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## The gastrointestinal (GI) system

is a complex tube bounded by the mouth at one end and the anus at the other. Food enters the mouth travels through the esophagus, stomach, small intestine (duodenum, jejunum, and ileum), large intestine )ascending, transverse, and descending colon), and rectum; and then exits via the anus. Primary function of it:

- **Digestion:** is prepare nutrients for absorption, the body mechanically and chemically breaks down food into smaller, simpler particles. The chemical breakdown of food and the mechanical breakdown of food involves smooth (i.e., as in mixing) or skeletal (i.e., as in chewing) muscle contractions.
- **Secretion:** is the act of transporting molecules or fluid from the body to the gastrointestinal lumen . Secretion facilitates digestion by delivering enzymes and water and protects the endothelial surface by secreting $HCO_3^-$ and mucus.
- **Absorption** is the process of transporting dietary contents across the gastrointestinal barrier into the body.
- **Excretion:** of undigested materials and biliary waste products.

## INNERVATION AND NEUROTRANSMITTERS:

GI function is regulated by three divisions of the autonomic nervous system (ANS): the parasympathetic nervous system (PSNS), sympathetic nervous system (SNS), and the (ENS) Enteric nervous system.

| Neurotransmitter | Releasing Nerves | Structures | Function |
|---|---|---|---|
| Acetylcholine | Parasympathetic, cholinergic | Smooth muscle, glands | Contracts wall muscle; relaxes sphincters; increases salivary, gastric, and pancreatic secretion |
| Vasoactive intestinal peptide | Parasympathetic, cholinergic, enteric | Smooth muscle, glands | Relaxes sphincters; increases pancreatic and intestinal secretion |
| Norepinephrine | Sympathetic, adrenergic | Smooth muscle, glands | Relaxes wall muscle; contracts sphincters; decreases salivary secretions |
| Neuropeptide Y | Sympathetic, adrenergic, enteric | Smooth muscle, glands | Relaxes wall muscle; decreases intestinal secretions |
| Gastric-releasing peptide | Parasympathetic, cholinergic, enteric | Glands | Increases gastrin secretion |
| Substance P | Parasympathetic, cholinergic, enteric | Smooth muscle, glands | Contracts wall muscle; increases salivary secretions |
| Enkephalins | Enteric | Smooth muscle, glands | Constrict sphincters; decrease intestinal secretions |

Enteric nervous system:

PSNS and SNS nerves usually synapse with components of the ENS. Although the ENS is modulated by these extrinsic neural inputs, it can operate autonomously via intrinsic regulation and sensory reflexes . ENS nerves are organized into:

-1 The myenteric plexuses that primarily regulates intestinal smooth muscle and participates in tonic and rhythmic contractions.

-2 The submucosal plexus primarily regulates intestinal secretions and the local absorptive environment.

## Reflexes:

Many GI reflex actions are regulated solely by neural circuits in which a mechanoreceptor or chemoreceptor is stimulated in the mucosa and transmits the signal back to neurons in the submucosal plexus, which stimulates other neurons in the submucosal or myenteric plexus that regulate endocrine or secretory cells.

## NON NEURONAL SIGNALING MOLECULES:

In addition to neurotransmitters, hormones and paracrine signaling molecules also regulate and control GI function.

A. Hormones:

| Hormone | Releasing Cells | Structures | Function |
|---|---|---|---|
| Cholecystokinin | I cells | Pancreas, gallbladder, stomach | Increases enzyme secretion; contracts gallbladder; increases gastric empting |
| Glucose-dependent insulinotropic peptide | K cells | Pancreas, stomach | Releases insulin; inhibits acid secretion |
| Gastrin | G cells | Stomach | Increases gastric acid secretion |
| Motilin | M cells | Gastrointestinal smooth muscle | Increases contractions and migrating motor complexes |
| Secretin | S cells | Pancreas, stomach | Releases $HCO_3^-$ and pepsin |

B. Paracrines: GI paracrines are both released and act locally.

| Paracrine | Releasing Cells | Structures | Function |
|---|---|---|---|
| Histamine | Enterochromaffin-like cells, mast cells | Stomach | Increases gastric acid secretion |
| Prostaglandins | Cells lining gastrointestinal tract | Mucosa | Increase blood flow and mucus and $HCO_3^-$ secretion |
| Somatostatin | D cells | Stomach and pancreas | Inhibits peptide hormones and gastric acid secretion |

## DIGESTIVE PHASES: Stomach and duodenal function can be divided into three discrete phases:

A. Cephalic phase

The cephalic phase is triggered by the thought of food or conditions suggestive of previous food intake. Chemoreceptors and mechanoreceptors in the oral and nasal cavities and throat that are stimulated by tasting, chewing, swallowing, and smelling food also contribute. The cephalic phase is primarily neural and causes ACh and VIP release. ACh and VIP stimulate secretion by the salivary glands, stomach ، pancreas, and intestines.

**B. Gastric phase**

The gastric phase begins when food and oral secretions enter the stomach. It coincides with distention and stomach contents (amino acids and peptides) and elicits neural, hormonal, and paracrine GI responses. For example of this combination of signaling molecules is in gastric acid secretion, which includes ACh (neural), gastrin (hormonal), and histamine (paracrine.(

**C. Intestinal phase**

The intestinal phase begins when stomach contents enter the duodenum. It is linked to digested constituents of proteins and fats as well as $H^+$ and initiates primarily hormonal but also paracrine and neural responses. CCK, gastrin, secretin, and GIP are all secreted during this phase.

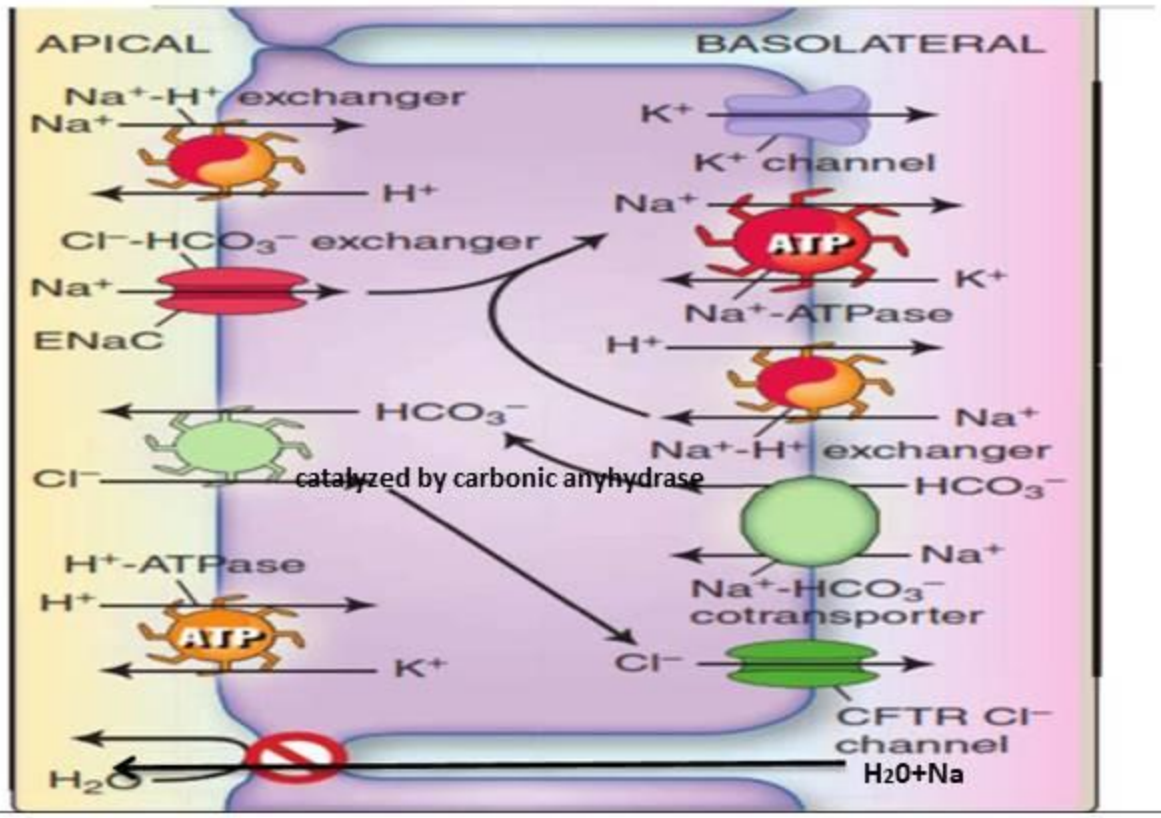
## MOUTH:

The mouth serves as the first site of mechanical and chemical digestion of food. Mastication (chewing( breaks food down into smaller pieces to increase the surface area available to digestive enzymes and to ease swallowing. Saliva provides the majority of the oral hydration and lubrication and performs some protective and digestive functions. The tongue changed shape, and extrinsic skeletal muscles that the tongue uses to change position, such as to protrude and to move from side to side for help in mastication of food. The tongue also contains taste buds and serous and mucous glands.

**Salivary glands:**

Salivary glands produce a watery fluid that lubricates the mouth, begins food digestion, and is protective. Individuals normally produce1.0–1.5 liters of saliva daily, the majority of which is secreted by the sublingual, submandibular, and parotid glands. Salivary secretions are controlled by both the sympathetic and parasympathetic nervous systems, although stimulation of either increases secretions ، the sympathetic component is transient and produces lower volume secretions than does the parasympathetic system. Salivary flow is increased by smell, taste, mechanical pressure in the mouth ، whereas it is decreased by stress, dehydration, and during sleep. Production saliva involve a two-step process: First, $Cl^-$, $Na^+$, and water are transported into the duct lumen. Second, ductal cells modify this

fluid by reabsorbing $Na^+$ and $Cl^-$ and secreting $K^+$ and $HCO3^-$. Saliva also contains low concentrations of protective proteins and enzymes that are secreted by acinar, mucous, and ductal cells.




H2O follows transcellularly and paracellularly, driven by the osmotic gradients created by ion secretion and facilitated by aquaporins and leaky tight junctions between acinar cells.

ion transport. ATP = adenosine

Addition function of saliva

a. Lysozyme: Secreted lysozyme has the potential to disrupt bacterial cell walls.

b. Lactoferrin: Lactoferrin is an iron-binding protein that can inhibit microbial growth.

c. Immunoglobulin A: Constituents for immunoglobulin A are secreted in the saliva and are active against both bacteria and viruses.

d. Proline-rich proteins: Proline-rich proteins aid in tooth enamel formation and also possess antimicrobial properties.

e. Salivary amylase: Salivary amylase (also known as -amylase, or ptyalin) begins the process of carbohydrate digestion but is denatured by low pH in the stomach. Amylase is then reintroduced into the GI tract from the pancreas.

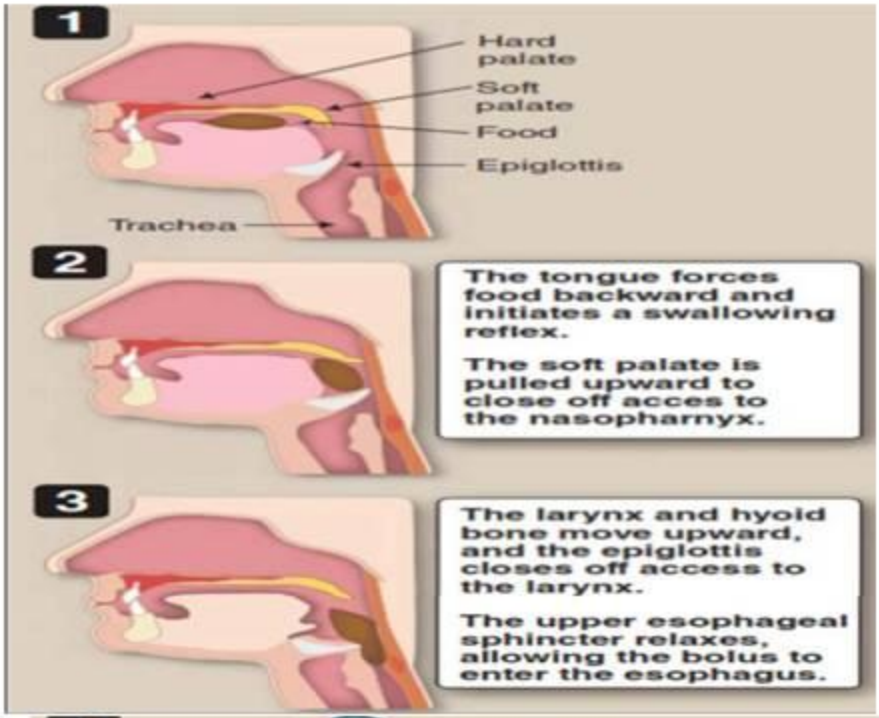
f. Lingual lipase: Lingual lipase hydrolyses lipids and remains active throughout the GI tract.

## ESOPHAGUS:

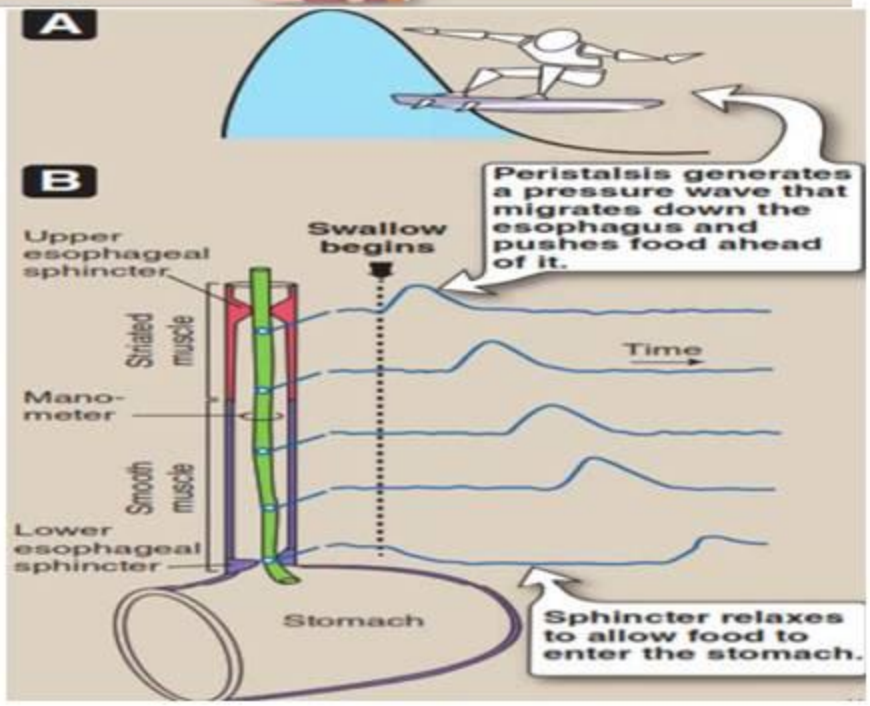
The oropharynx and esophagus convey dietary contents and oral secretions from the back of the oral cavity to the stomach.

### Swallowing:

The act of swallowing is a coordinated act involving many structures. Swallowing is largely initiated voluntarily but becomes involuntary once initiated . Swallowing control is a parasympathetic process involving afferent feedback to the swallowing center followed by:




The peristaltic wave reaches the sphincter, it relaxes and allows food to enter the stomach. Changes in sphincter tone are mediated by ACh, Nitric oxide )NO), and vasoactive intestinal peptide )VIP). Food traverses the esophagus in about 6–10 seconds. If food is not cleared by the first pressure wave )primary peristalsis), repetitive waves )secondary peristalsis) may be initiated.




## STOMACH:

The stomach serves a number of important physiologic functions: accepting and storing food, mixing food with secretions, digesting food, and delivering food to the small intestine in timed increments. The fundus, body, and antrum comprise the three anatomic areas of the stomach.

The primary function of the upper half of the stomach is to accommodate food from the esophagus. During swallowing, the LES relaxes, allowing food to move from an area of higher pressure in the esophagus to an area of lower pressure in the stomach. The stomach must be prepared for this bolus . This is accomplished by relaxing the upper portion of the stomach, which normally is contracted. This relaxation is termed receptive relaxation and is mediated by NO (nitric oxide) and VIP (vasoactive intestinal peptide). This relaxation is coordinated by the vagus nerve in response to vagus afferent stimulation and, thus, is referred to as a vagovagal reflex. The average stomach can accommodate1.5 of food.

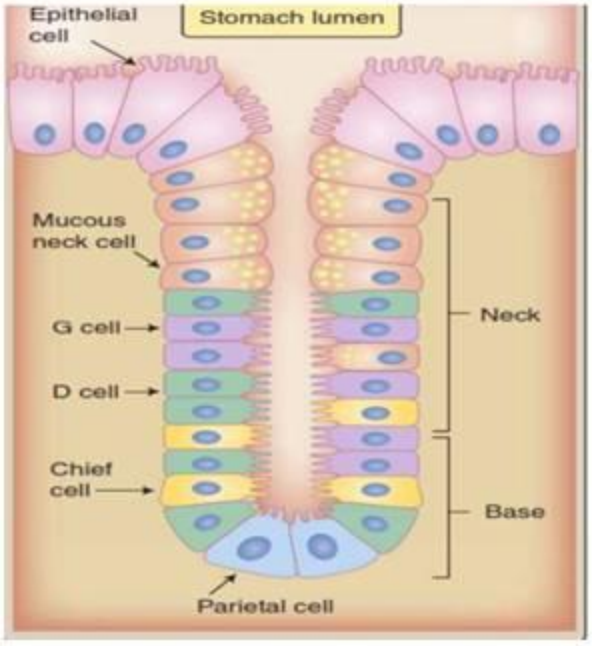
A. **The mechanical mixing** and grinding of food occurs in the lower half of the stomach.
Mechanical stomach contraction occurs as:

Slow waves are generated by interstitial cells at a rate of 3–5 cycles/min and propagate toward the pylorus. These electrical signals inhibited by norepinephrine. A threshold related to voltage amplitude and duration is reached in normal conditions and a greater frequency when stimulated by ACh . Interestingly, this contraction induced pressure wave eventually overtakes the food bolus and, thus , begins to push food in both directions.This results in a small amount of food entering the duodenum and the majority of the food being pushed back toward the middle of the stomach. This brief backward movement, termed retropulsion, allows for better food mixing and mechanical breakup.

**B. Secretions:**

are derived from gastric invaginations called pits. Pits are lined with many different secretory cell types.

a( Mucous neck cells: secrete mucus, which is vital to the gastric lining's barrier function in protecting the stomach from gastric acid and pepsin.
b( Chief cells: produce gastric lipase and pepsinogen, which is the inactive form of pepsin.
c( parietal cells (also known as oxyntic cells) secrete $H^+$ and intrinsic factor.
d( G and D cells are endocrine cells that secrete gastrin and somatostatin, respectively.

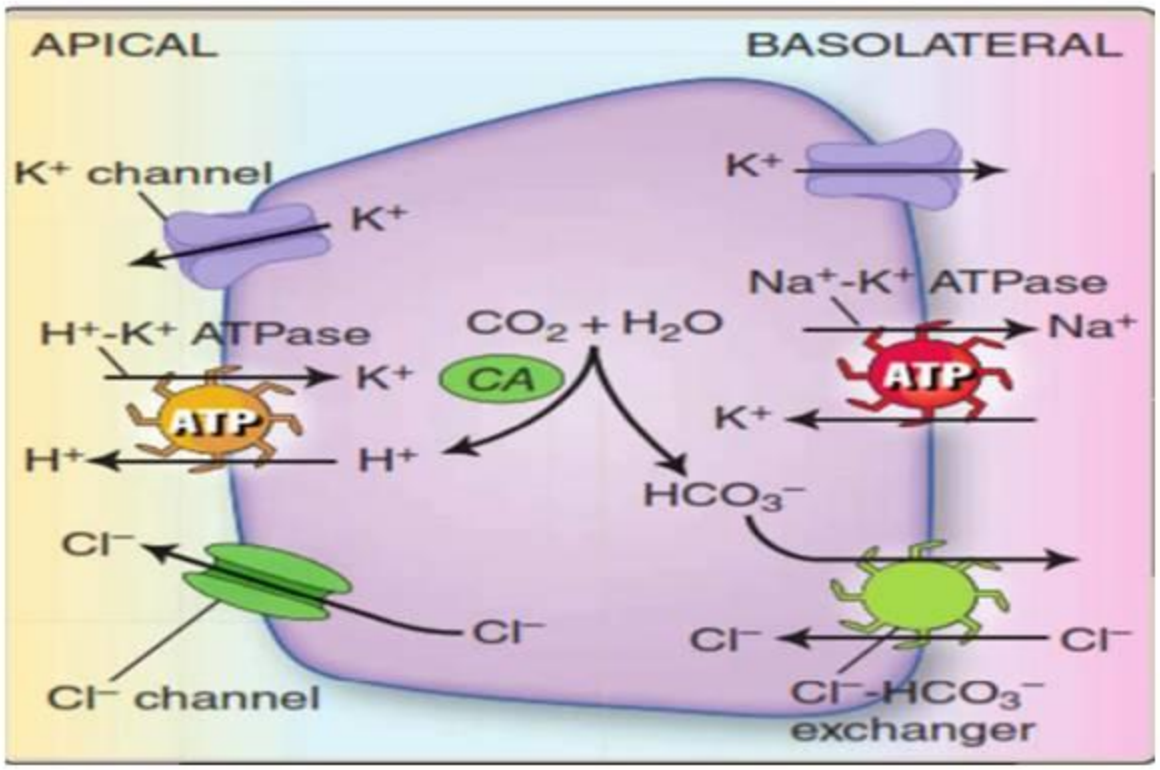



Regional differences exist in the number of cell types lining a gastric pit. Pits near the lower esophageal and pyloric sphincters contain more cells that produce more of the

protective secretions, such as mucus and $HCO3^-$ whereas pits in the rest of the stomach contain more of the secretory cells that produce more of the digestive secretions, such as $H^+$ and pepsinogen.

## Hydrogen ion secretion mechanism:

Acidification of the gastric lumen is accomplished by the transport of $H^+$ through:




Control of hydrogen ion secretions control involves both direct and indirect neural pathways.

-1 The direct parietal pathway involves:

a( The vagus nerve releasing ACh to stimulate M3 receptors .

b( Gastrin binding to cholecystokinin type-B (CCKB) receptors .

-2 Indirect stimulation involves:

a( Histamine increases cAMP. Histamine release from ECL(Enterochromaffin-like) cells, binding to H 2 receptors on the parietal cell. The ECL cells are stimulated by both ACh and gastrin.

b( Both somatostatin and prostaglandins decrease H production via binding to their own cell surface receptors on the parietal cell.Somatostatin and prostaglandins decrease cAMP.

## The control of gastric secretions is dependent on the phase of digestion:

### a. Cephalic phase:

%40of gastric secretions via the vagus nerve's actions caused: derived ACh that stimulates H+ production by parietal cells directly.

The vagus nerve also releases ACh to initiate H+ production by the stimulation of ECL cells to produce histamine, G cells to produce gastrin and mucus secretion to protect the stomach lining from H.+

**b. Gastric phase:** This primarily occurs via:

(1Directly through vagus afferents

(2Via local enteric refl exes. Distention appears to be the primary stimulant acting via vagal afferents and local refl exes. Besides distention, proteins, peptides, and, especially, amino acids additionally stimulate G cells to release gastrin.

c. **Intestinal phase**: The digestion of chyme (post-stomach food and secretion mix), in particular the digestion of proteins, continues to directly stimulate intestinal G cells as well as to stimulate gastric G cells via proteins and amino acids in the portal circulation. The negative feedback in the intestinal phase is provided by intestinal distension, which releases glucose-dependent insulinotropic peptide, which, in turn, inhibits parietal cells.

## Digestion

The low pH of the gastric contents helps denature and break down proteins. Breakdown is assisted by the proteolytic enzyme pepsin, which is secreted in inactive form (pepsinogen) by chief cells and converted to
pepsin by the low pH.Pepsin will be deactivated in the duodenum once pH increases toward the neutral range.
Gastric lipase also has a low optimal pH (3–6), and acts primarily on ester bonds to form fatty acid and diglyceride products.