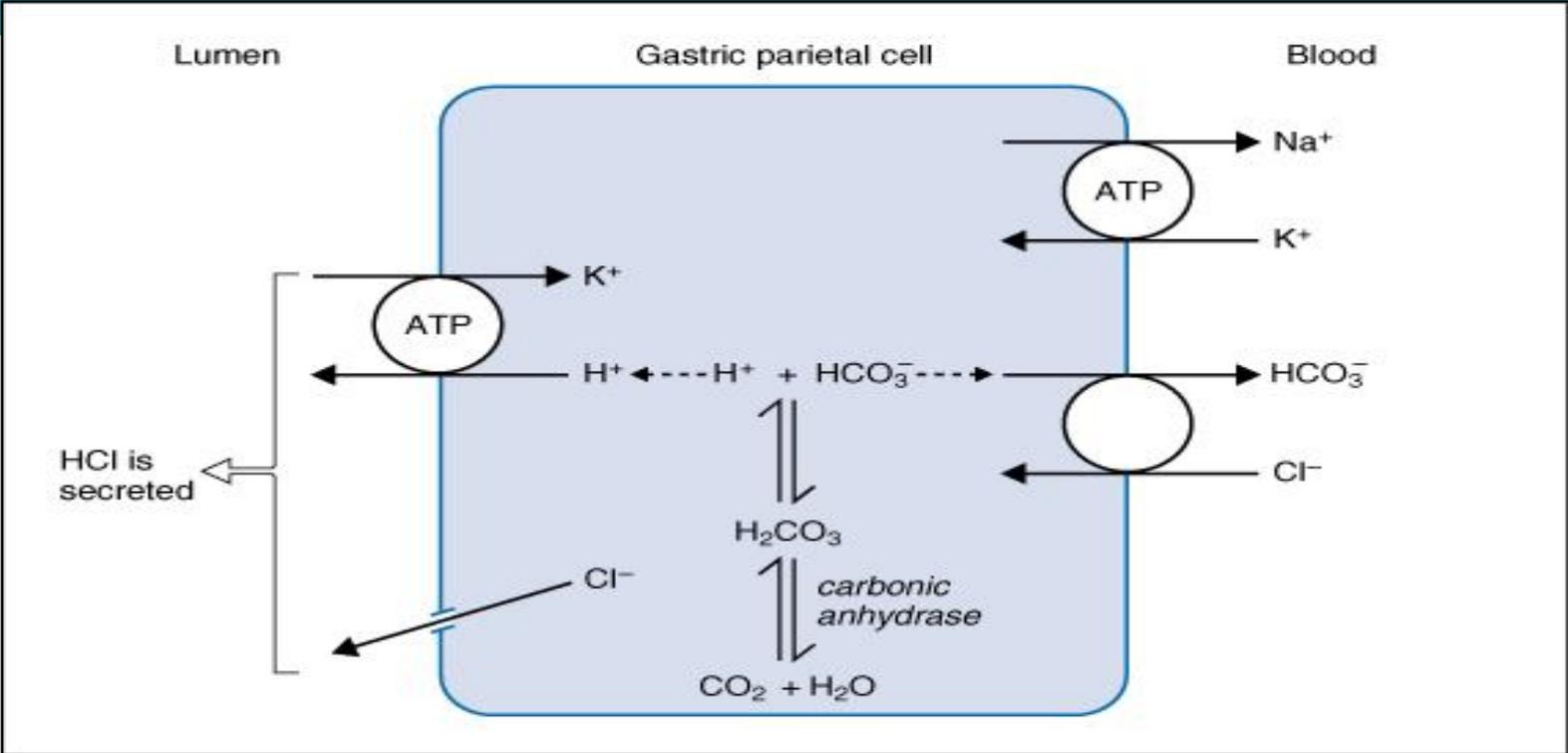


HCl Secretion

- **Parietal cells** secrete **HCl** which converts *inactive* pepsinogen to pepsin

- 1. Within cell, CO_2 combines with H_2O to form H^+ and HCO_3^-
- 2. At **apical membrane**, H^+ secreted into lumen of stomach via **H^+-K^+ ATPase**
 - Cl^- follows H^+ into the lumen by diffusing through **Cl^- channels**
- 3. At **basolateral membrane**, HCO_3^- absorbed into blood via a **Cl^- - HCO_3^- exchanger**
 - Eventually 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⁺ secretion by parietal cells
- **Atropine** blocks muscarinic receptors on parietal cells

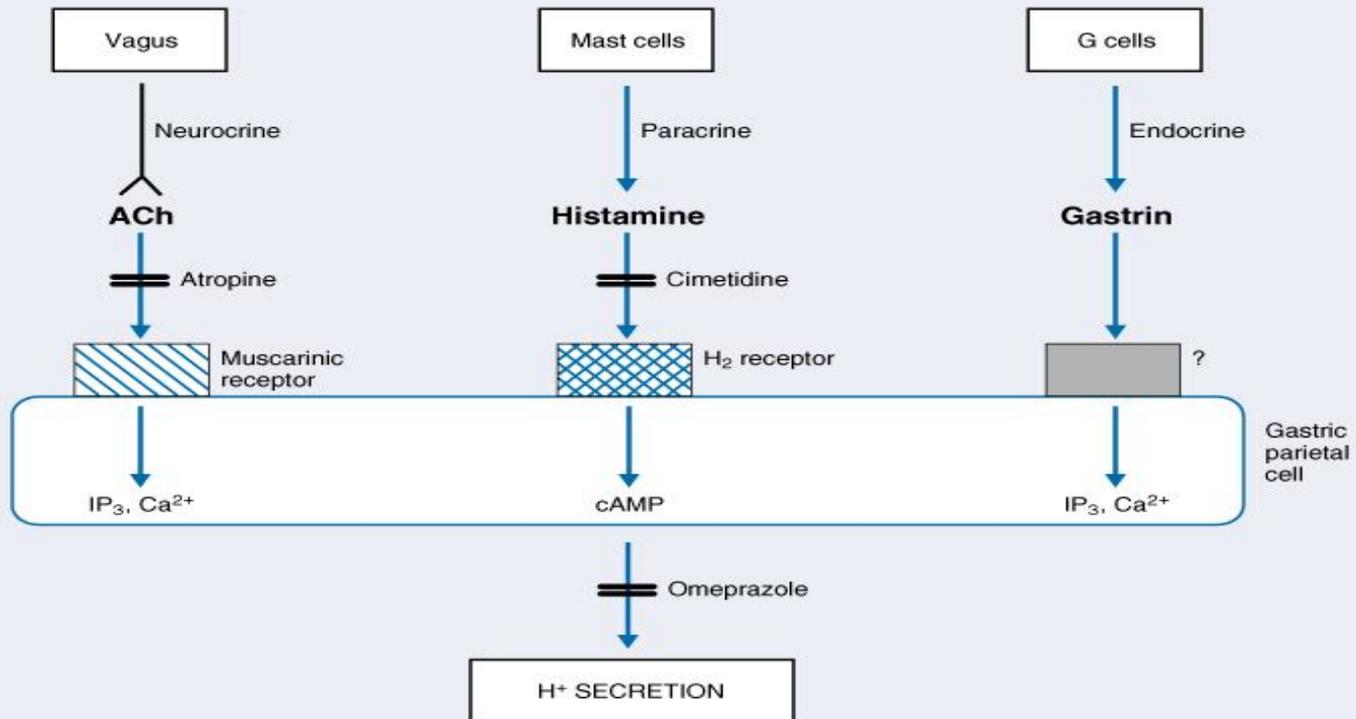
□ Histamine

- Released from mastlike cells in gastric mucosa
- Binds to **H₂ receptors** on parietal cells
- Produces H⁺ secretion by parietal cells
- **Cimetidine** blocks H₂ receptors

□ Gastrin

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

REGULATION OF H⁺ 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

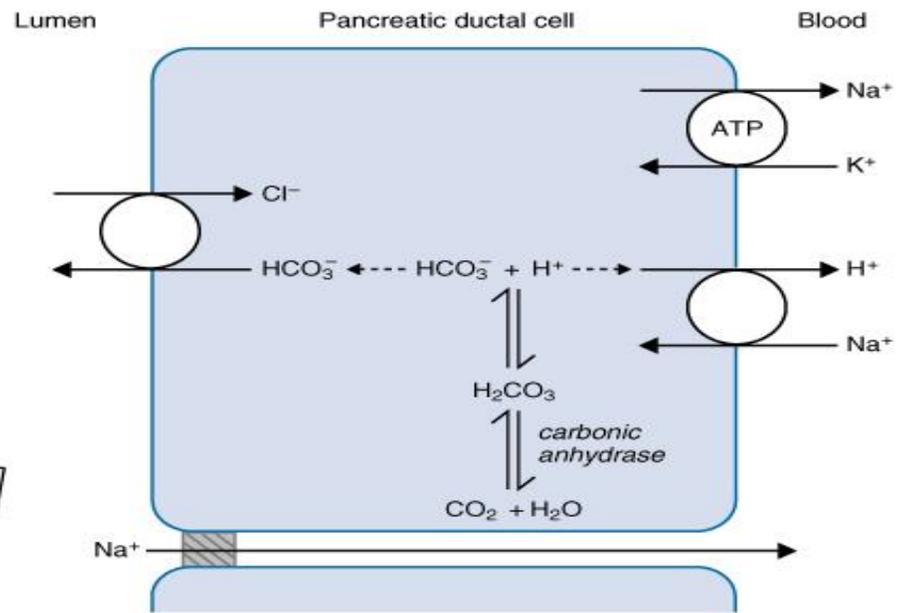
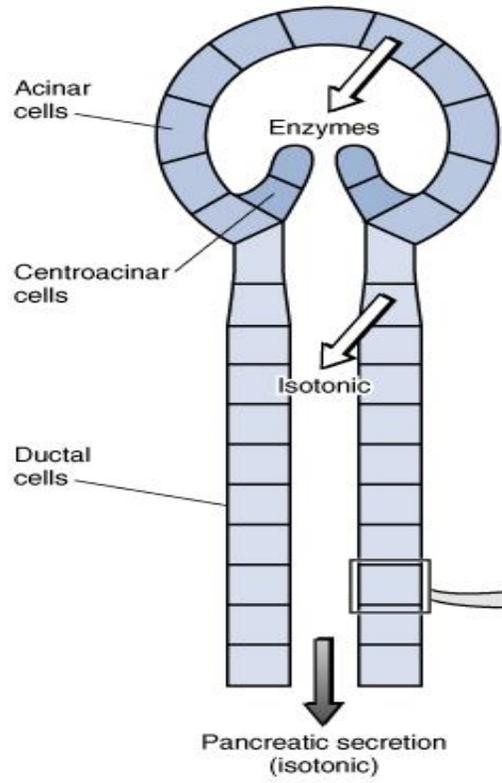
Pancreatic Secretion

- Exocrine pancreas secretes ~1 L/day into duodenum
 - Fluid consists of HCO_3^- and enzymes
 - HCO_3^- neutralizes 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 HCO_3^- component

HCO₃⁻ Secretion

- Apical membrane of ductal cells contains a Cl⁻-HCO₃⁻ exchanger
- Basolateral membrane contains Na⁺-K⁺ ATPase and a Na⁺-H⁺ exchanger
- 1. CO₂ and H₂O combine in cells to form H⁺ and HCO₃⁻
- 2. HCO₃⁻ is secreted into pancreatic juice by Cl⁻-HCO₃⁻ exchanger
- 3. H⁺ is transported into blood by Na⁺-H⁺ exchanger
 - Absorption of H⁺ causes acidification of pancreatic venous blood

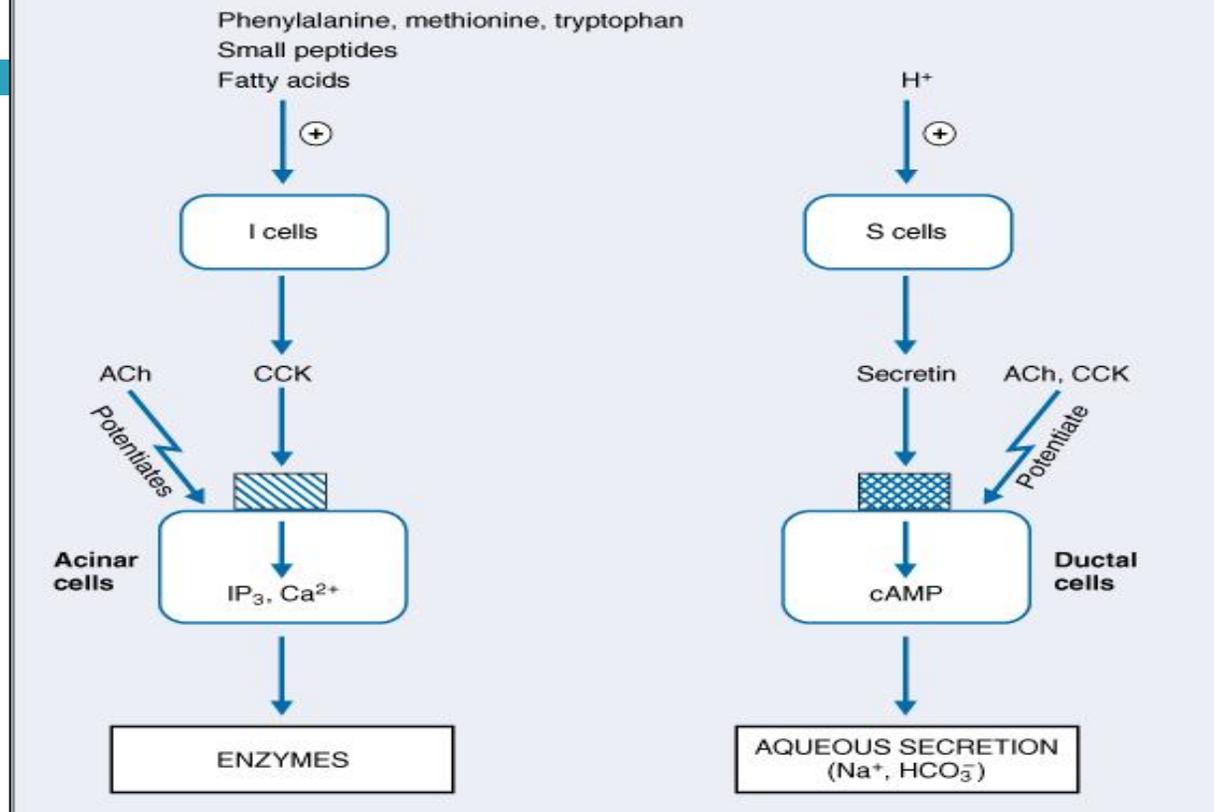
PANCREATIC SECRETION



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 HCO_3^-)**
 - Receptors for CCK, ACh, and secretin
 - **Secretin** (from S cells of duodenum) is major stimulant
 - Secreted in response to 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

