DIGESTIVE

PHYSIOLOGY

Plan

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Introduction

The animal organism requires a constant supply of proteins, carbohydrates, lipids, vitamins, and salts for its growth and the maintenance of its metabolism. These substances exist in food only in very small proportions in a directly absorbable form; they must therefore be transformed in order to be utilized.

Digestion is the set of processes of ingestion, transformation within the gastrointestinal tract, and elimination of non-absorbed solid and liquid residues.

Digestion involves a large number of mechanical and chemical processes closely linked and perfectly synchronized thanks to nervous regulation complemented by hormonal regulation.

Functional organization of the digestive wall

Whatever the segment considered, identical histological layers are found at all levels of the digestive tract, which is explained by the existence of certain functions common to the entire digestive tract. However, the composition of these layers varies from one region to another. The wall of the digestive tract is composed of four concentric layers:

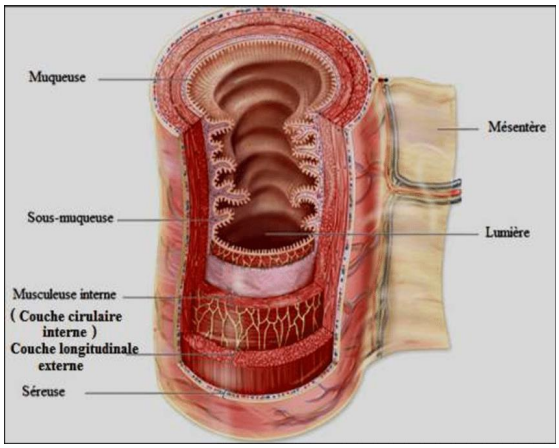
The mucosa consists of a surface epithelium resting on a connective tissue layer called the lamina propria containing glands, and the muscularis mucosa composed of smooth muscle fibers allowing folding of the mucosa.

The submucosa is composed of loose connective tissue rich in elastic fibers containing a network of small blood vessels called the Heller plexus; it also includes numerous lymphatic vessels and a nerve plexus (Meissner's submucosal plexus) involved in the regulation of gastrointestinal secretions and local blood flow.

The muscular layer consists of two thick layers of smooth muscle cells: an inner circular layer and an outer longitudinal layer. In most parts of the stomach, an additional inner oblique layer is

present. A nerve plexus called Auerbach's plexus is located between the muscle layers and controls contractions.

The serosa is the outermost layer, composed of loose connective tissue often containing adipose tissue.



Functions of the digestive tract

Motility

Ensures the propulsion of food along the digestive tract through contractions of the two layers of smooth muscle forming the digestive wall.

Secretion

Salivary, gastric, pancreatic, biliary, and intestinal secretions consist mainly of water, electrolytes, and organic substances such as enzymes (essential for digestion), mucus, immunoglobulins (IgA), and growth factors necessary for renewal of the digestive wall.

Digestion

Its main site is the small intestine.

Absorption

Its main site is the small intestine. It results from continuous and abundant flows of water and dissolved substances from the digestive lumen to the extracellular environment and vice versa, thus contributing to the regulation of the internal environment.

Immunity

The digestive mucosa constitutes a large exchange surface in contact with an environment rich in antigens of dietary, microbial, or viral origin.

Regulation of digestion

Neural regulation

The neural regulation of the gastrointestinal tract is ensured by two systems:

➤ **Intrinsic nervous system** (enteric nervous system, "little brain" or gut brain):
It relays information from the sympathetic and parasympathetic nervous systems to and from the gastrointestinal (GI) tract and controls most of its functions, particularly motility and secretion. It consists of:

- **Myenteric plexus (Auerbach):**
  Controls the motility of the GI tract by acting on smooth muscle cells. It ensures coordination of contractions of the circular and longitudinal muscle layers in an oral-to-aboral direction.

- **Submucosal plexus (Meissner):**
  Receives sensory information from chemoreceptors and mechanoreceptors of the GI tract and mainly controls secretion and blood flow.

➤ **Extrinsic nervous system** (ANS: sympathetic and parasympathetic):

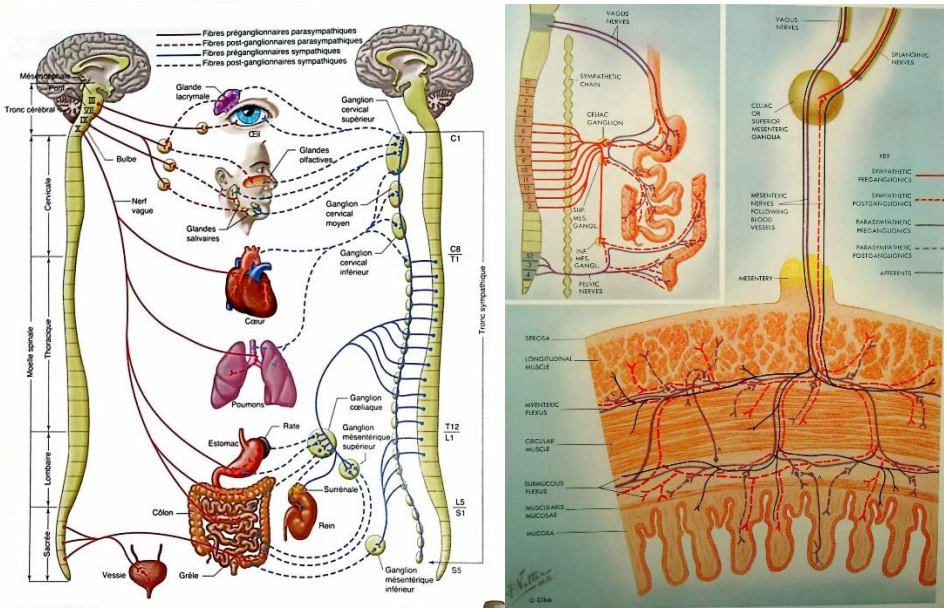
Afferent fibers transmit sensory information from chemoreceptors and mechanoreceptors of the GI tract to the brainstem and spinal cord.

Efferent fibers transmit information from the brainstem and spinal cord to the GI tract.

- **Sympathetic nervous system:**
  Inhibits gastrointestinal tract functions. Preganglionic cholinergic fibers synapse in the paravertebral ganglia, and postganglionic adrenergic fibers originate from these ganglia and synapse in the submucosal and myenteric plexuses. There is also postganglionic adrenergic innervation of blood vessels and some smooth muscles.
- **Parasympathetic nervous system:**
  Stimulates gastrointestinal tract functions and follows the pathways of the vagus nerve and pelvic nerves. Preganglionic parasympathetic fibers synapse in the submucosal and myenteric plexuses. Postganglionic fibers from these plexuses transmit information to smooth muscle cells, secretory cells, and endocrine cells of the gastrointestinal tract.

The vagus nerve carries information to the esophagus, stomach, pancreas, small intestine, and upper large intestine.

The pelvic nerves carry information to the lower large intestine, rectum, and anus.



Hormonal regulation

Throughout the gastrointestinal (GI) tract, endocrine cells secrete hormones responsible for the regulation of digestion. The secretion of these hormones is stimulated by distension of the GI tract wall, the osmolarity and acidity of the chyme, and certain digestion products (amino acids, fatty acids). The best-known digestive hormones are gastrin, secretin, cholecystokinin (CCK), and glucose-dependent insulinotropic peptide (GIP). There are other molecules involved in the regulation of GI tract functions such as:

Hormone	Site of Secretion	Stimulus for Secretion	Actions
Gastrin	G cells of the stomach	Small peptides Amino acids Gastric distension Vagus nerve (GRP)	Increases HCl secretion Stimulates growth of gastric mucosa Enhances gastric contractions
Cholecystokinin (CCK)	I cells of the duodenum and jejunum	Small peptides Amino acids Fatty acids Monoglycerides	Stimulates gallbladder contraction Increases pancreatic secretion of HCO_3^- and enzymes Promotes growth of pancreas and gallbladder Inhibits gastric emptying
Secretin	S cells of the duodenum	H^+ ions and fatty acids in the duodenum	Increases HCO_3^- secretion Inhibits HCl secretion Inhibits gastrin action
GIP (Glucose-dependent insulinotropic	Duodenum and jejunum	Fatty acids Amino acids Glucose (oral	Increases insulin secretion Inhibits H^+ secretion

peptide) intake)

- **Paracrines** are produced by endocrine cells of the GI mucosa and diffuse over short distances to act on target cells located within the GI tract. These include:
- **Somatostatin**

  It is secreted by cells distributed throughout the GI tract in response to the presence of H^+ in the lumen. Its secretion is inhibited by the vagus nerve.

  It inhibits the release of all GI hormones, as well as gastric H^+ secretion.
- **Histamine**

  It is secreted by mast cells of the gastric mucosa. It increases gastric H^+ secretion directly and by potentiating the effects of gastrin and vagal stimulation.
- **Neurocrines:** are synthesized in the cell bodies of neurons, travel along the axon, and are released at the nerve terminal in response to a nerve action potential. Neurocrines then diffuse across the synaptic cleft to reach the target cell, where they interact with a specific receptor.
- **Vasoactive intestinal peptide (VIP)**

  It is produced by nerves in the mucosa and smooth muscle of the GI tract. It causes relaxation of GI smooth muscle, stimulates pancreatic HCO_3 secretion, and inhibits gastric H^+ secretion. It is therefore homologous to secretin.

  In its actions, it resembles secretin.
- **Gastrin-releasing peptide (GRP) or bombesin**

  It is released by nerves in the gastric mucosa in response to vagal stimulation. It stimulates the release of gastrin.
- **Enkephalins (met-enkephalin and leu-enkephalin)**

  They are secreted by nerves in the mucosa and smooth muscle of the GI tract. They cause contraction of GI smooth muscle, particularly the lower esophagus and the pyloric and ileocecal sphincters. They inhibit intestinal secretion of water and electrolytes.

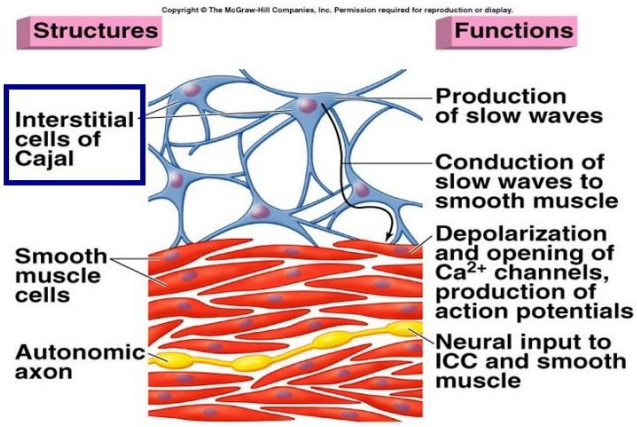
Digestive motility and mechanical digestion

With the exception of the pharynx, the upper third of the esophagus, and the external anal sphincter, which are all composed of striated muscle, the contractile tissue of the gastrointestinal (GI) tract is almost exclusively made up of smooth muscle. Depolarization of the circular musculature results in contraction of the smooth muscle ring and a reduction in the diameter of that segment of the GI tract. Depolarization of the longitudinal musculature results in contraction in the longitudinal direction and shortening of that segment of the GI tract; this is referred to as the law of the intestine or peristalsis.

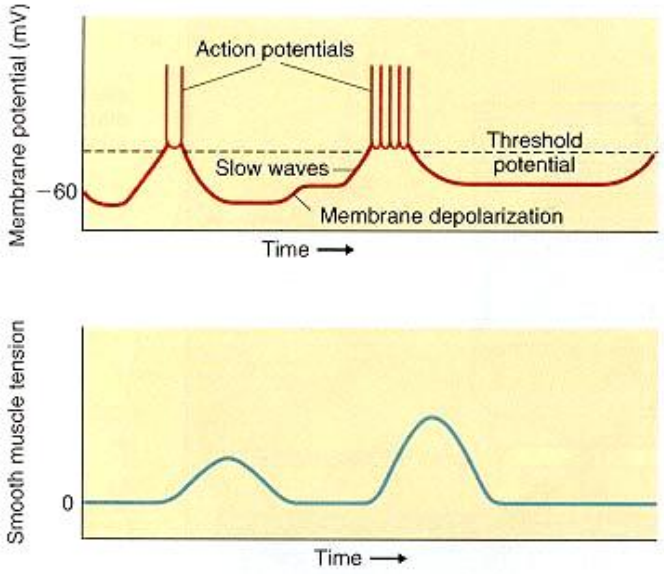
Intestinal peristalsis is a ring of contraction that moves at varying speeds and distances in an oral-to-aboral direction. Downstream of the contraction zone, there is a relaxed region that facilitates the forward movement of the chyme. This spatiotemporal coordination is referred to as the law of the intestine.

Slow waves and automaticity of digestive motility

The smooth muscle of the digestive tract exhibits intrinsic automaticity. This property is due to the presence of specialized cells called interstitial cells of Cajal (ICC). These cells act as pacemakers of the digestive tract and are located between the circular and longitudinal muscle layers, near the myenteric plexus. They develop numerous interconnected branches to form a network. They are connected to smooth muscle cells through tight junctions, giving the system properties similar to a syncytium or cable. They ensure depolarization of smooth muscle cells by opening voltage-dependent calcium channels. This activity gives rise to slow waves, which are regular oscillations of the resting membrane potential of smooth muscle fibers. These waves determine a basic electrical rhythm (BER), the frequency of which is specific to different segments of the digestive tract.



ICC ensure communication between smooth muscle cells and excitatory and inhibitory motor neurons of the autonomic nervous system. The depolarization produced by each slow wave brings the membrane potential of smooth muscle cells closer to the threshold and thus increases the probability of generating action potentials. The action potentials produced (at the peak of the slow wave) trigger excitation–contraction coupling and ultimately the contraction of smooth muscle cells.



The frequency of slow waves varies along the GI tract. It is constant and characteristic of each segment and is not influenced by neural or hormonal actions. In contrast, the frequency of action potentials is modified by neural and hormonal influences.

The frequency of slow waves determines the maximum contraction frequency of a given segment of the GI tract. The frequency of slow waves decreases in the oral-to-aboral direction: it is 3–6 slow waves/min in the stomach, 12–17 slow waves/min in the small intestine, and 9–16 slow waves/min in the large intestine in humans.

Mastication, swallowing, and esophageal peristalsis

Mastication: lubricates food by mixing it with saliva. It reduces the size of food particles, facilitating swallowing and initiating the digestion process.

Swallowing:

The swallowing reflex is coordinated by the brainstem. Information to and from the brainstem travels via the vagus and glossopharyngeal nerves. The mechanism of swallowing is as follows:

- The nasopharynx closes and ventilation is inhibited.
- The laryngeal muscles contract to close the glottis and elevate the larynx.
- Peristalsis begins in the pharynx to propel the food bolus toward the esophagus.
- Simultaneously, the upper esophageal sphincter relaxes to allow entry of the food bolus into the esophagus.

Esophageal motility

The esophagus propels swallowed food into the stomach. The sphincters at both ends of the esophagus prevent the entry of air (upper esophagus) and gastric acids (lower esophagus). The mechanism of esophageal motility is as follows:

- First, the upper esophageal sphincter relaxes to allow the swallowed bolus to enter the esophagus.
- Then, the upper esophageal sphincter contracts, preventing reflux.
- A primary peristaltic contraction creates a zone of high pressure just behind the bolus.
- The peristaltic wave travels down the esophagus, propelling the bolus along its length. Gravity accelerates the movement.

- A secondary peristaltic contraction clears any remaining food particles from the esophagus.
- The lower esophageal sphincter relaxes as the bolus approaches. This relaxation is mediated by the vagus nerve, with VIP as the neurotransmitter. At the same time, the proximal region of the stomach relaxes (receptive relaxation), allowing the bolus to enter the stomach.

Note:

Achalasia, resulting from failure of relaxation of the lower esophageal sphincter, is common in dogs.

In ruminants, during regurgitation, inspiration against a closed glottis creates negative pressure, and the bolus moves upward at a speed of 1 m/s via an antiperi staltic wave.

Gastric motility

The stomach has three layers of smooth muscle: a longitudinal layer, a circular layer, and a third oblique layer. The proximal (oral) region of the stomach is responsible for receiving the ingested meal. The distal (caudal) region is responsible for contractions that mix the food and propel it toward the duodenum.

Receptive relaxation

The proximal region of the stomach relaxes to accommodate the ingested meal. This vagovagal reflex is triggered by gastric distension and is abolished by vagotomy. CCK contributes to receptive relaxation by increasing the distensibility of the proximal stomach.

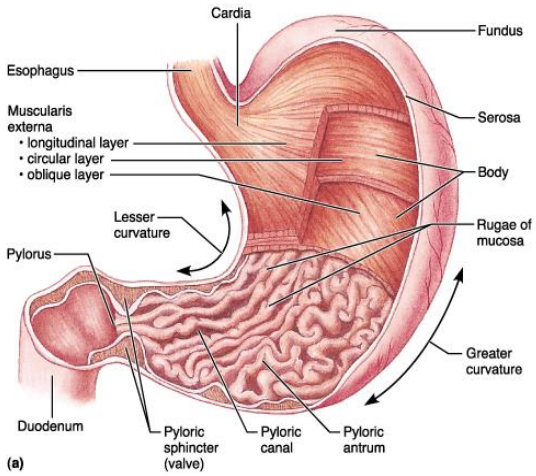
Mixing and digestion

The caudal region of the stomach contracts to mix food with gastric secretions and initiate the digestion process. The size of food particles is further reduced. Slow waves in the caudal stomach occur at a frequency of 3 to 5 waves/min. They depolarize smooth muscle cells. If the threshold is

reached during the slow waves, action potentials are triggered, followed by contraction. Thus, the frequency of slow waves determines the maximum frequency of contractions.

When the pylorus is closed, the contraction wave closes the distal antrum. Contraction of the caudal stomach causes the food to be pushed backward toward the stomach to be mixed: this is the retropulsive emulsifying jet. Gastric contractions are increased by vagal stimulation and decreased by sympathetic stimulation.

Even during periods of fasting, contractions called the migrating myoelectric complex (MMC) occur at intervals of 90 minutes and clear the stomach of any residual food. Motilin triggers these contractions.

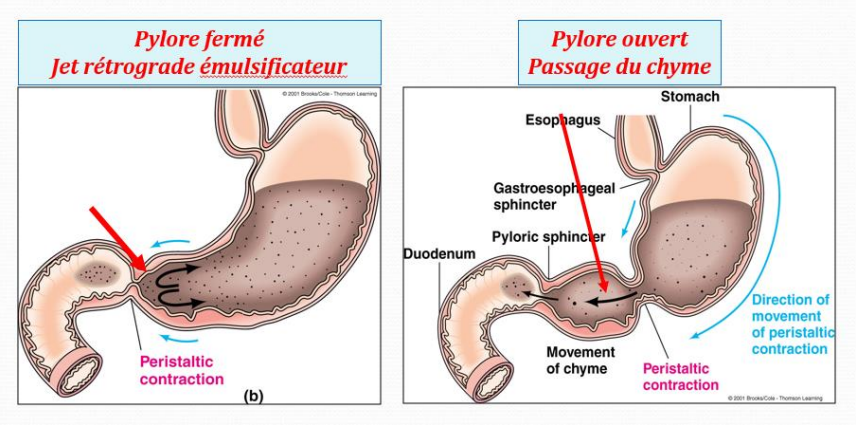


Gastric emptying

When the pylorus is open, the caudal region of the stomach contracts to propel food into the duodenum. The rate of gastric emptying depends on the nature of the gastric contents and their tonicity. Gastric emptying is faster for liquids than for solids. It is faster when the stomach contents are isotonic. The emptying of hypertonic and hypotonic contents is slower.

To avoid exceeding the capacity of the small intestine, gastric emptying is regulated by a negative feedback mechanism originating from the duodenum (in response to excessive chyme,

acidity, high lipid content, or tonicity). The duodenum and jejunum cannot tolerate hypo- or hypertonic fluids, which can cause water shifts leading to osmotic diarrhea (mannitol).



Fats inhibit gastric emptying (in other words, they increase the time required for the stomach to empty) by triggering the release of CCK.

The presence of H^+ in the duodenum inhibits gastric emptying through a direct neural reflex. H^+ receptors in the duodenum transmit information to gastric smooth muscle via interneurons of the GI plexuses.

Small intestine motility

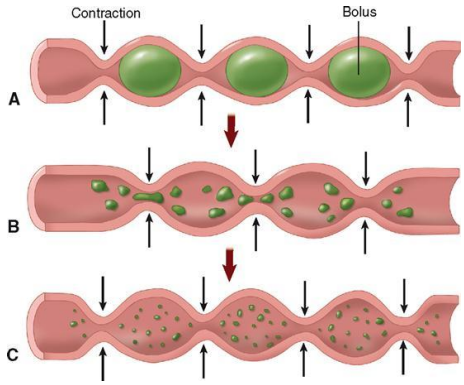
The small intestine participates in digestion and absorption of food. Therefore, its motility serves to mix and expose nutrients to digestive enzymes, allows absorption through the mucosa, and propels the residue toward the large intestine.

As in the stomach, slow waves set the basic electrical rhythm but occur at a frequency of 12 waves/min. Action potentials occur at the peak of the slow waves and induce contractions.

Parasympathetic stimulation increases intestinal smooth muscle contraction, whereas sympathetic stimulation decreases it.

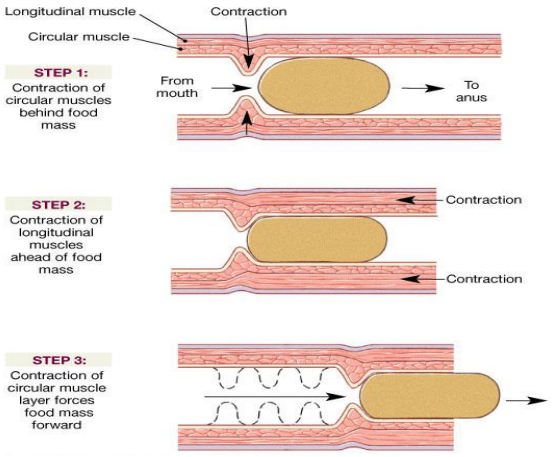
Segmentation contractions

They serve to mix the contents of the small intestine. A segment of the small intestine contracts in isolation, sending its contents in both oral and caudal directions. When this segment relaxes, the expelled contents return. This back-and-forth movement, produced by segmentation contractions, results in mixing but does not produce a net forward movement of the chyme along the small intestine.



Peristaltic contractions

They are highly coordinated and serve to propel intestinal contents along the small intestine toward the large intestine. This process occurs once digestion and absorption have been completed. A contraction occurs behind the bolus, and a relaxation occurs in front of it, resulting in its propulsion in the caudal direction. The peristaltic reflex is coordinated by the enteric nervous system.



Gastro-ileal reflex

It is maintained by the autonomic nervous system and possibly by gastrin. The presence of food in the stomach causes an increase in ileal peristalsis and relaxation of the ileocecal sphincter. This results in the passage of small intestinal contents into the large intestine.

Motility of the large intestine

The development of the cecocolic region varies greatly among species: it is very large in the horse and rabbit and much more reduced and simple in humans and carnivores.

In humans

Fecal matter passes from the cecum to the colon (ascending, transverse, descending, and sigmoid colon), then to the rectum, and finally into the anal canal. Haustra are sac-like segmentations produced by contractions of the large intestine.

Cecum and proximal colon

As soon as the proximal colon is distended by fecal matter coming from the ileum, the ileocecal sphincter contracts, preventing any reflux toward the ileum. Segmentation contractions in the proximal colon mix the intestinal contents and are responsible for the haustral appearance.

Mass movements of the contents of the large intestine occur one to three times per day and move colonic material over long distances (for example, from the transverse colon to the sigmoid colon).

Distal colon

Since most water absorption in the colon occurs in its proximal part, fecal material becomes semi-solid in the distal colon and moves slowly. Mass movements propel it into the rectum.

Rectum, anal canal, and defecation

The mechanism of defecation is as follows:

- When the rectum fills with fecal matter, it contracts and the anal sphincter relaxes (recto-sphincteric reflex).
- When the rectum is filled to about 25% of its capacity, a strong urge to defecate appears. Defecation is prevented by tonic contraction of the external anal sphincter.
- When defecation is desired, the external anal sphincter is voluntarily relaxed, and the smooth muscle of the rectum contracts to generate pressure that expels the feces.
- Intra-abdominal pressure can be increased with a closed glottis (Valsalva maneuver).

Gastrocolic reflex

The presence of food in the stomach increases colonic motility and the frequency of mass movements. A rapid parasympathetic component of the gastrocolic reflex is triggered by gastric distension. A slower hormonal component that increases colonic motility is due to CCK and gastrin.

Abnormalities of intestinal motility

Emotional factors strongly influence intestinal motility via the autonomic nervous system. An irritable bowel syndrome may occur during periods of stress, characterized by constipation (increased segmentation contractions) or diarrhea (decreased segmentation contractions).

Vomiting

A reverse peristaltic wave begins in the small intestine and moves gastrointestinal contents in the oral direction. Retching occurs when gastric contents are pushed into the esophagus while the upper esophageal sphincter remains closed. Vomiting occurs when the pressure in the esophagus becomes high enough to open the upper esophageal sphincter.

Note:
In carnivores, during weaning of the young, a type of vomiting known as epimelitic vomiting is observed. This vomiting is explained by short lactation and the need to provide a transitional diet to young carnivores.

In the horse

In the horse, the cecum and colon represent 70% of the volume of the digestive tract (30 L for the cecum, 100 L for the colon). Microbial digestion takes place at this level. More than half of the energy required by the horse is absorbed here, and it is also the site of major exchanges involved in water balance.

Cecal motility

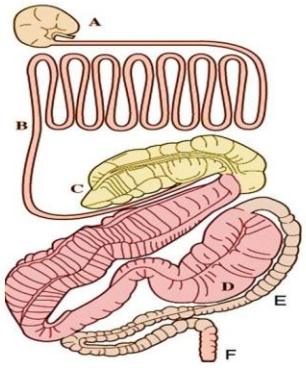
In the horse, ileal contents enter the cecum and not the colon as in other species. The horse cecum is a blind sac exhibiting two types of activity:

Propagated activities between the base and the apex and vice versa. Between meals, there are 1 to 2 base-to-apex contractions every 10 minutes and 2 to 3 retrograde apex-to-base contractions. The propagation speed is 10 cm/s and pressure increases by 20 mmHg.

Localized activities that occur independently at different levels of the cecum, especially at the cecal apex.

Cecal activity appears to be coordinated with that of the ileum and colon. Ileal peristaltic contractions are associated with propagated contractions of the cecum. This suggests that the arrival of an MMC triggers base-to-apex propagated activity aimed at dispersing chyme within the cecum. Retrograde contractions are followed by propagated contractions without involving the colon.

A. Petit estomac
B. Intestin grêle
C. Cæcum:
D. Colon replié
E. Colon flottant
F. Rectum



Colonic motility

In the horse, the colon is highly developed and is divided into two parts: the folded (fixed) colon and the floating colon, which is much narrower and suspended by a mesentery, allowing wide movements.

Colonic motility is coordinated with that of the cecum. Following retrograde contractions moving up the cecum from apex to base, contractions propagate at a speed of 5 cm/s from the right ventral colon to the left ventral colon and stop, for half of them, at the pelvic flexure. While the colon is active, the cecum is at rest. In other parts of the colon, activity is independent of the cecum. It occurs in periods of activity lasting 10 minutes, with contractions in both directions.

In carnivores

The colon of carnivores is different: it is not sacculated and does not exhibit antiperistalsis. It presents two types of activity:

- Propagated activity in the form of cyclic organized contractions (3 to 5 per hour)
- Localized activity dominant in constipation and disappearing in diarrhea

Cycles are ileum-dependent for the proximal colon and ileum-independent for the transverse colon.

Gastrointestinal Secretions

Gastrointestinal secretions play an important role in the chemical digestion of food thanks to the enzymes they produce.

Salivary Secretion

Saliva is mainly produced by three pairs of major glands: the parotid, submandibular, and sublingual glands. The structure of each of these glands resembles a bunch of grapes.

At the blind end of each primary excretory duct, there is an acinus, bounded by mucous and serous cells that secrete the initial saliva. The drainage system consists of branched ducts lined with columnar epithelial cells that modify the saliva.

Acinar cells secrete amylase, mucins, and electrolytes (in concentrations similar to plasma). As with most exocrine glands, the primary secretion is modified in the excretory duct. Ductal cells actively reabsorb sodium (in exchange for K^+) and secrete bicarbonate.

This is the first digestive secretion. Its daily production is about 1 L in humans, 40 L in horses, and 200 L in cattle. It initiates starch digestion through α-amylase (ptyalin) and triglyceride digestion through lingual lipase. It lubricates ingested food via mucus and protects the mouth and esophagus by diluting and buffering ingested substances.

Saliva is produced in large quantities; it is hypotonic and has a high concentration of K^+ and HCO_3^- and a low concentration of Na^+ and Cl^-. It contains α-amylase, lingual lipase, and kallikrein.

Saliva production is controlled by the autonomic nervous system (ANS) and not by gastrointestinal hormones. It is increased by the combined action of the sympathetic and parasympathetic systems, with parasympathetic activity being more predominant. Anticholinergic drugs (such as atropine) inhibit salivary secretion.

In ruminants, saliva has an anti-foaming role by reducing the surface tension of rumen contents, thereby preventing the risk of bloat. It also plays a buffering role in controlling rumen pH. It contains urea, which represents a significant nitrogen source for protein synthesis in the rumen.

Gastric Secretion (Gastric Juice)

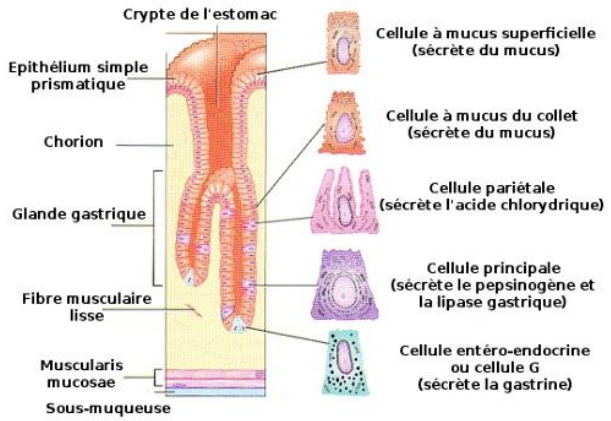
Gastric juice is the digestive secretion that transforms food into a semi-liquid chyme suitable for the small intestine. Its production is about 2 L per day in humans, 1.5 L/h in horses, and 3 mL/h in dogs.

The glands that secrete gastric juice extend from the gastric pits, which are invaginations of the fundic mucosa. Gastric glands are composed of several cell types:

- **Parietal (oxyntic) cells**: secrete HCl and intrinsic factor (a glycoprotein that binds vitamin B12 in the gastric lumen, allowing its absorption in the ileum).
- **Chief cells**: secrete pepsinogen
- **Mucous cells**: secrete mucus
- **Endocrine G cells**: secrete gastrin

Notes

In preruminants, the parietal cells of the abomasum produce rennin (also called chymosin, rennet, or lab ferment), a proteolytic enzyme involved in milk coagulation and digestion.

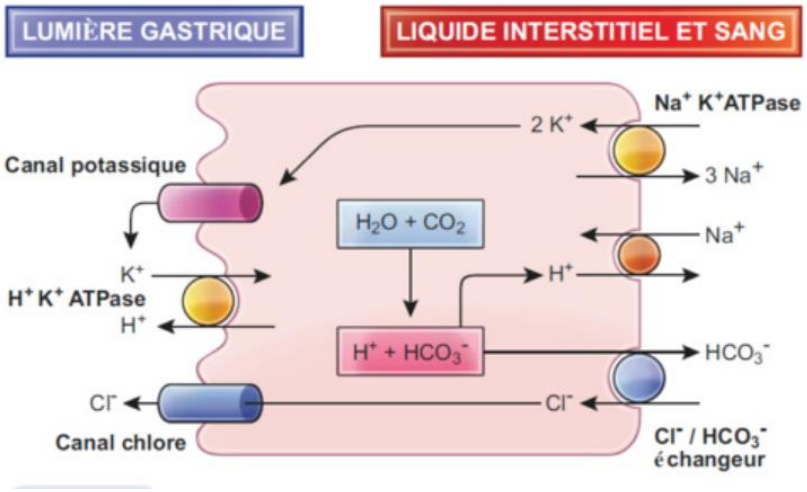


HCl Secretion

Parietal cells secrete HCl into the lumen of the stomach. CO_2 and H_2O are converted into H^+ and HCO_3^- by carbonic anhydrase. H^+ is secreted into the lumen via the H^+-K^+-ATPase pump. Since Cl^- is secreted simultaneously with H^+, the secretion product of parietal cells is HCl.

HCO_3^- produced within the cell is absorbed and released into the bloodstream in exchange for Cl^-. The addition of HCO_3^- increases venous blood pH and results in the postprandial alkaline tide. Later, HCO_3^- returns to the gastrointestinal lumen through pancreatic secretions to neutralize H^+ in the intestine.

Note: In cases of vomiting, and therefore absence of H^+ to neutralize in the intestine, metabolic alkalosis occurs due to the accumulation of HCO_3^- added by parietal cells.



Regulation of HCl Secretion

HCl secretion is stimulated by:

- **The parasympathetic nervous system**
  Acetylcholine (ACh) stimulates H^+ secretion by activating muscarinic receptors on parietal cell membranes.

- **Histamine**
  Released by mucosal mast cells, histamine diffuses to parietal cells and stimulates H^+ secretion via H_2 receptors.
- **Gastrin**
  Released in response to food intake (small peptides, gastric distension, vagal stimulation). The gastrin receptor on parietal cells has not been clearly identified.

Note: There is a potentiation between ACh, histamine, and gastrin because each acts through a different mechanism.

HCl secretion by parietal cells is inhibited by a negative feedback mechanism. A low gastric pH (< 3.0) inhibits gastrin secretion and therefore reduces H^+ secretion. After a meal, H^+ secretion is stimulated; once digestion is complete and the stomach empties, continued H^+ secretion lowers gastric pH. When pH falls below 3.0, gastrin release is inhibited, preventing further H^+ secretion.

The arrival of gastric chyme in the duodenum inhibits H^+ secretion either directly or via mediators such as:

- **GIP** (released in response to fatty acids in the duodenum)
- **Secretin** (released in response to H^+ in the duodenum)

Pharmacological Notes

- **Omeprazole** inhibits the H^+-K^+-ATPase pump and blocks H^+ secretion → used to treat ulcers (especially in dogs and horses).
- **Cimetidine** blocks H_2 receptors → inhibits histamine action.
- **Atropine** blocks muscarinic receptors → inhibits ACh-mediated H^+ secretion.

Mucus Secretion

Mucus consists of mucins (glycoproteins), phospholipids, water, and electrolytes secreted by mucous cells. It forms a protective barrier for the gastric mucosa against H^+ ions and pepsin.

HCO_3^- produced by mucous cells locally neutralizes H^+ that penetrates the barrier and inactivates pepsin. Prostaglandins E_2 (PGE_2) stimulate HCO_3^- secretion and help maintain this protective barrier.

Pancreatic Secretion

Gastric acidity must be rapidly neutralized to prevent duodenal damage, and macromolecules (proteins, fats, carbohydrates) must be digested into absorbable units. These functions are ensured by pancreatic secretion.

Like salivary glands, the exocrine pancreas has a grape-like structure. Acinar cells constitute most of the organ's mass.

The acinus produces a small volume of pancreatic juice containing mainly enzymes, Na^+, and Cl^-. Ductal cells modify this initial secretion by secreting HCO_3^- and absorbing Cl^- via a Cl^-/HCO_3^- exchange mechanism. Since pancreatic ducts are permeable to water, H_2O enters the lumen, making the pancreatic juice iso-osmotic.

It is a colorless, viscous fluid with an alkaline pH (7.1–8.2 in dogs, 7.6–8.4 in cattle), produced in large volumes (about 6 L in cattle and dogs). It is isotonic, with Na^+ and K^+ concentrations similar to plasma, higher HCO_3^- levels (to neutralize duodenal content), and lower Cl^- levels.

It contains Proteases (trypsinogen, chymotrypsinogen); Lipases; α-amylase. These are essential for digestion of proteins, lipids, and carbohydrates, respectively. Pancreatic secretion is under neuro-hormonal control, predominantly hormonal:

- **Secretin**: stimulates ductal cells to secrete bicarbonate (neutralizes H^+ in duodenum).
- **CCK (cholecystokinin)**: stimulates acinar enzyme secretion and potentiates secretin's effect.
- **ACh (vagus nerve)**: stimulates enzyme secretion and also potentiates bicarbonate secretion.

Biliary Secretion

The liver parenchyma consists of acini drained by a duct system. It includes hepatocytes (bile secretion) and ductal cells (electrolyte secretion). The liver produces about 0.7 L of bile per day.

Bile is essential for lipid digestion. It enables micelle formation (due to amphiphilic bile salts), which is necessary for fat digestion by pancreatic lipase. It also promotes lipid absorption and neutralizes acidic chyme via bicarbonate ions.

Bile is a viscous, bitter, green fluid with an alkaline pH (7.6–8.6), containing:

- Bile salts (lipid emulsification)
- Bile pigments (bilirubin)
- Cholesterol and lecithin
- Trace elements
- Electrolytes (especially HCO_3^-)

Enterohepatic Circulation

Bile salts undergo enterohepatic circulation to prevent excessive loss. After secretion into bile, they reach the duodenum, are reabsorbed in the terminal ileum, pass into the portal vein, and return to the liver for resecretion. This cycle occurs 6–8 times per day.

Roles of Bile Salts

- Emulsification of lipids
- Increase in duodenal pH
- Absorption of cholesterol and fat-soluble vitamins
- Enhancement of intestinal peristalsis
- Antibacterial/anti-fermentation role
- Micelle formation for fatty acid solubilization

Regulation

Bile is produced continuously and stored in the gallbladder. It is released under sympathetic conditions when the sphincter of Oddi is closed. It becomes concentrated by reabsorption of H_2O, Na^+, and Cl^-.

During meals, the gallbladder contracts and the sphincter of Oddi relaxes under the action of:

- Parasympathetic nervous system
- CCK

Note: The gallbladder is absent in horses, rats, camels, elephants, deer, giraffes, and pigeons.

Digestion and Absorption

In Monogastric Animals

Carbohydrates, proteins, and lipids are digested and absorbed in the small intestine. The absorptive surface of the small intestine is greatly increased by the presence of the brush border.

Carbohydrates

Digestion of Carbohydrates

Only monosaccharides are absorbed. Carbohydrates must be digested into glucose, galactose, and fructose for absorption to occur.

Salivary and pancreatic α-amylases hydrolyze the 1,4-glycosidic bonds of starch, producing maltose, maltotriose, and α-limit dextrins.

Maltase, α-dextrinase, and sucrase of the intestinal brush border hydrolyze oligosaccharides into the final products, monosaccharides: glucose, galactose, and fructose.

Lactase, trehalase, and sucrase break down their respective disaccharides into monosaccharides.

Absorption of Carbohydrates

Glucose and galactose are absorbed from the intestinal lumen into cells by secondary active cotransport with Na^+ at the luminal membrane. Sugar moves against its gradient, while Na^+ moves down its gradient. They are then transported from the cell into the blood by facilitated diffusion. The Na^+-K^+ ATPase pump in the basolateral membrane maintains low intracellular Na^+, preserving the gradient across the luminal membrane. Fructose is absorbed exclusively by facilitated diffusion and cannot be absorbed against a concentration gradient.

Note : Lactose intolerance is due to the absence of lactase in the brush border, preventing hydrolysis of lactose into absorbable glucose. Lactose remains in the GI tract as a non-absorbed solute, retaining water osmotically and causing osmotic diarrhea.

Proteins

Proteins can be absorbed as amino acids, dipeptides, and tripeptides (unlike carbohydrates, which are absorbed only as monosaccharides).

Digestion of Proteins

Endopeptidases break down proteins by hydrolyzing internal peptide bonds. Exopeptidases remove one amino acid at a time from the C-terminal end of proteins and peptides.

Pepsin is secreted as pepsinogen by chief cells of the stomach. It is activated into pepsin by gastric H^+. Its optimal pH is between 1 and 3. It is denatured when pH > 5 and inactivated in the duodenum by bicarbonate secretion. It is not essential for protein digestion.

Pancreatic proteases are secreted in inactive forms and activated by brush border enzymes. Trypsinogen is activated into trypsin by enterokinase in the small intestine.

Pancreatic proteases can digest each other and are absorbed along with dietary proteins.

Absorption of Proteins

Absorption of free amino acids

Amino acids are absorbed via Na^+-dependent secondary active cotransport at the luminal membrane, similar to glucose and galactose. They then move into the blood by facilitated diffusion and simple diffusion.

There are four transport systems for amino acids: neutral, acidic, basic, and imino acids.

Absorption of dipeptides and tripeptides

This process is faster than amino acid absorption and occurs via H^+-dependent secondary active transport at the luminal membrane.

Once inside intestinal cells, cytoplasmic peptidases hydrolyze them into amino acids, which are then transported into the blood by simple and facilitated diffusion.

Lipids

Lipids are absorbed into intestinal cells as fatty acids, monoglycerides, and cholesterol. Inside the cells, they are re-esterified into triglycerides and phospholipids and transported into the lymph as chylomicrons.

Digestion of Lipids Along the GI Tract

Lingual lipases digest part of the lipids.

Mechanical mixing in the stomach breaks lipids into droplets, increasing the surface area available for pancreatic enzymes.

Most dietary lipids are digested by pancreatic lipases. Gastric emptying is slowed by CCK, allowing sufficient time for digestion and absorption.

In the small intestine, bile components emulsify lipids.

Pancreatic enzymes hydrolyze lipids into fatty acids, monoglycerides, and cholesterol. These enzymes include:

- Pancreatic lipase
- Cholesterol ester hydrolase
- Pancreatic phospholipase A_2

Micelles are formed, which solubilize hydrophobic digestion products.

Absorption of Lipids

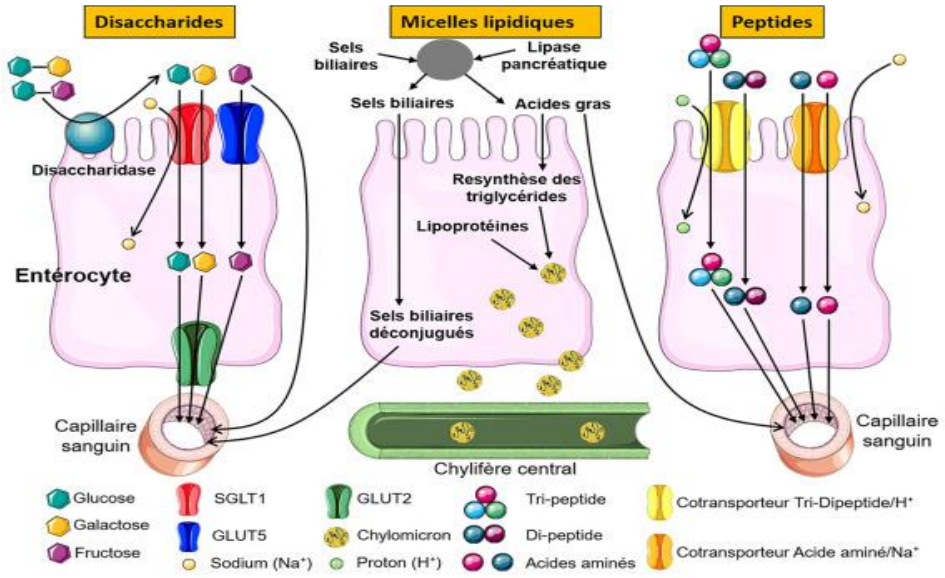
Micelles transport lipid digestion products to the intestinal absorptive surface. Fatty acids, monoglycerides, and cholesterol then diffuse into cells across the luminal membrane.

Hydrophilic glycerol is not included in micelles.

Inside intestinal cells, lipids are re-esterified into triglycerides and phospholipids, and together with cholesterol and apoproteins form chylomicrons.

A deficiency in apoprotein B synthesis prevents the transport of chylomicrons out of intestinal cells.

Chylomicrons are secreted by exocytosis. Because they are too large to enter capillaries, they pass into lymphatic vessels and are eventually released into the bloodstream via the thoracic duct.



In Polygastric Animals

Rumen Environment

Inside the rumen, there is a dense and stable population of microorganisms that live in symbiosis with the host and play a major role in digestion and animal nutrition.

The rumen provides very specific physicochemical conditions that allow the development of a highly active anaerobic microbiota:

- **Anaerobiosis** maintained by the rapid consumption of O_2 by facultative anaerobic bacteria
- **pH between 5.5 and 7.3**, significantly lower 2 to 6 hours after feeding
- **Buffer systems**: saliva regulates rumen fluid content and pH, prevents foam formation (surfactant role), and supplies nitrogen, 80% of which is in the form of urea
- **Temperature** between 39 and 40°C

Main Microbial Species

➤ **Anaerobic Bacteria**

- **Cellulolytic bacteria**
  The most important group. These bacteria can completely hydrolyze plant cellulose. They produce acetate (C2) and butyrate (C4). Optimal pH ≈ 6.5
- **Amylolytic bacteria**
  These species hydrolyze starch but cannot use cellulose. They produce propionate (C3) and tolerate acidic pH (5–6)
- **Lactic bacteria**
  Active at pH ≈ 5 and produce lactic acid

➤ **Protozoa (Ciliates)**

They are strictly anaerobic. Their optimal pH ranges from 5.5 to 7.6. Diets too rich in concentrates cause their disappearance due to pH decrease.

They digest carbohydrates, proteins, and lipids within digestive vacuoles. They cannot utilize non-protein nitrogen nor synthesize vitamin B.

They metabolize lactic acid and reduce the risk of acidosis.

➤ **Fungi**

They are anaerobic. Their role is not yet fully understood; they contribute to plant cell wall digestion but are not essential.

Microbial Digestion

Anaerobic bacteria, protozoa, and fungi produce enzymes that digest carbohydrates, proteins, and lipids. The products of fermentation are:

- Volatile fatty acids (VFAs): acetate, propionate, butyrate
- Methane (CH_4) + CO_2
- Ammonia (NH_3)

Carbohydrate Digestion

Carbohydrates represent about 75% of plant tissue mass:

- Structural carbohydrates (cellulose, hemicellulose, pectin)
- Storage carbohydrates (starch)
- Simple sugars

Their degradation occurs in two phases:

➤ **Hydrolysis Phase**

Carried out by bacterial enzymes, producing simple sugars that are taken up by bacteria and converted into pyruvate according to:

$$\text{D-glucose} + 2\ NAD^+ + 2\ ADP + 2\ Pi \rightarrow 2\ \text{Pyruvate} + 2\ NADH + 2\ ATP + 2\ H^+$$

➤ **Fermentation Phase**

Produces:

- VFAs (acetate, propionate, butyrate) from pyruvate
- CO_2 (via decarboxylation of pyruvate)
- CH_4 (of no nutritional value, eliminated by eructation)

VFAs are absorbed through ruminal papillae by diffusion or facilitated diffusion and transported to the liver via the portal circulation.

They provide **60–80% of dietary energy**, contribute to milk fatty acid synthesis (propionate → glucose; acetate & butyrate → fat synthesis).

Protein Digestion

Ruminants utilize both proteins and non-protein nitrogen (NPN). Nitrogen utilization involves two processes:

➤ **Degradation**

All NPN and part of fermentable dietary proteins are degraded by bacteria into ammonia (NH_3).

Undegradable dietary proteins pass to the intestine, forming **digestible undegraded dietary protein (PDIA)**.

Ammonia follows two pathways:

- **Excess ammonia**
  - Absorbed in the rumen
  - Converted into urea in the liver
  - Recycled via saliva (rumino-hepatic cycle) or excreted in urine
- **Low ammonia availability**
  - Reused by bacteria for protein synthesis

➤ **Synthesis**

Microbial proteins are synthesized from ammonia.

In the intestine, these microbial proteins form **PDIM**, which, together with PDIA, are the main sources of amino acids for the animal.

Lipid Digestion

Plant material contains 2–5% lipids in the form of:

- Galactolipids
- Triglycerides (oilseeds)
- Phospholipids
- Fatty acids

Galactolipids are completely hydrolyzed by lipases produced by bacteria and protozoa, releasing fatty acids. Glycerol and galactose are fermented into VFAs. Lipid digestion and absorption occur in the intestine and are similar to those in monogastric mammals.