Physiology of the Gastrointestinal Tract

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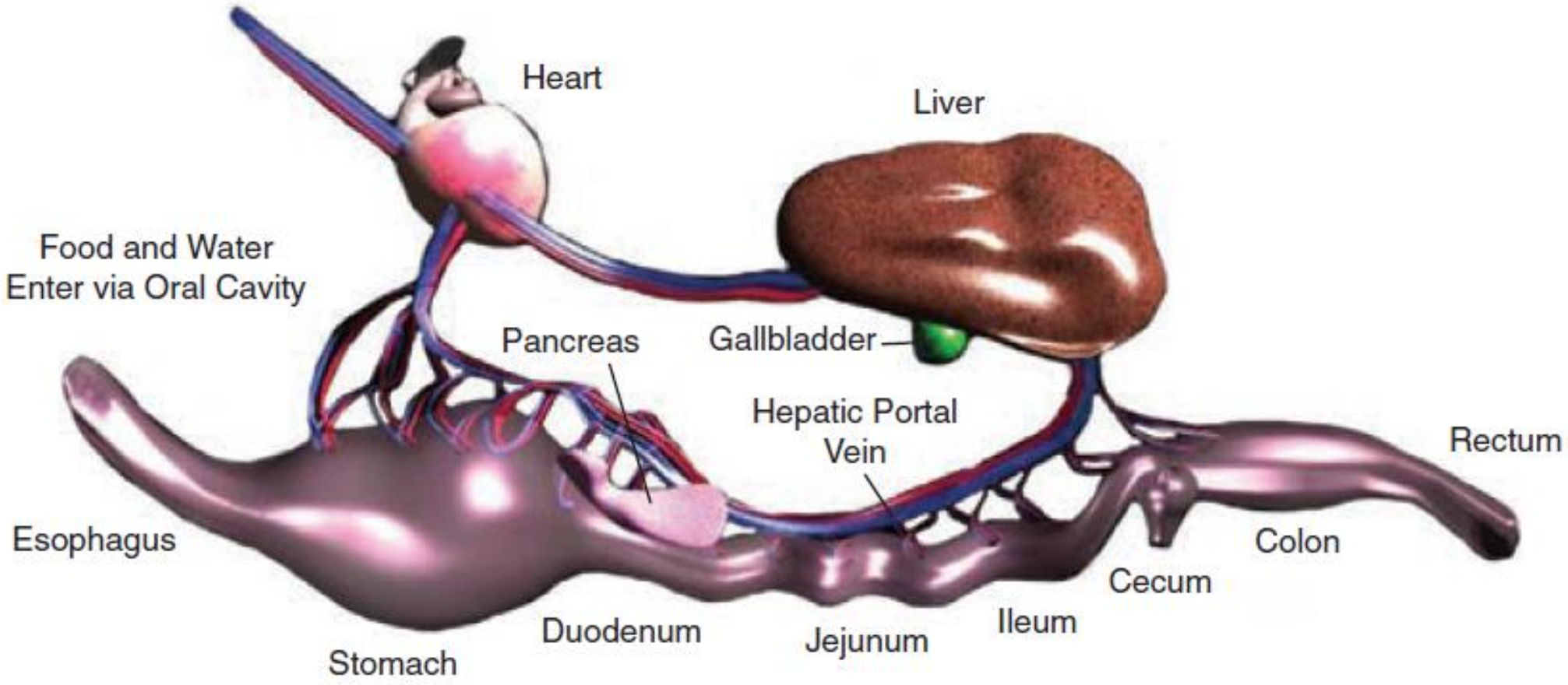
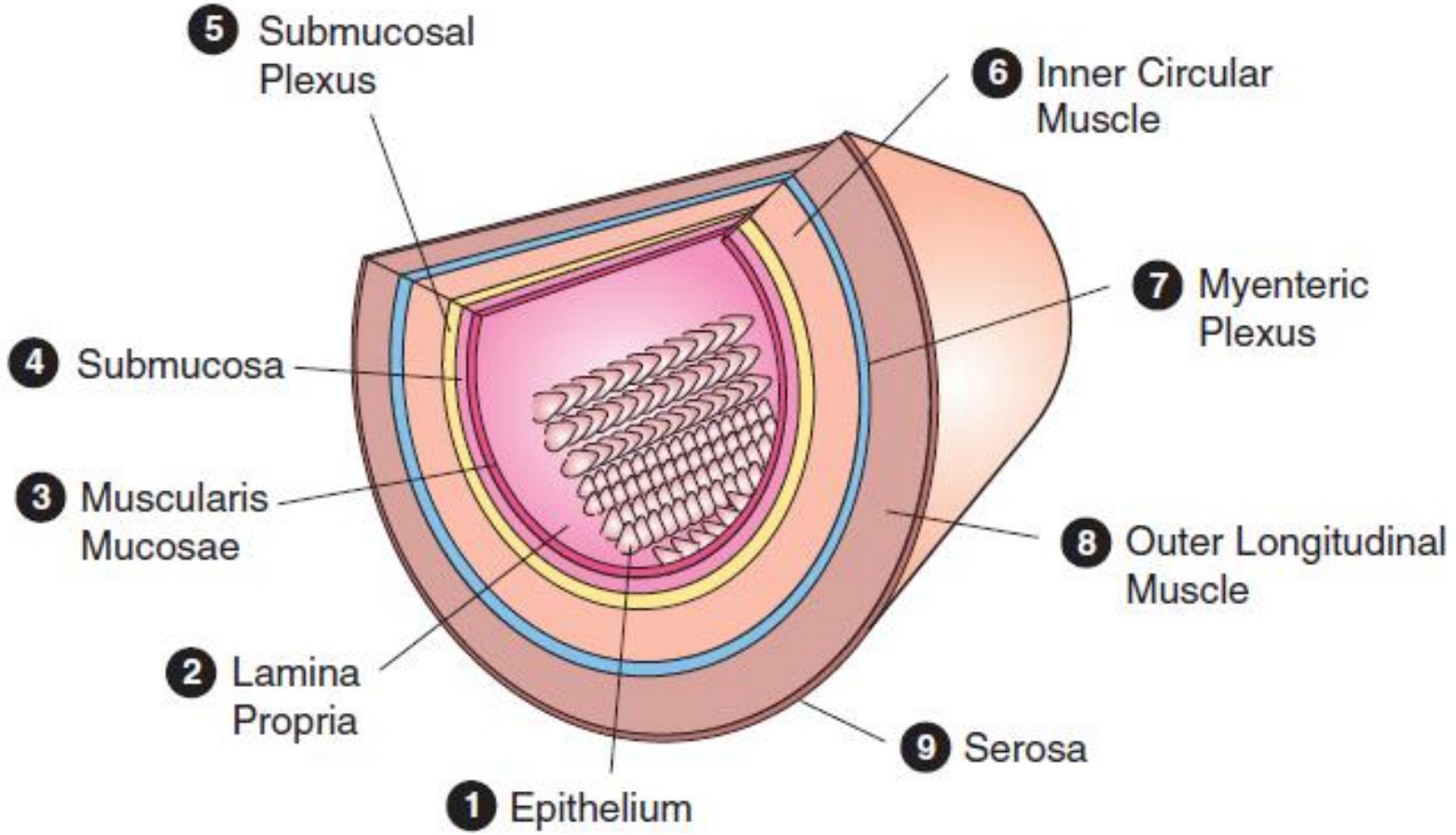
Functional Anatomy

Functional Anatomy and Blood Supply



Layers of the GI tract wall



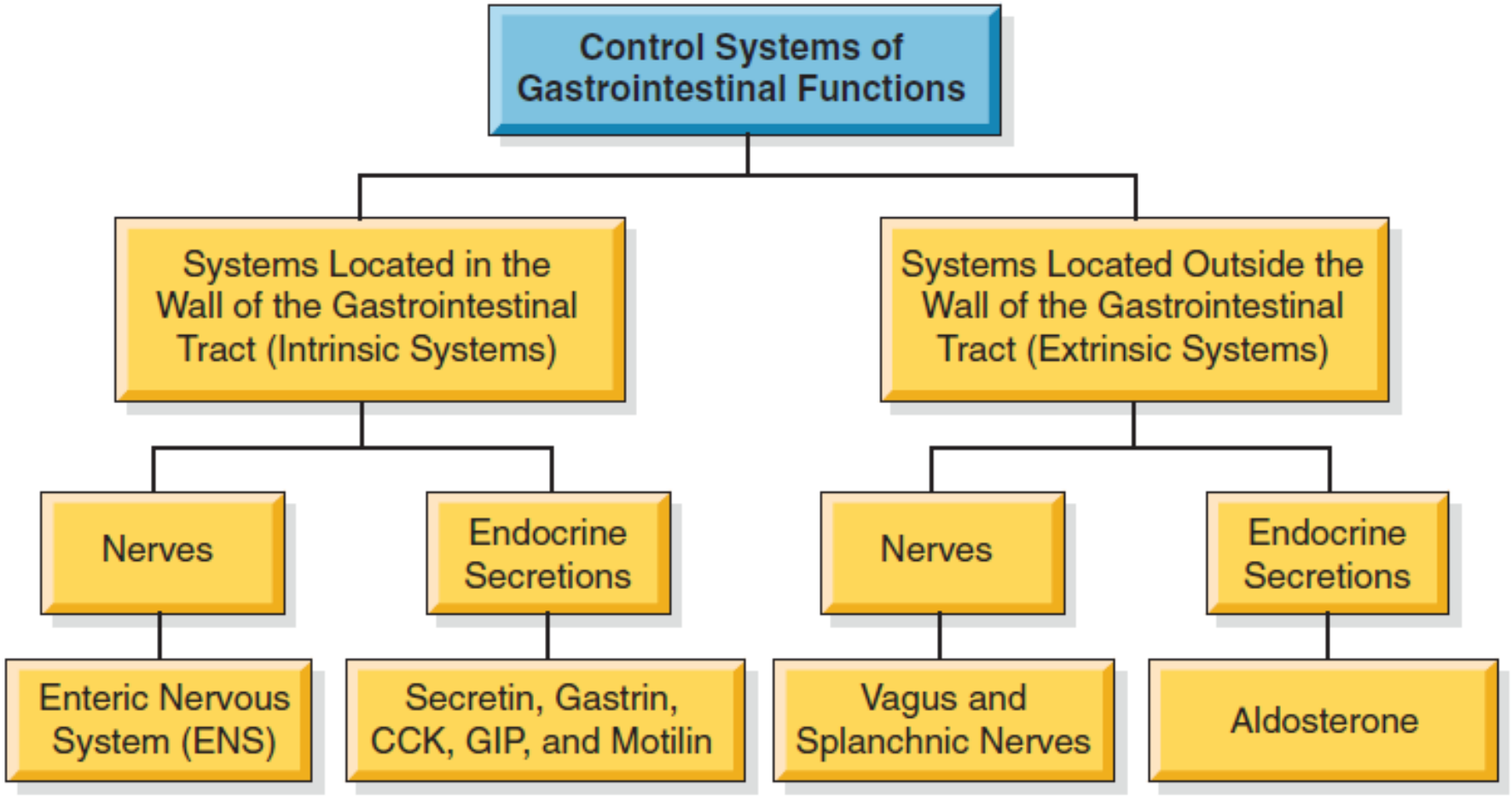
Functions of the digestive system

the GI tract supplies the body, including the gut itself, with nutrients, electrolytes, and water

- Ingestion
  - Taking food into the GI tract
- Digestion
  - Breaking down the food into nutrients
- Absorption
  - Pulling nutrients into the blood stream
- Excretion
  - Getting rid of waste materials

Control Systems

Control System of GI Functions

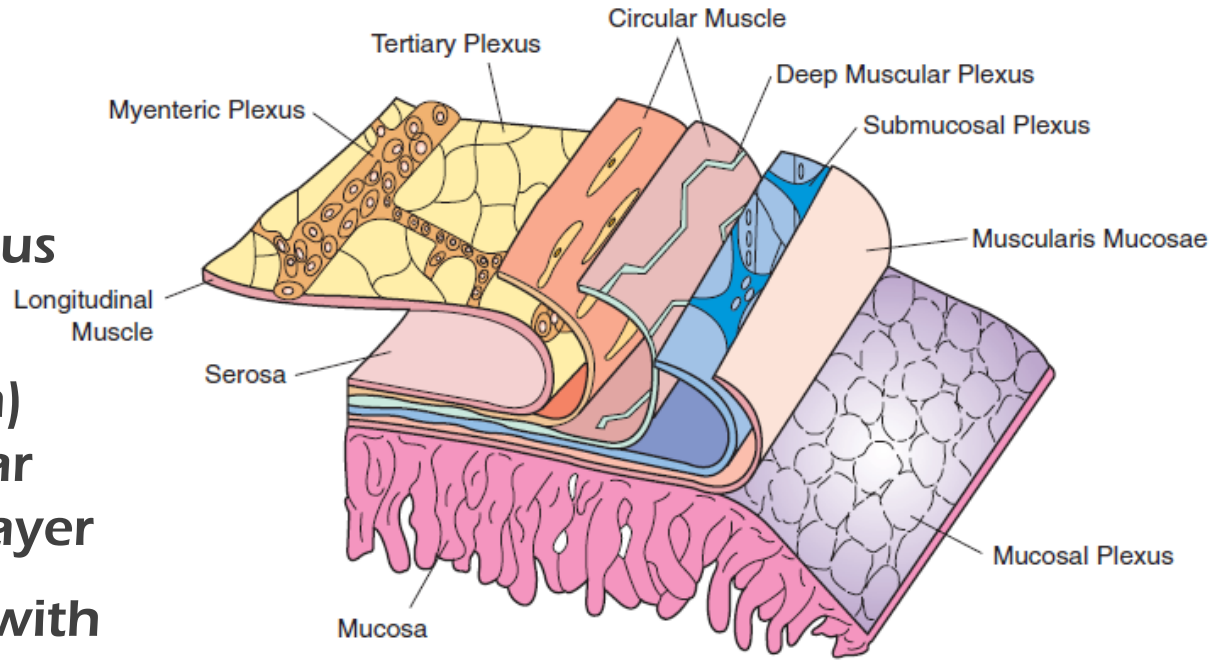


various systems that control the different functions of the GI tract: intrinsic and extrinsic control systems. Each system contains nerves and endocrine secretions.

CCK, Cholecystokinin; GIP, gastric inhibitory peptide (or glucose-dependent insulotropic peptide).

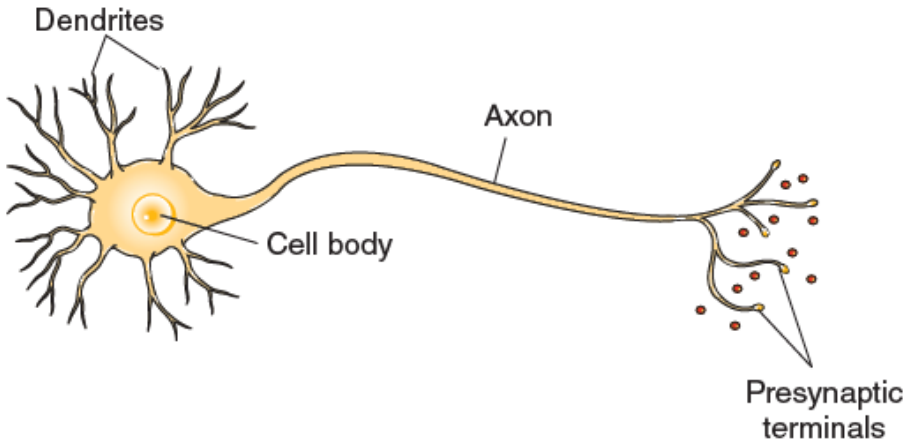
Control System of GI Functions

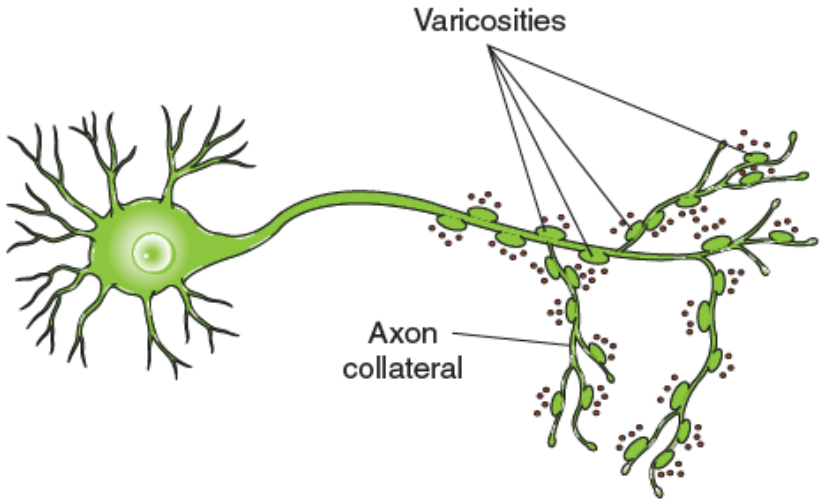
- Intrinsic Systems
  - Nerves
    - Enteric Nervous System (ENS):
      - The submucosal (Meissner) plexus locate under submucosal layer,
      - the myenteric plexus (Auerbach) locate between the inner circular and outer longitudinal muscle layer
    - The enteric plexuses communicate with each other through interneurons and with the CNS through vagal, pelvic, and splanchnic nerves.
    - Interstitial cell of Cajal (ICC): pacemaker-like activity



Control System of GI Functions

- **Intrinsic Systems**
  - **Nerves**
    - Unlike classical neurons, the enteric neurons release their neurotransmitter/neuromodulator molecules from vesicles located in swellings along often extensive branches of the axon, not just at the level of the distal synaptic terminals. These swellings are referred to as **varicosities**.
    - The varicosities contain regulatory peptides, substances collectively known as **neurocrines**.

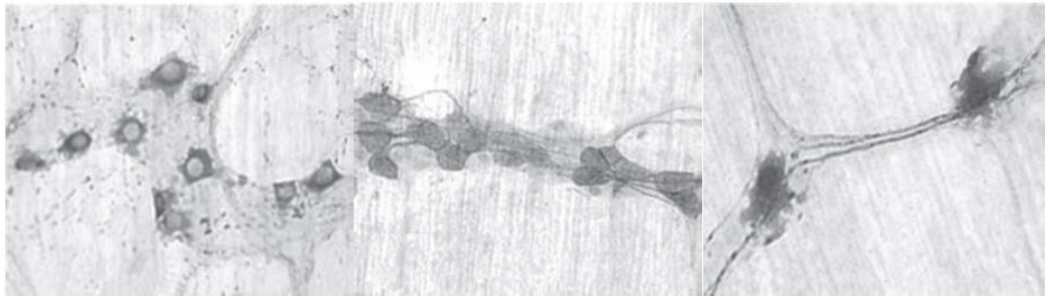




Control System of GI Functions

- **Intrinsic Systems**
  - **Nerves**
    - Four classification methods to study enteric nerves:

1. **Morphology**: Dogiel type I, II, and III
2. **Chemical coding**:
   - cholinergic neurons (Stimulatory),
   - adrenergic neurons (Inhibitory)
3. **Electrophysiology**:
   - S-type (S for synaptic) neurons, fast (e.g., millisecond) action potential,
   - AH neurons (AH for the long after hyperpolarization phase), longer lasting action potential (e.g., seconds)
4. **Function**: Excitatory, Inhibitory, Sensory, or Motor neurons.



Dogiel type I Dogiel type II Dogiel type III

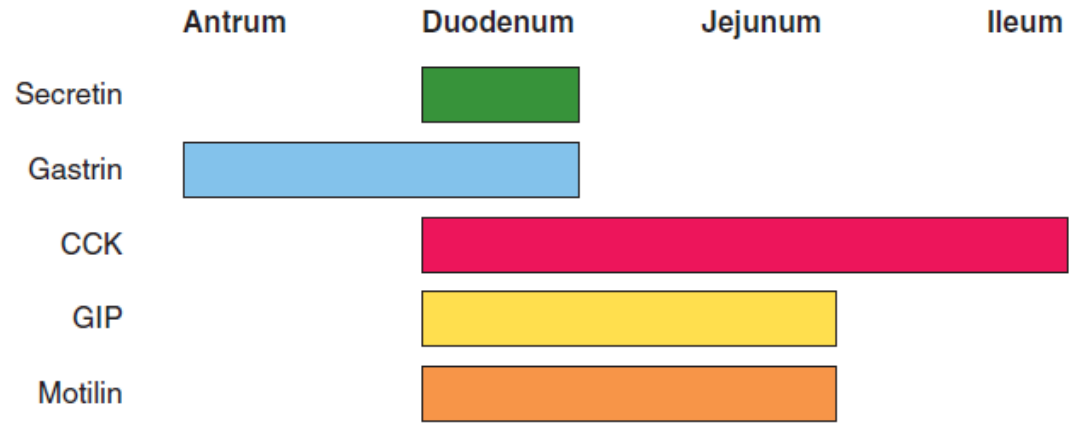
Function
Motor
S-type
Dogiel type I
Sensory
AH-type
Dogiel type II
Excitatory
Acetylcholine (Ach)
Substance P (Sub P)
Inhibitory
Nitric oxide (NO)
Vasoactive intestinal peptide (VIP)

Control System of GI Functions

- **Intrinsic Systems**
  - **Hormones**

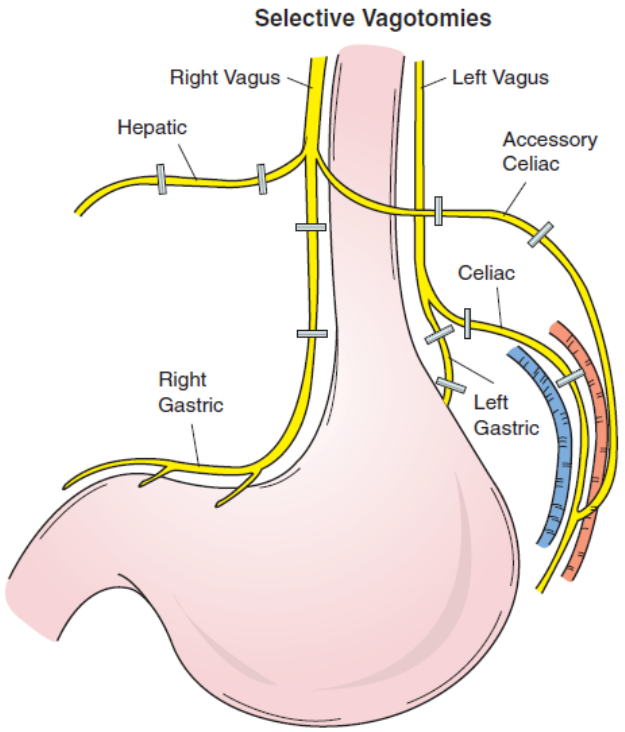
Hormone	Production Site	Action	Release Stimulus
Secretin	Duodenum and upper jejunum	Stimulates bicarbonate secretion and inhibits acid secretion (nature's anti-acid)	Acid, fat, and protein
Gastrin	Stomach and duodenum	Stimulates acid secretion and growth of stomach epithelium (marker for cancer)	Protein, increased high gastric acidity
Cholecystokinin	Duodenum, jejunum, and ileum	Stimulates pancreatic enzyme secretion and gallbladder contractions; inhibits food intake and gastric emptying	Fats and proteins
Gastric inhibitory polypeptide	Duodenum and jejunum	Inhibits gastric secretions and stimulates insulin secretion	Fat and glucose
Motilin	Duodenum and jejunum	Induction of phase III of the MMC during fasting (digestive state)	Acetylcholine

MMC, Migrating motor complex.

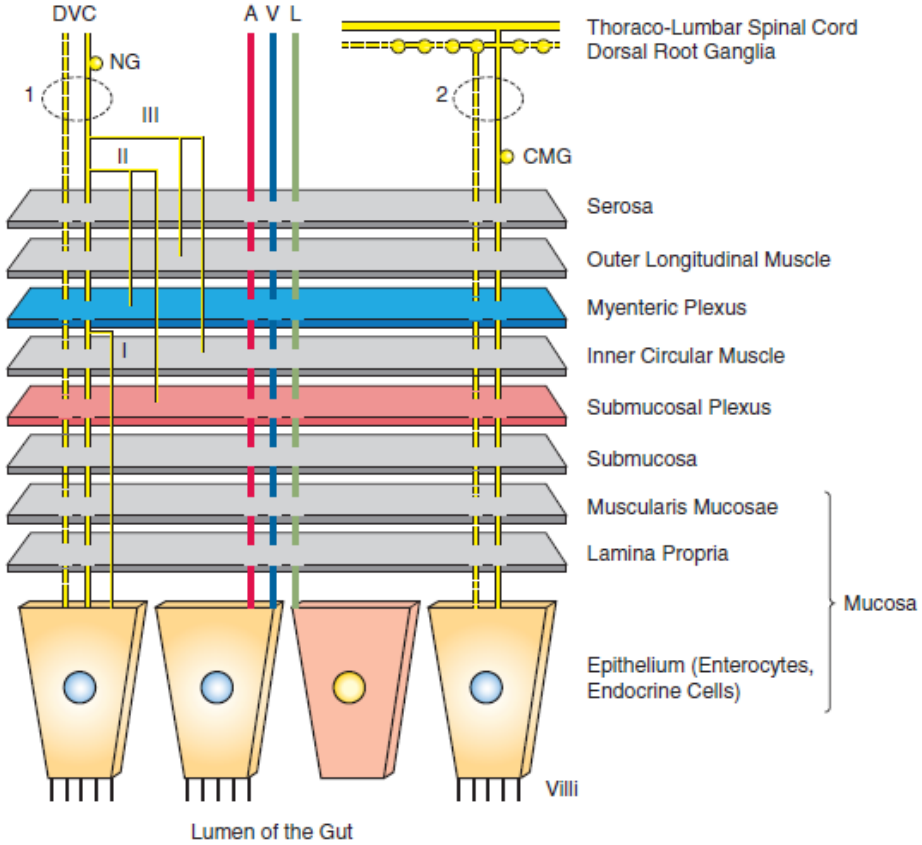


Control System of GI Functions

- **Extrinsic Systems**
  - **Nerves**:
    - The Vagus nerve:
      - **Afferents (sensory):** chemoreceptors, mechanoreceptors
      - **Efferent (motor):** increase gut blood flow, motility, and glandular secretions
    - The Splanchnic Nerve:
      - **Spinal afferent**: carry signals regarding pathological conditions in the gut (distention of the gut wall, inflammation, or the presence of noxious chemicals or substances in the lumen of the gut with associated colic or abdominal pain)
      - **Sympathetic efferent:** inhibition of gut motility and increased glandular secretions.



location of both vagi along the esophagus and their branches. The right vagus provides hepatic, right gastric, and accessory celiac branches; and the left vagus provides a celiac and left gastric branch. The *thin rectangles* along the branches represent potential locations for vagotomy in the treatment of gastric/peptic ulcers.



A schematic showing the layers of the gut and the locations of the innervations that regulate the various functions of the gut.
the vagus nerve *(1).* the splanchnic nerve *(2).* nodose ganglia [NG]), celiaco-mesenteric ganglia *(CMG),* dorsal vagal complex *(DVC).*

Control System of GI Functions

- **Extrinsic Systems**
  - **Hormone**: Aldosterone
    - Steroid hormone (mineralocorticoid)
    - secreted by the outer zona glomerulosa section of the adrenal cortex
    - following stimulation by a low-salt (low sodium) diet, angiotensin, adrenocorticotropic hormone, or high potassium levels.
    - In the GI tract,
      - Stimulates sodium and water reabsorption from the gut and salivary glands in exchange with potassium ions.
      - In addition, although it is species-dependent, aldosterone promotes increased absorption of water and sodium in the proximal colon and decreased absorption in the distal colon.

Motility

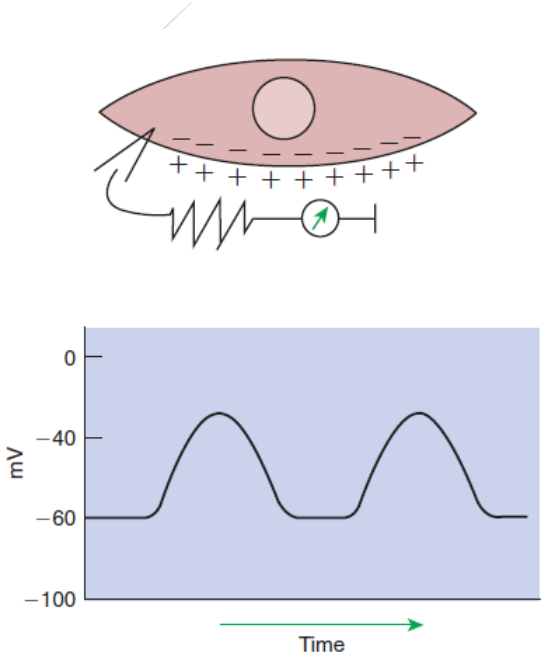
Motility Patterns of the GI Tract

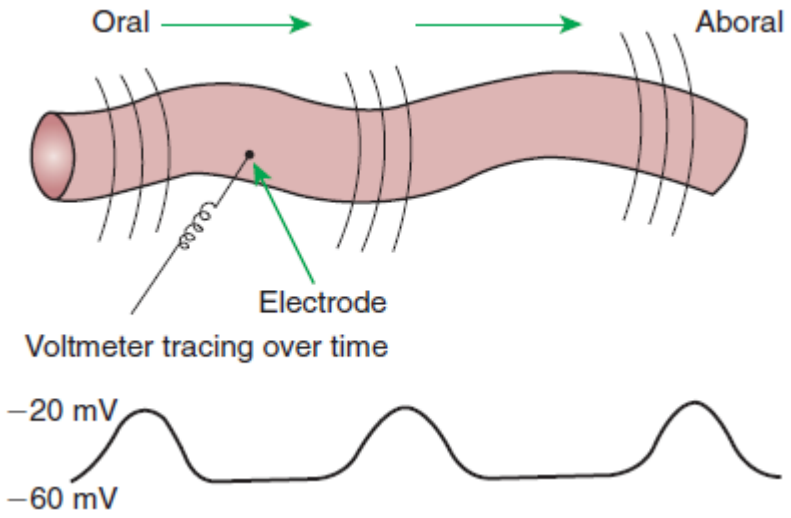
- GI movements have several functions:
  1. to **propel** ingesta from one location to the next;
  2. to **retain** ingesta at a given site for digestion, absorption, or storage;
  3. to **break up** food material physically and mix it with digestive secretions;
  4. to **circulate** ingesta so that all portions come into contact with absorptive surfaces.
- Movement of the gut wall is referred to as ***motility***, and motility may be of a **propulsive**, **retentive**, or **mixing** nature.
- The time it takes material to travel from one portion of the gut to another is referred to as the **transit time**.

Motility Patterns of the GI Tract

- **interstitial cells of Cajal (ICC)** form an interconnecting lattice of cells that surrounds the circular and longitudinal layers of muscle over the entire length of the gut.
- These cells are very similar in structure and function to the **Purkinje cells** of the heart.
- The ICC exhibit rhythmical and spontaneous oscillation in their transmembrane electrical potentials, and **fluctuations in intracellular calcium** concentrations is responsible for the spontaneous changes in membrane polarization.
  - Changes in membrane potential begin high in the duodenum and are propagated aborally (away from the mouth) along the length of the small intestine.
  - These aborally moving waves are called **slow waves** or the **basic electrical rhythm** of the gut.

Motility Patterns of the GI Tract





Spontaneous changes in membrane polarity of the interstitial cells of Cajal, specialized gastrointestinal (GI) smooth muscle cells that are responsible for spontaneous electrical rhythmicity in gut muscle

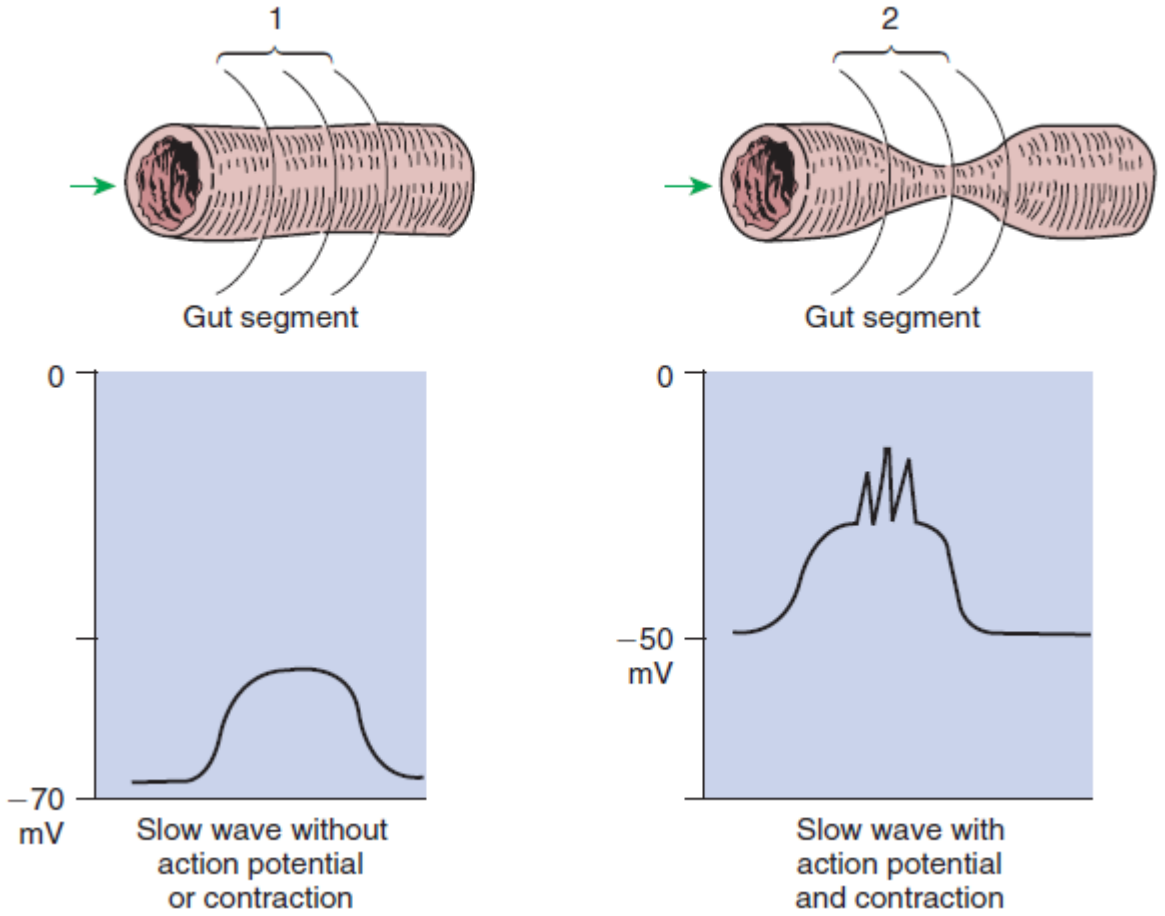
Partial membrane depolarizations of GI smooth muscle cells occur in a coordinated manner, creating waves of depolarization that sweep over large segments of muscle

Motility Patterns of the GI Tract

- **Action potentials** in the GI smooth muscle occur only in association with **slow waves**. Thus the presence of slow waves is necessary but not sufficient to cause muscle contractions.
- When slow waves pass over an area of smooth muscle and action potentials are **superimposed** on the slow waves, gut muscle contracts.
- **Control and coordination** of smooth muscle activity is achieved by influencing the likelihood that action potentials will be superimposed on slow waves.
- Such control is a function of peptides and regulatory substances produced by the **ENS** and enteric **endocrine** and **paracrine** cells.

Motility Patterns of the GI Tract

1, No muscle contraction occurs in the absence of action potentials. *2,* Muscle contracts when the crest of the slow waves reaches a critical point of depolarization, allowing action potentials to occur. The probability of action potentials occurring during the passage of a slow wave over a segment of gut muscle is influenced by the degree of baseline depolarization. Norepinephrine lowers the baseline (increases its absolute value), whereas acetylcholine raises the baseline (decreases its absolute value). *mV,* Millivolts.



Motility of the Stomach

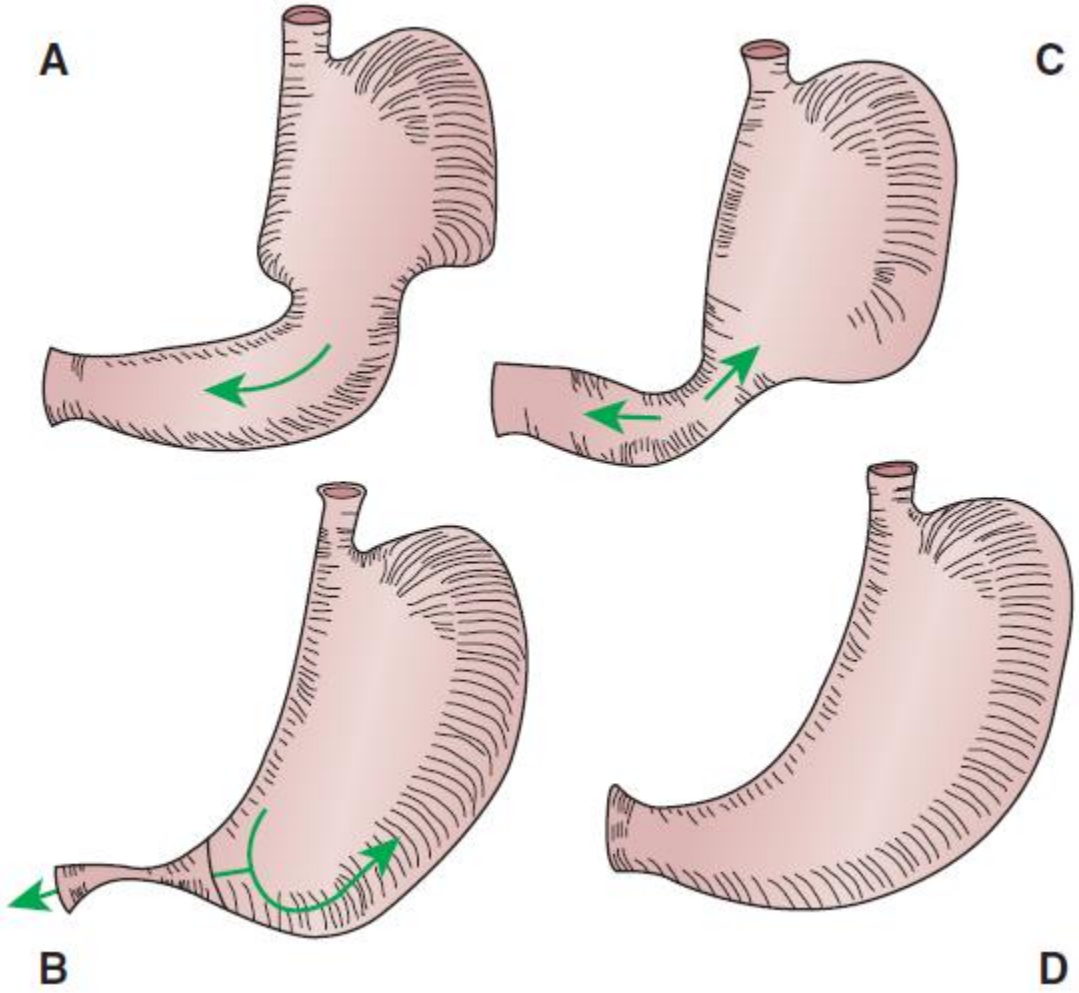
- The stomach is divided into two physiological regions:
  - The proximal region
    - **adaptive relaxation**: relaxation of the muscles as food enters the stomach
  - The distal region (antrum)
    - Strong waves of peristalsis begin at about the middle of the stomach and migrate, with the slow waves, toward the pylorus.
    - the pylorus constricts, blocking the gastric exit of all but the smallest particles (less than 2mm in diameter).
    - Particles too large to pass the pylorus are crushed and ejected back into the antrum
    - the peristaltic actions of the distal stomach are:

1) propel food 2) grind and mix it.

Motility of the Stomach

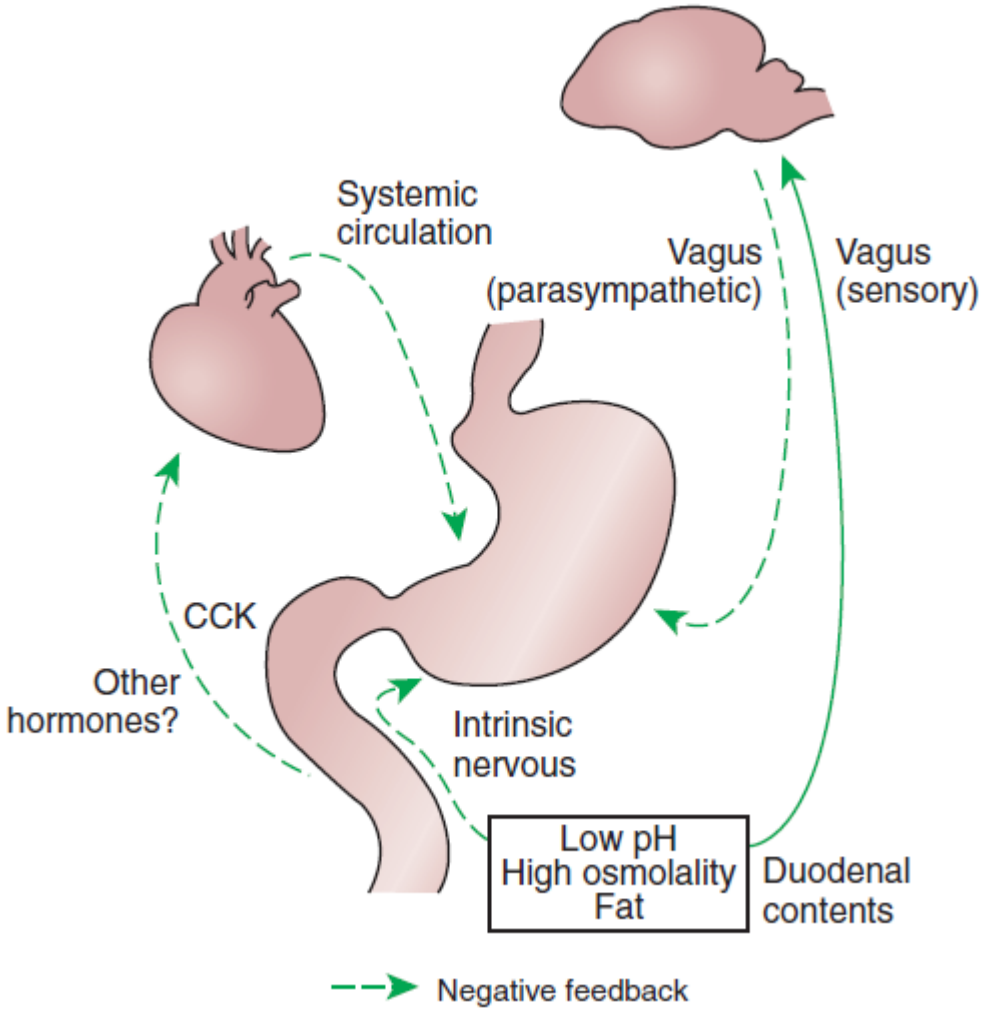
Grinding and churning activity
of the distal stomach.

A, Wave of peristalsis begins at the junction of the proximal and distal areas of the stomach and moves toward the pylorus. **B,** As the peristaltic wave approaches the pylorus, the pylorus constricts, causing some of the ingesta to be crushed within the peristaltic ring and propelled back toward the proximal stomach. **C,** As the peristaltic wave reaches the pylorus, some finely ground and liquefied material passes through into the duodenum, but the majority of material has been propelled back into the stomach. **D,** Between contractions, no gross movement of gastric contents occurs.



Motility of the Stomach

- The rate at which food leaves the stomach must match the rate at which it can be digested and absorbed by the small intestine.
- There are reflexes that regulate gastric emptying and allow the stomach to serve as a storage site. They called **enterogastrc reflex**.
- The afferent receptors of these reflexes are in the duodenum and are activated by **low pH**, **high osmolality**, and the presence of **fat**.

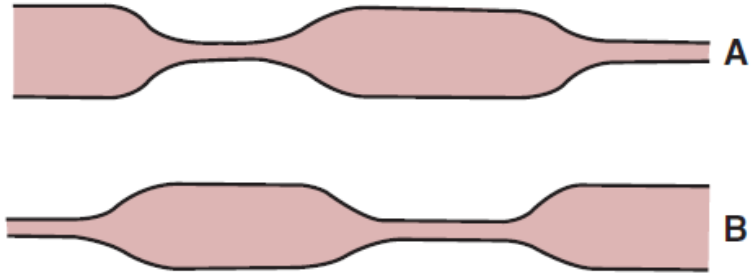


Vomiting Reflex

- Vomiting is a complex reflex activity, and its integration, or coordination, is centered in the **vomit center** in brainstem.
- Afferent stimulation of the vomiting reflex comes from **mechanoreceptors** in the pharynx and tension receptors and **chemoreceptors** in the gastric and duodenal mucosa.
- **The chemoreceptor trigger zone (CTZ)**
  - an area of the brainstem that lies in contact with the third ventricle
  - is sensitive to the presence of some drugs and toxins in the blood.
  - When stimulated, this zone sends signals to the vomit center and induces vomiting
- The semicircular canals of the **inner ear** may induce vomiting, by stimulation of the CTZ, as occurs in **motion sickness**

Motility of the Small Intestine

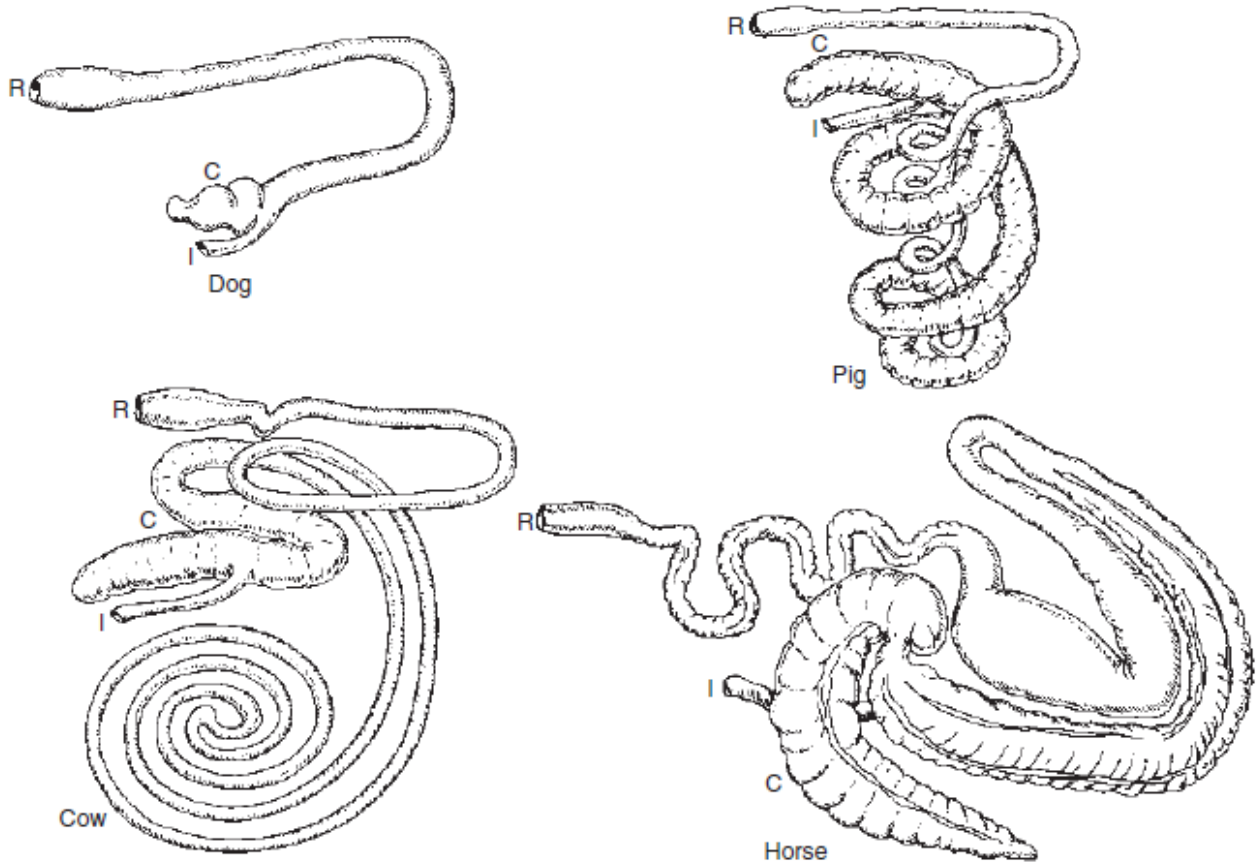
- **Digestive phase**:
  - **Nonpropulsive pattern (Segmentation)**: localized contractions of circular muscle which tends to "**milk**" gut contents back and forth.
  - **Propulsive activity** consists of peristaltic contractions that **migrate** down the gut in phase with the slow waves ("two steps forward, one step back.")



- **Interdigestive phase**:
  - **Migrating motility complex (MMC)** or, alternatively, the migrating myoelectric complex: powerful peristaltic contractions that sweep over a large length of small intestine.
    - "housekeeping" function and controlling the bacterial population by preventing the migration of bacteria from the ileum to the duodenum.

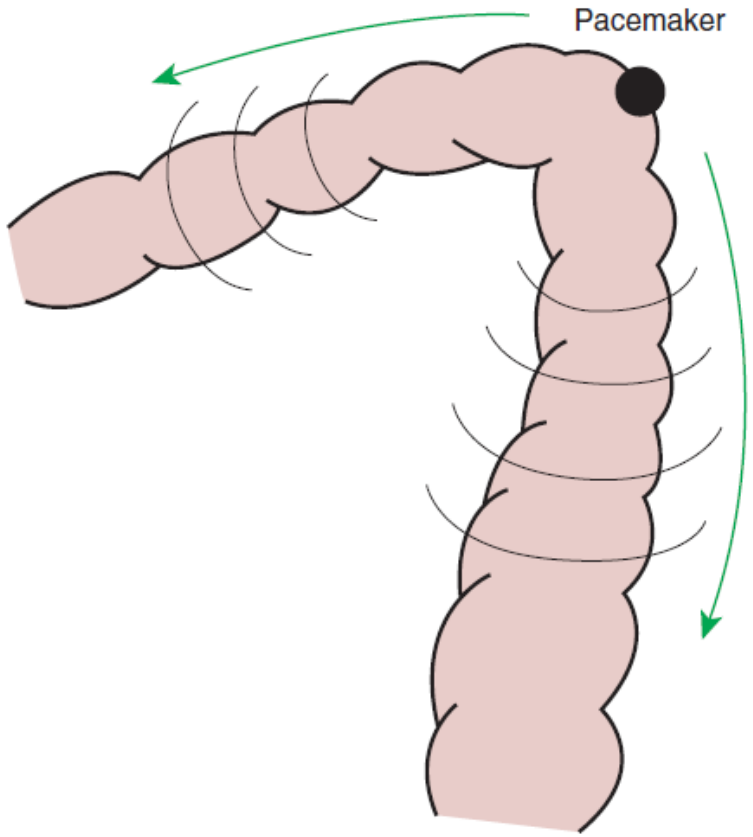
Motility of the Colon

- The colon has multiple functions, including (1) absorption of water and electrolytes, (2) storage of feces, and (3) fermentation of organic matter that escapes digestion and absorption in the small intestine.
- The importance of colonic fermentation to the energy needs determines the size of colon among animals.



Motility of the Colon

- **Mixing** activity is prominent in the colons of all species because mixing and circulating are important to both absorptive and fermentative functions.
- **Retropulsion**, or antiperistalsis motility are contractions that migrate orally, the opposite of normal peristaltic movement.
- Slow waves originate in the ICC but ENS can influence in such a manner as to shift the direction of slow waves propagation.
- Under resting conditions in the colon, slow waves originate from **pacemakers** in one or more central sites.



Secretions

Secretions of the GI Tract

- Digestion and absorption can take place only in the **aqueous milieu of** digestive secretions.
- Synthesis and secretion of these fluids represent a well-controlled process regulated by **endocrine**, **paracrine**, and **neural** events.
- most of the digestive secretions have a relatively large concentration of **electrolytes**.
- one of the major life-threatening ramifications of digestive diseases is the loss of water and electrolytes from the body caused by inadequate **reabsorption** of digestive secretions.

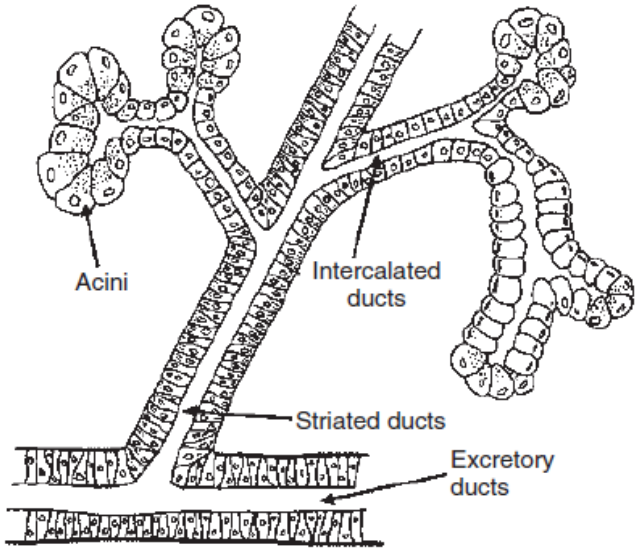
Secretions of the GI Tract- Saliva

- Salivary secretions allow the food to be well-lubricated boluses that **facilitate swallowing**.
- Saliva has antibacterial, digestive, and evaporative cooling functions, depending on the species.
  - **Lysosomes**: antibacterial
  - **Salivary amylase**: starch-digesting enzyme in omnivorous animals.
  - **Lingual lipase**: in young animals while they are on milk diet.
- The salivary gland is a typical acinar gland
  - The glandular cells lining the acini secrete water, electrolytes, enzymes, and mucus.
  - The duct epithelium **reabsorbs electrolytes**, especially sodium and chloride like in the kidney tubules.

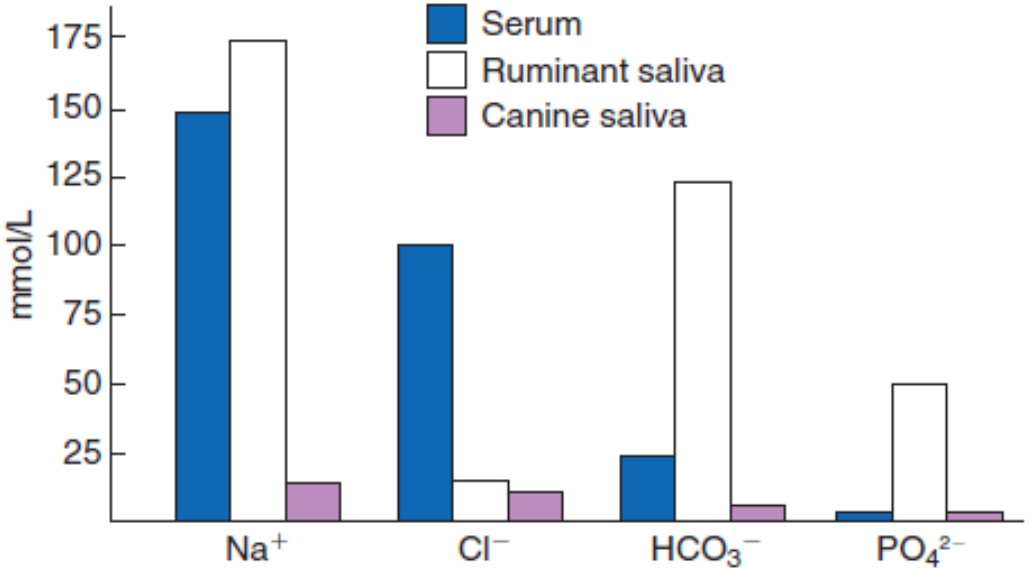
Secretions of the GI Tract- Ruminants Saliva

- The normal composition of ruminant parotid saliva, compared with blood serum, has high concentrations of **bicarbonate** and **phosphate** and a **high pH**.
  - This well-buffered solution is necessary for neutralizing acids formed by fermentation.
  - An adult cow may secrete **100 to 200 L** of saliva **per day**.
  - In abnormal circumstances, such as blockage of the esophagus, in which the flow of saliva is diverted from the gastrointestinal (GI) tract, cattle quickly become **dehydrated** and **acidotic**.

Secretions of the GI Tract- Saliva



Schematic illustration of the salivary gland. Saliva is initially secreted by the acinar cells and is then modified as it passes through the intercalated, or collecting, ducts. Modification of acinar secretions by duct epithelia is a physiological phenomenon common among several types of glands, including the pancreas.



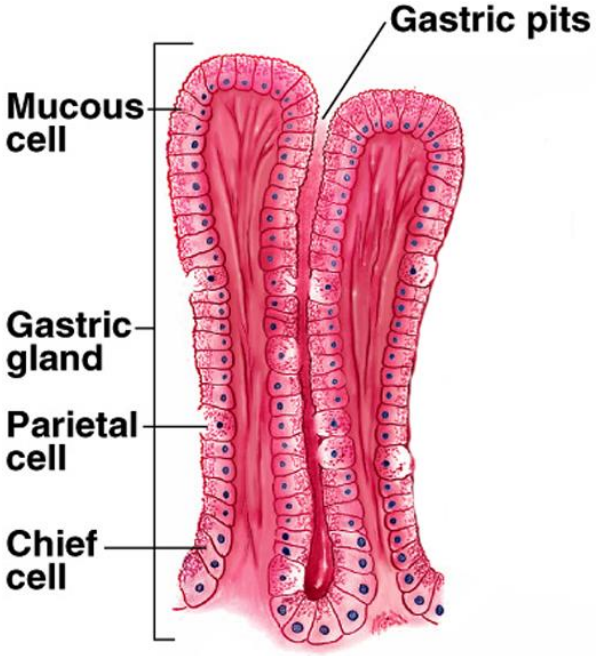
Electrolyte composition of blood serum and of canine and ruminant saliva. Note that the electrolyte concentration of canine saliva is much lower than that of serum, in contrast to the concentration in ruminant saliva. Also note the high concentrations of bicarbonate (HCO_{3-}) and phosphate (PO_4^{2-}) in ruminant saliva; these ions give ruminant saliva its alkalizing quality.

Gastric Secretions

- **Non-glandular area**:
  - only in horse and pig
  - Function unclear (probably rumen like activity)
- **Glandular area**:
  - Divide into 3 regions: **cardiac** mucosa, **parietal** mucosa, **pyloric** mucosa
  - These areas contain glands of similar structure but with different types of secretions
  - In most species the cardiac mucosa forms a narrow band around the gastric opening of the esophagus.
  - In the pig, however, the cardiac mucosa covers a substantial portion of the proximal stomach.

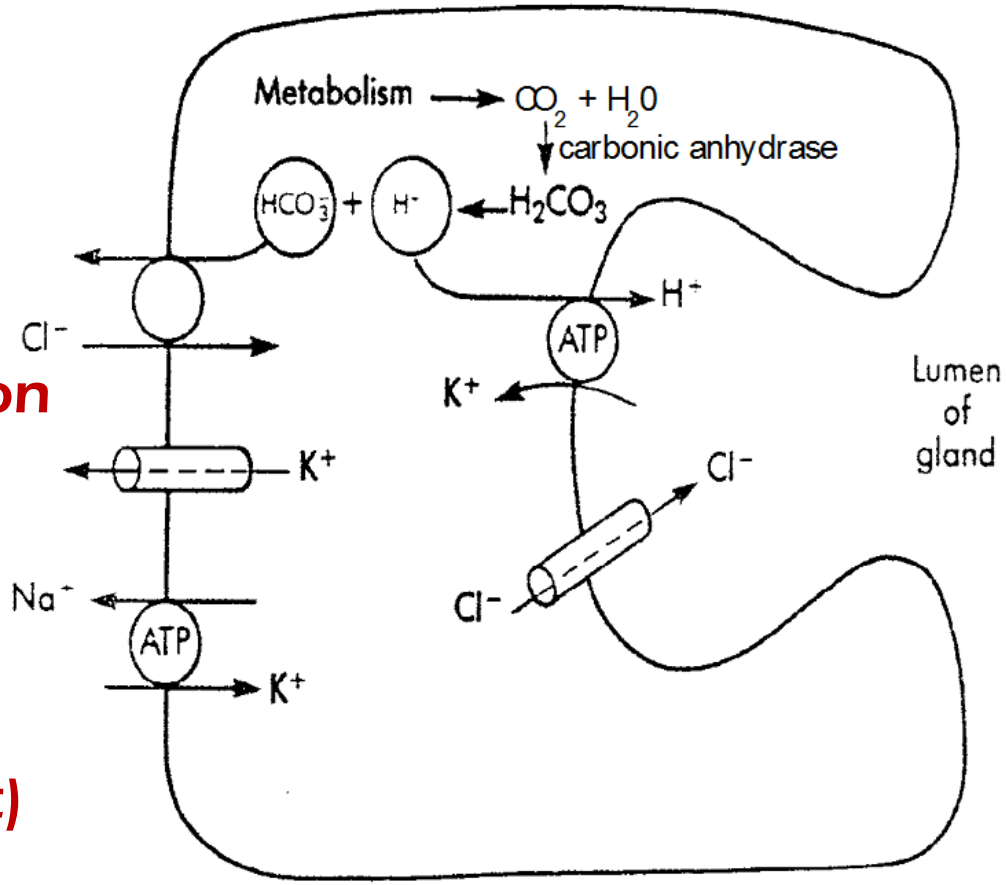
Gastric Secretions

- Gastric Mucosa
  - Surface mucous cells secrete thick, tenacious mucus
  - Parietal cells secrete HCl & intrinsic factor (necessary for B12 absorption in intestine)
  - mucous neck cells, secrete thin mucus,
    - They are only stomach cells that can divide.
    - They can differentiate into any of the several types of mature cells of the gastric surface and glands
  - Chief cells secrete pepsinogen (precursor for pepsin)
  - G cells produce gastrin in the pyloric region
  - Enterochromaffin-like cells secrete histamine & serotonin
  - D cells secrete somatostatin



Gastric Secretions

- Gastric Glands: Secrets HCl
  - H+ Is produced by parietal cells which ATP H+ into lumen via an H+/ K+ pump (pH ≈1)
  - Cl- is secreted by facilitated diffusion
  - H+ comes from dissociation of H2CO3 (Carbonic anhydrase enzyme)
  - Cl- comes from blood side of cell in exchange for HC03- (Chloride shift)
- HCl Is secreted in response to the hormone gastrin; & ACh from vagus by releasing histamine

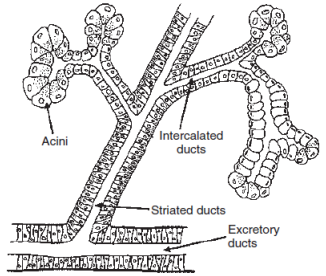


Pancreatic Exocrine Secretions

- Acinar Cells Secrete Enzymes, Whereas Centroacinar Cells and Duct Cells Secrete an Electrolyte Solution Rich in Sodium Bicarbonate
- Pancreatic Cells Have Cell Surface Receptors Stimulated by Acetylcholine, Cholecystokinin, and Secretin

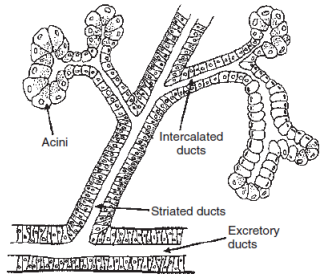
Enzyme	Action	Source	Precursor	Activator
Pepsin	Endopeptidase	Gastric glands	Pepsinogen	Hydrochloric acid, pepsin
Chymosin (rennin)	Endopeptidase	Gastric glands	Chymosinogen	?
Trypsin	Endopeptidase	Pancreas	Trypsinogen	Enterokinase, trypsin
Chymotrypsin	Endopeptidase	Pancreas	Chymotrypsinogen	Trypsin
Elastase	Endopeptidase	Pancreas	Proelastase	Trypsin
Carboxypeptidase A	Exopeptidase	Pancreas	Procarboxypeptidase A	Trypsin
Carboxypeptidase B	Exopeptidase	Pancreas	Procarboxypeptidase B	Trypsin

Pancreatic Exocrine Secretions



- The exocrine pancreas is a typical acinar gland in which the end-pieces, or acini, are connected by an arborizing system of ducts; thus the gland conceptually resembles a bunch of grapes.
  - The cells of the **acini** secrete **protein-digesting enzymes**
  - **Centroacinar** cells near the junction of the acini and ducts, modify the electrolyte composition of the fluid secreted by the acinar cells.
    - **Cl^- - $HC03^-$** exchange protein on the **luminal** surface
    - Na^+,K^+-ATPase, **Na^+-$HCO3^-$ co-transporter**, H+- Na+ exchanger, and an **H^+-ATPase** on the **basolateral** membrane.
    - The net result is that pancreatic fluid is a bicarbonate-rich, **alkaline fluid** that neutralizes the acid ingesta arriving **in the duodenum** from the stomach. In addition, the **H+ ions** transported into the basal interstitial fluid of the pancreas are absorbed **into the blood**, balancing the "alkaline tide" that was created by gastric acid secretion.

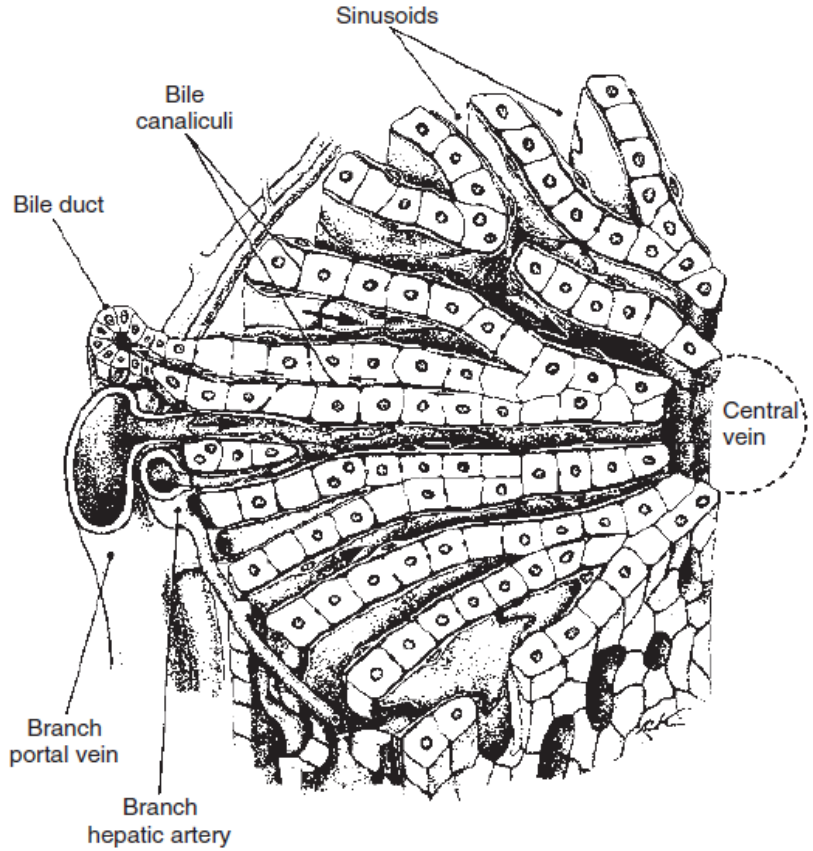
Pancreatic Exocrine Secretions



- **CCK** is the primary hormonal stimulus for **acinar** cells, whereas **secretin** is the primary hormonal stimulus for **centroacinar** and duct cells.
- **Ach** released from nerve endings stimulate both CCK and secretin.
  - The sight and smell of food induce centrally integrated vagal responses, leading to pancreatic secretion (**Cephalic phase**).
  - Distention of the stomach causes a vagovagal reflex stimulating pancreatic secretion, (**gastric phase**).
  - As food material from the stomach enters the duodenum, enteric nerve impulses begin, resulting in ACh stimulation of pancreatic secretory cells (**intestinal phase**).
- **Peptides** in the duodenal lumen stimulate **CCK**, **Fats** in gastric ingesta also stimulate **CCK**, **low pH** of material entering the duodenum stimulates the secretion of **secretin**.

Bile Secretion

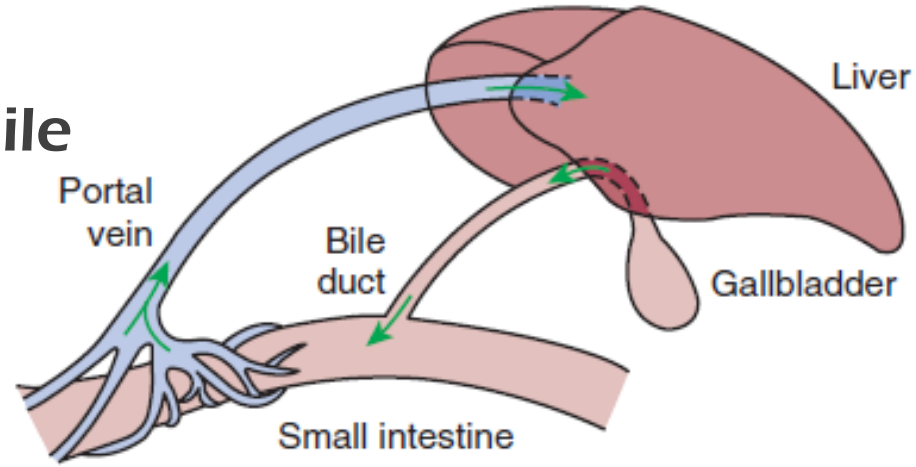
- The liver Is an **acinar gland** with small acinar lumina known as canaliculi.
- The liver is composed of plates, or one-cell–thick layers of hepatocytes that are bathed on either side by blood from the hepatic sinusoids.
- Within the plates of cells, these spaces join to form channels, or canaliculi, that connect to the bile ductules.
- Bile is secreted from the hepatocytes into the canaliculi (acini), from which it flows into the bile duct system.



Hepatic microanatomy is complex and can be visualized in several ways. Note the relationship of the bile canaliculi to the bile ducts; the biliary system may be viewed as an acinar gland with the bile canaliculi forming a long, narrow acinus.

Bile Secretion

- Bile Contains **Phospholipids** and **Cholesterol** Maintained in Aqueous Solution by the Detergent Action of Bile Acids
- Hepatocytes form bile acids from cholesterol.
- Bile acids are molecules with a water-soluble (hydrophilic, or "water-loving") side and a lipid-soluble (hydrophobic, or "water-hating") side.
- Bile acids can **emulsify** dietary lipids and to solubilize the products of fat digestion.



Bile acids and other molecules circulate in an enterohepatic cycle. Phases of the cycle include the portal vein, biliary system, and intestinal lumen.

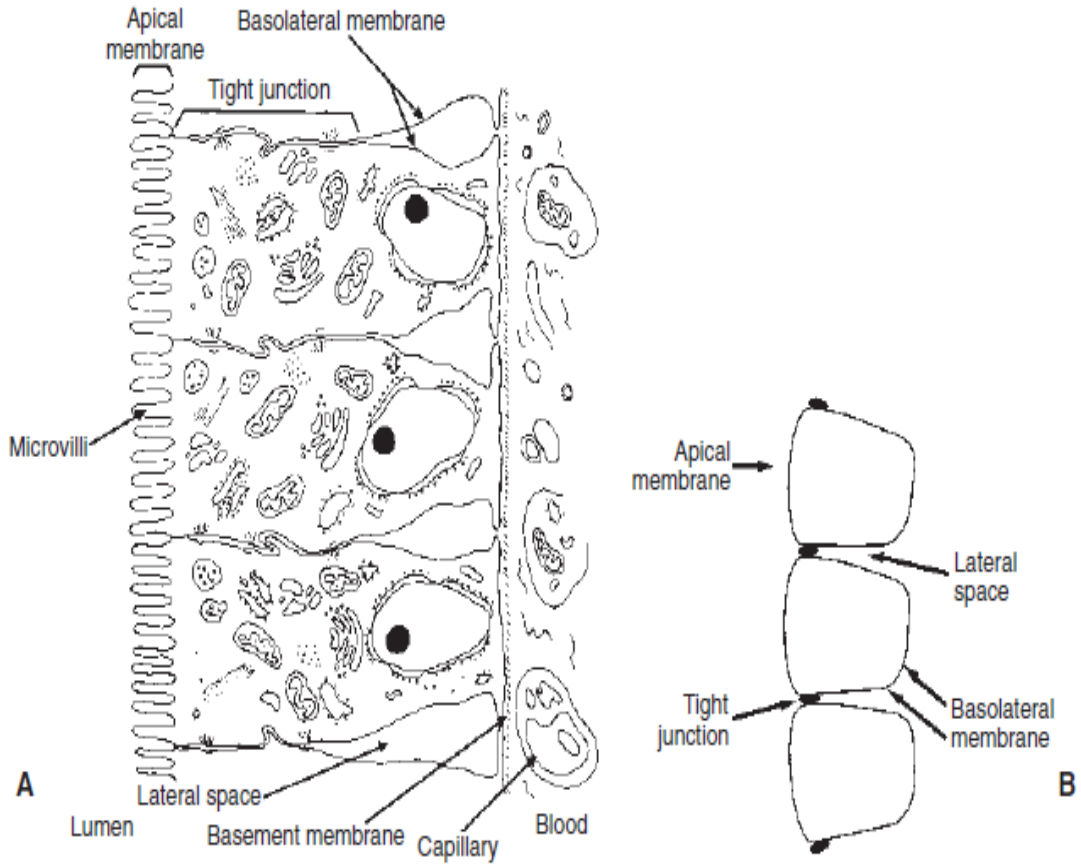
Bile Secretion

- When food, especially fat-containing food, reaches the duodenum:
  - the GI endocrine cells → CCK, → the sphincter of Oddi relaxes → the gallbladder contracts.
  - Bile acids aid in the digestion and absorption of fats in the jejunum.
  - Bile acids absorb in the ileum and travel via the hepatic portal vein to the liver, stimulates further bile synthesis (positive feedback).
    - Further bile absorption → Further bile synthesis
- When fats have been digested and absorbed, the stimulus for CCK secretion is removed, resulting in closure of the sphincter of Oddi and diversion of bile to the gallbladder.
- Secretin stimulates water and bicarbonate secretion from the bile ducts in a manner similar to that of its effects on the duct cells of the pancreas.

Digestion/Absorption
The Nonfermentative Processes

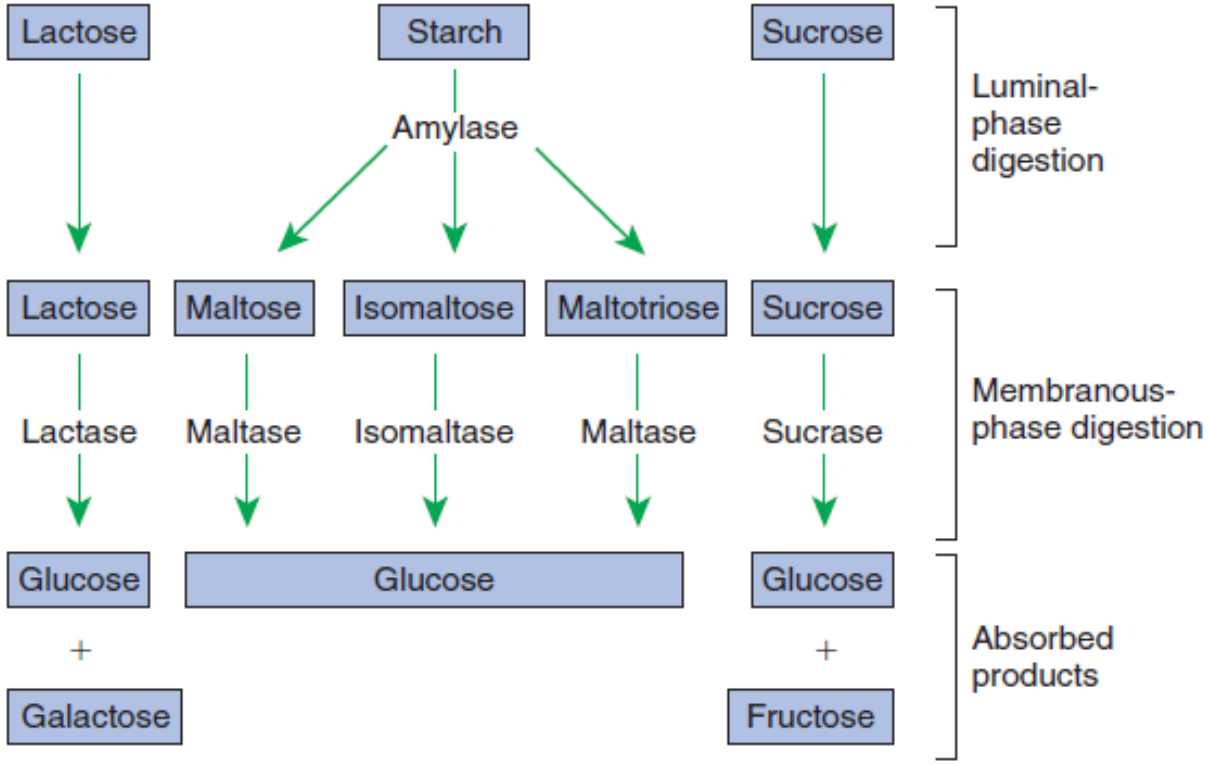
Digestion

Understanding the anatomical relationships of the enterocytes, tight junctions, apical membrane, basolateral membrane, and lateral spaces is critical to an understanding of the physiology of intestinal absorption. **A**, Anatomic illustration of the intestinal epithelium. **B**, Stylized sketch of the epithelium, including a capillary containing formed elements of blood. It is important to understand the relationship between part *A* and part *B* of this diagram.



Carbohydrate Digestion

Luminal-phase and membranous-phase digestion of carbohydrate. Note that specific enzymes exist for each polysaccharide, and that a limited number of monomers are formed eventually from a relatively large number of starches and polysaccharides.

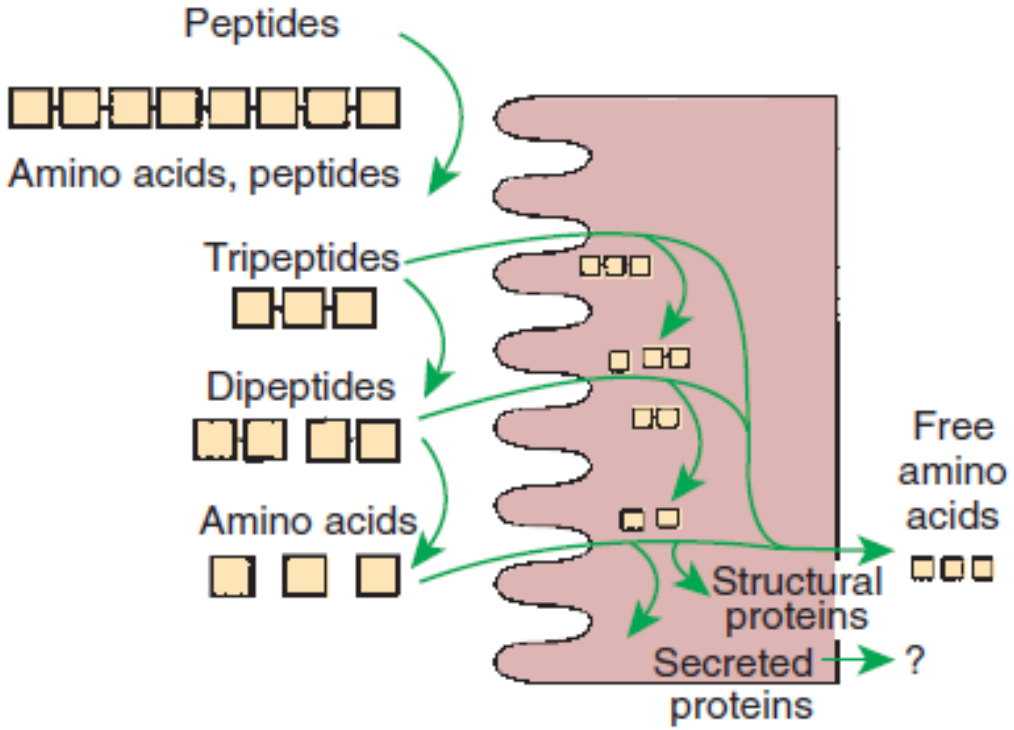


Protein Digestion

Luminal-Phase
Enzymes of
Protein Digestion

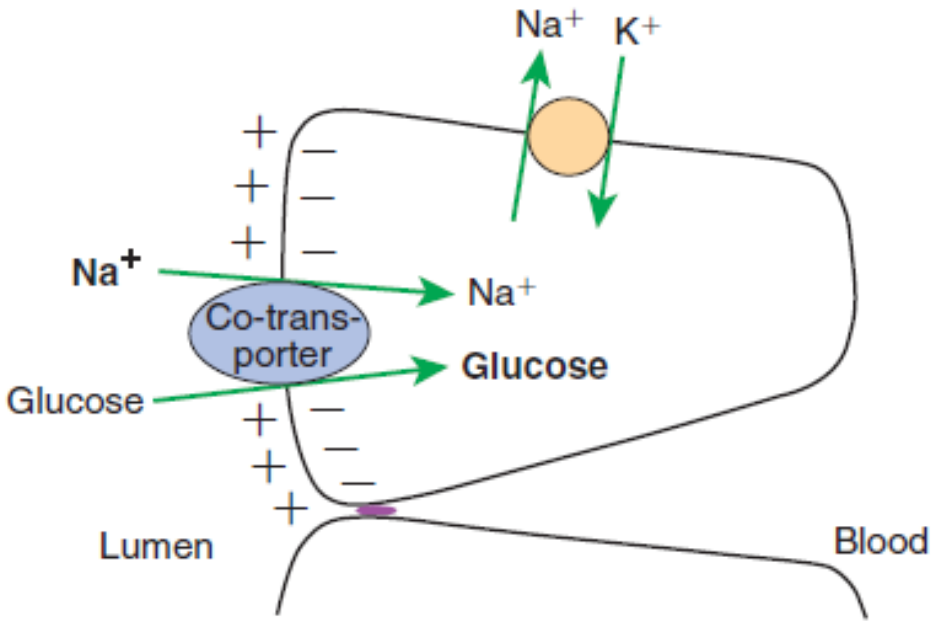
Enzyme	Action	Source	Precursor	Activator
Pepsin	Endopeptidase	Gastric glands	Pepsinogen	Hydrochloric acid, pepsin
Chymosin (rennin)	Endopeptidase	Gastric glands	Chymosinogen	?
Trypsin	Endopeptidase	Pancreas	Trypsinogen	Enterokinase, trypsin
Chymotrypsin	Endopeptidase	Pancreas	Chymotrypsinogen	Trypsin
Elastase	Endopeptidase	Pancreas	Proelastase	Trypsin
Carboxypeptidase A	Exopeptidase	Pancreas	Procarboxypeptidase A	Trypsin
Carboxypeptidase B	Exopeptidase	Pancreas	Procarboxypeptidase B	Trypsin

Membranous-phase digestion of peptides. Note that tripeptides and dipeptides may be hydrolyzed to their constituent amino acids either on the apical membrane or within the enterocyte the product absorbed into the blood is free amino acid

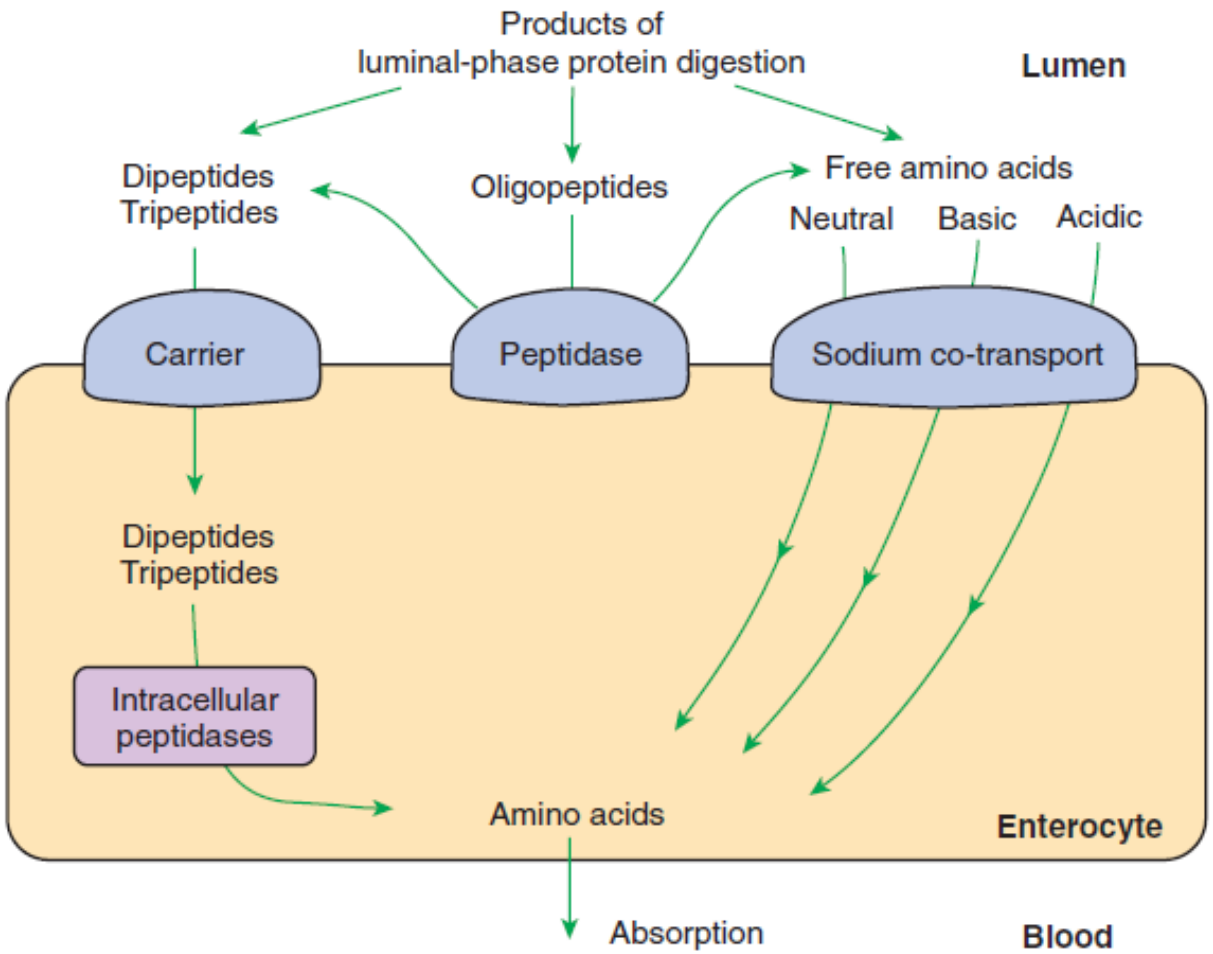


Intestinal Absorption - Glucose

During co-transport, glucose is transported against an unfavorable concentration gradient. This diagram illustrates that the large sodium concentration difference across the apical membrane provides energy to transport glucose against its concentration gradient. The sodium concentration gradient, created by the action of the Na_+,K_+-ATPase pump, provides energy to drive this reaction. Amino acids, several vitamins and bile acids also absorb by this way.



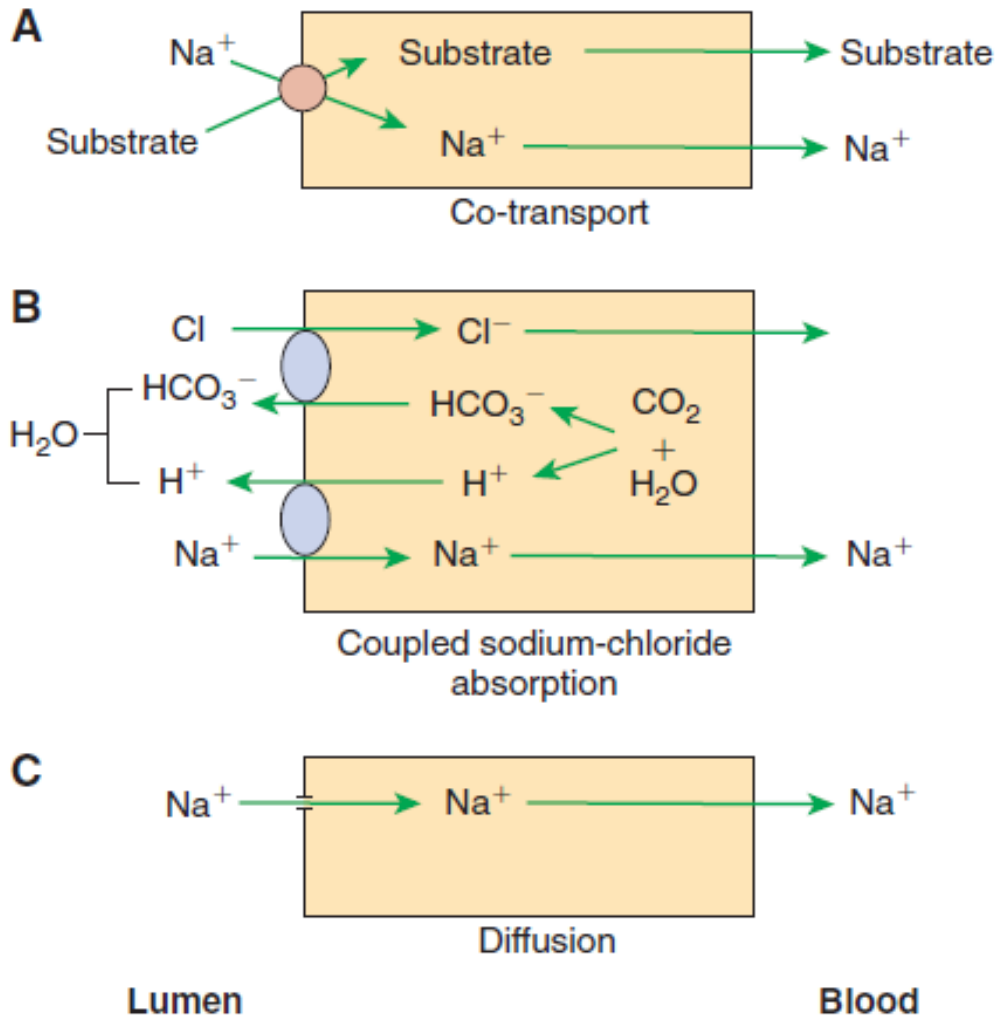
Intestinal Absorption - Proteins



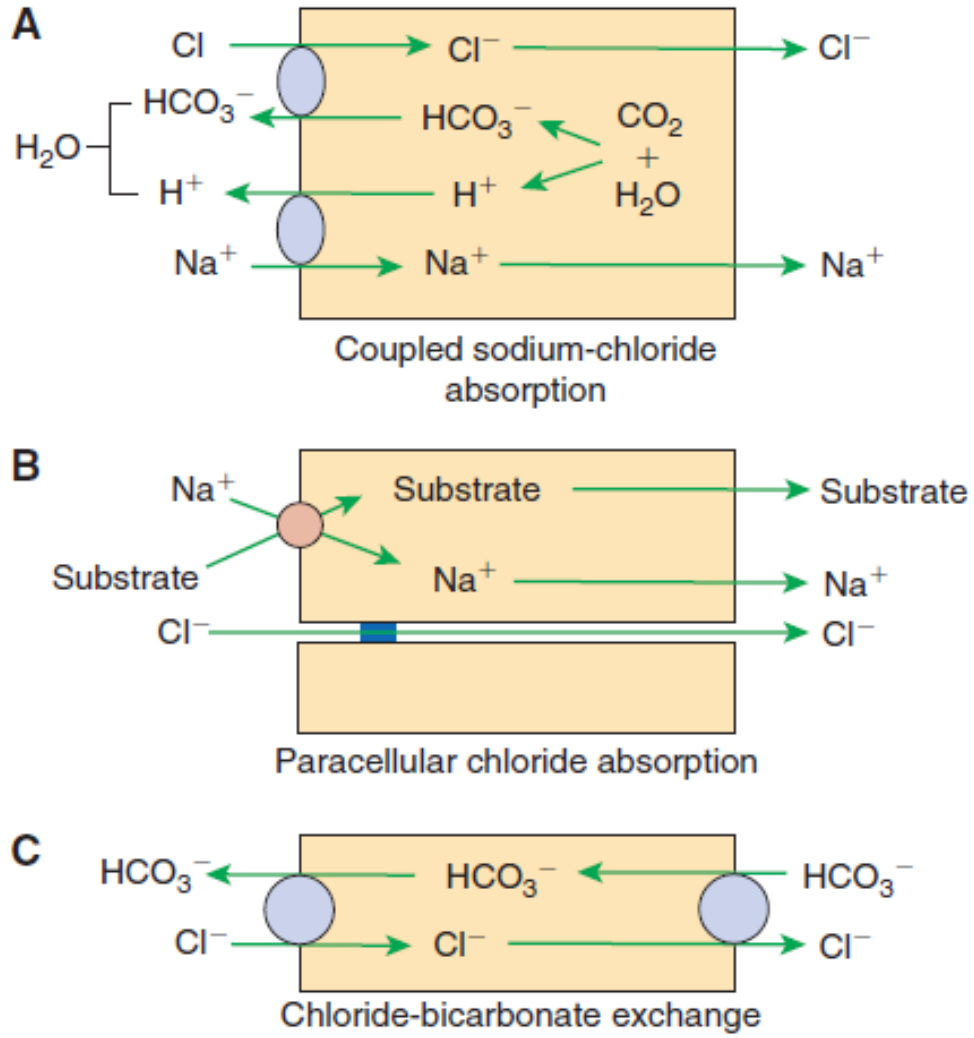
At least three different sodium co-transport proteins exist for the transport of amino acids: those for neutral, basic, and acidic amino acids. A sodium co-transport process might be involved in the absorption of dipeptides and tripeptides, but this possibility is not well established

Intestinal Absorption - Sodium

Three mechanisms of sodium *(Na_+)* absorption. **A**, Sodium co-transport with organic molecules is a major means of sodium uptake during active digestion and absorption. **B**, Chloride-coupled sodium absorption is also an important means of sodium absorption and requires the action of carbonic anhydrase and the existence on the apical membrane of bicarbonate-chloride *(HCO_{3-}/Cl_-)* and sodium-hydrogen *(Na_+/H_+)* exchange mechanisms. **C**, Simple diffusion of sodium across the apical membrane may occur because of the large, favorable concentration gradient, but it is a relatively minor means of sodium absorption. *CO_2,* Carbon dioxide; *H_2O,* water.



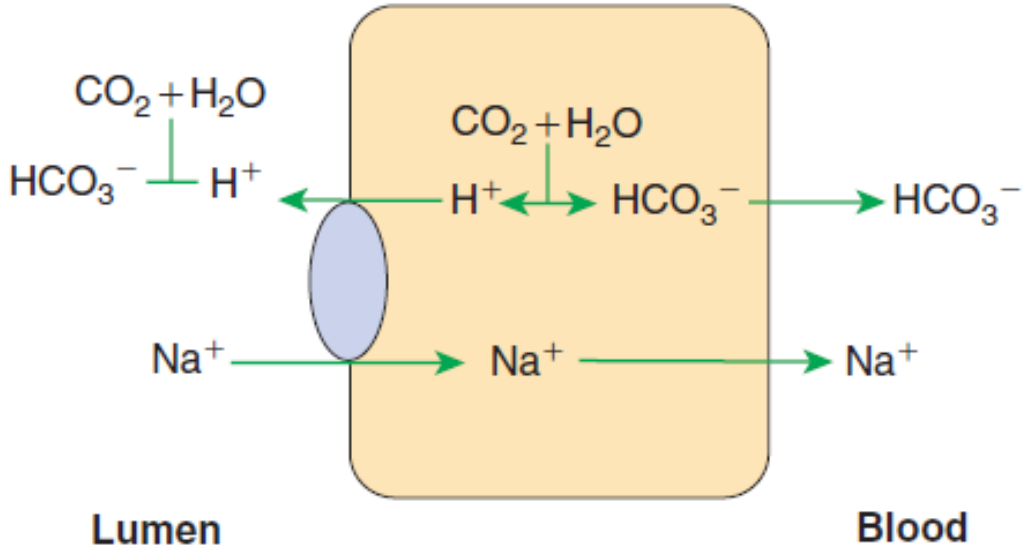
Intestinal Absorption - Chloride



Three mechanisms of chloride *(Cl^-)* absorption. **A**, Chloride-coupled sodium absorption is directly related to sodium *(Na^+)* uptake. **B**, Paracellular chloride absorption is indirectly related to sodium absorption that occurs during co-transport. **C**, Chloride-bicarbonate *(Cl^-/ HCO_3^-)* exchange occurs especially in areas where bicarbonate secretion into the intestinal lumen is important.

Intestinal Absorption - Bicarbonate

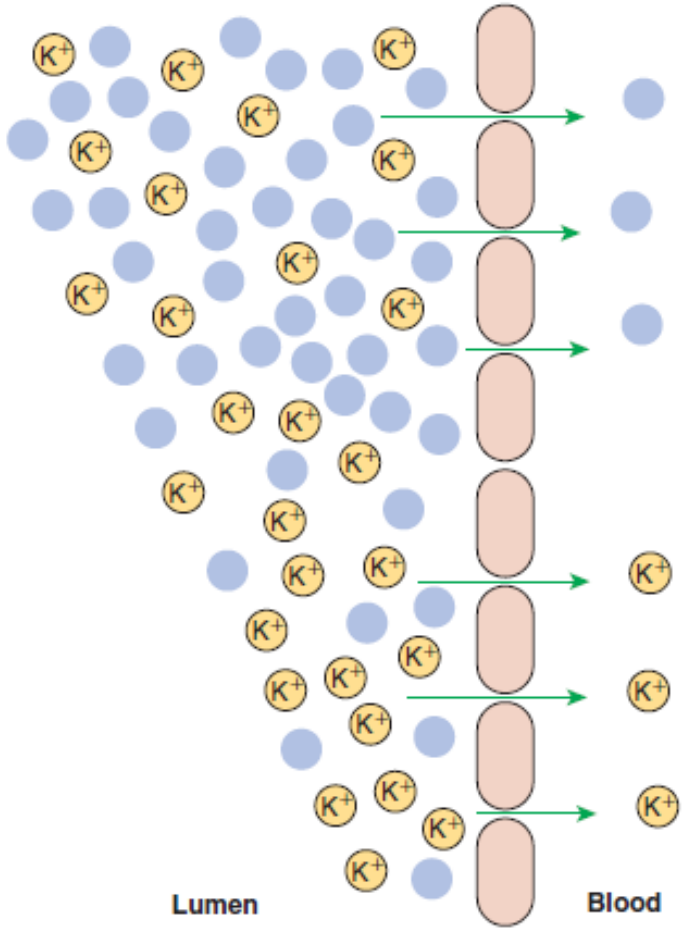
- Much of bicarbonate **neutralize** by **HCl**
- However, considerable bicarbonate remains in the intestine after the neutralization of stomach acid. This remaining bicarbonate is reabsorbed, primarily in the **ileum** and **colon** via an ion-exchange mechanism.
- The result is that sodium is transferred through the membrane. However, luminal bicarbonate is converted to water and carbon dioxide in the gut lumen, whereas bicarbonate anion is regenerated intracellularly. The net effect is the absorption of sodium bicarbonate.



Absorption of bicarbonate *(HCO3–)* is facilitated by sodium-hydrogen *(Na+/H+)* exchange at the apical membrane. The bicarbonate ion is regenerated by the action of carbonic anhydrase.

Intestinal Absorption - Potassium

Potassium *(K_+)* is absorbed by simple diffusion through the paracellular route. Water absorption in the upper intestine increases K_+ concentration in the lower intestine, creating a favorable diffusion gradient for potassium. Note that the removal of water *(solid blue circles)* in the upper part results in a relative increase in the number of K_+ ions in the lower part.



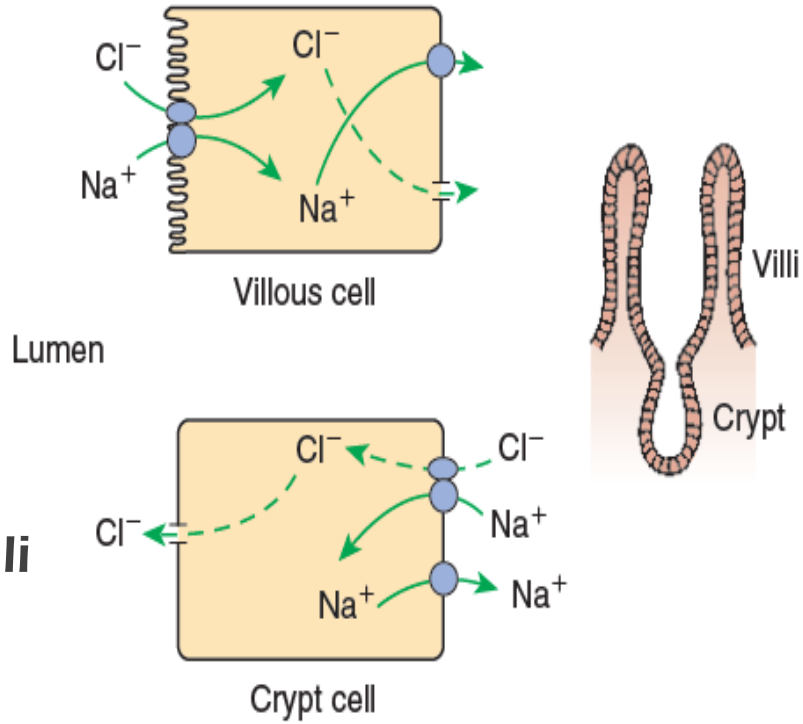
Intestinal Secretion of Water and Electrolytes

- All water secretion form intestinal surface is osmotic, but the osmotic gradient driving water secretion may occur in response to either **passive** or **active** processes.

- **Passive movement** of water in the intestines:
  - Digestion of foods creates many osmotically active molecules from one giant precursor molecule; thus the **osmotic activity** of ingesta is **increased initially** by digestion.
  - As solute molecules are **absorbed**, water follows them osmotically back through the epithelium and **into the blood** vascular system.
  - The rule of water movement in the intestine: *water moves in whatever direction necessary to keep ingesta iso-osmotic*.

Intestinal Secretion of Water and Electrolytes

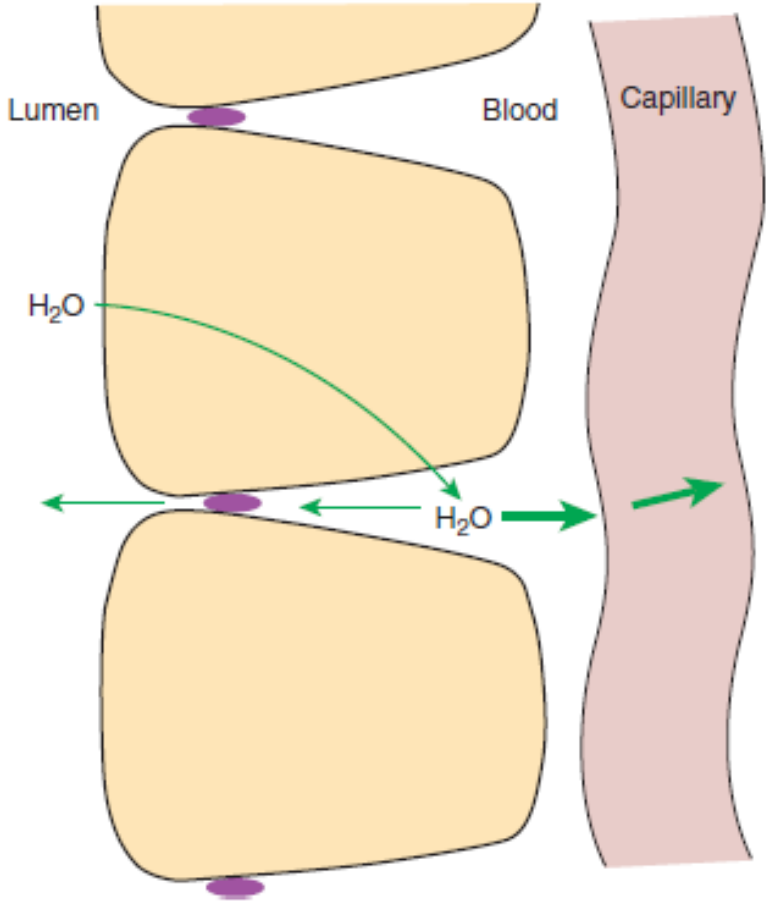
- **Active movement of electrolytes** and water in the intestines:
  - The **villous** cells have secretory function, the **crypt** cells have secretory function.
  - The mechanism is coupled **Na+/Cl- transport**:
    - In **crypt** cell it is on the **basolateral** membrane:
      - **pump Na+ and Cl– into the crypt** enterocytes
      - Na+ pumps back by Na+/K+ ATPase pump while Cl- diffuses to the crypt lumen under appropriate stimuli (cAMP↑, VIP) Cl- secretion draws Na+ and then water to the lumen.
    - In **villus** cell it is on the **apical** membrane:
      - reabsorbs Na+, Cl- and H20 to maintain an appropriate hydration and ionic environment for digestion and absorption.



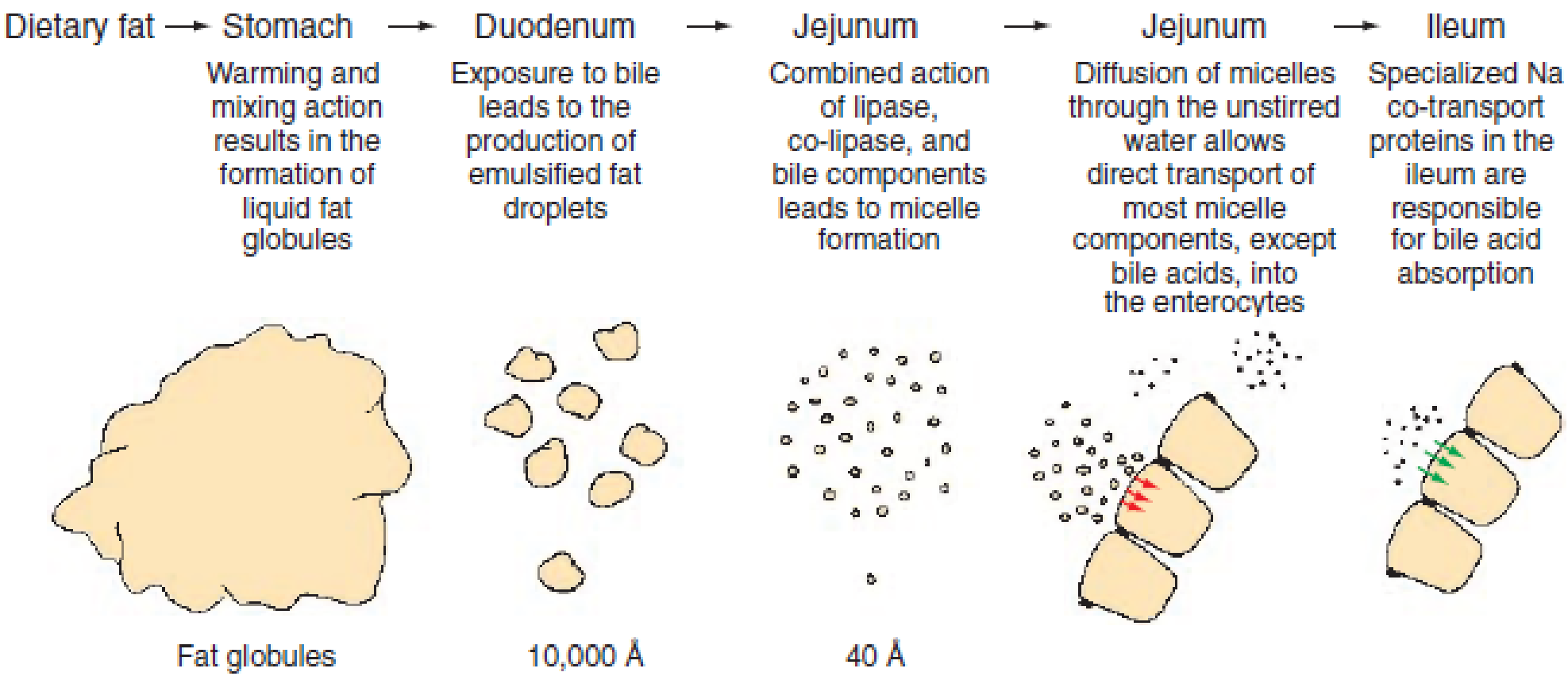
The cells of the intestinal crypts will eventually mature and migrate up the villi.

Intestinal Absorption - Water

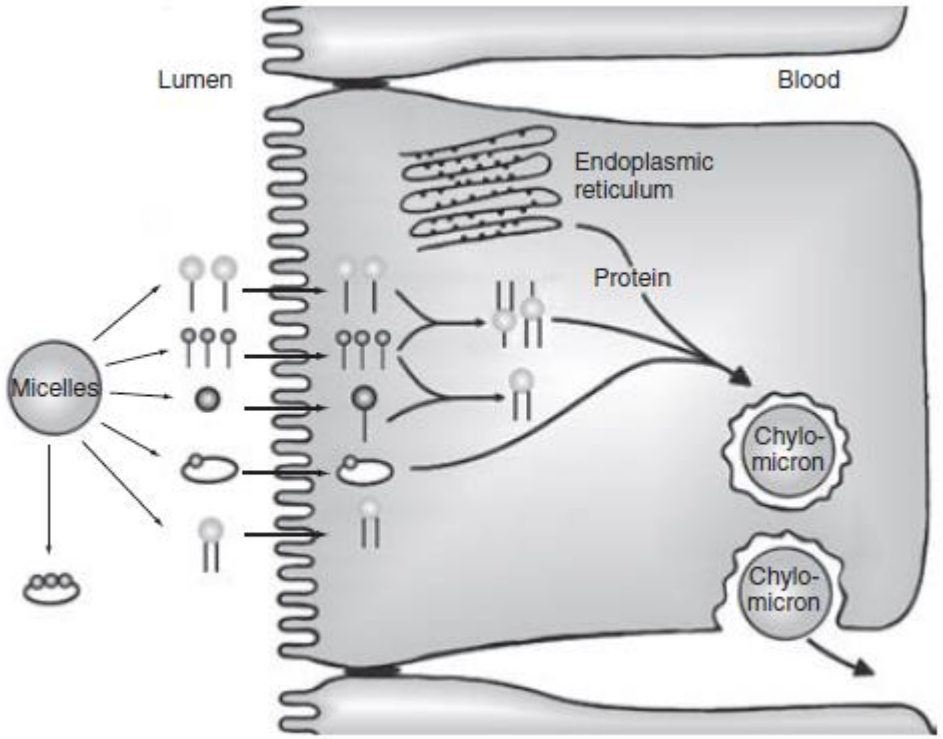
Water *(H_2O)* enters the lateral spaces because of osmotic effects created by absorbed solutes, thus creating a hydrostatic pressure head in the lateral spaces. Under pressure, the lateral-space solution can exit through the tight junctions or through the basement membrane of the capillaries. Under normal conditions the route of least resistance is into the capillaries, resulting in little movement of water from the lateral space into the intestinal lumen



Digestion and Absorption - Fats



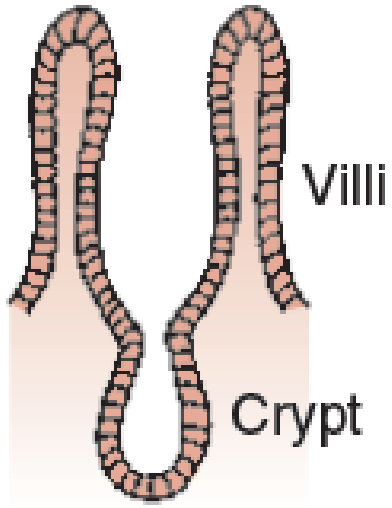
Digestion and Absorption - Fats



Lipid absorption from micelles with subsequent formation of chylomicrons. As micelles come close to the apical membrane, lipid constituents, except bile acids, are transported through the membrane into the cell. When in the enterocyte, triglycerides are re-formed from fatty acids and monoglycerides. Triglycerides are then packaged into the core of chylomicrons for transport out of the cell. The chylomicron surface is coated with phospholipids, cholesterol, and proteins.

Growth and Development of Intestinal epithelium

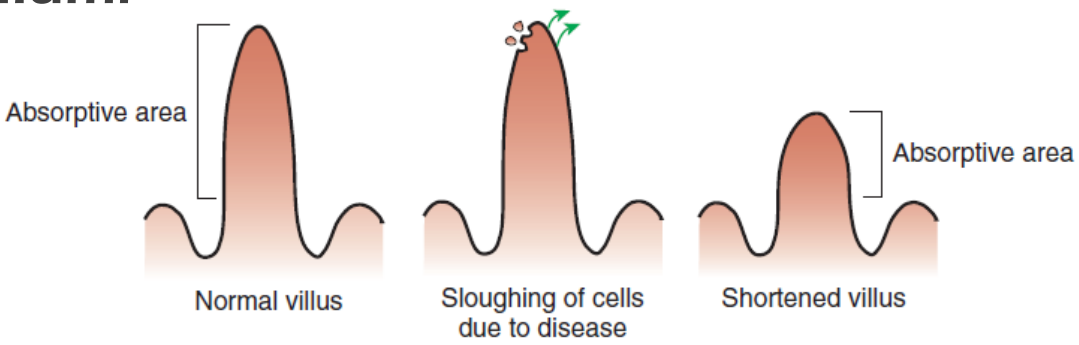
- **Crypt enterocytes** are highly mitotic and regenerate rapidly.
- As crypt cells multiply, they **migrate upward** onto the villi, pushing other villous cells ahead of them.
- As the cells migrate they mature, changing from relatively **undifferentiated cells** in the crypts **to highly specialized** absorptive cells on the **villi**.
- As the cells reach the tips of the villi, they are lost because of age and exposure to gut contents.
- on average, however, the turnover time of enterocytes is **4 to 7 days.**



Pathophysiology of Diarrhea

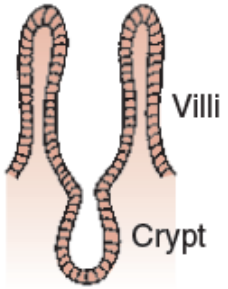
- **Diarrhea** refers to an increase in **frequency** of defecation or fecal **volume**. Volume often increases in diarrhea primarily because of increased **water** content.
- The amount of water in the feces is the result of the balance between **secretion** and **absorption**.
- **Malabsorptive diarrhea** occurs when absorption is inadequate
  - Usually occurs because of the loss of GI epithelium.
  - Viral (e.g. parvovirus), bacterial, or protozoal infections often cause severe destruction of villous epithelium.

Shortening of villi caused by increased cell loss. Many infectious diseases result in an increased rate of cell sloughing from the villi. when the rate of cell loss exceeds the capacity for cell replacement, shortened villi with reduced absorptive surfaces



Pathophysiology of Diarrhea

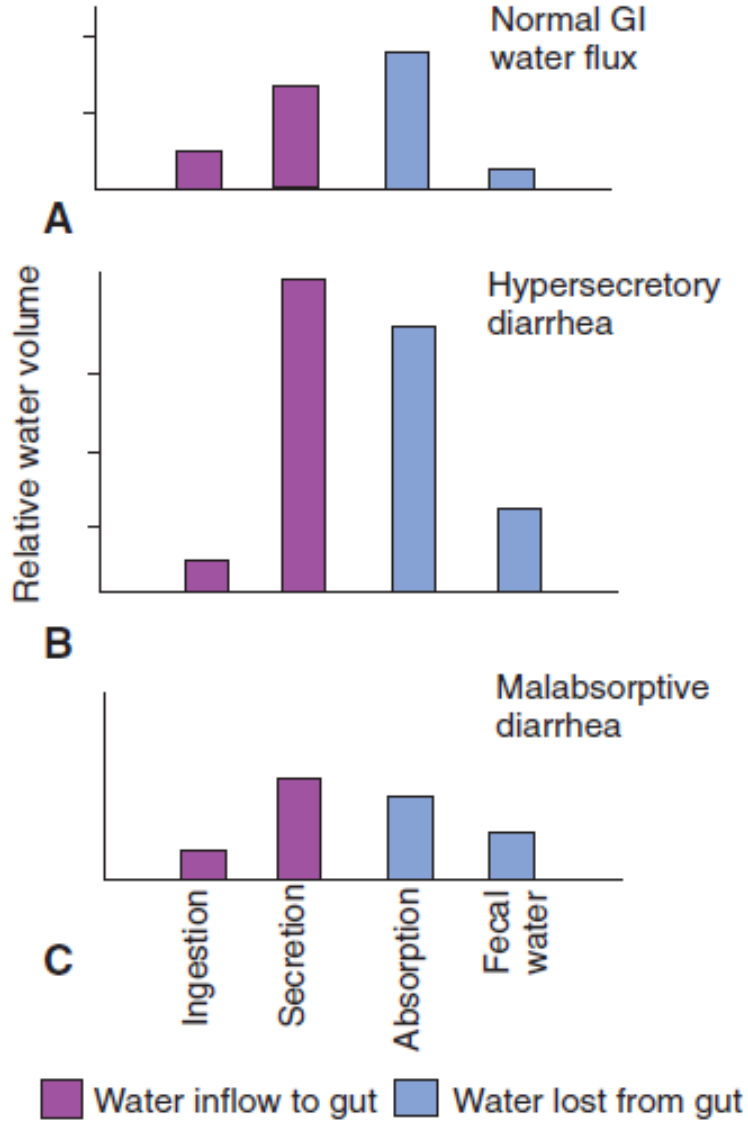
- **Secretory diarrhea** occurs when the rate of intestinal secretion increases and overwhelms the absorptive capacity.
- **Enterotoxins** which are produced by some types of pathogenic bacteria can abnormally stimulate the secretory mechanisms of crypt epithelium.
- These toxins bind to enterocytes → cAMP↑ → open Cl- gates → secretion of water and electrolytes from crypt epithelium.
- when the **secretion exceeds** the capacity of the gut to increase **absorption**, diarrhea results.
- Hypersecretory diarrhea has devastating effects on the water, electrolyte, and acid-base status of animals



Pathophysiology of Diarrhea

Pathophysiology of diarrhea. The bars represent the relative amounts of water entering or leaving the gut. Fecal volume is the sum of the water ingested and the water secreted minus the water absorbed.

Therefore, fecal volume depends not on the amount of water entering the gut, but rather on the balance between water influx and efflux.



Digestion/Absorption
The Fermentative Processes

Fermentation

- In **fermentative digestion**, molecular substrates are broken down by the action of bacteria and other microorganisms. **Enzymatic hydrolysis** of large molecules is an essential part of fermentative digestion, just as it is for glandular digestion.
- Fermentative vs. glandular digestion:
  - Enzymes are microbial in origin
  - Much slower
  - Substrates are altered to a much greater degree
- Fermentative compartments positioned before the stomach are called **forestomachs** (ruminants and camelids)
- Fermentation compartments positioned in the cecum and colon, often collectively called the **hindgut**.

Fermentation

- Forestomach and colon vs. stomach and small intestine:
  - In the stomach, bacterial numbers are kept low by the acid pH, whereas in the small intestine, bacterial numbers are kept in check by the constant flushing action of ingesta and secretions.
  - The pH in the forestomach and large colon is close to neutral, and the flow rate is comparatively slow.
- Microbial ecosystem of fermentative digestion:
  - The bacterial population is vast, Most of them are strict anaerobes although facultative organisms are also present.
  - In the rumen, fungi are present, play an important role in the digestion of plant cell walls.
  - Large population of protozoa in the rumen as well as in the cecum and colon. They are anaerobic and slow down the digestion of starch and some proteins.

Substrates and Products of Fermentative digestion

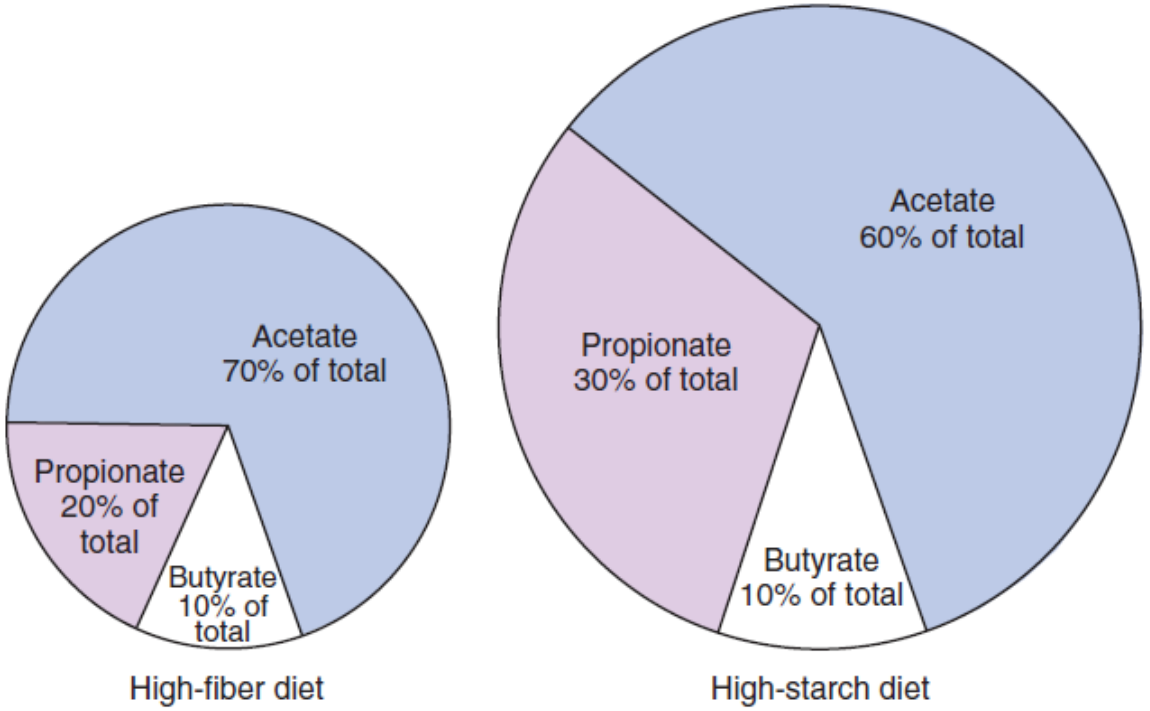
- **Plant Cell Walls** Are Important Substrates for Fermentative Digestion.
  - **Cellulose**, **hemicellulose**, and **pectin** are subject to the hydrolytic action of a complex of microbial enzymes known as **cellulase**.
  - **Lignin**, a heterogeneous group of phenolic chemicals, is resistant to the action of either mammalian or microbial enzymes.
    - The lignin concentration of plants increases with age and ambient temperature; thus young, cool-season plants are more digestible than mature plants grown in hot weather.
- Almost all dietary **protein** and **carbohydrate** are potentially subject to fermentative digestion.
  - Forestomach fermentative digestion of these, can potentially lead to the inefficient use of other nutrients because of **microbial alteration**.

Substrates and Products of Fermentative digestion

- Anaerobic Conditions in the Rumen Result in Metabolic Activities Leading to the Production of **Volatile Fatty Acids (VFAs)**.
  - The primary VFAs are **acetic acid**, **propionic acid**, and **butyric acid**; often referred to acetate, propionate, and butyrate, respectively.
  - Other quantitatively minor but metabolically important VFAs are **valeric acid**, **isovaleric acid**, **isobutyric acid**, and **2-methylbutyric acid**.
- The relative concentrations of the VFAs have important nutritional and metabolic consequences
  - The ruminal acetic/propionic/butyric acid concentration ratio: in rum
    - **70 : 20 : 10** for animals eating **high-forage** diets
    - **60 : 30 : 10** for animals eating **high-grain** diets
- These bacterial "waste products" are the major energy fuels.

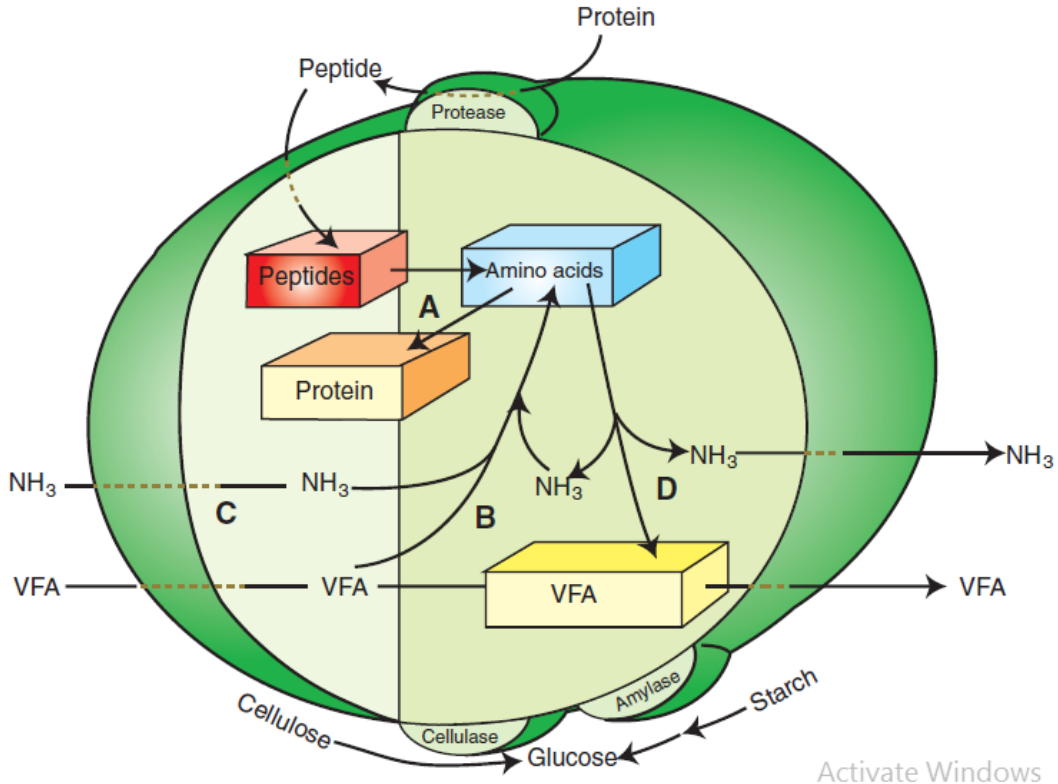
Substrates and Products of Fermentative digestion

VFA production on high-fiber and high-starch diets. Although the percentage of acetate is lower on the high-starch diet, the total amount of acetate produced is greater on the high-starch diet. In contrast, propionate increases in both amount and proportion on the high-starch diet.



Fermentative digestion of Protein

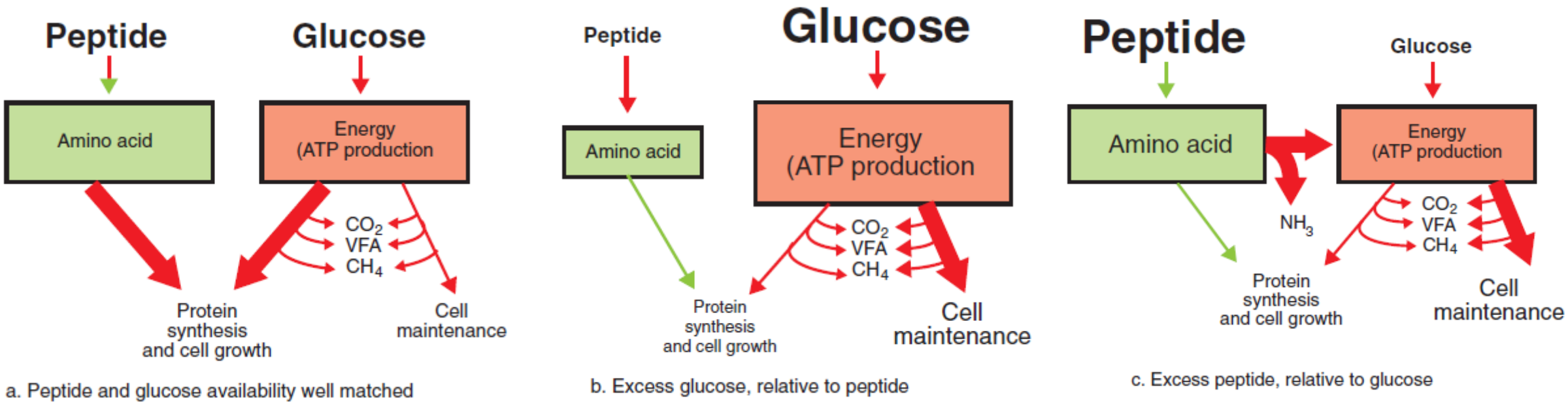
Protein metabolism by rumen microbes:
Protease enzymes on the microbe surfaces generate peptides that are then taken up by many types of organisms. Absorbed peptides contribute to an intracellular pool of amino acids from which microbial proteins are synthesized **(A).** Another source of amino acids is from intracellular synthesis **(B),** using ammonia *(NH_3)* and volatile fatty acid *(VFA).* Many microbes appear capable of deriving their amino acids from either extracellular peptides or intracellular synthesis; however, several types of bacteria seem incapable of using peptides for an amino acid source and are thus dependent on an extracellular source of ammonia **(C)** for amino acid synthesis. Amino acids not used for protein synthesis can be metabolized to VFA and ammonia **(D).**



Protein and Energy Availability in the Forestomach for Efficient Protein Utilization

- Ruminant animals depend, to a large extent, on **microbial protein** to meet their own protein needs.
- Digestive efficiency is optimized in ruminants when the **growth rate of the microbial mass** is maximal, resulting in maximal delivery of microbial protein to the host animal.
- The overall reaction in the rumen may be greatly simplified to this equation:
  - Glucose + Peptide = Microbes + VFA + NH_3 + CH_4 + CO_2
- When glucose and peptide availability are appropriately matched, energy for cellular growth comes primarily from glucose, with peptides directed toward microbial protein synthesis.

Protein and Energy Availability in the Forestomach for Efficient Protein Utilization



The efficiency with which dietary energy is used for protein synthesis in the rumen depends on the balance between energy and nitrogen sources. The proportion of energy used for protein synthesis and cell maintenance (as indicated by the size of the *arrows*) changes in relation to the balance of peptide (nitrogen) and glucose supplies. *ATP,* Adenosine triphosphate; *VFA,* volatile fatty acid.

Good Luck!