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ZAPOROZHYE STATE MEDICAL UNIVERSITY
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THE GASTROINTESTINAL SYSTEM

Methodical manual for 2^{d}-year students of international faculty, discipline "normal physiology"

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Methodical recommendations compiled in accordance with the program of "normal physiology". Guidelines are intended to help students prepare for practical classes and learn the material. Can be used for training of 2th-years students of international faculty, discipline "normal physiology".

CONTENTS

Theme actuality. The gastrointestinal tract is a continuous tube that stretches from the mouth to the anus. Its primary function is to serve as a portal whereby nutrients and water can be absorbed into the body. Residues of the meal that cannot be absorbed, along with cellular debris and lipid-soluble metabolic end products that are excreted in the bile rather than the urine, are expelled from the body. All of these functions are tightly regulated in concert with the ingestion of meals. Diseases in the digestive systems, also called gastrointestinal diseases, have become quite common in the modern day world. The health of a body depends on the health of the digestive system and any barrier in its functioning will ultimately affect the body. Future doctors should know about the functional peculiarities of the digestive system in order to diagnose various disorders and use appropriate methods of treatment.

Study purposes: to know the functions of the digestive system and principles of their regulation.

Concrete purposes of the module:

A student must know:

- the functional significance of the gastrointestinal system, and in particular, its roles in nutrient assimilation, excretion, and immunity.
- the structure of the gastrointestinal tract, the glands that drain into it, and its subdivision into functional segments.
- the major gastrointestinal secretions, their components, and the stimuli that regulate their production.
- the major hormones, other peptides, and key neurotransmitters of the gastrointestinal system.
- the special features of the enteric nervous system and the splanchnic circulation.
- differences between mechanical and chemical digestion.
- the general neural and chemical controls over digestive function.

Digestive Function

The **digestive system** is the organ system that processes food, extracts nutrients from it, and eliminates the residue. It does this in four stages:

1. **ingestion,** the selective intake of food;

2. **digestion,** the mechanical and chemical breakdown of food into a form usable by the body;

3. **absorption,** the uptake of nutrient molecules into the epithelial cells of the digestive tract and then into the blood or lymph; and finally

4. **defecation,** the elimination of undigested residue.

The digestion stage itself has two facets, mechanical and chemical. **Mechanical digestion** is the physical breakdown of food into smaller particles. It is achieved by the cutting and grinding action of the teeth and the churning contractions of the stomach and small intestine. Mechanical digestion exposes more food surface to the action of digestive enzymes. **Chemical digestion** is a series of hydrolysis reactions that break dietary macromolecules into their monomers (residues): polysaccharides into monosaccharides, proteins into amino acids, fats into glycerol and fatty acids, and nucleic acids into nucleotides. It is carried out by digestive enzymes produced by the salivary glands, stomach, pancreas, and small intestine. Some nutrients are already present in usable form in the ingested food and are absorbed without being digested: vitamins, free amino acids, minerals, cholesterol, and water.

Digestion involves the processes of motility, secretion, and membrane transport. *Motility* refers to the muscular contractions that break up food, propel it through the canal, mix it with digestive enzymes, and eliminate the waste. *Secretion* releases enzymes, hormones, and other products that carry out or regulate digestion. *Membrane transport* includes all the mechanisms such as active transport and facilitated diffusion that absorb nutrients and transfer them to the blood and lymph.

General principles of anatomical organization of the digestive system

The digestive system has two anatomical subdivisions, the digestive tract and the accessory organs (fig. 1). The **digestive tract** is a tube extending from mouth to anus, measuring about 9 m (30 ft) long in the cadaver. It is also known as the *alimentary canal.* It includes the oral cavity, pharynx, esophagus, stomach, small intestine, and large intestine. Part of this, the stomach and intestines, constitute the *gastrointestinal (GI) tract.* The **accessory organs** are the teeth, tongue, salivary glands, liver, gallbladder, and pancreas.

The digestive tract is open to the environment at both ends. Most of the material in it has not entered any body tissues and is considered to be external to the body until it is absorbed by epithelial cells of the alimentary canal. In the strict sense, defecated food residue was never in the body.

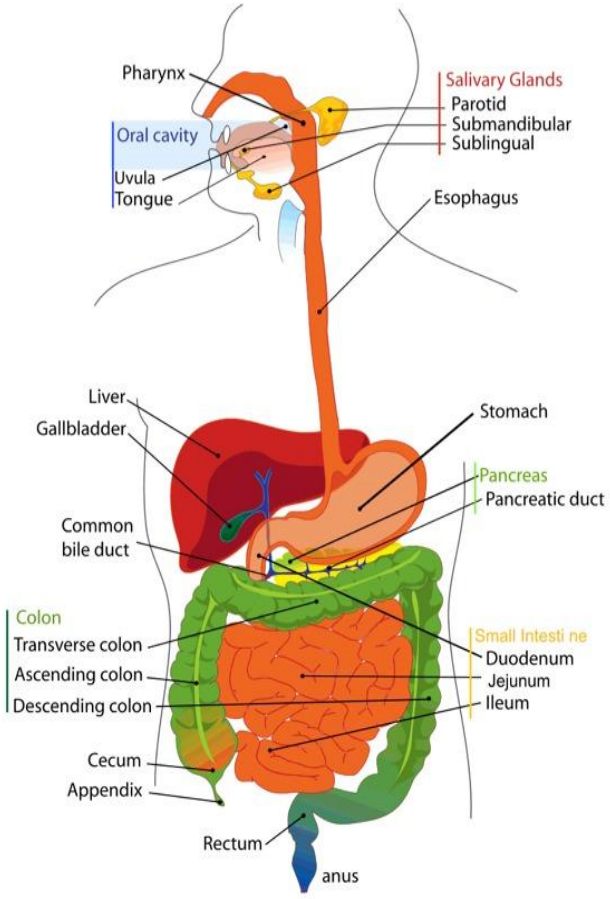


Fig.1. The digestive system

Most of the digestive tract follows the basic structural plan shown in figure 2, with a wall composed of the following tissue layers, in order from the inner to the outer surface:

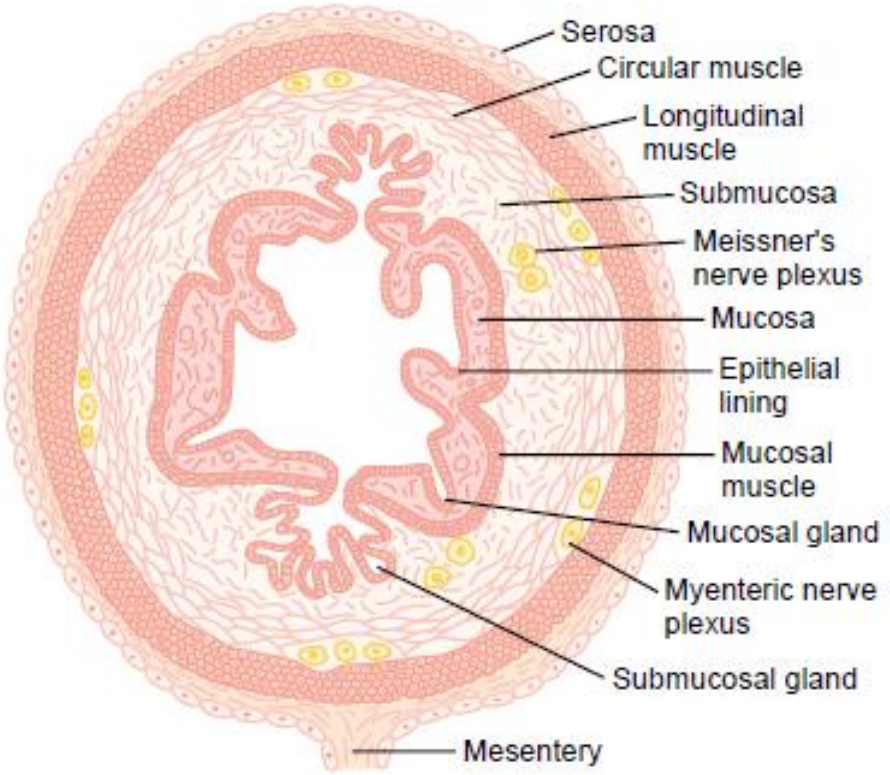


Fig.2. Tissue Layers of the Digestive Tract

Mucosa

- Epithelium
- Lamina propria
- Muscularis mucosae

Submucosa

Muscularis externa

- Inner circular layer
- Outer longitudinal layer

Serosa

- Areolar tissue
- Mesothelium

Slight variations on this theme are found in different regions of the tract.

The **mucosa,** lining the lumen, consists of an inner epithelium, a loose connective tissue layer called the **lamina propria,** and a thin layer of smooth muscle called the **muscularis mucosae**. The epithelium is simple columnar in most of the digestive tract, but of the nonkeratinized stratified squamous type from the oral cavity through the esophagus and in the lower anal canal, where the tract is subject to more abrasion.

The **submucosa** is a thicker layer of loose connective tissue containing blood vessels, lymphatic vessels, a nerve plexus, and in some places, glands that secrete lubricating mucus into the lumen.

The **muscularis externa** consists of usually two layers of smooth muscle near the outer surface. Cells of the inner layer encircle the tract while those of the outer layer run longitudinally.

The **serosa** is composed of a thin layer of areolar tissue topped by a simple squamous mesothelium. The serosa begins in the lower 3 to 4 cm of the esophagus and ends with the sigmoid colon. The oral cavity, pharynx, most of the esophagus, and the rectum are surrounded by a fibrous connective tissue layer called the **adventitia.**

The esophagus, stomach, and intestines have a nervous network called the **enteric nervous system,** which regulates digestive tract motility, secretion, and blood flow. Two nerve networks make up this system: the **submucosal (Meissner) plexus** in the submucosa and the **myenteric (Auerbach) plexus** between the two layers of the muscularis externa.

Digestion in the mouth

Mouth is the first part of the alimentary tract, where digestion of food starts. The mouth is otherwise known as oral cavity or buccal cavity. It is formed by cheeks, lips and palate. It encloses the teeth and tongue. It opens outside anteriorly through the lips and posteriorly through fauces.

The functions of mouth are the ingestion of food materials, chewing and mixing the food with saliva, appreciation of the taste of food and transfer of food (bolus) to the esophagus by swallowing. Digestive juice present in the mouth is saliva. It is secreted by the salivary glands.

First of all food must be broken down into smaller particles for adequate action of different enzymes. It is achieved by the cutting and grinding action of the teeth during the process of mastication.

Mastication (Chewing)

The teeth are admirably designed for chewing, the anterior teeth (incisors) providing a strong cutting action and the posterior teeth (molars), a grinding action. All the jaw muscles working together can close the teeth with a force as great as 55 pounds on the incisors and 200 pounds on the molars.

Most of the muscles of chewing are innervated by the motor branch of the fifth cranial nerve, and the chewing process is controlled by nuclei in the brain stem. Stimulation of specific reticular areas in the brain stem taste centers will cause rhythmical chewing movements. Also, stimulation of areas in the hypothalamus, amygdala, and even the cerebral cortex near the sensory areas for taste and smell can often cause chewing.

Much of the chewing process is caused by a *chewing reflex*, which may be explained as follows: the presence of a bolus of food in the mouth at first initiates reflex inhibition of the muscles of mastication, which allows the lower jaw to drop. The drop in turn initiates a stretch reflex of the jaw muscles that leads to *rebound* contraction. This automatically raises the jaw to cause closure of the teeth, but it also compresses the bolus again against the linings of the mouth, which inhibits the

jaw muscles once again, allowing the jaw to drop and rebound another time; this is repeated again and again.

Chewing is important for digestion of all foods, but especially important for most fruits and raw vegetables because these have indigestible cellulose membranes around their nutrient portions that must be broken before the food can be digested. Also, chewing aids the digestion of food for still another simple reason: digestive enzymes act only on the surfaces of food particles; therefore, the rate of digestion is absolutely dependent on the total surface area exposed to the digestive secretions. In addition, grinding the food to a very fine particulate consistency prevents excoriation of the gastrointestinal tract and increases the ease with which food is emptied from the stomach into the small intestine, then into all succeeding segments of the gut.

Saliva and salivary glands

Saliva moistens the mouth, digests a little starch and fat, cleanses the teeth, inhibits bacterial growth, dissolves molecules so they can stimulate the taste buds, and moistens food and binds particles together to aid in swallowing. It is a hypotonic solution of 97.0% to 99.5% water and the following solutes:

- **salivary amylase,** an enzyme that begins starch digestion in the mouth;
- **lingual lipase,** an enzyme that is activated by stomach acid and digests fat after the food is swallowed;
- **mucus,** which binds and lubricates the food mass and aids in swallowing;
- **lysozyme,** an enzyme that kills bacteria;
- **immunoglobulin A** (IgA), an antibody that inhibits bacterial growth;
- **electrolytes,** including sodium, potassium, chloride, phosphate, and bicarbonate ions.

Saliva has a pH of 6.8 to 7.0. Daily secretion of saliva normally ranges between 800 and 1500 milliliters, saliva contains two major types of protein secretion: a *serous secretion* that contains *ptyalin* (an α-amylase), which is an

enzyme for digesting starches, and *mucus secretion* that contains *mucin* for lubricating and for surface protective purposes.

There are two kinds of salivary glands, intrinsic and extrinsic. The **intrinsic salivary glands** are an indefinite number of small glands dispersed amid the other oral tissues. They include *lingual glands* in the tongue, *labial glands* on the inside of the lips, and *buccal glands* on the inside of the cheeks. They secrete relatively small amounts of saliva at a fairly constant rate whether we are eating or not. This saliva contains lingual lipase and lysozyme and serves to moisten the mouth and inhibit bacterial growth.

The **extrinsic salivary glands** are three pairs of larger, more discrete organs located outside of the oral mucosa; they communicate with the oral cavity by way of ducts:

1. The **parotid gland** is located just beneath the skin anterior to the earlobe. Its duct passes superficially over the masseter, pierces the buccinator, and opens into the mouth opposite the second upper molar tooth.

2. The **submandibular gland** is located halfway along the body of the mandible, medial to its margin, just deep to the mylohyoid muscle. Its duct empties into the mouth at a papilla on the side of the lingual frenulum, near the lower central incisors.

3. The **sublingual gland** is located in the floor of the mouth. It has multiple ducts that empty into the mouth posterior to the papilla of the submandibular duct.

The parotid glands secrete almost entirely the serous type of secretion, while the submandibular and sublingual glands secrete both serous secretion and mucus. The buccal glands secrete only mucus.

Salivary glands are formed by the cells arranged in small groups around a central globular cavity called acinus or alveolus. The central cavity or lumen is continuous with the lumen of the duct. The fine duct draining each acinus is called the intercalated ducts. Many of the intercalated ducts join together to form intralobular ducts. Two or more intralobular ducts join to form interlobular ducts,

which unite to form the main duct of the gland. The gland with this type of structure and duct system is called racemose type (Fig.3).

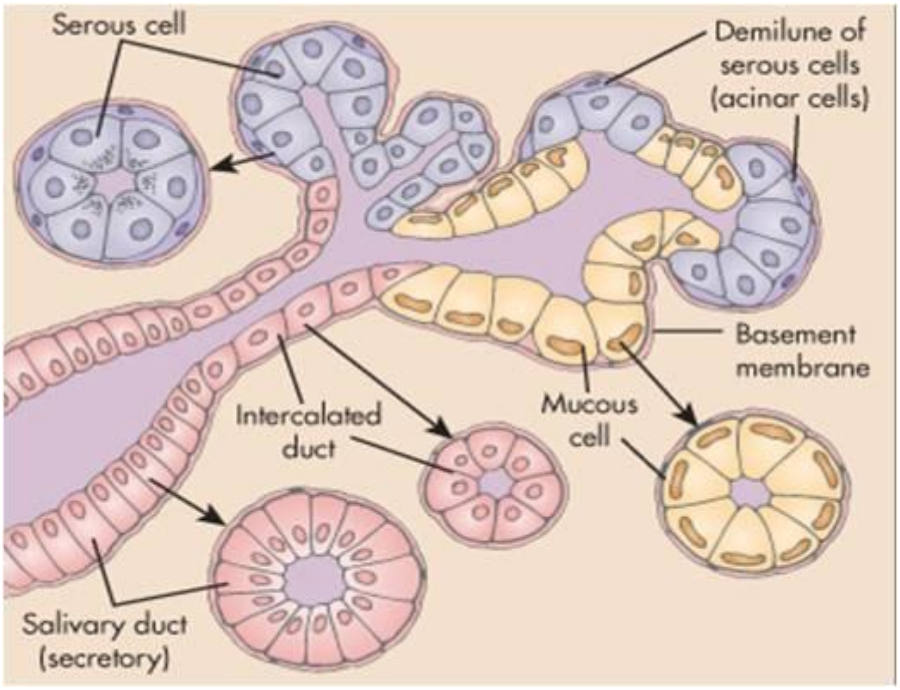


Fig. 3. Structure of salivary gland

Secretion of Ions in Saliva

Saliva contains especially large quantities of potassium and bicarbonate ions. Conversely, the concentrations of both sodium and chloride ions are several times less in saliva than in plasma. One can understand these special concentrations of ions in the saliva from the following description of the mechanism for secretion of saliva. Figure 4 shows secretion by the submandibular gland, a typical compound gland that contains *acini* and *salivary ducts*. Salivary secretion is a two-stage operation: the first stage involves the acini, and the second, the salivary ducts.

First, *sodium ions* are actively reabsorbed from all the salivary ducts and *potassium ions* are actively secreted in exchange for the sodium. Therefore, the sodium ion concentration of the saliva becomes greatly reduced, whereas the potassium ion concentration becomes increased. However, there is excess sodium reabsorption over potassium secretion, and this creates electrical negativity of about -70 millivolts in the salivary ducts; this in turn causes chloride ions to be

reabsorbed passively. Therefore, the chloride ion concentration in the salivary fluid falls to a very low level, matching the ductal decrease in sodium ion concentration.

Second, *bicarbonate ions* are secreted by the ductal epithelium into the lumen of the duct. This is at least partly caused by passive exchange of bicarbonate for chloride ions, but it may also result partly from an active secretory process.

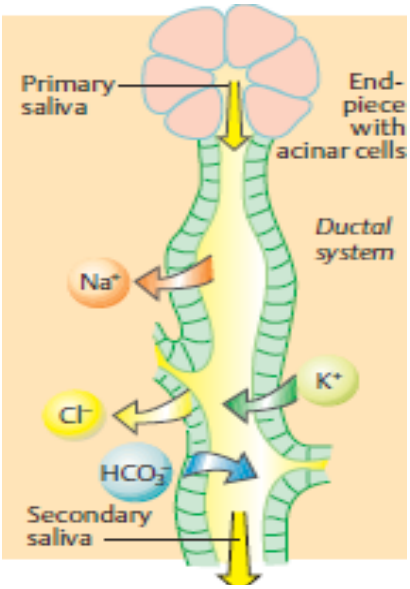


Fig. 4. Formation and secretion of saliva by a submandibular salivary gland.

Nerve supply to salivary glands

Salivary glands are under the control of autonomic nervous system and receive efferent nerve fibers from both parasympathetic and sympathetic divisions of autonomic nervous system.

The parasympathetic nerve fibers supplying the salivary glands arise from the superior and the inferior salivatory nuclei, which are situated in pons and medulla, respectively (fig. 5).

Parasympathetic fibers to submandibular and sublingual glands. The preganglionic parasympathetic fibers to submandibular and sublingual glands arise from the superior salivatory nucleus situated in pons. After taking origin from this nucleus, the preganglionic fibers pass through nervous intermedius of Wrisberg, geniculate ganglion, the motor fibers of facial nerve, chorda tympani

branch of facial nerve and lingual branch of trigeminal nerve and finally reach the submaxillary ganglion. The postganglionic fibers arising from this ganglion supply the submaxillary and sublingual glands.

Parasympathetic fibers to parotid gland. The preganglionic fibers to parotid gland arise from inferior salivatory nucleus situated in the upper part of medulla oblongata. From here, the fibers pass through the tympanic branch of glossopharyngeal nerve, tympanic plexus and lesser petrosal nerve and end in otic ganglion. The postganglionic fibers from otic ganglion reach the parotid gland by passing through the auriculotemporal branch in mandibular division of trigeminal nerve.

Sympathetic fibers. The preganglionic sympathetic preganglionic fibers to salivary glands arise from the lateral horns of first and second thoracic segments of spinal cord. The fibers leave the cord through the anterior nerve roots and end in superior cervical sympathetic ganglion. The postganglionic fibers from this ganglion are distributed to the salivary glands along the nerve plexus around the arteries supplying the glands.

Function of Parasympathetic Fibers. When the parasympathetic fibers of salivary glands are stimulated, profuse and watery saliva is secreted. The amount of organic constituents is less. The parasympathetic fibers activate the acinar cells and dilate the blood vessels of salivary glands. The neurotransmitter is acetylcholine.

Function of Sympathetic Fibers. The stimulation of sympathetic fibers causes less secretion of saliva, which is thick and rich in mucus. This is because, these fibers activate the acinar cells and cause vasoconstriction by secreting noradrenaline.

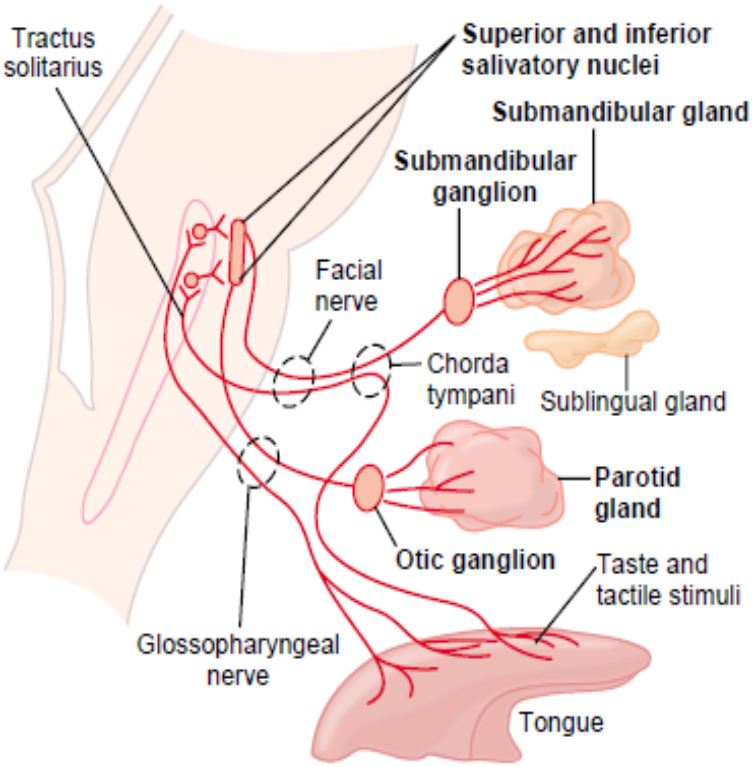


Fig. 5. Parasympathetic nervous regulation of salivary secretion.

Stomach: structure and function

The major function of the stomach is storage, but it also absorbs water-soluble and lipid-soluble substances (e.g., alcohol and some drugs). An important function of the stomach is to prepare the chyme for digestion in the small intestine. **Chyme** is the semi-fluid material produced by the gastric digestion of food. Chyme results partly from the conversion of large solid particles into smaller particles via the combined peristaltic movements of the stomach and contraction of the pyloric sphincter.

The stomach is divided into four regions: (1) The **cardiac region (cardia)** is a small area immediately inside the cardiac orifice. (2) The **fundic region (fundus)** is the domeshaped portion superior to the esophageal attachment. (3) The **body (corpus)** makes up the greatest part of the stomach inferior to the cardiac orifice. (4) The **pyloric region** is a slightly narrower pouch at the inferior end; it is subdivided into a funnel-like **antrum** and a narrower **pyloric canal.** The latter terminates at the **pylorus,** a narrow passage into the duodenum. The pylorus is surrounded by a thick ring of smooth muscle, the **pyloric (gastroduodenal) sphincter,** which regulates the passage of chyme into the duodenum (fig. 6).

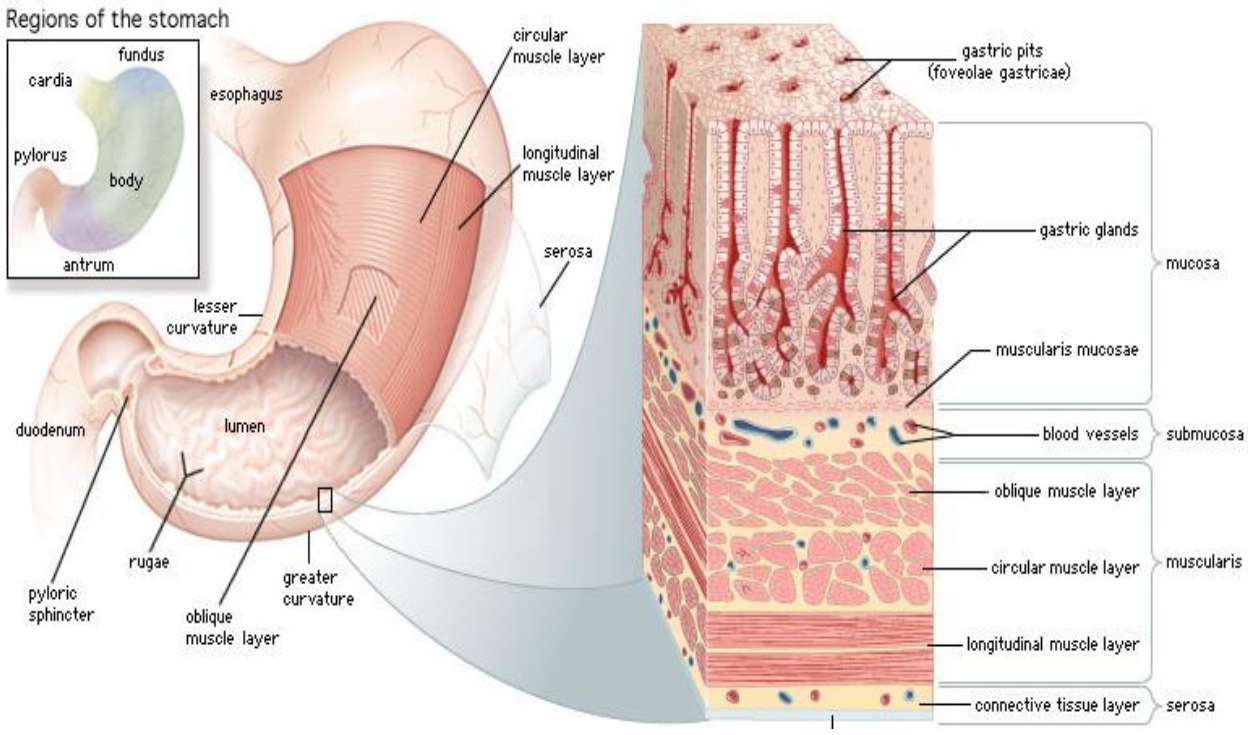


Fig.6. Parts of the stomach and gastric glands

Structure of the stomach wall

The wall of the stomach has four layers:

1. Outer serous layer: This is formed by peritoneum which covers the stomach except at the lesser and greater curvatures, where omenta are attached.
2. Muscular coat: This consists of three layers of smooth muscle fibers namely, inner oblique, middle circular and outer longitudinal layers. Auerbach's plexus is situated between the longitudinal and circular muscle fibers.
3. Submucus layer: This is formed by areolar tissue. Blood vessels, lymph vessels and Meissner's nerve plexus are present in this layer.
4. Inner mucus layer: This is lined by mucus secreting columnar epithelial cells.

The gastric glands are situated in this layer. Under resting conditions, the mucosa of the stomach is thrown into many folds. These folds are called rugae. However, the rugae disappear when the stomach is distended after meals. Throughout the inner surface of stomach, small depressions are seen. These are called gastric pits. The glands of the stomach open into these pits. The inner surface of mucus layer is covered by 2 mm thick mucus.

Classification of glands of the stomach

The glands of the stomach or gastric glands are of three types depending upon the situation: f*undic glands:* these are situated in body and fundus of stomach. These glands are also called main gastric glands or oxyntic glands; *pyloric glands:* these are present in the pyloric part of the stomach; *cardiac glands:* these glands are situated in the cardiac region of the stomach.

Structure and Functions of Fundic Glands. The fundic glands are long and tubular glands, which secrete hydrochloric acid, pepsinogen, mucin and intrinsic factor of Castle. These tubular glands have body, neck and isthmus. Many glands open into a common gastric pit, which in turn opens on the surface of gastric mucosa. The fundic glands are considered as the typical glands. The different cells of these glands are (fig. 7):

- **chief cells** or pepsinogen cells, which secrete pepsinogen, rennin and gelatinase
- **parietal cells or oxyntic cells,** which secrete hydrochloric acid and intrinsic factor of Castle. The structure of resting parietal cells is unique in that they have intracellular canaliculi as well as an abundance of mitochondria. Hydrochloric acid is secreted across the parietal cell microvillar membrane and flows out of the intracellular canaliculi into the oxyntic gland lumen.
- **mucus neck cells,** which secrete mucin and HCO^{3-} ions, which protect the stomach from the acid in the stomach lumen.

Structure and Functions of Pyloric Glands. The pyloric glands are short and tortuous in structure formed by G cells and columnar epithelial cells. Columnar epithelial cells secrete mucin and G cells secrete gastrin.

Structure and Functions of Cardiac Glands. Cardiac glands are also short and tortuous. These glands have more mucus cells, which are columnar in nature. Cardiac glands secrete more mucus and small quantity of pepsinogen.

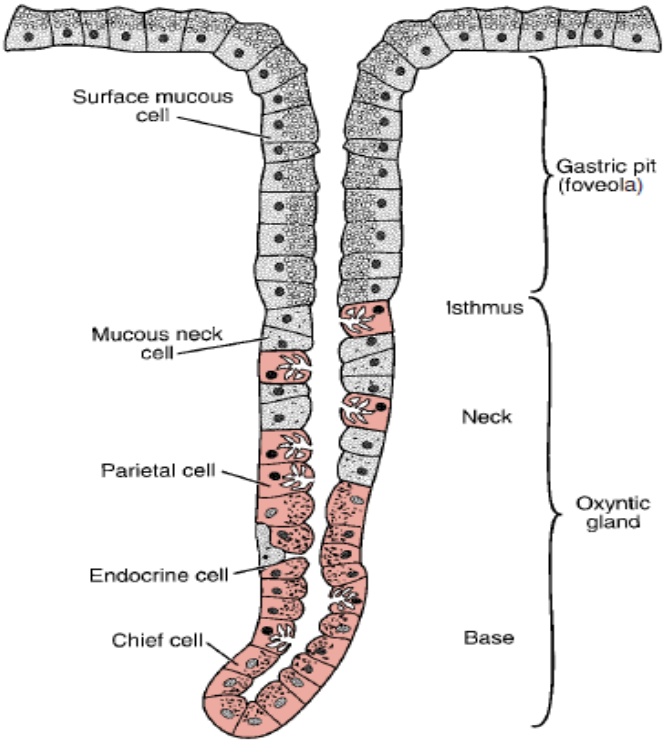


Fig. 7. Structure of the gastric (oxyntic) gland

Gastric juice

Gastric juice is the mixture of secretions from different glands of the stomach.

Properties of gastric juice:

Volume: 1200 to 1500 ml/day.

Reaction: Gastric juice is highly acidic with pH of 0.9 to 1.2. The acidity of gastric juice is due the hydrochloric acid.

Specific gravity: 1.002 to 1.004

Composition of gastric juice: gastric juice contains 99.5% of water and 0.5% solids. The solids are organic and inorganic substances. **The organic substances** present in gastric juice are the enzymes, mucus and intrinsic factor.

Gastric Enzymes

1.Pepsin: this is the major protein splitting (proteolytic) enzyme in the gastric juice. The precursor of pepsin is pepsinogen.

2.Rennin: it is a milk curdling enzyme. It is not present in man.

3.Gastric lipase: gastric lipase is a weak lipid splitting (lipolytic) enzyme.

4.Other gastric enzymes: the other enzymes of gastric juice are the gelatinase and urase.

Gastric Mucus

Gastric mucus is secreted by neck cells of the gastric glands and surface mucus cells in fundus, body and other parts of stomach. It is like a flexible gel covering the gastric mucus membrane. Mucus is a glycoprotein.

Intrinsic Factor

This is necessary for absorption of the extrinsic factor.

Functions of gastric juice:

1. Digestive function. The gastric juice mainly acts on proteins. The enzymes of the gastric juice acting on protein digestion are pepsin and rennin. Gastric juice also contains some other enzymes like gastric lipase, gelatinase and urase. ***Pepsin*** is the major proteolytic enzyme in gastric juice. It is secreted as pepsinogen, which is inactive. Pepsinogen is formed in zymogen granules in the

cytoplasm of chief cells. Pepsinogen is converted into pepsin by some catalytic enzyme in acid medium at a pH below 6. The acid medium is provided by the hydrochloric acid secreted from parietal cells. HCl removes some of the amino acids from pepsinogen and coverts it to pepsin. Pepsin catalyzes the production of more pepsin (autocatalytic effect), as well as partially digesting dietary protein (fig. 8).

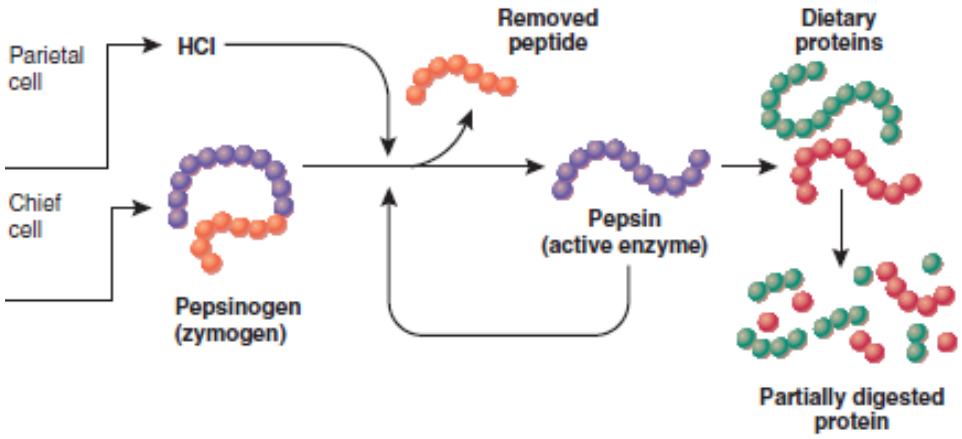


Fig. 8. The Production and Action of Pepsin.

Gastric Lipase is a weak lipolytic enzyme when compared to pancreatic lipase. Gastric lipase is inactive at a pH below 2.5 and it becomes active only when the pH is between 4 and 5. The products of lipid digestion by gastric lipase are fatty acids and glycerols.

Gelatinase acts on gelatin, ***urase*** acts on urea and produces ammonia.

2. Hemopoietic function: the intrinsic factor present in gastric juice plays an important role in erythropoiesis. This is necessary for absorption of the extrinsic factor (vitamin B_{12}) from gastrointestinal tract into the blood. Absence of intrinsic factor in gastric juice causes deficiency of vitamin B_{12}. And, the deficiency of vitamin B_{12} leads to pernicious anemia.

3. Protective function. The mucus lubricates the gastric mucosa and protects it from irritation or mechanical injury by virtue of its high viscosity. It also prevents the digestive action of pepsin on the wall of the stomach particularly gastric mucosa. Because of alkaline nature and its acid combining power, mucus protects the gastric mucosa from hydrochloric acid of gastric juice.

4. Function of hydrochloric acid:

- It activates pepsinogen into pepsin

- It has bacteriolytic action. It kills some of the bacteria entering the stomach along with food substances

- It causes acidity of the chyme. When the acid chyme leaves stomach and enters intestine, the acidity of the chyme causes release of hormones-secretin and cholecystokinin. These hormones, in turn stimulate the release of other digestive juices into intestine

- It provides acid medium for the action of enzymes.

Mechanism of secretion of gastric juice

Secretion of pepsinogen: pepsinogen is synthesized from amino acids. The synthesis occurs in ribosomes attached to endoplasmic reticulum in chief cells. The pepsinogen molecules are packed into zymogen granules by Golgi apparatus. When zymogen granule is secreted into stomach from chief cells, the granule is dissolved and pepsinogen is released into gastric juice. Pepsinogen is activated into pepsin by hydrochloric acid.

The mechanism of HCl production is depicted in fig. 9. An **H^+/K^+-ATPase** in the apical (luminal) cell membrane of the parietal cell actively pumps H^+ out of the cell in exchange for K^+ entering the cell. The H^+/K^+-ATPase is inhibited by omeprazole. Although the secreted H^+ is often depicted as being derived from carbonic acid (see Fig. 9), the source of H^+ is probably mostly from the dissociation of H_2O. Carbonic acid (H_2CO_3) is formed from carbon dioxide (CO_2) and H_2O in a reaction catalyzed by carbonic anhydrase. The CO_2 is provided by metabolic sources inside the cell and from the blood. The H^+/K^+-ATPase recycles K^+ ions back into the cell in exchange for H^+ ions. The basolateral cell membrane has an electroneutral Cl^-/HCO^{3-} exchanger that balances the entry of Cl^- into the cell with an equal amount of HCO^{3-} entering the bloodstream. The Cl^- inside the cell then leaks into the lumen through Cl^- channels, down an electrochemical gradient. Consequently, HCl is secreted into the lumen. The

osmotic gradient created by the HCl concentration in the gland lumen drives water passively into the lumen, thereby, maintaining the isoosmolality of the gastric secretion.

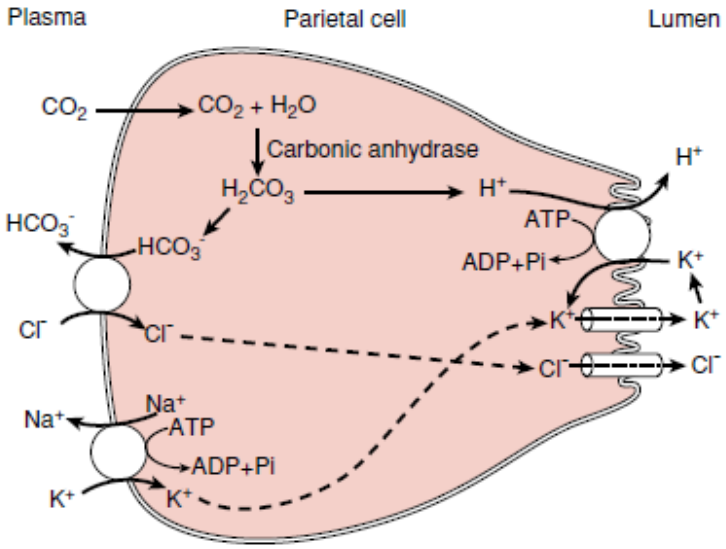


Fig.9. The mechanism of HCl production

Phases of gastric secretion

Secretion of gastric juice occurs when the food is taken in the mouth. Neural and hormonal mechanisms are involved in gastric secretion, which occurs in three phases (Fig. 10): cephalic phase, gastric phase and intestinal phase. In human beings, a fourth phase called interdigestive phase exists, i.e. secretion of small amount of gastric juice in between meals. Thus, the gastric secretion tends to be continuous.

1. Cephalic Phase

This is solely under nervous control. While taking food, the secretion of gastric juice starts even before food enters the stomach. The impulses are sent from head and so this phase is called cephalic phase. The gastric juice secreted in this phase is called appetite juice. This occurs as conditioned and unconditioned reflex. In both, pepsinogen and hydrochloric acid are secreted.

Unconditioned Reflex: this causes gastric secretion when food is placed in the mouth. Afferent impulses arise from taste buds and other receptors in the mouth and reach the appetite center in amygdala and hypothalamus. From here, the efferent impulses pass through dorsal nucleus of vagus and vagal fibers to the wall of the stomach. The gastric secretion occurs by the release of acetylcholine.

Conditioned Reflex: in this, the sight, smell, hearing or thought of food causes gastric secretion. The impulses arising from cerebral cortex reach stomach via vagus.

2. Gastric Phase

This phase is under both nervous and hormonal control. When the food enters the stomach, secretion of gastric juice increases which is rich in pepsinogen and hydrochloric acid mechanisms involved in this phase of gastric secretion are:

-Local myenteric reflex - nervous mechanism

-Vagovagal reflex - nervous mechanism and

-Gastrin - hormonal mechanism

The stimuli, which activate these mechanisms, are the distention of stomach, mechanical stimulation of gastric mucosa by food and, the chemical stimulation by the contents of food.

Local Myenteric Reflex: when food enters the stomach, the food particles stimulate the local nerve plexus in the wall of the stomach. These nerves, in turn activate the glands of the stomach, and, a large quantity of gastric juice is secreted.

Vagovagal Reflex: presence of food in stomach stimulates the sensory nerve endings. Now, the sensory impulses pass to the brainstem via sensory fibers of vagus. The efferent impulses pass through the motor fibers of vagus back to stomach and cause secretion. As both afferent and efferent impulses pass through vagus, this is called vagovagal reflex.

Gastrin Mechanism: gastrin is one of the gastrointestinal hormones. It is secreted by the G cells present in pyloric glands of stomach. Small amount is also secreted in mucosa of upper small intestine. Gastrin is a polypeptide containing G14, G17 or G34 amino acids. Gastrin is released when food enters stomach. The mechanism involved may be the local nervous reflex or vagovagal reflex. The neurotransmitter called gastrin releasing peptide is released at vagal nerve ending. This acts on the G cells and causes release of the hormone.

Actions of Gastrin

- It stimulates the secretion of pepsinogen and hydrochloric acid by the gastric glands
- It increases the motility of stomach
- It promotes growth of gastric mucosa
- It causes secretion of pancreatic juice, which is rich in enzymes
- It also stimulates the production of hormones by pancreas.

3. Intestinal Phase. When the chyme enters the intestine from stomach, initially the secretion of gastric juice is increased and later it is inhibited. This is due to enterogastrone and some other hormonal substances like gastric inhibitory peptide and vasoactive intestinal polypeptide secreted in small intestine.

- e*nterogastrone:* is a gastrointestinal hormone secreted in the mucosa of duodenum, when acid chyme enters from stomach. Enterogastrone inhibits gastric secretion and also gastric motility. This is the major hormone involved in intestinal phase.

- *gastric inhibitory peptide (GIP):* it is secreted in deodenum and in jejunum. This is secreted, when chyme containing glucose and fat enters the duodenum. GIP inhibits the secretion of gastric juice and the motility of stomach. It also stimulates the islets of Langherhans in pancreas to release insulin.

- *Vasoactive intestinal polypeptide (VIP):* this polypeptide is also secreted in intestine. This causes inhibition of secretion of hydrochloric acid in gastric juice. It also causes peripheral vasodilatation. The VIP stimulates the secretion of succus entericus with more amounts of electrolytes and water in the small intestine.

- apart from these hormones, secretin, cholecys-tokinin and somatostatin secreted from intestine are also responsible for inhibition of gastric secretion.

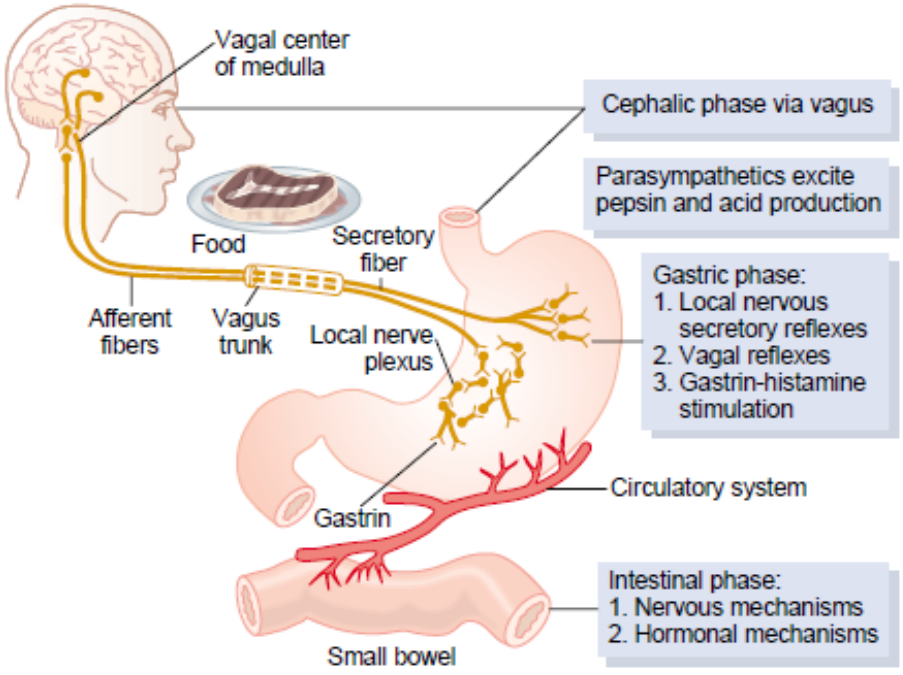


Fig. 10. Phases of gastric secretion

Digestion in the small intestine. Role of pancreas

The small intestine receives not only chyme from the stomach but also secretions from the liver and pancreas, which enter the digestive tract near the junction of the stomach and small intestine. These secretions are so important to the digestive processes of the small intestine that it is necessary to understand them before continuing with intestinal physiology.

The human pancreas is located in close apposition to the duodenum. It performs both endocrine and exocrine functions, but here we discuss only its exocrine function. The exocrine pancreas is composed of numerous small, sac-like dilatations called acini composed of a single layer of pyramidal **acinar cells** (Fig. 11). These cells are actively involved in the production of enzymes. Their cytoplasm is filled with an elaborate system of ER and Golgi apparatus. Zymogen granules are observed in the apical region of acinar cells. A few **centroacinar cells** line the lumen of the acinus. In contrast to acinar cells, these cells lack an elaborate ER and Golgi apparatus. Their major function seems to be modification of the electrolyte composition of the pancreatic secretion.

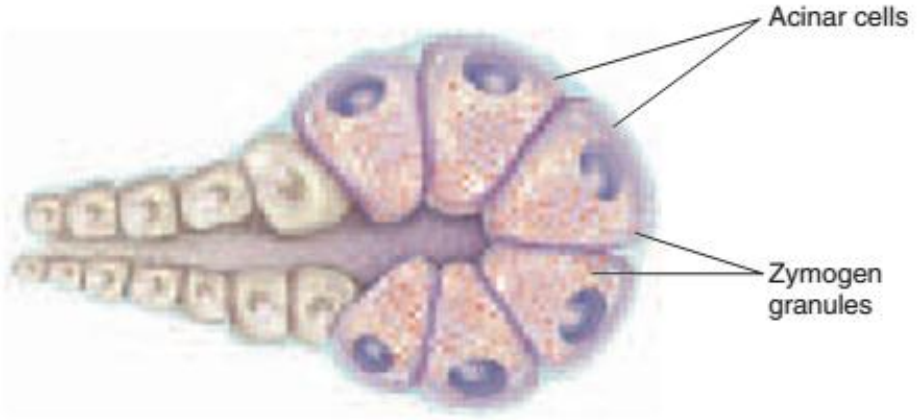


Fig. 11. Structure of pancreatic acinus.

The acini empty their secretions into intercalated ducts, which join to form intralobular and then interlobular ducts. The interlobular ducts empty into two pancreatic ducts: a major duct, the duct of Wirsung, and a minor duct, the duct of

Santorini. The duct of Santorini enters the duodenum more proximally than the duct of Wirsung. The pancreatic digestive enzymes are secreted by pancreatic acini, and large volumes of sodium bicarbonate solution are secreted by the small ductules and larger ducts leading from the acini. The combined product of enzymes and sodium bicarbonate then flows through a long pancreatic duct of Wirsung, which enters the duodenum usually together with the common bile duct. A ring of smooth muscle, the **sphincter of Oddi**, surrounds the opening of these ducts in the duodenum. The sphincter of Oddi not only regulates the flow of bile and pancreatic juice into the duodenum but also prevents the reflux of intestinal contents into the pancreatic ducts (fig. 12).

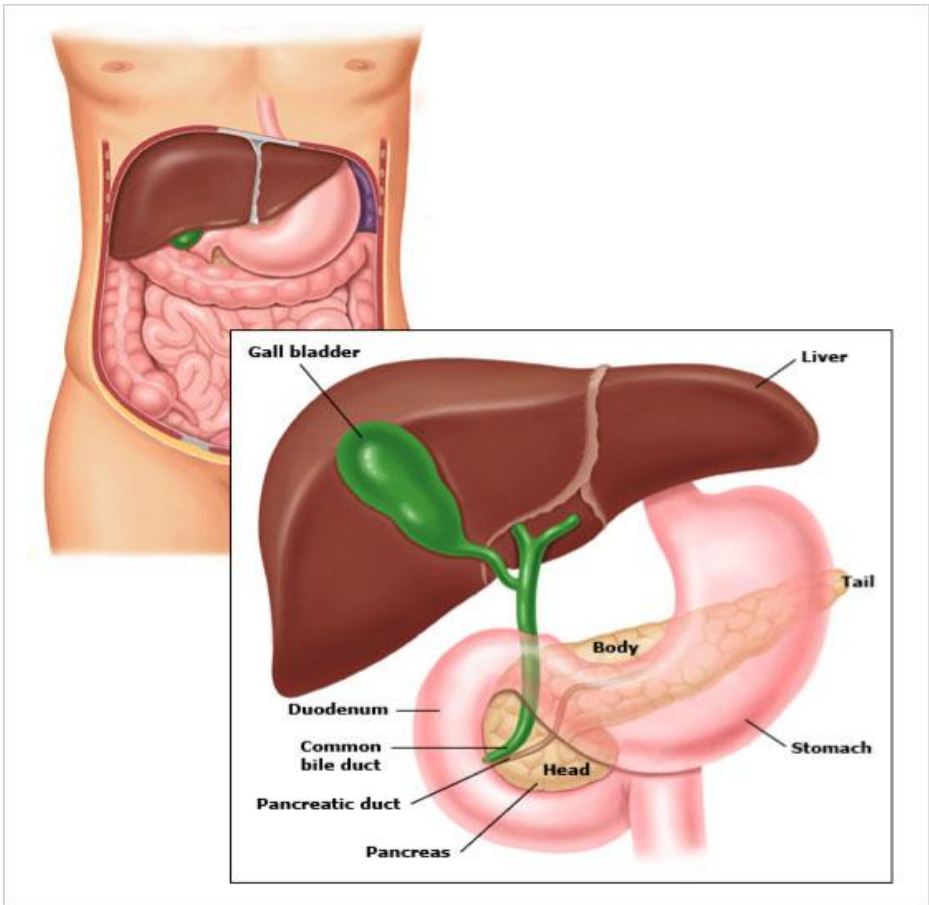


Fig.12. Anatomy of the pancreas

Properties and composition of pancreatic juice

Pancreatic juice is an alkaline with pH of 8 to 8.3, volume is 500 to 800 ml/day. Pancreatic juice contains 99.5% of water and 0.5% of solids. The solids are

the organic and inorganic substances. The organic substances are enzymes and other organic substances.

Enzymes of Pancreatic Juice

Proteolytic Enzymes

1. Trypsin
2. Chymotrypsin
3. Carboxypeptidase A
4. Carboxypeptidase B
5. Nuclease
6. Elastase
7. Collagenase

Lipolytic Enzymes

1. Pancreatic lipase
2. Cholesterol ester hydrolase
3. Phospholipase A
4. Phospholipase B

Amylolytic Enzyme: pancreatic amylase

Inorganic Substances Present in Pancreatic Juice: sodium, calcium, potassium, magnesium, bicarbonate, chloride, sulfate and phosphate. The bicarbonate content is very high in pancreatic juice. It is about 110 to 150 mEq/ L against the concentration of 24 mEq/L in plasma. This high concentration of bicarbonate is responsible for the alkalinity of pancreatic juice.

Functions of pancreatic juice

Pancreatic juice has digestive functions and the neutralizing action.

Digestive functions of pancreatic juice

Pancreatic juice plays an important role in the digestion of proteins and lipids. It also digests the carbohydrates.

Digestion of Proteins

The major proteolytic enzymes of pancreatic juice are trypsin and chymotrypsin. Other proteolytic enzymes are carboxypeptidases, nuclease, elastase and collagenase.

1. Trypsin is secreted as inactive trypsinogen. Trypsinogen is converted into trypsin by the enzyme enterokinase. Enterokinase is also called enteropeptidase. It is secreted by the brush bordered cells of duodenal mucus membrane. Once formed, trypsin itself activates trypsinogen by means of autocatalytic action.

Actions of trypsin (fig.13):

- digestive action: trypsin is the most powerful protein splitting enzyme. It is an **endopeptidase** because, it breaks the interior bonds of the protein molecules. By means of hydrolysis, it converts proteins into proteoses and polypeptides.

- at a pH of 8 to 9, trypsin curdles the milk.

- it accelerates blood clotting.

- activates other enzymes of pancreatic juice. It converts: chymotrypsinogen into chymotrypsin, procarboxypeptidases into carboxypeptidases, proelastase into elastase, procolipase into colipase. Trypsin also activates collagenase, phospholipase A and B.

- autocatalytic action. Conversion of trypsinogen into trypsin by trypsin itself is called autocatalytic action.

2. Chymotrypsin

Chymotrypsin is secreted as inactive chymotrypsinogen. Chymotrypsinogen is activated into chymotrypsin by trypsin. Chymotrypsin is a polypeptide with 246 amino acids and a molecular weight of 25,700.

Actions of chymotrypsin: chymotrypsin is also a proteolytic enzyme. Its actions are:

- digestive action on proteins: this is also an endopeptidase. It hydrolyses the proteins into polypeptides.

- digestion of milk: digests casein faster than trypsin. The combination of both enzymes causes more rapid digestion of milk. Chymotrypsin does not affect blood clotting.

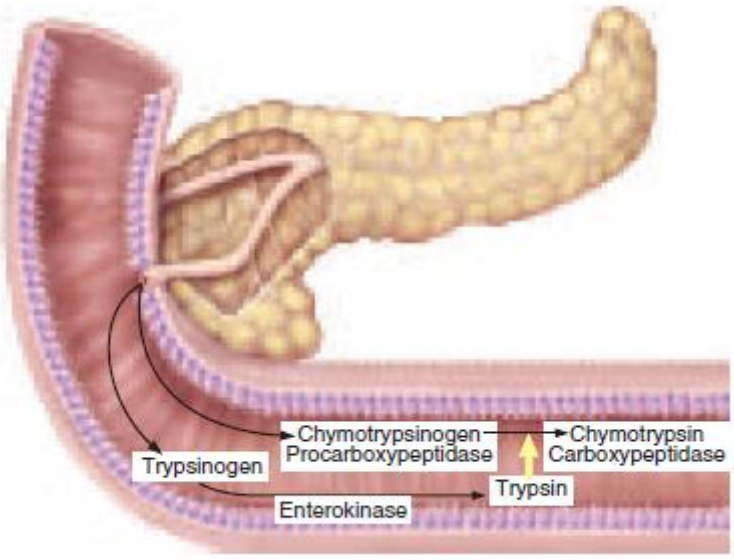


Fig. 13. Trypsin and its action

3. Carboxypeptidases

The two carboxypeptidases are carboxypeptidase A and carboxypeptidase B. Procarboxypeptidase A is the precursor of carboxypeptidase A. Procarboxypeptidase B is the precursor for carboxypeptidase B. The procarboxypeptidases are activated into carboxypeptidases by trypsin.

Actions of carboxypeptidases: they break the terminal bond of protein molecules. Therefore, these enzymes are called **exopeptidases.** The exopeptidases act on polypeptides and other proteins and convert them into amino acids. Carboxypeptidase A splits the proteins into amino acids having **aromatic or aliphatic side chains.** Carboxypeptidase B converts the proteins into amino acids having **basic side chains.**

4. Nucleases

The nucleases present in pancreatic juice are ribonuclease and deoxyribonuclease, which are responsible for the digestion of nucleic acids. These enzymes convert the ribonucleic acid and deoxyribonucleic acid into mononucleotides.

5. Elastase

Proelastase is activated into elastase by trypsin. Elastase is an important enzyme, which digests the elastic fibers.

6. Collagenase

This enzyme is also activated by trypsin. Collagenase causes digestion of collagen.

Digestion of Lipids

The lipolytic enzymes present in pancreatic juice are pancreatic lipase, phospholipase A and phospholipase B.

1. Pancreatic Lipase

Pancreatic lipase is a powerful lipolytic enzyme. It hydrolyses the natural fats such as triglycerides. It converts triglycerides into monoglycerides and fatty acids. The activity of pancreatic lipase is accelerated in the presence of bile. The optimum pH required for activity of this enzyme is 7 to 9. Digestion of fat by pancreatic lipase requires two more factors namely bile salts and colipase. Bile salts are responsible for the emulsification of fat prior to their digestion. Colipase is a coenzyme necessary for the pancreatic lipase to hydrolyze the dietary lipids. Procolipase is activated into colipase by trypsin.

2. Cholesterol Ester Hydrolase

Cholesterol ester hydrolase or cholesterol esterase hydrolyses cholesterol ester into free cholesterol and fatty acid.

3. Phospholipase A

This is activated by trypsin. Phospholipase A acts on the phospholipids and convert them into lysophospholipids. It converts lecithin into lysolecithin and cephalin into lysocephalin.

4. Phospholipase B

Phospholipase B is also activated by trypsin. This enzyme acts on lysophospholipids, i.e. lysolecithin and lysocephalin and converts them into phosphoryl choline and free fatty acids.

Digestion of Carbohydrates

Pancreatic amylase is the only amylolytic enzyme present in pancreatic juice. Its action on carbohydrates is like that of salivary amylase. It converts starch into maltose.

Mechanism of pancreatic secretion

Secretion of pancreatic enzymes. The pancreatic enzymes are synthesized in ribosomes, which are attached to the endoplasmic reticulum of acinar cells in pancreas. The raw materials for the synthesis of pancreatic enzymes are the amino acids. The amino acids are derived from the blood. These enzymes synthesized in the ribosomes are packed into different zymogen granules by Golgi apparatus and stored in cytoplasm. When stimulated, the acinar cells release the zymogen granules into the pancreatic duct. From the granules, the enzymes are liberated into intestine where these enzymes are activated.

Secretion of Bicarbonate Ions

Although the enzymes of the pancreatic juice are secreted entirely by the acini of the pancreatic glands, the other two important components of pancreatic juice, bicarbonate ions and water, are secreted mainly by the epithelial cells of the ductules and ducts that lead from the acini. When the pancreas is stimulated to secrete copious quantities of pancreatic juice, the bicarbonate ion concentration can rise to as high as 145 mEq/L, a value about five times that of bicarbonate ions in the plasma. This provides a large quantity of alkali in the pancreatic juice that serves to neutralize the hydrochloric acid emptied into the duodenum from the stomach.

The basic steps in the cellular mechanism for secreting sodium bicarbonate solution into the pancreatic ductules and ducts are shown in Figure 14.They are the following:

1. Carbon dioxide diffuses to the interior of the cell from the blood and, under the influence of carbonic anhydrase, combines with water to form carbonic acid (H_2CO_3). The carbonic acid in turn dissociates into bicarbonate ions and hydrogen ions (HCO^{3-} and H^+). Then the bicarbonate ions are actively transported in association with sodium ions (Na^+) through the *luminal border* of the cell into the lumen of the duct.

2. The hydrogen ions formed by dissociation of carbonic acid inside the cell are *exchanged for sodium ions through the blood border* of the cell by a secondary active transport process. This supplies the sodium ions (Na^+) that are transported through the *luminal border* into the pancreatic duct lumen to provide electrical neutrality for the secreted bicarbonate ions.

3. The overall movement of sodium and bicarbonate ions from the blood into the duct lumen creates an osmotic pressure gradient that causes osmosis of water also into the pancreatic duct, thus forming an almost completely isosmotic bicarbonate solution.

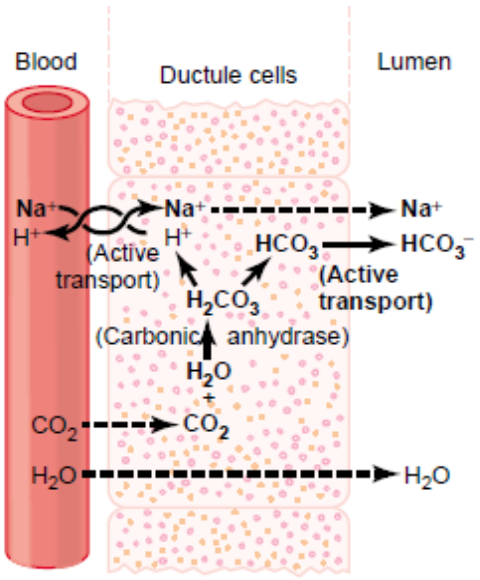


Fig. 14. Secretion of isosmotic sodium bicarbonate solution by the pancreatic ductules and ducts.

Neutralizing action of pancreatic juice. When acid chyme enters intestine from stomach, immediately pancreatic juice with more bicarbonate is secreted and released into intestine. Due to the presence of large quantity of bicarbonate ions, the pancreatic juice is highly alkaline. Because of this, pancreatic juice neutralizes acidity of chyme in the intestine. This is an important function, because, the acid chyme can destroy the intestinal mucus membrane. Thus, the pancreatic juice protects the intestine from destructive action of acid chyme.

Regulation of Pancreatic Secretion

Basic Stimuli That Cause Pancreatic Secretion. Three basic stimuli are important in causing pancreatic secretion:

1. *Acetylcholine*, which is released from the parasympathetic vagus nerve endings and from other cholinergic nerves in the enteric nervous system.

2. *Cholecystokinin*, which is secreted by the duodenal and upper jejunal mucosa when food enters the small intestine.

3. *Secretin*, which is also secreted by the duodenal and jejunal mucosa when highly acid food enters the small intestine.

The first two of these stimuli, acetylcholine and cholecystokinin, stimulate the acinar cells of the pancreas, causing production of large quantities of pancreatic digestive enzymes but relatively small quantities of water and electrolytes to go with the enzymes. Without the water, most of the enzymes remain temporarily stored in the acini and ducts until more fluid secretion comes along to wash them into the duodenum. Secretin, in contrast to the first two basic stimuli, stimulates secretion of large quantities of water solution of sodium bicarbonate by the pancreatic ductal epithelium.

Phases of Pancreatic Secretion. Pancreatic secretion occurs in three phases, the same as for gastric secretion: the *cephalic phase*, the *gastric phase*, and the *intestinal phase*. Their characteristics are as follows.

Cephalic phase. During the cephalic phase of pancreatic secretion, the same nervous signals from the brain that cause secretion in the stomach also cause

acetylcholine release by the vagal nerve endings in the pancreas. This causes moderate amounts of enzymes to be secreted into the pancreatic acini, accounting for about 20 per cent of the total secretion of pancreatic enzymes after a meal. But little of the secretion flows immediately through the pancreatic ducts into the intestine because only small amounts of water and electrolytes are secreted along with the enzymes.

Gastric phase. When food enters stomach, the nervous mechanism may continue. However, the important factor in this phase is the hormonal mechanism. The hormone involved is gastrin. Gastrin is the gastrointestinal hormone secreted from stomach when food enters the stomach. The gastrin is transported by blood, and while reaching the pancreas, it causes release of the pancreatic juice. During the gastric phase, the nervous stimulation of enzyme secretion continues, accounting for another 5 to 10 per cent of pancreatic enzymes secreted after a meal. But, again, only small amounts reach the duodenum because of continued lack of significant fluid secretion.

Intestinal Phase (fig.15)**.** After chyme leaves the stomach and enters the small intestine, pancreatic secretion becomes copious, mainly in response to the hormone ***secretin*****. Secretin** stimulates secretion of copious quantities of bicarbonate ions—neutralization of acidic stomach chyme. Secretin is a polypeptide, containing 27 amino acids (molecular weight about 3400), present in an inactive form, prosecretin, in so-called S cells in the mucosa of the duodenum and jejunum. When acid chyme with pH less than 4.5 to 5.0 enters the duodenum from the stomach, it causes duodenal mucosal release and activation of secretin, which is then absorbed into the blood. The one truly potent constituent of chyme that causes this secretin release is the hydrochloric acid from the stomach.

Secretin in turn causes the pancreas to secrete large quantities of fluid containing a high concentration of bicarbonate ion (up to 145 mEq/L) but a low concentration of chloride ion. The secretin mechanism is especially important for two reasons: First, secretin begins to be released from the mucosa of the small intestine when the pH of the duodenal contents falls below 4.5 to 5.0, and its

release increases greatly as the pH falls to 3.0. This immediately causes copious secretion of pancreatic juice containing abundant amounts of sodium bicarbonate. The net result is then the following reaction in the duodenum:

$$HCl + NaHCO_3 \rightarrow NaCl + H_2CO_3$$

Then the carbonic acid immediately dissociates into carbon dioxide and water. The carbon dioxide is absorbed into the blood and expired through the lungs, thus leaving a neutral solution of sodium chloride in the duodenum. In this way, the acid contents emptied into the duodenum from the stomach become neutralized, so that further peptic digestive activity by the gastric juices in the duodenum is immediately blocked. Because the mucosa of the small intestine cannot withstand the digestive action of acid gastric juice, this is an essential protective mechanism to prevent development of duodenal ulcers.

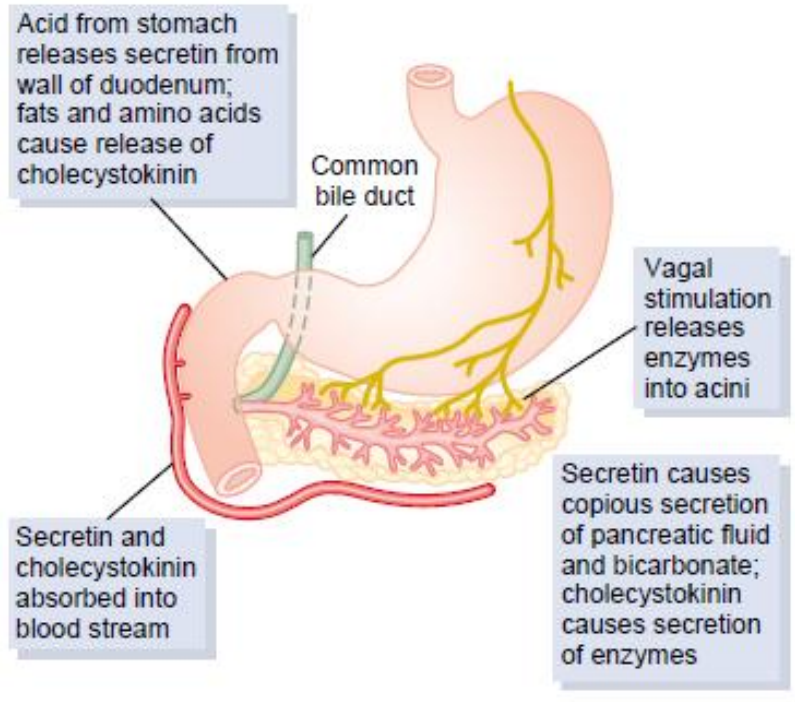


Fig. 15. Regulation of pancreatic secretion

Bicarbonate ion secretion by the pancreas provides an appropriate pH for action of the pancreatic digestive enzymes, which function optimally in a slightly

alkaline or neutral medium, at a pH of 7.0 to 8.0. Fortunately, the pH of the sodium bicarbonate secretion averages 8.0.

Cholecystokinin—its contribution to control of digestive enzyme secretion by the pancreas. The presence of food in the upper small intestine also causes a second hormone, *cholecystokinin*, a polypeptide containing 33 amino acids, to be released from yet another group of cells, the *I cells*, in the mucosa of the duodenum and upper jejunum. This release of cholecystokinin results especially from the presence of *proteoses* and *peptones* (products of partial protein digestion) and *long-chain fatty acids* in the chyme coming from the stomach.

Cholecystokinin, like secretin, passes by way of the blood to the pancreas but instead of causing sodium bicarbonate secretion causes mainly secretion of still much more pancreatic digestive enzymes by the acinar cells. This effect is similar to that caused by vagal stimulation but even more pronounced, accounting for 70 to 80 per cent of the total secretion of the pancreatic digestive enzymes after a meal.

Functions of liver and biliary tree

Liver

Liver is both secretory and excretory organ. It is the largest gland in the body. It weighs about 1.5 kg in man. It is located in the upper and right side of the abdominal cavity immediately beneath diaphragm.

Liver is made up of liver cells called hepatocytes and a system of blood vessels. Liver consists of many lobes. Each lobe consists of large number of lobules. Each lobule is a honey comb like structure. The hepatocytes are arranged in different plates. Each plate is one cell thick with a central vein. In between the cells, are bile canaliculi. Each lobule is surrounded by portal triads. Each portal triad consists of a branch of hepatic artery, a branch of portal vein and a tributary of bile duct.

In between the plates, the sinusoids or blood spaces are present. The sinusoid receives blood from a branch of portal vein and a branch of hepatic artery of the portal triad. Sinusoids are lined by endothelial cells. Few macrophage cells called Kupffer's cells are also found in between the endothelial cells.

Functions of liver:

1. **metabolic function** (it is the organ where maximum metabolic actions are carried out);
2. **storage function** (many substances like glycogen, amino acids, iron, folic acid and vitamins A, B_{12}, and D are stored in liver);
3. **synthetic function** (liver produces glucose by gluconeogenesis. It synthesizes all the plasma proteins. It synthesizes other proteins (except immunoglobulins) such as clotting factors and complement factors, steroids, hormone binding proteins, somatomedin and heparin);
4. **secretion of bile**
5. **excretory function** (liver excretes cholesterol, bile pigments, heavy metals (like lead, arsenic and bismuth), toxins, bacteria like typhoid and virus (like that of yellow fever).
6. **heat production**

7. hemopoietic function (in fetus the blood cells are produced in liver. It stores vitamin B_{12} necessary for erythropoiesis and iron necessary for synthesis of hemoglobin in red blood cells. Liver produces thrombopoietin that promotes production of thrombocytes);

8. hemolytic function (the senile red blood cells after the life span of 120 days are destroyed by reticuloendothelial cells of the liver. The Kupffer's cells are the reticuloendothelial cells in liver.

9. inactivation of hormones and drugs;

10. defensive and detoxification functions (the foreign bodies like bacteria or antigens are swallowed and digested by reticuloendothelial cells of liver by means of phagocytosis, liver cells are involved in removal of toxic property of various harmful substances. The removal of toxic property of the harmful agent is known as detoxification).

Physiologic Anatomy of Biliary Secretion

Bile is secreted in two stages by the liver:

(1) The initial portion is secreted by the principal functional cells of the liver, the hepatocytes; this initial secretion contains large amounts of bile acids, cholesterol, and other organic constituents. It is secreted into minute bile canaliculi that originate between the hepatic cells

(2) Next, the bile flows in the canaliculi toward the interlobular septa, where the canaliculi empty into terminal bile ducts and then into progressively larger ducts, finally reaching the hepatic duct and common bile duct. From these the bile either empties directly into the duodenum or is diverted for minutes up to several hours through the cystic duct into the gallbladder, shown in Fig. 15.

In its course through the bile ducts, a second portion of liver secretion is added to the initial bile. This additional secretion is a watery solution of sodium and bicarbonate ions secreted by secretory epithelial cells that line the ductules and ducts. This second secretion sometimes increases the total quantity of bile by as much as an additional 100 per cent. The second secretion is stimulated especially

by secretin, which causes release of additional quantities of bicarbonate ions to supplement the bicarbonate ions in pancreatic secretion (for neutralizing acid that empties into the duodenum from the stomach).

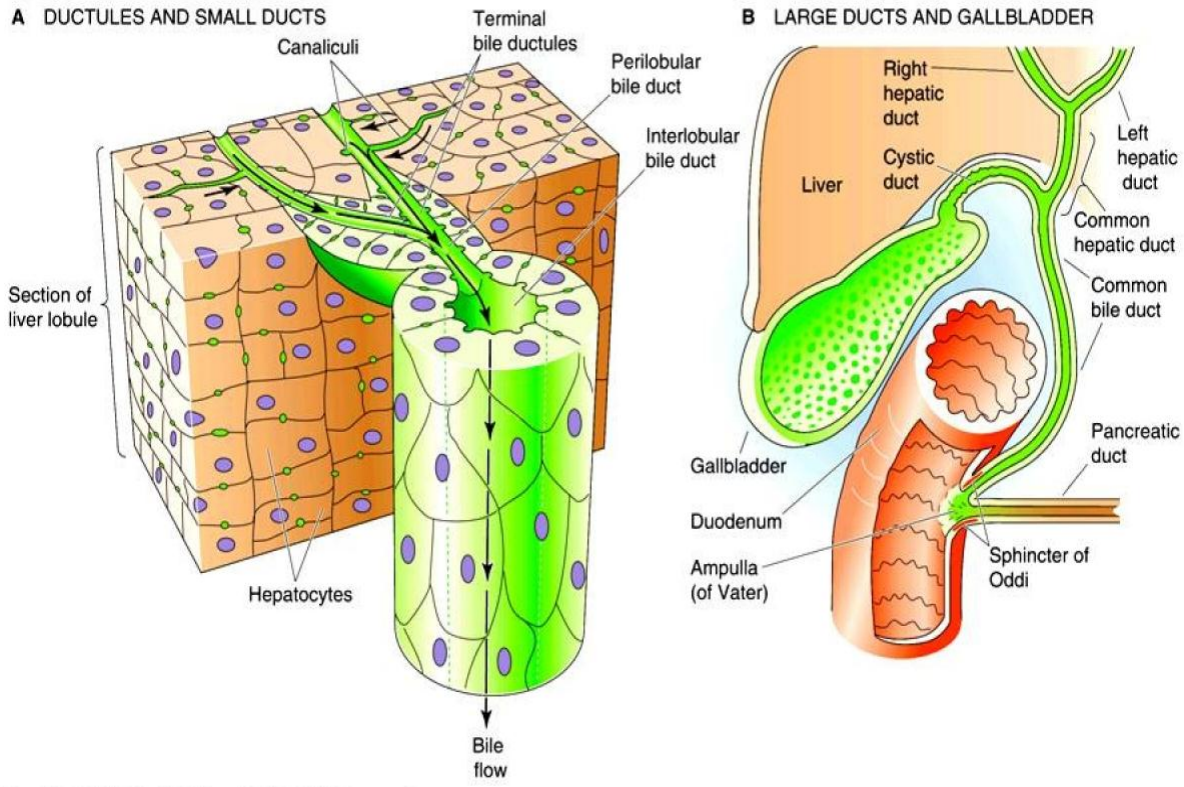


Fig. 15. Bile is secreted by the liver, stored in the gallbladder and ejected in the small intestine

Bile

Composition of Bile. By far the most abundant substances secreted in the bile are bile salts, which account for about one half of the total solutes also in the bile. Also secreted or excreted in large concentrations are bilirubin, cholesterol, lecithin, and the usual electrolytes of plasma.

In the concentrating process in the gallbladder, water and large portions of the electrolytes (except calcium ions) are reabsorbed by the gallbladder mucosa; essentially all other constituents, especially the bile salts and the lipid substances cholesterol and lecithin, are not reabsorbed and, therefore, become highly concentrated in the gallbladder bile.

Bile serves two important functions:

First, bile plays an important role in fat digestion and absorption, not because of any enzymes in the bile that cause fat digestion, but because bile acids in the bile do two things: (1) they help to emulsify the large fat particles of the food into many minute particles, the surface of which can then be attacked by lipase enzymes secreted in pancreatic juice, and (2) they aid in absorption of the digested fat end products through the intestinal mucosal membrane.

Second, bile serves as a means for excretion of several important waste products from the blood. These include especially bilirubin, an end product of hemoglobin destruction, and excesses of cholesterol.

Function of Bile Salts in Fat Digestion and Absorption

The liver cells synthesize about 6 grams of bile salts daily. The precursor of the bile salts is cholesterol, which is either present in the diet or synthesized in the liver cells during the course of fat metabolism. The cholesterol is first converted to **cholic acid** or **chenodeoxycholic acid** in about equal quantities. These acids in turn combine principally with glycine and to a lesser extent with taurine to form **glyco-and tauroconjugated bile acids.** The salts of these acids, mainly sodium salts, are then secreted in the bile.

The **bile salts have two important actions** in the intestinal tract:

1. They have a detergent action on the fat particles in the food. This decreases the surface tension of the particles and allows agitation in the intestinal tract to break the fat globules into minute sizes. This is called the **emulsifying** or detergent function of bile salts.

2. Bile salts help in the absorption of (1) fatty acids, (2) monoglycerides, (3) cholesterol, and (4) other lipids from the intestinal tract. They do this by forming very small physical complexes with these lipids; the complexes are called **micelles,** and they are semi-soluble in the chyme because of the electrical charges of the bile salts. The intestinal lipids are "ferried" in this form to the intestinal mucosa, where they are then absorbed into the blood. Without the presence of bile salts in the intestinal tract, up to 40 per cent of the ingested fats are lost into the feces, and the person often develops a metabolic deficit because of this nutrient loss.

3. Choliretic action: bile salts stimulate the secretion of bile from liver.

4. Cholagogue action: cholagogue is an agent, which increases the release of bile from gallbladder into the intestine. Bile salts act as cholagogues indirectly by stimulating the secretion of hormone CCK-PZ. This hormone causes contraction of gallbladder and release of bile.

5. Laxative is an agent which induces defecation. Bile salts show this action by stimulating peristaltic movements of the intestine.

6. Prevention of gallstone formation: Bile salts prevent the formation of gallstone by keeping the cholesterol and lecithin in solution. In the absence of bile salts, cholesterol precipitates along with lecithin and forms gallstone.

The Enterohepatic Circulation Recycles Bile Salts Between the Small Intestine and the Liver

The enterohepatic circulation of bile salts is the recycling of bile salts between the small intestine and the liver. The total amount of bile acids in the body, primary or secondary, conjugated or free, at any time is defined as the total bile acid pool. In healthy people, the bile acid pool ranges from 2 to 4g. The enterohepatic circulation of bile acids in this pool is physiologically extremely

important. By cycling several times during a meal, a relatively small bile acid pool can provide the body with sufficient amounts of bile salts to promote lipid absorption. In a light eater, the bile acid pool may circulate 3 to 5 times a day; in a heavy eater, it may circulate 14 to 16 times a day. The intestine is normally extremely efficient in absorbing the bile salts by carriers located in the distal ileum. Inflammation of the ileum can lead to their malabsorption and result in the loss of large quantities of bile salts in the feces. Depending on the severity of illness, malabsorption of fat may result.

Bile salts in the intestinal lumen are absorbed via four pathways (Fig. 16). First, they are absorbed throughout the entire small intestine by passive diffusion, but only a small fraction of the total amount of bile salts is absorbed in this manner. Second, and most important, bile salts are absorbed in the terminal ileum by an active carrier-mediated process, an extremely efficient process in which usually less than 5% of the bile salts escape into the colon. Third, bacteria in the terminal ileum and colon deconjugate the bile salts to form bile acids, which are much more lipophilic than bile salts and, thus, can be absorbed passively. Fourth, these same bacteria are responsible for transforming the primary bile acids to secondary bile acids (deoxycholic and lithocholic acids) by dehydroxylation. Deoxycholic acid may be absorbed, but lithocholic acid is poorly absorbed.

Although bile salt and bile acid absorption is extremely efficient, some salts and acids are nonetheless lost with every cycle of the enterohepatic circulation. About 500 mg of bile acids are lost daily. They are replenished by the synthesis of new bile acids from cholesterol. The loss of bile acid in feces is, therefore, an efficient way to excrete cholesterol.

Absorbed bile salts are transported in the portal blood bound to albumin or high-density lipoproteins (HDLs). The uptake of bile salts by hepatocytes is extremely efficient. In just one pass through the liver, more than 80% of the bile salts in the portal blood is removed. Once taken up by hepatocytes, bile salts are secreted into bile. The uptake of bile salts is a primary determinant of bile salt secretion by the liver.

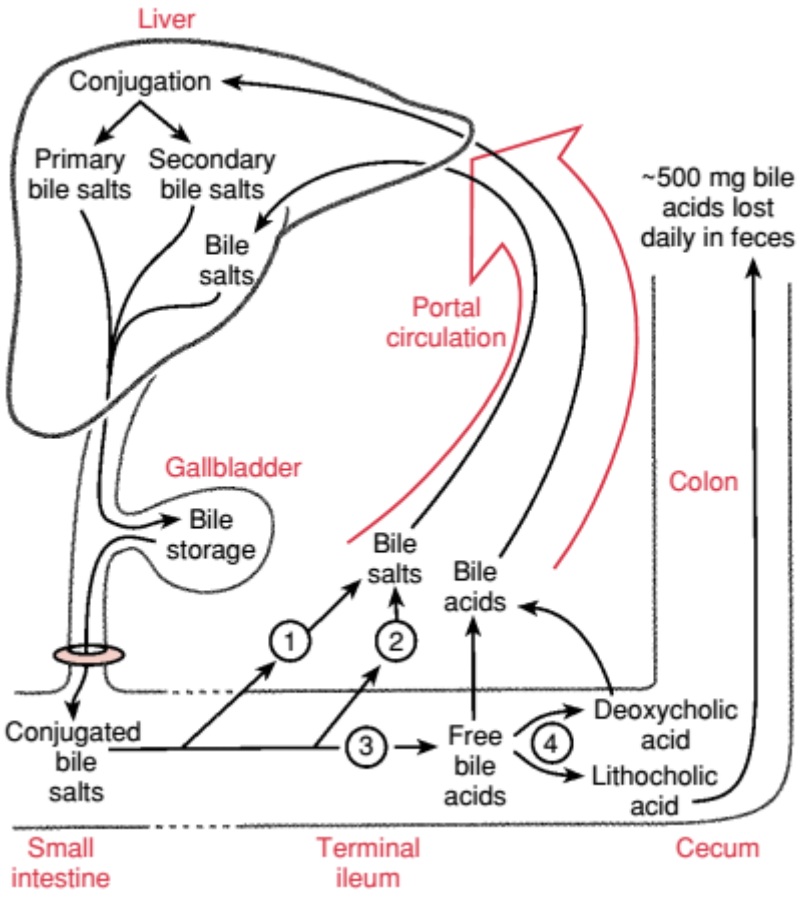


Fig. 16. The Enterohepatic Circulation of Bile Salts

The Liver Secretes Bile Pigments

The major pigment present in bile is the orange compound bilirubin, an end-product of hemoglobin degradation in the monocyte-macrophage system in the spleen, bone marrow, and liver (Fig. 17). Hemoglobin is first converted to biliverdin with the release of iron and globin. Biliverdin is then converted into bilirubin, which is transported in blood bound to albumin. The liver removes bilirubin from the circulation rapidly and conjugates it with glucuronic acid. The glucuronide is secreted into the bile canaliculi through an active carrier-mediated process.

In the small intestine, bilirubin glucuronide is poorly absorbed. In the colon, however, bacteria deconjugate it, and part of the bilirubin released is converted to the highly soluble, colorless compound called urobilinogen. Urobilinogen can be oxidized in the intestine to stercobilin or absorbed by the small intestine. It is

excreted in either urine or bile. Stercobilin is responsible for the brown color of the stool.

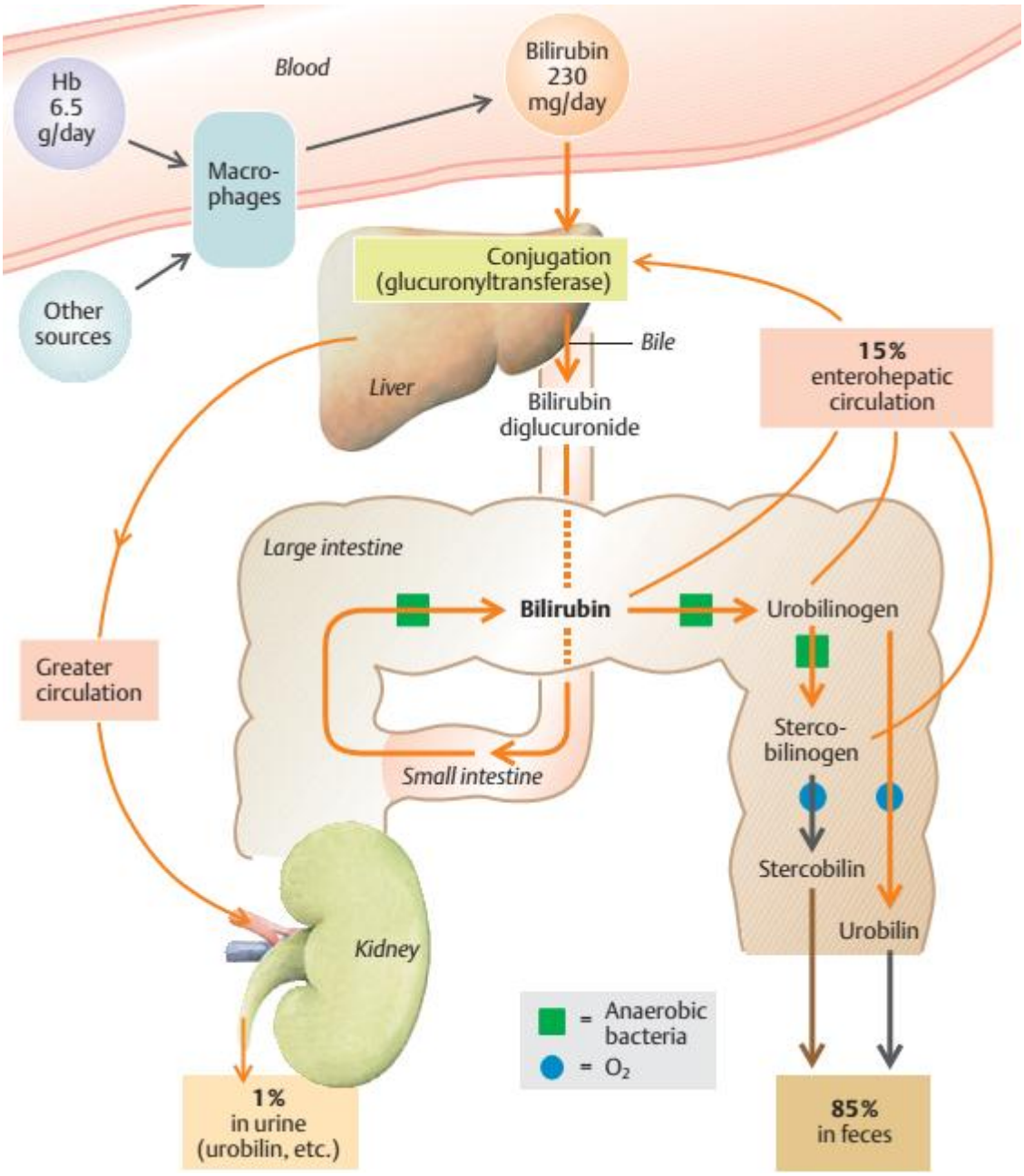


Fig. 17. Bilirubin metabolism and excretion

Storing and Concentrating Bile in the Gallbladder. Bile is secreted continually by the liver cells, but most of it is normally stored in the gallbladder until needed in the duodenum. The maximum volume that the gallbladder can hold is only 30 to 60 milliliters. Nevertheless, as much as 12 hours of bile secretion

(usually about 450 milliliters) can be stored in the gallbladder because water, sodium, chloride, and most other small electrolytes are continually absorbed through the gallbladder mucosa (fig. 18-1), concentrating the remaining bile constituents that contain the bile salts, cholesterol, lecithin, and bilirubin.

Most of this gallbladder absorption is caused by active transport of sodium through the gallbladder epithelium, and this is followed by secondary absorption of chloride ions, water, and most other diffusible constituents. Bile is normally concentrated in this way about 5-fold, but it can be concentrated up to a maximum of 20-fold.

Gallbladder contraction is triggered by CCK, which binds to CCKA receptors, and the neuronal plexus of the gallbladder wall, which is innervated by preganglionic parasympathetic fibers of the vagus nerve (fig. 18-2). Calcitonin gene-related peptide CGRP and substance P released by sensory fibers appear to stimulate the gallbladder musculature indirectly by increasing acetylcholine release. The sympathetic nervous system inhibits gallbladder contractions via α2 adrenoreceptors located on cholinergic fiber terminals. As cholagogues, fatty acids and products of protein digestion as well as egg yolk and $MgSO_4$ effectively stimulate CCK secretion.

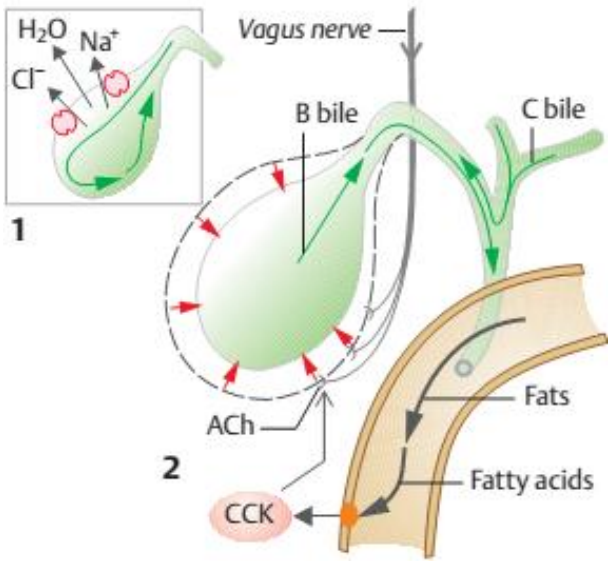


Fig. 18. Regulation of gallbladder emptying

Secretions of the Small Intestine

Secretion of Mucus by Brunner's Glands in the Duodenum

An extensive array of compound mucous glands, called Brunner's glands, is located in the wall of the first few centimeters of the duodenum, mainly between the pylorus of the stomach and the papilla of Vater where pancreatic secretion and bile empty into the duodenum. These glands secrete large amounts of alkaline mucus in response to (1) tactile or irritating stimuli on the duodenal mucosa; (2) vagal stimulation, which causes increased Brunner's glands secretion concurrently with increase in stomach secretion; and (3) gastrointestinal hormones, especially secretin.

The function of the mucus secreted by Brunner's glands is to protect the duodenal wall from digestion by the highly acid gastric juice emptying from the stomach. In addition, the mucus contains a large excess of bicarbonate ions, which add to the bicarbonate ions from pancreatic secretion and liver bile in neutralizing the hydrochloric acid entering the duodenum from the stomach.

Brunner's glands are inhibited by sympathetic stimulation; therefore, such stimulation in very excitable persons is likely to leave the duodenal bulb unprotected and is perhaps one of the factors that cause this area of the gastrointestinal tract to be the site of peptic ulcers in about 50 per cent of ulcer patients.

Secretion of Intestinal Digestive Juices by the Crypts of Lieberkühn

Located over the entire surface of the small intestineare small pits called crypts of Lieberkühn, one of which is illustrated in figure 19. These crypts lie between the intestinal villi. The surfaces of both the crypts and the villi are covered by an epithelium composed of two types of cells: (1) a moderate number of goblet cells, which secrete mucus that lubricates and protects the intestinal surfaces, and (2) a large number of enterocytes, which, in the crypts, secrete large quantities of water and electrolytes and, over the surfaces of adjacent villi, reabsorb the water and electrolytes along with end products of digestion.

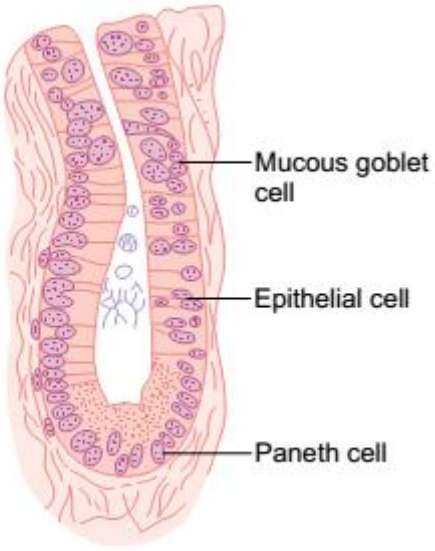


Fig. 19. A crypt of Lieberkühn

The intestinal secretions are formed by the enterocytes of the crypts at a rate of about 1800 ml/day. These secretions are almost pure extracellular fluid and have a slightly alkaline pH in the range of 7.5 to 8.0. The secretions also are rapidly reabsorbed by the villi. This flow of fluid from the crypts into the villi supplies a watery vehicle for absorption of substances from chyme when it comes in contact with the villi. Thus, the primary function of the small intestine is to absorb nutrients and their digestive products into the blood.

Mechanism of Secretion of the Watery Fluid. The exact mechanism that controls the marked secretion of watery fluid by the crypts of Lieberkühn is not known. It is believed to involve at least two active secretory processes: (1) active secretion of chloride ions into the crypts and (2) active secretion of bicarbonate ions. The secretion of both of these ions causes electrical drag as well of positively charged sodium ions through the membrane and into the secreted fluid. Finally, all these ions together cause osmotic movement of water.

Digestive Enzymes in the Small Intestinal Secretion. When secretions of the small intestine are collected without cellular debris, they have almost no enzymes. The enterocytes of the mucosa, especially those that cover the villi, do contain digestive enzymes that digest specific food substances while they are being

absorbed through the epithelium. These enzymes are the following: (1) several peptidases for splitting small peptides into amino acids, (2) four enzymes—sucrase, maltase, isomaltase, and lactase—for splitting disaccharides into monosaccharides, and (3) small amounts of intestinal lipase for splitting neutral fats into glycerol and fatty acids.

The epithelial cells deep in the crypts of Lieberkühn continually undergo mitosis, and new cells migrate along the basement membrane upward out of the crypts toward the tips of the villi, thus continually replacing the villus epithelium and also forming new digestive enzymes. As the villus cells age, they are finally shed into the intestinal secretions. The life cycle of an intestinal epithelial cell is about 5 days. This rapid growth of new cells also allows rapid repair of excoriations that occur in the mucosa.

Regulation of Small Intestine Secretion—Local Stimuli

By far the most important means for regulating small intestine secretion are local enteric nervous reflexes, especially reflexes initiated by tactile or irritative stimuli from the chyme in the intestines.

Secretions of the Large Intestine

Mucus Secretion. The mucosa of the large intestine, like that of the small intestine, has many crypts of Lieberkühn; however, unlike the small intestine, there are no villi. The epithelial cells contain almost no enzymes. Instead, they consist mainly of mucous cells that secrete only mucus. The great preponderance of secretion in the large intestine is mucus. This mucus contains moderate amounts of bicarbonate ions secreted by a few non–mucus-secreting epithelial cells. The rate of secretion of mucus is regulated principally by direct, tactile stimulation of the epithelial cells lining the large intestine and by local nervous reflexes to the mucous cells in the crypts of Lieberkühn.

Stimulation of the pelvic nerves from the spinal cord, which carry parasympathetic innervation to the distal one half to two thirds of the large intestine, also can cause marked increase in mucus secretion. This occurs along with increase in peristaltic motility of the colon.

During extreme parasympathetic stimulation, often caused by emotional disturbances, so much mucus can occasionally be secreted into the large intestine that the person has a bowel movement of ropy mucus as often as every 30 minutes; this mucus often contains little or no fecal material.

Mucus in the large intestine protects the intestinal wall against excoriation, but in addition, it provides an adherent medium for holding fecal matter together. Furthermore, it protects the intestinal wall from the great amount of bacterial activity that takes place inside the feces, and, finally, the mucus plus the alkalinity of the secretion (pH of 8.0 caused by large amounts of sodium bicarbonate) provides a barrier to keep acids formed in the feces from attacking the intestinal wall.

Digestion and Absorption in the Gastrointestinal Tract

Digestion and absorption of carbohydrates

The digestion and absorption of dietary carbohydrates takes place in the small intestine. These are extremely efficient processes, in that essentially all of the carbohydrates consumed are absorbed. Carbohydrates are an extremely important component of food intake, since they constitute about 45 to 50% of the typical Europian diet and provide the greatest and least expensive source of energy. Carbohydrates must be digested to monosaccharides before absorption.

The Diet Contains Both Digestible and Nondigestible Carbohydrates. Humans can digest most carbohydrates; those we cannot digest constitute the dietary fiber that forms roughage. Carbohydrate is present in food as monosaccharides, disaccharides, oligosaccharides, and polysaccharides. **The monosaccharides** are mainly hexoses (six-carbon sugars), and **glucose** is by far the most abundant of these. Glucose is obtained directly from the diet or from the digestion of disaccharides, oligosaccharides, or polysaccharides. The next most common monosaccharides are **galactose, fructose, and sorbitol.** Galactose is present in the diet only as milk lactose, a disaccharide composed of galactose and glucose. Fructose is present in abundance in fruit and honey and is usually present as disaccharides or polysaccharides. Sorbitol is derived from glucose and is almost as sweet as glucose, but sorbitol is absorbed much more slowly and, thus, maintains a high blood sugar level for a longer period when similar amounts are ingested. It has been used as a weight-reduction aid to delay the onset of hunger sensations.

The major disaccharides in the diet are **sucrose, lactose, and maltose.** Sucrose, present in sugar cane and honey, is composed of glucose and fructose. Lactose, the main sugar in milk, is composed of galactose and glucose. Maltose is composed of two glucose units.

The digestible **polysaccharides are starch, dextrins, and glycogen.** Starch, by far the most abundant carbohydrate in the human diet, is made of amylose and amylopectin. Amylose is composed of a straight chain of glucose units;

amylopectin is composed of branched glucose units. Dextrins, formed from heating (e.g., toasting bread) or the action of the enzyme amylase, are intermediate products of starch digestion. Glycogen is a highly branched polysaccharide that stores carbohydrates in the body. Normally, about 300 to 400 g of glycogen is stored in the liver and muscle, with more stored in muscle than in the liver. Muscle glycogen is used exclusively by muscle, and liver glycogen is used to provide blood glucose during fasting.

Dietary fiber is made of polysaccharides that are usually poorly digested by the enzymes in the small intestine. They have an extremely important physiological function in that they provide the "bulk" that facilitates intestinal motility and function. Many vegetables and fruits are rich in fibers, and their frequent ingestion greatly decreases intestinal transit time.

Carbohydrates Are Digested in Different Parts of the GI Tract

The digestion of carbohydrates starts when food is mixed with saliva during chewing. The enzyme salivary amylase acts on the α-1,4-glycosidic linkage of amylose and amylopectin of polysaccharides to release the disaccharide maltose and oligosaccharides maltotriose and α-limit dextrins (Fig. 20). Because salivary amylase works best at neutral pH, its digestive action terminates rapidly after the bolus mixes with acid in the stomach. However, if the food is thoroughly mixed with amylase during chewing, a substantial amount of complex carbohydrates is digested before this point. **Pancreatic amylase** continues the digestion of the remaining carbohydrates. However, the chyme must first be neutralized by pancreatic secretions, since pancreatic amylase works best at neutral pH. The products of pancreatic amylase digestion of polysaccharides are also maltose, maltotriose, and α-limit dextrins.

The digestion products of starch and glycogen, together with disaccharides (sucrose and lactose), are further digested by enzymes located at the brush border membrane of the enterocytes. The final products are glucose, fructose, and galactose.

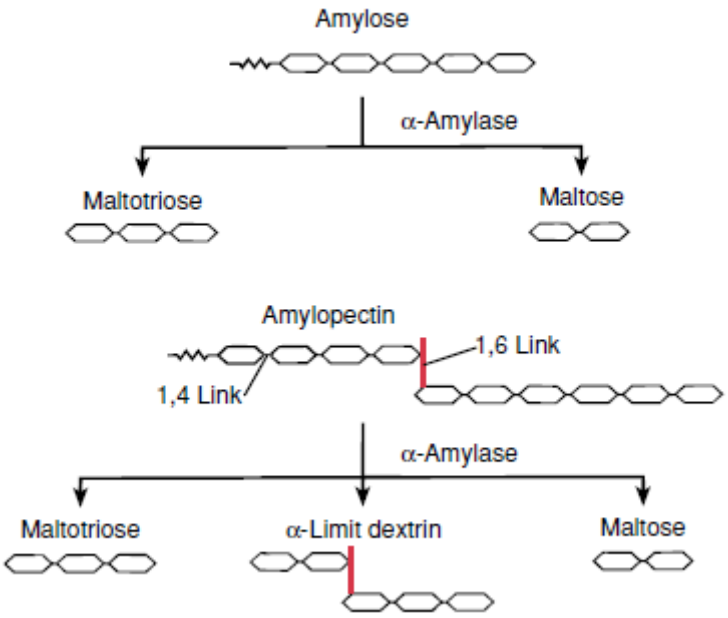


Fig. 20. The digestion products of starch after exposure to salivary or pancreatic α-amylase.

Role of enterocytes in carbohydrate absorption and metabolism

Monosaccharides are absorbed by enterocytes either actively or by facilitated transport. Glucose and galactose are absorbed via secondary active transport by a symporter that transports two Na^+ ions for every molecule of monosaccharide (Fig. 21). The movement of Na^+ into the cell, down concentration and electrical gradients, effects the uphill movement of glucose into the cell. The low intracellular Na^+ concentration is maintained by the basolateral membrane Na^+/K^+-ATPase. Sugars accumulate in the cell at a higher concentration than in plasma and leave the cell by Na^+-independent facilitated transport or passive diffusion through the basolateral cell membrane. Glucose and galactose share a common transporter at the brush border membrane of enterocytes and, thus, compete with each other during absorption.

Fructose is taken up by facilitated transport. Although facilitated transport is carrier-mediated, it is not an active process. Fructose absorption is much slower than glucose and galactose absorption and is not Na^+-dependent.

The sugars absorbed by enterocytes are transported by the portal blood to the liver where they are converted to glycogen or remain in the blood. After a meal, the level of blood glucose rises rapidly, usually peaking at 30 to 60 minutes. The concentration of glucose can be as high as 150 mg/dL.

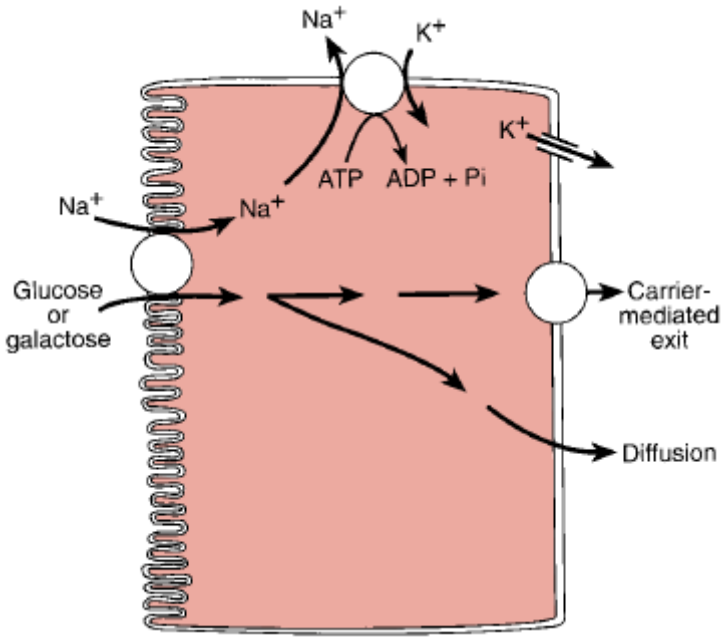


Fig. 21. The enterocyte Na^+-dependent carrier system for glucose and galactose.

Dietary Fiber Plays an Important Role in GI Motility

Dietary fiber includes indigestible carbohydrates and carbohydrate- like components mainly found in fruits and vegetables. The most common are cellulose, hemicellulose, pectins, and gums. Cellulose and hemicellulose are insoluble in water and are poorly digested by humans, thus, providing the bulkiness of stool.

Dietary fiber imparts bulk to the bolus and, therefore, greatly shortens transit time. It has been proposed that dietary fiber reduces the incidence of colon cancer by shortening GI transit time, which, in turn, reduces the formation of carcinogenic bile acids (e.g., lithocholic acid). Because dietary fiber also binds bile acids, which are formed from cholesterol, fiber consumption can result in a lowering of blood cholesterol by promoting excretion.

Digestion and absorption of lipids

Lipids are a concentrated form of energy. Lipids are also essential for normal body functions, as they form part of cellular membranes and are precursors of bile acids, steroid hormones, prostaglandins, and leukotrienes. The human body is capable of synthesizing most of the lipids it requires with the exception of the **essential fatty acids** linoleic acid and arachidonic acid. Both of these acids belong to the family of omega-6 fatty acids. Recently, researchers have provided convincing evidence that **eicosapentaenoic acid** and **docosahexaenoic acid** are also essential for the normal development of vision in newborns. Both of these acids are omega-3 fatty acids and are abundant in seafood and algae.

Lipids are comprised of several classes of compounds that are insoluble in water but soluble in organic solvents. By far the most abundant dietary lipids are **triglycerides**. They consist of a glycerol backbone esterified in the three positions with fatty acids. More than 90% of the daily dietary lipid intake is in the form of triglycerides.

The other lipids in the human diet are cholesterol and phospholipids. Cholesterol is a sterol derived exclusively from animal fat. Humans also ingest a small amount of plant sterols, notably β-sitosterol and campesterol. The phospholipid molecule is similar to a triglyceride with fatty acids occupying the first and second positions of the glycerol backbone (Fig. 27.23B). However, the third position of the glycerol backbone is occupied by a phosphate group coupled to a nitrogenous base (e.g., choline or ethanolamine), for which each type of phospholipid molecule is named.

Bile serves as an endogenous source of cholesterol and phospholipids. Bile contributes about 12 g/day of phospholipid to the intestinal lumen, most in the form of phosphatidylcholine, whereas dietary sources contribute 2 to 3 g/day. Another important endogenous source of lipid is desquamated intestinal villus epithelial cells.

Role of Different Lipases in Lipid Hydrolysis

Lipid digestion mainly occurs in the lumen of the small intestine. Humans secrete an overabundance of **pancreatic lipase**. Depending on the substrate being digested, pancreatic lipase has an optimal pH of 7 to 8.0, allowing it to work well in the intestinal lumen after the acidic contents from the stomach have been neutralized by pancreatic HCO^{3-} secretion. Pancreatic lipase hydrolyzes the triglyceride molecule to a 2-monoglyceride and two fatty acids (Fig. 22). It works on the triglyceride molecule at the oil-water interface; thus, the rate of lipolysis depends on the surface area of the interface. The products from the partial digestion of dietary triglyceride by gastric lipase and the churning action of the stomach produce a suspension of oil droplets (an emulsion) that help increase the area of the oil-water interface. Pancreatic juice also contains the peptide **colipase,** which is necessary for the normal digestion of fat by pancreatic lipase. Colipase binds lipase at a molar ratio of 1:1, thereby allowing the lipase to bind to the oil-water interface where lipolysis takes place. Colipase also counteracts the inhibition of lipolysis by bile salt, which, despite its importance in intestinal fat absorption, prevents the attachment of pancreatic lipase to the oil-water interface.

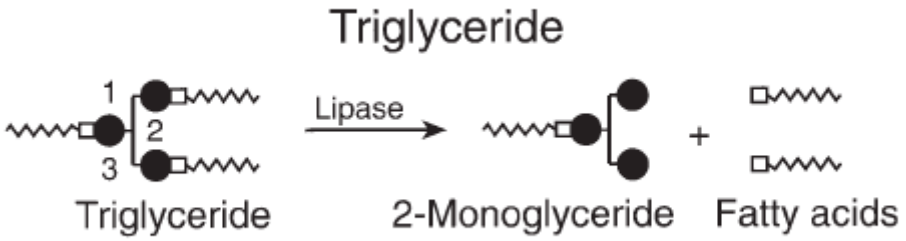


Fig. 22. The digestion of dietary lipids by pancreatic lipase

Phospholipase A2 is the major pancreatic enzyme for digesting phospholipids, forming lysophospholipids and fatty acids. For instance, phosphatidylcholine (lecithin) is hydrolyzed to form lysophosphatidylcholine (lysolecithin) and fatty acid.

Dietary cholesterol is presented as a free sterol or as a sterol ester (cholesterol ester). The hydrolysis of cholesterol ester is catalyzed by the pancreatic enzyme **cholesterol esterase**. The digestion of cholesterol ester is important because cholesterol can be absorbed only as the free sterol.

Bile Salt Plays an Important Role in Lipid Absorption

A layer of poorly stirred fluid called the **unstirred water layer** coats the surface of the intestinal villi (Fig. 23A). The unstirred water layer reduces the absorption of lipid digestion products because they are poorly soluble in water. They are rendered water-soluble by **micellar solubilization** by bile salts in the small intestinal lumen. This mechanism greatly enhances the concentration of these products in the unstirred water layer (Fig. 23B). The lipid digestion products are then absorbed by enterocytes, mainly by passive diffusion. Fatty acid and monoglyceride molecules are taken up individually. Similar mechanisms seem to operate for cholesterol and lysolecithin.

Bile salts are derived from cholesterol, but they are different from cholesterol in that they are water-soluble. They are essentially detergents—molecules that possess both hydrophilic and hydrophobic properties. Because bile salts are polar molecules, they penetrate cell membranes poorly. This is significant because it ensures their minimal absorption by the jejunum where most fat absorption takes place. At or above a certain concentration of bile salts, the **critical micellar concentration,** they aggregate to form micelles; the concentration of luminal bile salts is usually well above the critical micellar concentration. When bile salts alone are present in the micelle, it is called a **simple micelle.** Simple micelles incorporate the lipid digestion products— monoglyceride and fatty acids—to form **mixed micelles.** This renders the lipid digestion products water-soluble by incorporation into mixed micelles. Mixed micelles diffuse across the unstirred water layer and deliver lipid digestion products to the enterocytes for absorption.

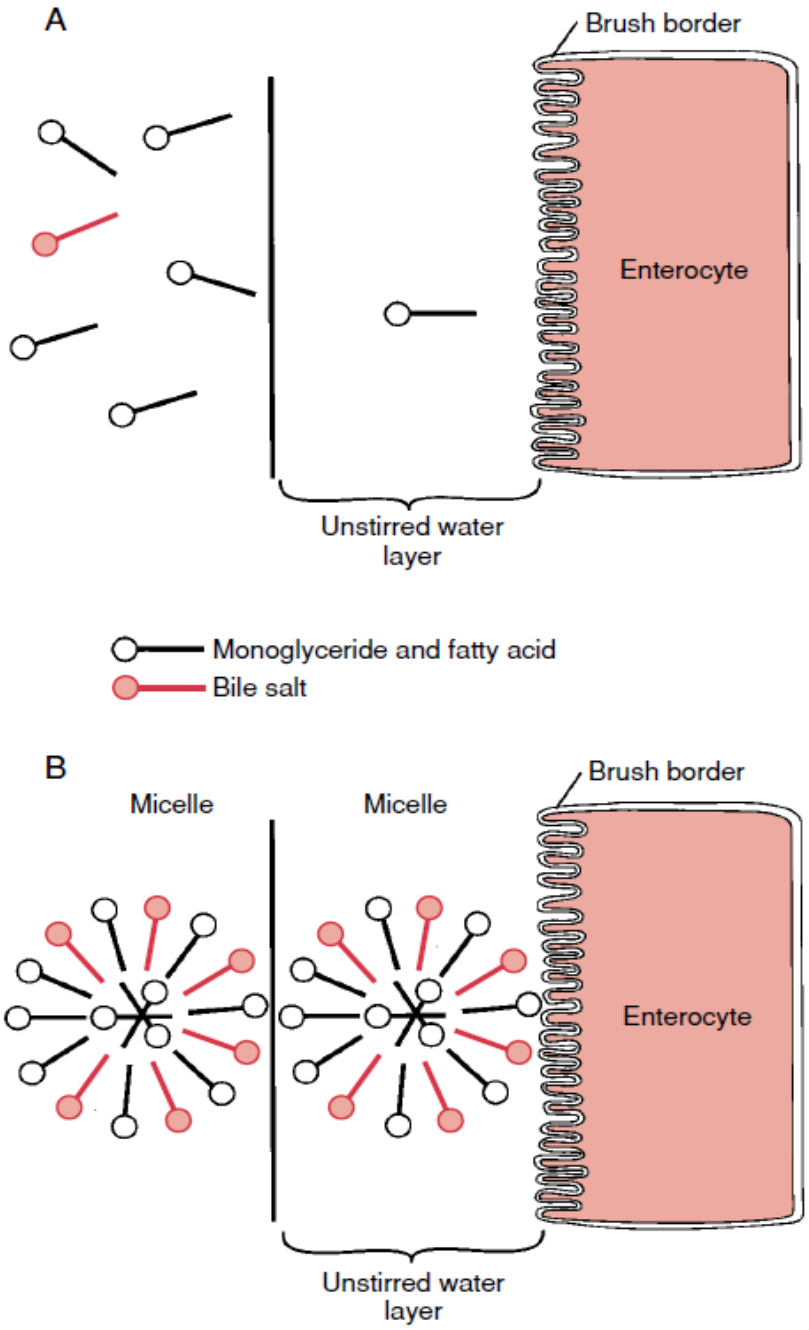


Fig. 23. Formation of micelles with the help of bile acids

Enterocytes Process Absorbed Lipid to Form Lipoproteins

After entering the enterocytes, the fatty acids and monoglycerides migrate to the smooth ER. In the smooth ER, monoglycerides and fatty acids are rapidly reconstituted to form triglycerides (Fig. 24). Fatty acids are first activated to form acyl-CoA, which is then used to esterify monoglyceride to form diglyceride, which

is transformed into triglyceride. The lysolecithin absorbed by the enterocytes can be reesterified in the smooth ER to form lecithin.

Cholesterol can be transported out of the enterocytes as free cholesterol or as esterified cholesterol. The enzyme responsible for the esterification of cholesterol to form cholesterol ester is **acyl-CoA cholesterol acyltransferase** (ACAT).

The reassembled **triglycerides, lecithin, cholesterol, and cholesterol esters** are then packaged into **lipoproteins** and exported from the enterocytes. The intestine produces two major classes of lipoproteins: chylomicrons and very low density lipoproteins (VLDLs). Both are triglyceriderich lipoproteins with densities less than 1.006 g/mL. **Chylomicrons** are made exclusively by the small intestine, and their primary function is to transport the large amount of dietary fat absorbed by the small intestine from the enterocytes to the lymph. Chylomicrons are large, spherical lipoproteins with diameters of 80 to 500 nm. They contain less protein and phospholipid than VLDLs and are, therefore, less dense than VLDLs. **VLDLs** are made continuously by the small intestine during both fasting and feeding, although the liver contributes significantly more VLDLs to the circulation.

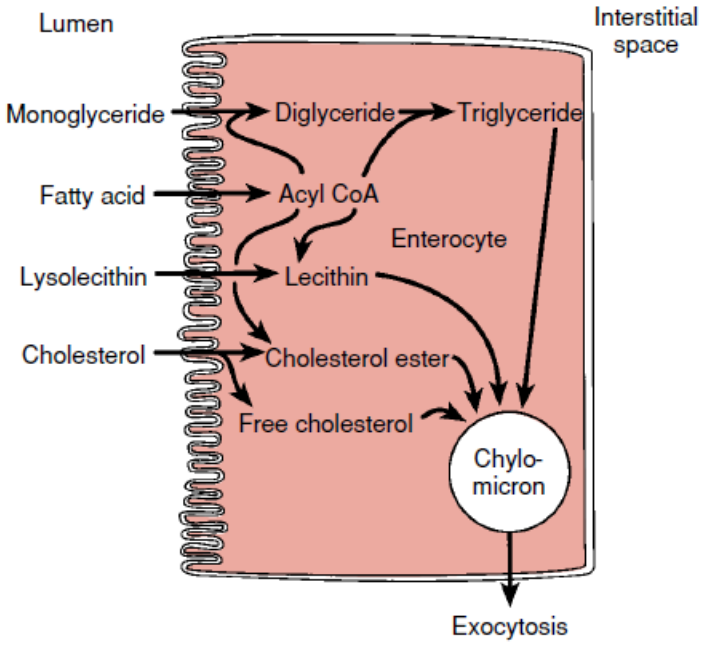


Fig. 24. The intracellular metabolism of absorbed lipid digestion products to form chylomicrons

Apoproteins—apo A-I, apo A-IV, and apo B—are among the major proteins associated with the production of chylomicrons and VLDLs. Apo B is the only protein that seems to be necessary for the normal formation of intestinal chylomicrons and VLDLs. This protein is made in the small intestine. It has a molecular weight of 250,000 and it is extremely hydrophobic.

Newly synthesized lipoproteins in the smooth ER are transferred to the Golgi apparatus, where they are packaged in vesicles. Chylomicrons and VLDLs are released into the intercellular space by exocytosis (Fig. 24). From there, they are transferred to the central lacteals (the beginnings of lymphatic vessels) by a process that is not well understood. Experimental evidence seems to indicate that the transfer probably occurs mostly by diffusion. Intestinal lipid absorption is associated with a marked increase in lymph flow called the **lymphagogic effect** of fat feeding. This increase in lymph flow plays an important role in the transfer of lipoproteins from the intercellular spaces to the central lacteal.

Fatty acids can also travel in the blood bound to albumin. While the most of the long-chain fatty acids are transported from the small intestine as triglycerides packaged in chylomicrons and VLDLs, some are transported in the portal blood bound to serum albumin. Most of the medium-chain (8 to 12 carbons) and all of the short-chain fatty acids are transported by the hepatic portal route.

Digestion and absorption of proteins

Protein digestion starts in the stomach (fig. 25-1). HCl in the stomach denatures proteins and converts the three secreted pepsinogens into about eight different **pepsins**. At a pH of 2–5, these endopeptidases split off proteins at sites where tyrosine or phenylalanine molecules are incorporated in the peptide chain. The pepsins become inactive in the small intestine (pH 7–8). Pancreatic juice also contains proenzymes of other peptidases that are activated in the duodenum. The endopeptidases **trypsin, chymotrypsin and elastase** hydrolyze the protein molecules into short-chain peptides. **Carboxypeptidase A and B** (from the pancreas) as well as **dipeptidases** and **aminopeptidase** (brush border enzymes) act on proteins at the end of the peptide chain, breaking them down into tripeptides, dipeptides, and (mostly) individual amino acids. These cleavage products are absorbed in the duodenum and jejunum.

Amino acids (AA) are transported by a number of specific carriers (fig.25-2). Neutral (without net charge) and anionic ("acid") L-amino acids are transported with Na^+ symporters (secondary active transport;) from the intestinal lumen into mucosal cells, from which they passively diffuse with carriers into the blood. Cationic ("basic") L-amino acids such as L-arginine$^+$, L-lysine$^+$ and L-ornithine$^+$ are partly taken up into the enterocytes by Na^+ independent mechanisms, as the membrane potential is a driving force for their uptake. Anionic amino acids like L-glutamate$^-$ and L-aspartate$^-$ which, for the most part, are broken down in the mucosal cells, also have their own (Na^+ and K^+ dependent) carrier systems. Neutral amino acids use several different transporters.

Dipeptides and tripeptides can be absorbed as intact molecules by a symport carrier (PepT1). The carrier is driven by an H^+ gradient (fig.25), which in turn is generated by H^+ secretion (tertiary active H^+-peptide symport). Amino acids generally are much more rapidly absorbed as dipeptides and tripeptides than as free amino acids. Once they enter the cells, the peptides are hydrolyzed to free amino acids.

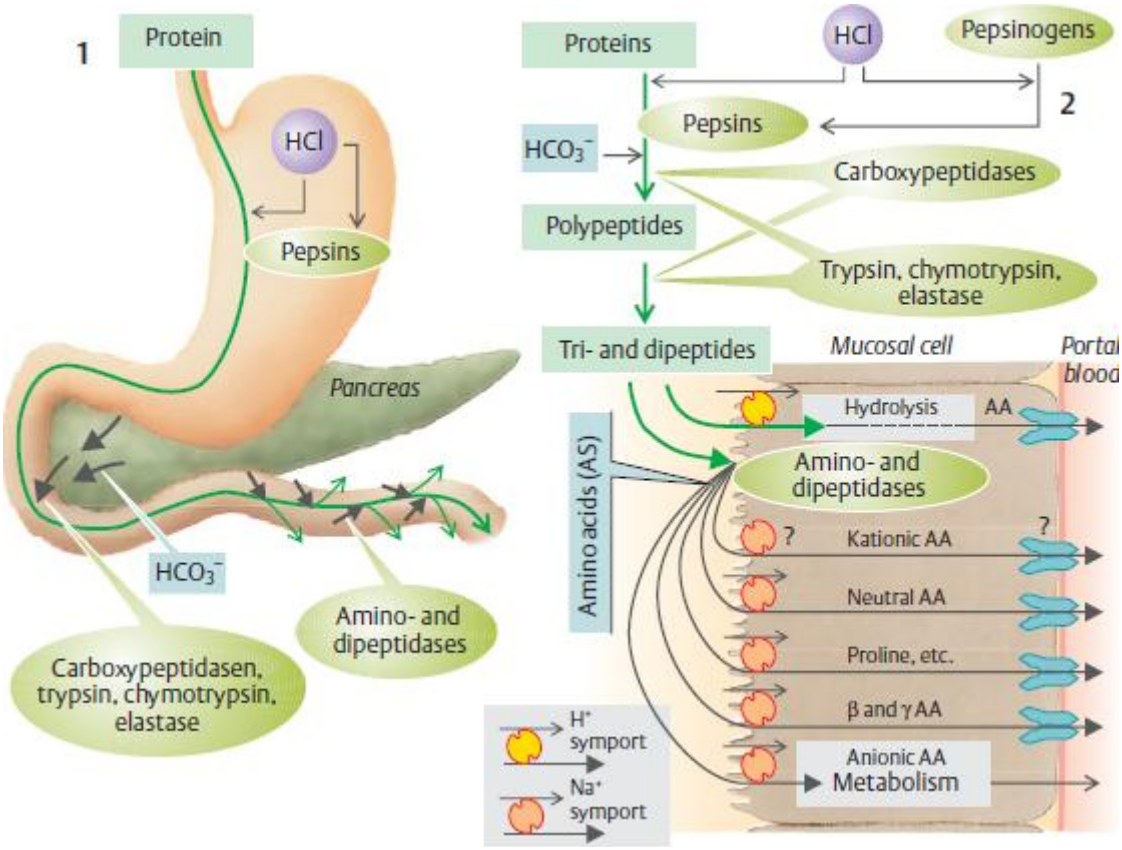


Fig. 25. Protein digestion and absorption of amino acids

Water and Mineral Absorption

GI **absorption of water** occurs mainly in the jejunum and ileum, with smaller quantities being absorbed by the colon (fig. 26). Water is driven through the intestinal epithelium by osmosis. When solutes (Na^+, Cl^-, etc.) are absorbed in the intestine, water follows (fig. 27). Conversely, the secretion of substances into the lumen or the ingestion of non-absorbable substances leads to water fluxes into the lumen. Poorly absorbable substances therefore act as laxatives (e.g. sulfate, sorbitol, polyethylene glycol).

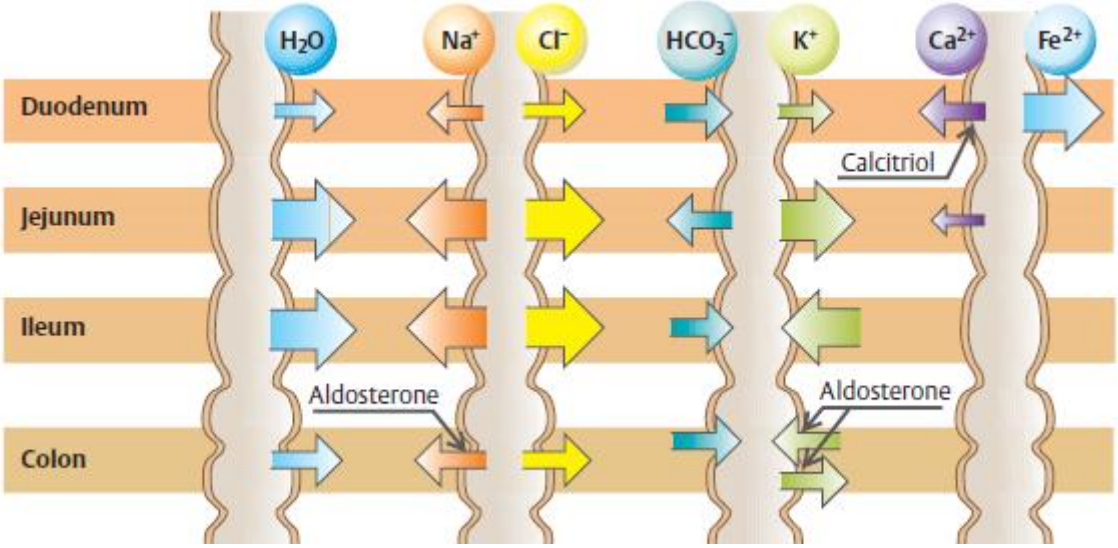


Fig. 26. Water and electrolyte absorption in the gut

Water absorption is mainly driven by the **absorption of Na^+, Cl^-** and **organic compounds**. The luminal concentration of Na^+ and Cl^- steadily decreases from the duodenum to the colon. Na^+ is absorbed by various mechanisms, and the Na+-K+-ATPase on the basolateral cell membrane is the primary driving mechanism for all of them (Fig. 27, 28).

Symport of Na^+ and organic substances. Na^+ passively influxes into cells of the duodenum and jejunum via symporter carriers, which actively cotransport glucose, amino acids, phosphates and other compounds (secondary active transport; fig.28-1). Since this is an electrogenic transport mechanism, a lumen-negative transepithelial potential that drives Cl^- out of the lumen forms (fig. 28-2).

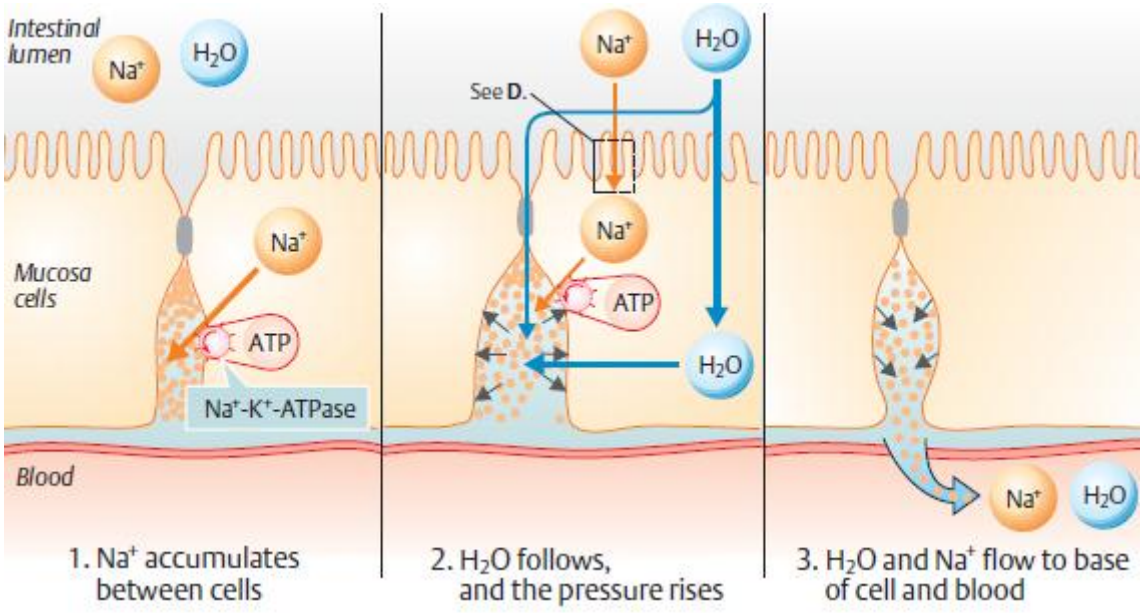


Fig. 27. Na^+ and water absorption in the gut

Parallel transport of Na^+ and Cl^-: Na^+ ions in the lumen of the ileum are exchanged for H^+ ions (fig. 28-3) while Cl^- is exchanged for HCO^{3-} at the same time (fig. 28-4). The H+ ions combine with HCO^{3-} to yield H_2O + CO_2, which diffuse out of the lumen. Most Na^+, Cl^- and, by subsequent osmosis, H_2O is absorbed by this electroneutral transport mechanism.

Na^+ diffusion: Na^+ in the colon is mainly absorbed through luminal Na+ channels (fig. 28-5). This type of Na^+ transport is electrogenic and aldosterone-dependent. The related lumen-negative transepithelial potential either leads to K^+ secretion or drives Cl^- out of the lumen (fig. 28-2).

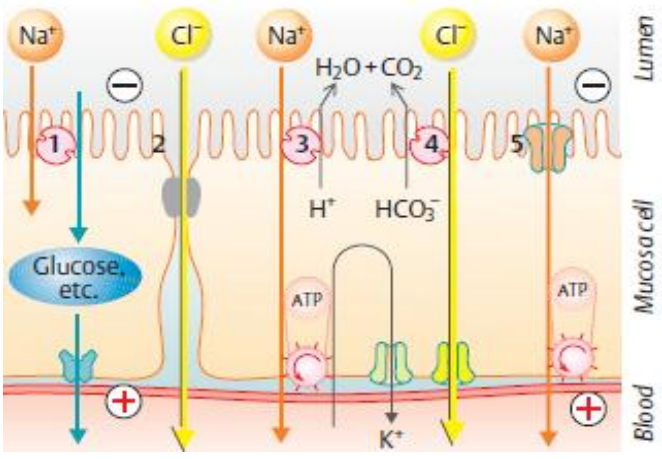


Fig. 28. Sodium and chloride absorption in the gut

General Principles of Gastrointestinal Motility

Electrical Activity of Gastrointestinal Smooth Muscle

The individual smooth muscle fibers in the gastrointestinal tract are 200 to 500 micrometers in length and 2 to 10 micrometers in diameter, and they are arranged in bundles of as many as 1000 parallel fibers. In the *longitudinal muscle layer*, the bundles extend longitudinally down the intestinal tract; in the *circular muscle layer*, they extend around the gut.

Within each bundle, the muscle fibers are electrically connected with one another through large numbers of *gap junctions* that allow low-resistance movement of ions from one muscle cell to the next. Therefore, electrical signals that initiate muscle contractions can travel readily from one fiber to the next within each bundle but more rapidly along the length of the bundle than sideways.

Each bundle of smooth muscle fibers is partly separated from the next by loose connective tissue, but the muscle bundles fuse with one another at many points, so that in reality each muscle layer represents a branching latticework of smooth muscle bundles. Therefore, each muscle layer functions as a *syncytium*; that is, when an action potential is elicited anywhere within the muscle mass, it generally travels in all directions in the muscle. The distance that it travels depends after only a few millimeters and at other times it travels many centimeters or even the entire length and breadth of the intestinal tract.

Also, a few connections exist between the longitudinal and circular muscle layers, so that excitation of one of these layers often excites the other as well.

The smooth muscle of the gastrointestinal tract is excited by almost continual slow, intrinsic electrical activity along the membranes of the muscle fibers. This activity has two basic types of electrical waves: (1) *slow waves* and (2) *spikes* (fig. 29). In addition, the voltage of the resting membrane potential of the gastrointestinal smooth muscle can be made to change to different levels, and this too can have important effects in controlling motor activity of the gastrointestinal tract.

Slow Waves. Most gastrointestinal contractions occur rhythmically, and this rhythm is determined mainly by the frequency of so-called "slow waves" of smooth muscle membrane potential. These waves are not action potentials. Instead, they are slow, undulating changes in the resting membrane potential. Their intensity usually varies between 5 and 15 millivolts, and their frequency ranges in different parts of the human gastrointestinal tract from 3 to 12 per minute: about 3 in the body of the stomach, as much as 12 in the duodenum, and about 8 or 9 in the terminal ileum. Therefore, the rhythm of contraction of the body of the stomach usually is about 3 per minute, of the duodenum about 12 per minute, and of the ileum 8 to 9 per minute.

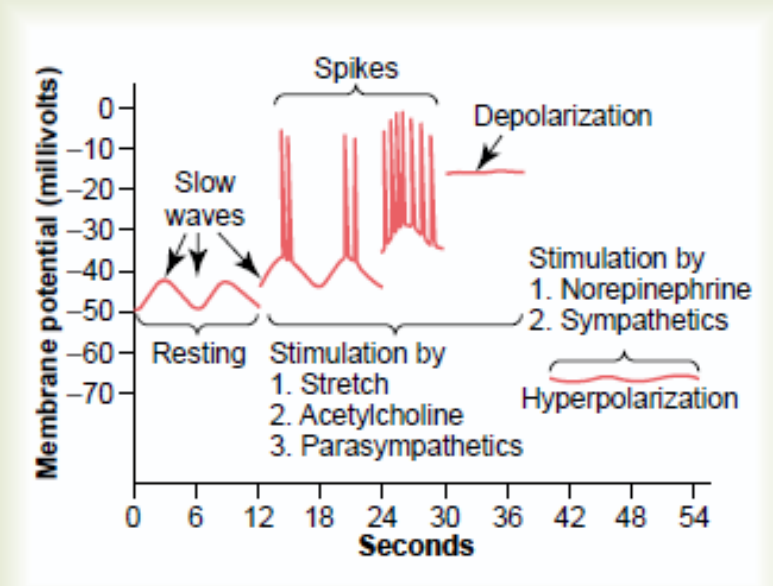


Fig. 29. Types of electrical activity in intestinal smooth muscle

The precise cause of the slow waves is not completely understood, although they appear to be caused by complex interactions among the smooth muscle cells and specialized cells, called the **interstitial cells of Cajal,** that are believed to act as **electrical pacemakers** for smooth muscle cells. These interstitial cells form a network with each other and are interposed between the smooth muscle layers, with synaptic-like contacts to smooth muscle cells. The interstitial cells of Cajal undergo cyclic changes in membrane potential due to unique ion channels that

periodically open and produce inward (pacemaker) currents that may generate slow wave activity.

The slow waves usually do not by themselves cause muscle contraction in most parts of the gastrointestinal tract, except perhaps in the stomach. Instead, they mainly excite the appearance of intermittent spike potentials, and the spike potentials in turn actually excite the muscle contraction.

Spike Potentials. The spike potentials are true action potentials. They occur automatically when the resting membrane potential of the gastrointestinal smooth muscle becomes more positive than about -40 millivolts (the normal resting membrane potential in the smooth muscle fibers of the gut is between -50 and -60 millivolts).Thus, each time the peaks of the slow waves temporarily become more positive than -40 millivolts, spike potentials appear on these peaks. The higher the slow wave potential rises, the greater the frequency of the spike potentials, usually ranging between 1 and 10 spikes per second. The spike potentials last 10 to 40 times as long in gastrointestinal muscle as the action potentials in large nerve fibers, each gastrointestinal spike lasting as long as 10 to 20 milliseconds.

Another important difference between the action potentials of the gastrointestinal smooth muscle and those of nerve fibers is the manner in which they are generated. In nerve fibers, the action potentials are caused almost entirely by rapid entry of sodium ions through sodium channels to the interior of the fibers.

In gastrointestinal smooth muscle fibers, the channels responsible for the action potentials are somewhat different; they allow especially large numbers of calcium ions to enter along with smaller numbers of sodium ions and therefore are called **calcium-sodium channels.** These channels are much slower to open and close than are the rapid sodium channels of large nerve fibers. The slowness of opening and closing of the calcium-sodium channels accounts for the long duration of the action potentials. Also, the movement of large amounts of calcium ions to the interior of the muscle fiber during the action potential plays a special role in causing the intestinal muscle fibers to contract.

Changes in Voltage of the Resting Membrane Potential. In addition to the slow waves and spike potentials, the baseline voltage level of the smooth muscle resting membrane potential also can change. Under normal conditions, the resting membrane potential averages about -56 millivolts, but multiple factors can change this level. When the potential becomes less negative, which is called **depolarization** of the membrane, the muscle fibers become more excitable. When the potential becomes more negative, which is called **hyperpolarization,** the fibers become less excitable.

Factors that depolarize the membrane—that is, **make it more excitable**—are 1) stretching of the muscle, 2) stimulation by acetylcholine, 3) stimulation by parasympathetic nerves that secrete acetylcholine at their endings, and 4) stimulation by several specific gastrointestinal hormones.

Important **factors that make the membrane potential more negative**—that is, hyperpolarize the membrane and make the muscle fibers **less excitable**—are 1) the effect of norepinephrine or epinephrine on the fiber membrane and 2) stimulation of the sympathetic nerves that secrete mainly norepinephrine at their endings.

Calcium Ions and Muscle Contraction. Smooth muscle contraction occurs in response to entry of calcium ions into the muscle fiber. Calcium ions, acting through a calmodulin control mechanism, activate the myosin filaments in the fiber, causing attractive forces to develop between the myosin filaments and the actin filaments, thereby causing the muscle to contract.

The slow waves do not cause calcium ions to enter the smooth muscle fiber (only sodium ions).Therefore, the slow waves by themselves usually cause no muscle contraction. Instead, it is during the spike potentials, generated at the peaks of the slow waves, that significant quantities of calcium ions do enter the fibers and cause most of the contraction.

Neural Control of Gastrointestinal Function—Enteric Nervous System

The gastrointestinal tract has a nervous system all its own called the *enteric nervous system*. It lies entirely in the wall of the gut, beginning in the esophagus and extending all the way to the anus. The number of neurons in this enteric system is about 100 million, almost exactly equal to the number in the entire spinal cord. This highly developed enteric nervous system is especially important in controlling gastrointestinal movements and secretion.

The enteric nervous system is composed mainly of two plexuses (fig. 30): 1) an outer plexus lying between the longitudinal and circular muscle layers, called the **myenteric plexus or Auerbach's plexus,** and 2) an inner plexus, called the **submucosal plexus or Meissner's plexus,** that lies in the submucosa.

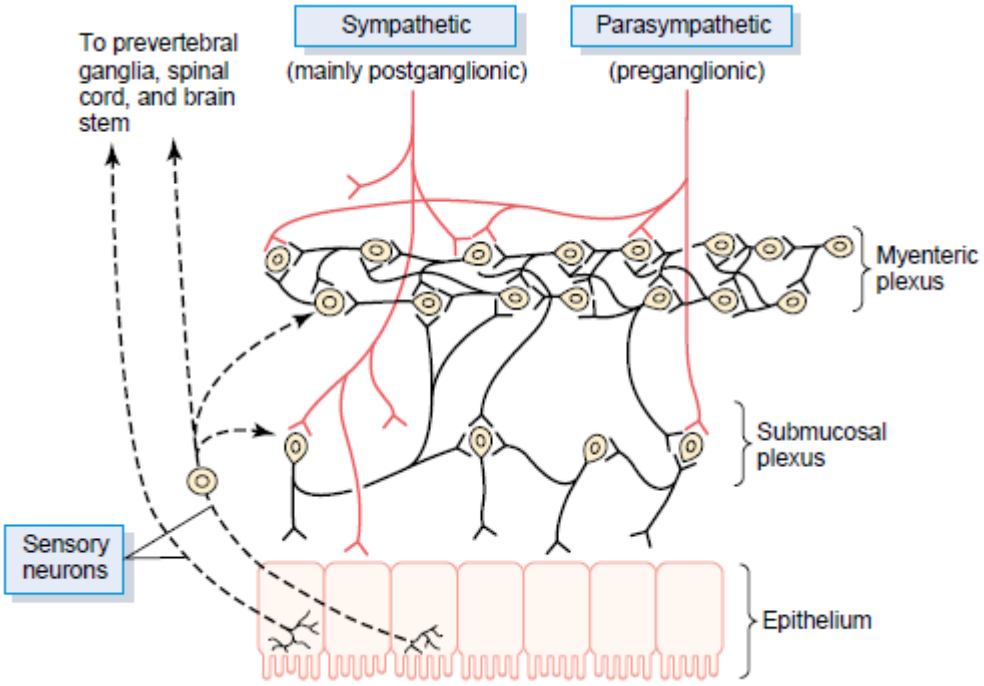


Fig. 30. Neural control of the gut wall

The myenteric plexus controls mainly the gastrointestinal movements, and the submucosal plexus controls mainly gastrointestinal secretion and local blood flow.

The extrinsic sympathetic and parasympathetic fibers connect to both the myenteric and submucosal plexuses. Although the enteric nervous system can

function on its own, independently of these extrinsic nerves, stimulation by the parasympathetic and sympathetic systems can greatly enhance or inhibit gastrointestinal functions.

Sensory nerve endings that originate in the gastrointestinal epithelium or gut wall and send afferent fibers to both plexuses of the enteric system, as well as 1) to the prevertebral ganglia of the sympathetic nervous system, 2) to the spinal cord, and 3) in the vagus nerves all the way to the brain stem. These sensory nerves can elicit local reflexes within the gut wall itself and still other reflexes that are relayed to the gut from either the prevertebral ganglia or the basal regions of the brain.

Differences Between the Myenteric and Submucosal Plexuses. The **myenteric plexus** consists mostly of a linear chain of many interconnecting neurons that extends the entire length of the gastrointestinal tract.

Because the myenteric plexus extends all the way along the intestinal wall and because it lies between the longitudinal and circular layers of intestinal smooth muscle, it is concerned mainly with controlling muscle activity along the length of the gut. When this plexus is stimulated, its principal effects are 1) increased tonic contraction, or "tone," of the gut wall, 2) increased intensity of the rhythmical contractions, 3) slightly increased rate of the rhythm of contraction, and 4) increased velocity of conduction of excitatory waves along the gut wall, causing more rapid movement of the gut peristaltic waves.

The myenteric plexus should not be considered entirely excitatory because some of its neurons are inhibitory; their fiber endings secrete an inhibitory transmitter, possibly vasoactive intestinal polypeptide or some other inhibitory peptide. The resulting inhibitory signals are especially useful for inhibiting some of the intestinal sphincter muscles that impede movement of food along successive segments of the gastrointestinal tract, such as the pyloric sphincter, which controls emptying of the stomach into the duodenum, and the sphincter of the ileocecal valve, which controls emptying from the small intestine into the cecum.

The **submucosal plexus,** in contrast to the myenteric plexus, is mainly concerned with controlling function within the inner wall of each minute segment

of the intestine. For instance, many sensory signals originate from the gastrointestinal epithelium and are then integrated in the submucosal plexus to help control local intestinal secretion, local absorption, and local contraction of the submucosal muscle that causes various degrees of infolding of the gastrointestinal mucosa.

Types of Neurotransmitters Secreted by Enteric Neurons. In an attempt to understand better the multiple functions of the gastrointestinal enteric nervous system, research workers the world over have identified a dozen or more different neurotransmitter substances that are released by the nerve endings of different types of enteric neurons. Two of them with which we are already familiar are *acetylcholine* and *norepinephrine*. Others are *adenosine triphosphate*, *serotonin*, *dopamine*, *cholecystokinin*, *substance P*, *vasoactive intestinal polypeptide*, *somatostatin*, *leu-enkephalin*, *metenkephalin*, and *bombesin*.

Acetylcholine most often excites gastrointestinal activity. **Norepinephrine** almost always inhibits gastrointestinal activity. This is also true of **epinephrine,** which reaches the gastrointestinal tract mainly by way of the blood after it is secreted by the adrenal medullae into the circulation. The other aforementioned transmitter substances are a mixture of excitatory and inhibitory agents.

Gastrointestinal Reflexes

The anatomical arrangement of the enteric nervous system and its connections with the sympathetic and parasympathetic systems support three types of gastrointestinal reflexes that are essential to gastrointestinal control. They are the following:

1. **Reflexes that are integrated entirely within the gut wall enteric nervous system.** These include reflexes that control much gastrointestinal secretion, peristalsis, mixing contractions, local inhibitory effects, and so forth.

2. **Reflexes from the gut to the prevertebral sympathetic ganglia and then back to the gastrointestinal tract.** These reflexes transmit signals long distances to other areas of the gastrointestinal tract, such as signals from the stomach to cause evacuation of the colon **(the *gastrocolic reflex*),** signals from the colon and small intestine to inhibit stomach motility and stomach secretion **(the enterogastric reflexes),** and reflexes from the colon to inhibit emptying of ileal contents into the colon **(the colonoileal reflex).**

3. **Reflexes from the gut to the spinal cord or brain stem and then back to the gastrointestinal tract.** These include especially 1) reflexes from the stomach and duodenum to the brain stem and back to the stomach—by way of the vagus nerves—to control gastric motor and secretory activity;

2) **pain reflexes** that cause general inhibition of the entire gastrointestinal tract;

3) **defecation reflexes** that travel from the colon and rectum to the spinal cord and back again to produce the powerful colonic, rectal, and abdominal contractions required for defecation (the defecation reflexes).

Propulsion and Mixing of Food in the Alimentary Tract

Swallowing (deglutition)

1. **Oral stage or first stage.**

This stage occurs after mastication. During mastication, food is rolled into a bolus. The passage of bolus through oral cavity into the pharynx occurs in this stage. And, this is a voluntary stage.

First, this bolus is placed over posterodorsal surface of the tongue. This is called the preparatory position. Now, the front part of tongue is retracted and depressed. The posterior part of tongue is elevated and retracted against hard palate. This makes the bolus to move back into the pharynx. The forceful contraction of tongue against the palate produces a positive pressure in the posterior part of oral cavity. This pressure in the oral cavity also pushes the food into pharynx to some extent (fig. 31-1).

2. **Pharyngeal stage or second stage**

In the pharyngeal or the second stage of deglutition, the bolus is pushed from pharynx into the esophagus. It is an involuntary stage. The pharynx is a common passage for food and air. It divides into larynx and esophagus. Larynx lies anteriorly and continues as respiratory passage. Esophagus lies behind the larynx and continues as gastrointestinal tract. During this stage of swallowing, the bolus from the pharynx can enter into four paths: 1) back into mouth; 2) upwards into nasopharynx; 3) forwards into larynx and 4) downwards into esophagus.

The various movements are coordinated so that, bolus enters only into the esophagus. The entrance of bolus through other paths is prevented as follows:

1. Return of bolus back into the mouth is prevented by: the position of tongue against the soft palate (roof of the mouth) and the high intraoral pressure developed by the movement of tongue.

2. The movement of bolus into the nasopharynx from pharynx is prevented by elevation of soft palate along with its extension called uvula (fig. 31-2).

3. The movement of bolus into the larynx is prevented by the following means (fig. 31-3):

- approximation of the vocal cords

- forward and upward movement of larynx

- the backward movements of epiglottis to seal the opening of the larynx.

Another important factor, which prevents entry of food into respiratory tract during deglutition, is the temporary arrest of breathing. This occurs during the second stage of swallowing. The temporary arrest of breathing is called the apnea. And, apnea during deglutition is called the deglutition apnea or swallowing apnea.

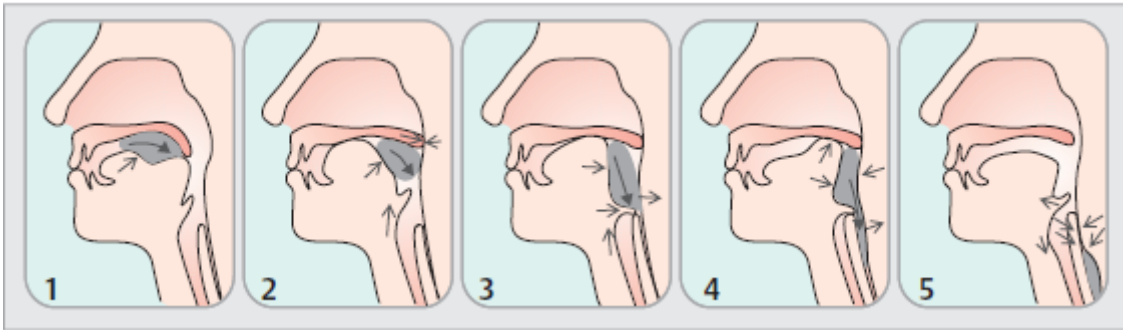


Fig. 31. Mechanism of swallowing.

3. Entrance of bolus into esophagus.

Since the other three paths are closed for the bolus, it has to pass only through the esophagus. This occurs by the combined effects of various factors given below: the upward movement of the larynx stretches the opening of the esophagus, simultaneously, the upper 3 to 4 cm of esophagus relaxes. This part of the esophagus is formed by the cricopharyngeal muscle and it is called upper esophageal sphincter or pharyngoesophageal sphincter (fig. 31-4). At the same time, the peristaltic contractions start in the pharynx due to the contraction of pharyngeal muscles. Elevation of larynx also lifts the glottis away from the food passage.

All the above-mentioned factors act together so that, the bolus moves easily into the esophagus. The whole process takes place within 1 to 2 seconds. And this process is purely involuntary.

3. Esophageal stage or third stage

This is also an involuntary stage. The function of esophagus is to transport the food from the pharynx to the stomach. The movements of esophagus are

specifically organized for this function and the movements are called peristaltic waves. Peristalsis means a wave of contraction followed by the wave of relaxation of muscle fibers of Gl tract, which travel in aboral direction (away from mouth). By this type of movement, the contents are propelled down along the Gl tract.

When bolus reaches the esophagus, the peristaltic waves are initiated, which propel the bolus into the stomach (fig. 31-5). Usually, two types of peristaltic contractions are produced in esophagus.

Primary Peristaltic Contractions. When bolus reaches the upper part of esophagus, the peristalsis starts. This is known as primary peristalsis. After origin, the peristaltic contractions pass down through the rest of the esophagus propelling the food towards stomach.

The pressure developed during the primary peristaltic contractions is important to propel the bolus. Initially, the pressure becomes negative in the upper part of esophagus. This is due to the stretching of the closed esophagus by the elevation of larynx. But, immediately the pressure becomes positive and increases up to 10 to 15 cm of H_2O.

Secondary Peristaltic Contractions. The secondary peristaltic contractions arise in esophagus locally due to the distention of upper esophagus by the bolus. After origin, these contractions pass down like the primary contractions, producing a positive pressure. If the primary peristaltic contractions are unable to propel the bolus into the stomach, the secondary peristaltic contractions appear and push the bolus into stomach.

Role of Lower Esophageal Sphincter. The distal 2 to 5 cm of esophagus acts like a sphincter. And, it is called lower esophageal sphincter. When bolus enters this part of the esophagus, this sphincter relaxes so that the contents enter the stomach. Later, the sphincter contracts. The relaxation and contraction of sphincter occur in sequence with the arrival of peristaltic contractions of esophagus.

Movements of stomach

1. Hunger contractions

The activities of smooth muscles of stomach are increased during gastric digestion (when stomach is filled with food) and when the stomach is empty. The movements of empty stomach are related to the sensations of hunger. So, these movements are called the hunger contractions.

Hunger contractions are the peristaltic waves superimposed over the contractions of gastric smooth muscle as a whole. This type of peristaltic waves is different from the digestive peristaltic contractions. The digestive peristaltic contractions usually occur in body and pyloric parts of the stomach. But, the peristaltic contractions of empty stomach involve the entire stomach. The hunger contractions are of three types:

- Type I Hunger Contractions. The type I hunger contractions are the first contractions to appear in the empty stomach when the tone of the stomach is low. The type I contractions are single contractions and each one lasts for 20 seconds. The interval between the contractions is about 3 to 4 seconds. The tonus of the stomach is not increased between the contractions. The pressure produced by these contractions is about 5 cm of water.

- Type II Hunger Contractions. Type II hunger contractions occur if the food intake is postponed even after the appearance of the type I contractions. Type II hunger contractions occur when the tonus of stomach is stronger. These contractions also last for 20 seconds. The pause between the contractions is absent. The pressure produced by these contractions is 10-15 cm of water.

- Type III Hunger Contractions. Type III hunger contractions appear when the hunger becomes severe. Otherwise called incomplete tetanus, these contractions are rare in man as the intake of food usually occurs before the appearance of these contractions. Type III contractions last for 1 to 5 minutes. The pressure rise is 10 to 20 cm of water. And the tonus is increased to a great extent.

When the stomach is empty, the type I contractions occur first followed by type II. If food intake is still postponed, then type 111 contractions appear and, as soon as food is consumed, hunger contractions disappear.

2. Receptive relaxation

Relaxation of the upper portion of the stomach when bolus enters the stomach from esophagus is called receptive relaxation. It involves the fundus and upper part of the body of stomach. Its significance is to accommodate the food without much increase in pressure inside the stomach.

3. Peristalsis of stomach

When the stomach contains food, the peristaltic contraction or peristaltic wave occurs regularly with a frequency of 3/minute. It starts from the lower part of the body of stomach.

The contraction first appears as a slight indentation on the greater and lesser curvatures and travels towards pylorus. The contraction becomes deeper while traveling. And finally, it ends with the contraction of pyloric sphincter. Some of the waves disappear before reaching the sphincter. Each peristaltic wave takes about one minute to travel from the point of origin to the point of ending.

These contractions are called digestive peristalsis because of their involvement in mixing of food with gastric juice, grinding of food particles and the digestive activities.

Filling of stomach. While taking food, the food arranges itself in the stomach in different layers. The first eaten food is placed against the greater curvature in the fundus and body of the stomach. The successive layers of food particles lie nearer the lesser curvature until the last portion of food eaten lies near the upper end of lesser curvature adjacent to cardiac sphincter.

The liquid remains near the lesser curvature and flows towards the pyloric end of the stomach along a V shaped groove. This groove is formed by the smooth muscle and it is called magenstrasse. But, if a large quantity of fluid is taken, it flows around the entire food mass and is distributed over the interior part of stomach between wall of the stomach and food mass.

Emptying of stomach

The emptying of stomach contents into the intestine occurs due to the peristaltic waves arising in pyloric part of the stomach and simultaneous relaxation of pyloric sphincter. Various factors influence the emptying of stomach.

1. *Volume of Gastric Content.* For any type of meal, gastric emptying is directly proportional to the volume. If the content of stomach is more, a large amount is emptied into the intestine.

2. *Consistency of Gastric Content.* Emptying of the stomach is proportional to the consistency of the contents. Liquids, particularly the inert liquids (which do not stimulate the stomach) leave the stomach rapidly. Water is emptied into intestine as soon as it is swallowed. But, the solids are moved out of stomach only after being converted into fluid or semifluid. Normally, the undigested solid particles are not easily emptied.

3. *Chemical Composition.* The chemical composition of the food also plays an important role in the emptying of the stomach. The gastric content with more carbohydrates leaves the stomach more rapidly than the content with proteins. The proteins leave the stomach more rapidly than the fat. Thus, the fatty food remains in stomach for a longer period.

4. *pH of the Gastric Content.* The strong acid content leaves the stomach slowly. The emptying of such content is accelerated by neutralizing the acid. This has an important function of protecting the duodenal mucosa from the acidity.

5. *Osmolar Concentration of Gastric Content.* The gastric content, which is isotonic to blood, leaves the stomach rapidly than the hypotonic or hypertonic content.

Regulation of gastric emptying

The emptying of stomach stops mainly due to the inhibition of gastric motility. The inhibition of motility of stomach is caused by both nervous and hormonal factors. The nervous factor, which regulates the emptying of stomach, is the enterogastric reflex.

Enterogastric Reflex. When the chyme enters the intestine, the gastric muscle is inhibited and the motility stops leading to stoppage of emptying. This is called enterogastric reflex. This reflex involves the vagus nerves.

Hormonal Factors. The major hormone, which controls the gastric emptying, is **enterogastrone.** When an acid chyme enters the duodenum, the hormone enterogastrone is released from the duodenal mucus membrane. When this hormone enters the stomach through blood it inhibits the motility of stomach. The other hormones, which inhibit the gastric motility and emptying, are VIP, GIP, secretin and cholecystokinin.

Movements of small intestine

The movements of small intestine are essential for mixing the chyme with digestive juices, propulsion of food and absorption. Four types of movements occur in small intestine.

1) Mixing movements: segmentation movements and pendular movements
2) Propulsive movements: peristaltic movements and peristaltic rush
3) Peristalsis in fasting - Migrating motor complex
4) Movements of villi.

Mixing movements. The mixing movements of small intestine are responsible for proper mixing of chyme with digestive juices like pancreatic juice, bile and intestinal juice. The mixing movements of small intestine are segmentation contractions and pendular movements.

Segmentation Contractions. The segmentation contractions are the common type of movements of small intestine, which occur regularly or irregularly but in a rhythmic fashion. So, these movements are also called rhythmic segmentation contractions. The contractions occur at spaced intervals along a section of intestine. The segment of the intestine involved in each contraction is about 1 to 5 cm long. The segments of intestine in between the contracted segments are relaxed. The length of the relaxed segments is same as that of the contracted segments. All the segments (both contracted and relaxed segments) give a ring like appearance resembling the chain of sausages. After some time, the contracted segments are relaxed and the relaxed segments are contracted (fig. 32). Therefore, the segmentation contractions chop the chyme many times. This helps in mixing of chyme with digestive juices.

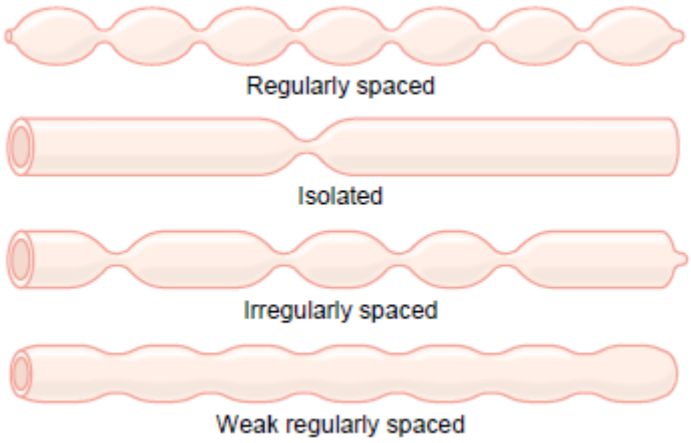


Fig. 32. Segmentation contractions

Pendular Movement. This is another type of mixing movement, which can be noticed only by close observation. Small constrictive waves sweep forward and backward or upward and downward and the intestinal loops move like the pendulum of the clock and, this movement is called the pendular movement.

Propulsive movements. The movements of small intestine involved in pushing the chyme towards the aboral end of intestine are called propulsive movements. The propulsive movements are of two types, peristaltic movements and peristaltic rush.

Peristaltic Movements. Peristalsis is defined as the wave of contraction followed by wave of relaxation, which travels aborally (fig. 33). The stimulation of smooth muscles of intestine initiates the peristalsis. It travels from point of stimulation in both directions. But under normal conditions, the progress of contraction in an oral direction is inhibited quickly and the contractions disappear. Only the contraction that travels in an aboral direction persists.

Starling law of intestine: depending upon the direction of the peristalsis, "Law of intestine" was put forth by Starling. According to this law of intestine, the response of the intestine for a local stimulus consists of a contraction of smooth muscle above and relaxation below the stimulated area.

The peristaltic contractions start at any part of the intestine travel towards anal end at a velocity of 1 to 2 cm/sec. The contractions are always weak and

usually disappear after traveling for about few cm distance. Because of this, the average movement of chyme through small intestine is very slow, and the average velocity of movement of the chyme is < 1 cm/sec. Thus, the chyme requires several hours to travel from duodenum to the end of small intestine.

The peristaltic waves in small intestine are increased very much immediately after a meal. This is caused by gastroenteric reflex. The gastroenteric reflex is initiated by the distention of stomach. And, the impulses are conducted through myenteric plexus from stomach along the wall of the intestine.

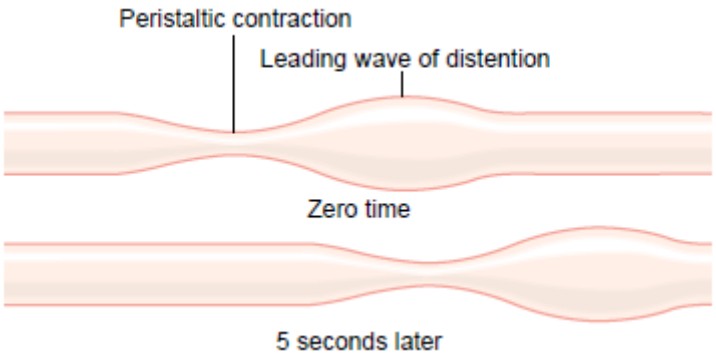


Fig. 33. Peristalsis

Peristaltic Rush. Sometimes, the small intestine shows a powerful peristaltic contraction. This is caused by excessive irritation of intestinal mucus membrane or extreme distention of the intestine. This type of powerful contraction begins in duodenum and passes through entire length of small intestine and finally reaches the ileocecal valve within few minutes. This is called peristaltic rush or rush waves. The peristaltic rush sweeps the contents of intestine into colon. Thus, it relieves the small intestine off either irritants or excessive distention.

Peristalsis in fasting-migrating motor complex. This is a type of peristaltic contraction, which occurs in stomach and small intestine during the long periods of fasting or several hours after the meals. It is different from the regular peristalsis because, a large portion of stomach or intestine is involved in

the contraction. The contraction extends to about 40 cm of the stomach or intestine. This type of movement occurs once in every 114 to 2 hours.

Migrating motor complex starts as a moderately active peristalsis in the body of stomach and runs through the entire length of small intestine. It travels at a velocity of 6 to 12 cm / min. Thus, it takes about 10 minutes to reach the colon after taking origin from stomach.

The migrating motor complex sweeps the excessive digestive secretions into the colon and prevents the accumulation of the secretions in stomach and intestine.

Movements of villi. During the movement of small intestine, there are simultaneous movements of villi also. This is because the smooth muscle fibers of the intestinal wall extend into the villi also. The movements of villi are shortening and elongation, which occur alternatively and help in emptying lymph from the central lacteal into the lymphatic system. The surface area of villi is increased during elongation. This helps absorption of digested food particles from the lumen of intestine.

Movements of villi are initiated by local nervous reflexes, which occur in response to the presence of chyme in small intestine. The hormone secreted from small intestinal mucosa called villikinin is also believed to play an important role in increasing the movements of villi.

Movements of large intestine

The movements of large intestine are mostly sluggish. Still, these movements are important for mixing, propulsive and absorptive functions. Two types of movements occur in large intestine.

1. Mixing movements—Segmentation contractions
2. Propulsive movements—Mass peristalsis.

Segmentation contractions. Large circular constrictions, which appear in the colon, are called mixing segmentation contractions. The length of the portion of colon involved in each contraction is nearly about 2.5 cm. The contractions occur at regular distance in colon.

Mass peristalsis. Mass peristalsis or mass movement propels the feces from colon towards anus. Usually, this movement is developed only a few times every day. The duration of the mass movement is about 10 minutes in the morning before or after breakfast. This is because of the neurogenic factors like gastrocolic reflex and parasympathetic stimulation.

Defecation

Voiding of feces is known as defecation. Feces is formed in the large intestine and stored in sigmoid colon. By the influence of an appropriate stimulus, it is expelled out through the anus. This is prevented by tonic constriction of anal sphincters in the absence of the stimulus.

Defecation reflex. The mass movement drives the feces into sigmoid or pelvic colon. In the sigmoid colon the feces is stored. The desire for defecation occurs when some feces enters rectum due to the mass movement. Usually, the desire for defecation is elicited by an increase in the intrarectal pressure to about 20 to 25 cm H2O.

The usual stimulus is intake of liquid like coffee or tea or water. But it differs from person to person.

The act of defecation is preceded by voluntary efforts like assuming an appropriate posture, voluntary relaxation of external sphincter and the compression of abdominal contents by voluntary contraction of abdominal muscles.

Usually, the rectum is empty. During the development of mass movement, the feces is pushed into rectum and the defecation reflex is initiated. The processes of defecation involves the contraction of rectum and relaxation of internal and external anal sphincters.

The internal anal sphincter is made up of smooth muscle and it is innervated by parasympathetic nerve fibers via pelvic nerve. The external anal sphincter is composed of skeletal muscle and it is controlled by somatic nerve fibers, which pass through pudendal nerve. The pudendal nerve always keeps the external sphincter constricted and the sphincter can relax only when the pudendal nerve is inhibited.

Usually, defecation occurs by the gastrocolic reflex mediated by intrinsic nerves of gastrointestinal tract. In this, the distention of stomach by food causes contraction of rectum followed by desire for defecation. However, this reflex causes only a weak contraction of rectum. The strong contraction of rectum and

the relaxation of anal sphincters occur due to the reflex mediated by parasympathetic nerves and the reflex center is in the sacral segment of spinal cord (fig. 34).

When rectum is distended due to the entry of feces by mass movement, sensory nerve endings are stimulated and the impulses are transmitted via afferent fibers of pelvic nerve to sacral segments (center) of spinal cord. Spinal cord, in turn sends motor impulses to the descending colon, sigmoid colon and rectum via efferent nerve fibers of pelvic nerve. The efferent impulses cause strong contraction of descending colon, sigmoid colon and rectum and relaxation of internal sphincter. Simultaneously, voluntary relaxation of external sphincter occurs. This is due to the inhibition of pudendal nerve by impulses arising from cerebral cortex.

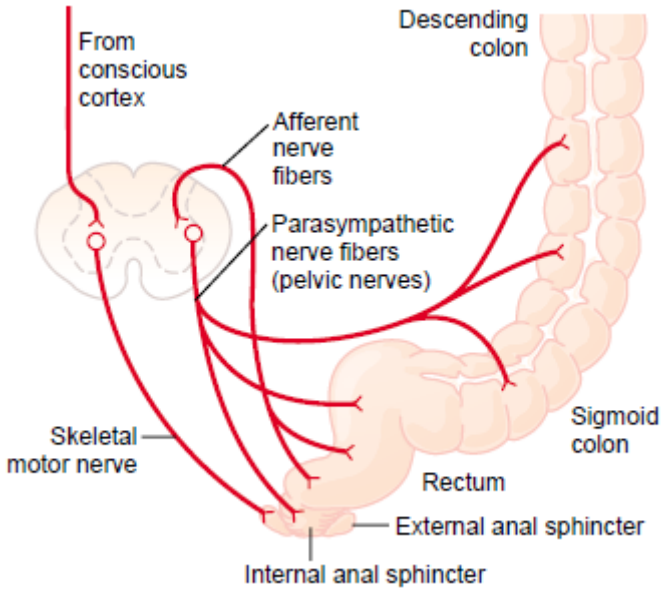


Fig. 34. Defecation reflex.

CONTROL QUESTIONS:

1. What are the different types of salivary glands? Describe the composition, functions and regulation of secretion of saliva.
2. Explain the composition and functions of gastric juice. And, give an account of hormonal regulation of gastric secretion.
3. Describe the different phases of gastric secretion with experimental evidences.
4. Explain the composition, functions and regulation of secretion of pancreatic juice.
5. Describe the composition, functions and regulation of secretion of bile. Enumerate the differences between the liver bile and gallbladder bile. Add a note on enterohepatic circulation.
6. Explain the mechanisms of absorption in GI tract.
7. Write an essay on gastric motility. What are the factors influencing gastric emptying?
8. Describe in detail the gastrointestinal movements.

Task for initial independent training

Topic: ***Gastrointestinal function. Digestion and absorption of substances. Digestion in the Mouth***

1. During a sharp experiment an animal's chorda tympani was electrically irritated. How does it influence the secretion of the parotid salivary gland?

A. Saliva is not secreted.

B. Little liquid saliva secreted.

C. Much liquid saliva secreted.

D. Little viscid saliva secreted.

E. Much viscid saliva secreted.

2. What kind of enzymes does Alimentary tract use for digestion of starch in the mouth?

A. Lingual lipase

B. Chymotrypsins

C. ά-amylase

D. Lactase

E. Pepsins

3. A peripheral part of sympathetic fibers which innervate the sublingual salivary gland of an experimental animal is irritated. How does it influence the secretion of the sublingual salivary gland?

A. Much viscid saliva secreted.

B. Little liquid saliva secreted.

C. Saliva is not secreted.

D. Much liquid saliva secreted.

E. Little viscid saliva secreted.

4. A patient has got a chronic neuritis of the trigeminus. Which of the digestive processes is considerably broken?

A. Mastication.

B. Salivation.

C. Formation of taste feeling.

D. Swallowing.

E. Formation of saliva.

5. Saliva decreases gingivitis and caries because it contains immunoglobulin A and

A. lysozyme

B. mucus

C. salivary amylase

D. water

E. A and C

6. The salivary gland that produces primarily mucus is the … salivary gland.

A. parotid

B. labial

C. submandibular.

D. A and B

E. sublingual

7. The salivary gland which is mixed but produces more serous than mucous secretions and whose duct opens inferiorly in the floor of the oral cavity next to the frenulum of the tongue is the … salivary gland.

A. submandibular

B. sublingual

C. palatine

D. A and B

E. parotid

8. A surgeon makes an incision in the jejunum starting at the serosal surface and ending in the lumen. What is the sequential order of bisected structures as the scalpel passes through the intestinal wall?

A. Circular muscle → longitudinal muscle → submucous plexus

B. Longitudinal muscle → myenteric plexus → circular muscle

C. Myenteric plexus → circular muscle → longitudinal muscle

D. Network of interstitial cells of Cajal → longitudinal muscle → circular muscle

E. Longitudinal muscle → network of interstitial cells of Cajal → submucous plexus

9. A mouse with a new genetic mutation is discovered not to have electrical slow waves in the small intestine. What cell type is most likely affected by the mutation?

A. Enteric neurons

B. Inhibitory motor neurons

C. Enterochromaffin cells

D. Interstitial cells of Cajal

E. Enteroendocrine cells

10. A 10-cm segment of small intestine is removed surgically and placed in a 37^0C physiological solution containing tetrodotoxin. A stimulus at one end of the segment evokes an action potential and an accompanying contraction that travels to the opposite end of the segment. This finding is best explained by

A. Electrical slow waves

B. Varicose motor nerve fibers

C. Interstitial cells of Cajal

D. Functional electrical syncytial properties

E. Release of neurotransmitters

11. Lactase is a brush border enzyme involved in the digestion of lactose. The digestion product or products of lactose are

A. Glucose

B. Glucose and galactose

C. Glucose and fructose

D. Galactose and fructose

E. Fructose

12. Maltase hydrolyzes maltose to form

A. Glucose

B. Glucose and galactose

C. Glucose and fructose

D. Galactose and fructose

E. Galactose

13. Which sugar is taken up by enterocytes by facilitated diffusion?

A. Glucose

B. Galactose

C. Fructose

D. Xylose

E. Sucrose

14. Dietary triglyceride is a major source of nutrient for the human body. It is digested mostly in the intestinal lumen by pancreatic lipase to release

A. Lysophosphatidylcholine and fatty acids

B. Glycerol and fatty acids

C. Diglyceride and fatty acids

D. 2-Monoglyceride and fatty acids

E. Lysophosphatidylcholine and diglyceride

15. After a meal of pizza, dietary lipid is absorbed by the small intestine and transported in the lymph mainly as:

A. VLDLs

B. Free fatty acids bound to albumin

C. Chylomicrons

D. LDLs

E. HDLs

16. The submucosal plexus, in contrast to the myenteric plexus, is mainly concerned with

A. Local intestinal secretion

B. Local absorption

C. Local contraction of the submucosal muscle

D. Increased tonic contraction, or “tone,” of the gut wall

E. True answers are A, B and C

17. The myenteric plexus, is mainly concerned with:

A. Increased tonic contraction, or “tone,” of the gut wall

B. Increased intensity of the rhythmical contractions

C. Slightly increased rate of the rhythm of contraction

D. Increased velocity of conduction of excitatory waves along the gut wall

E. All answers are correct

18. The extrinsic sympathetic and parasympathetic fibers connect to both the myenteric and submucosal plexuses. Stimulation by the parasympathetic system can greatly enhance gastrointestinal functions because neurotransmitter released at the nerve endings is:

A. Norepinephrine

B. Acetylcholine

C. VIP

D. substance P

E. Villikinin

19. The extrinsic sympathetic and parasympathetic fibers connect to both the myenteric and submucosal plexuses. Stimulation by the sympathetic system can greatly inhibit gastrointestinal functions because neurotransmitter released at the nerve endings is:

A. Norepinephrine

B. Acetylcholine

C. VIP

D. substance P

E. Villikinin

20. Absorption of glucose in the small intestine occurs with the help of:

A. Primary-active transport

B. Simple diffusion

C. Secondary-active transport

D. Osmosis

E. Facilitated diffusion

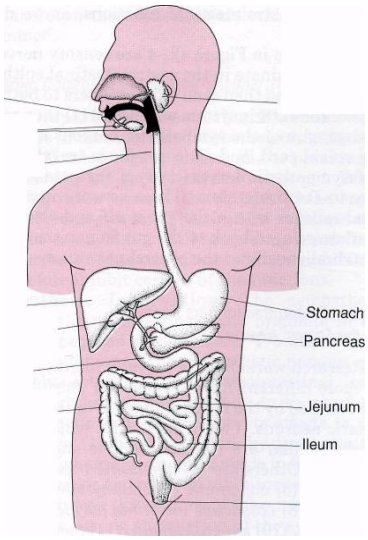
ANSWERS

1	**C**	**6**	**E**	**11**	**B**	**16**	**E**
2	**C**	**7**	**A**	**12**	**A**	**17**	**E**
3	**E**	**8**	**B**	**13**	**C**	**18**	**B**
4	**A**	**9**	**D**	**14**	**D**	**19**	**A**
5	**A**	**10**	**D**	**15**	**C**	**20**	**C**

PRACTICAL SKILLS

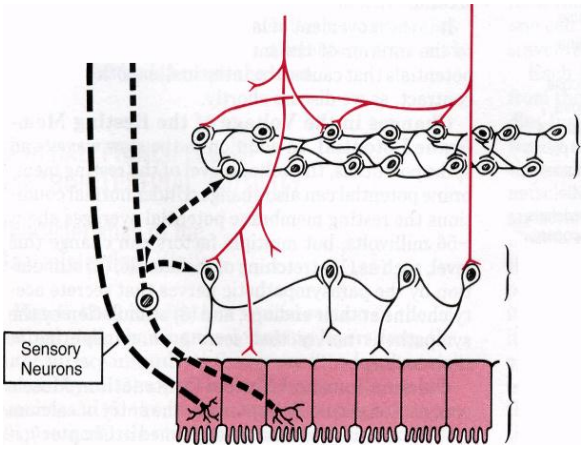
Topic: ***Gastrointestinal function. Digestion and absorption of substances. Digestion in the Mouth***

TASK1. **Draw and note at this figure the Mouth, the Salivary glands, the Esophagus, the liver, all parts of the intestine, the Anus. Describe their function**.



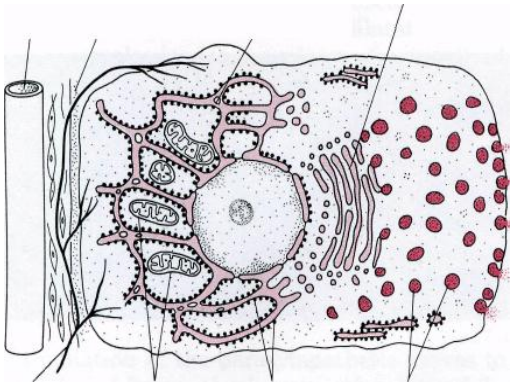
TASK 2. **Draw and note at this figure the Myenteric plexus, the Submucosal plexus, Epithelium. Explain and describe their function.**

To prevertebral ganglia,
Spinal cord and brai stem Sympathetic Parasypathetic
(mainly postganglionic) (preganglionic)



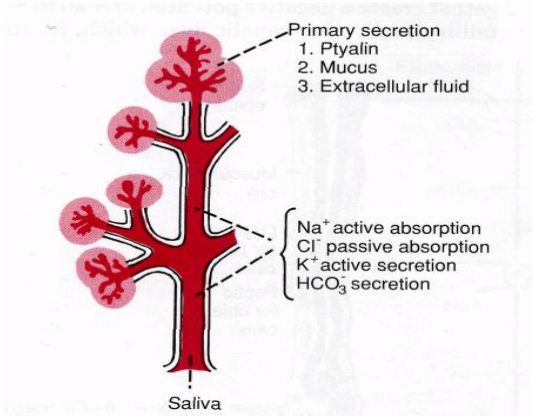
TASK 3. **Draw and note at figure the Capillary, the Basement membrane, the Endoplasmic reticulum, the Goldgy apparatus, the Nerve fiber, the**

Mitochondria, the Ribosomes and the Zymogen granules. Explain their function



Typical glandular cell.

The TASK4**. Draw this figure and write an explanation about the formation and secretion of saliva by a salivary gland.**



The TASK5**. Studying of reaction on Mucin.**

During 1-2 minutes rinse a mouth of distilled water of 20 ml. Repeat manipulation 3 times. Filter the collected saliva through a filtering paper. Add to 2 ml of a saliva

some drops of an acetic acid. After that Mucin drops out as a white sediment. And the saliva loses viscosity.

RESEARCH PROBLEMS

1. Describe this research and write a conclusion on value of saliva's Mucin.

The TASK6**. Studying of saliva's pH**

Eat one sweet before performance of work. Then, collect 2 ml of a saliva in a test tube. Place a strip of a display paper in a test tube with the help of a tweezers. Take out a strip and immediately compare the received colouring to a scale.

RESEARCH PROBLEMS

1.Describe this research and write a conclusion by the received results.

The TASK8. **Write the information about normal transport of substances by the intestine and location of maximum absorption or secretion in this table**

	Small intestine			
Absorption of	**Upper**	**Mid**	**Lower**	**Colon**
Sugars				
Amino acids				
Water-soluble and fast- soluble vitamins				
Betaine,sarcosine				
Antibodies in newborns				
Pyrimidines				
Long-chain fatty acid absorption and conversion to triglyceride				
Bile salts				
Vitamin B12				
Na+				
K+				
Ca+				
Fe+				
Cl+				

SO_4^{2-}				

TASK 7. **Write the information in the table**

source	enzyme	activator	substrate	Catalytic function or products
	Salivary ά-amylase			
	Lingual lipase			
	Pepsins			
	Gastric lipase			
	Trypsin			
	Chymotrypsins			
	Elastase			
	Carboxypeptidase			
	Colipase			
	Pancreatic lipase			
	Bile salt –acid lipase			
	Cholesteryl ester hydrolase			
	Pancreatic ά-amylase			
	Ribonuclease			
	Deoxyribonuclease			
	Phospholipase A_2			
	Enteropeptidase			
	aminopeptidases			
	Carboxypeptidases			
	Endopeptidases			
	Dipeptidases			
	Maltase			
	Lactase			
	Sucrase			
	Ά-Dextinase			
	Trehalase			
	Nuclease and related enzyms			
	Various peptidases			

Task for initial independent training

Topic: ***Digestive functions of Stomach and Pancreas***

1. 150 gr of meat broth was introduced into the gastric cavity of an experimental clog through a probe. The content of which of the following substances will be quickly increased in the dog's blood?

A. Vasointerstinal polypeptide.
B. Somatostatin.
C. Insulin.
D. Neurotensin.
E. Gastrin.

2. Deficit of what enzyme is the most often the reason for incomplete digestion of fats in the digestive tract and the increase of the neutral fat quantity in excrements?

A. Hepatic lipase.
B. Gastric lipase.
C. Pancreatic lipase.
D. Intestinal lipase.
E. Enterokinase.

3. During a patient's examination the decrease of the motor and evacuatory functions of the stomach was determined. The deficit of which of the following substances can it be connected with?

A. Secretin.
B. Gastrin.
C. Adenosine.
D. Somatostatin.
E. Gastric-inhibiting peptide.

4. In the process of aging of a human being there is a decrease of the synthesis and secretion of the pancreatic juice, a decrease of trypsin content in it. To the violation of the splitting of what substances does it lead first of all?

A. Polysaccharides.
B. Phospholipids.
C. Proteins.
D. Nucleic acids.
E. Lipids.

5. A patient's duodenum is ablated. The decrease of the secretion of what hormone will it cause?

A. Gastrin.
B. Cholecystokinin and secretin.
C. Histamine.
D. Gastrin and histamine.
E. Neurotensin.

6. A lean solution of hydrochloric acid was introduced into an experimental dog's duodenum through a probe. The secretion increase of what hormone will it cause?

A. Gastrin.
B. Secretin.
C. Histamin.
D. Cholecystokinin.
E. Neurotensin.

7. Which of the following processes of a hungry man who sees tasty food will be activated first of all?

A. Secretion of gastric juice.
B. Secretion of intestinal juice.
C. Colon motility.

D. Contraction of Oddi's sphincter.

E. Small intestine motor activity.

8. A person has got considerable violation in digestion of proteins, fats and carbonhydrates. Reduced secretion of what digestive juice is the result of it?

A. Saliva.

B. Pancreatic.

C. Gastric.

D. Bile.

E. Intestinal.

9. A part of a patient's pancreas was ablated. What products is it necessary for him to limit in his food ration?

A. Fruit.

B. Boiled vegetables.

C. Dairy produce.

D. Vegetables rich in proteins (beans, soy).

E. Fat meat, beef tea.

10. How many ml of Gastric juice does healthy Stomach produce a day?

A. 500- 600 ml

B. 700- 900 ml

C. 900- 1000 ml

D. 1200- 1500 ml

E. 2000- 2500 ml

11. What inactive enzymes does Pancreas produce for Proteins digestion?

A. lipase

B. Chymotrypsins

C. ά-amylase

D. Trypsinogens

E. Pepsins

12. Absence of intrinsic factor in gastric juice causes deficiency of …….

A. Lipase

B. Chymotrypsins

C. vitamin B12

D. Cholesteryl ester hydrolase

E. Pepsins

13. Which one of the following cells in the gastric glands produce pepsinogen?

A. endocrine cells

B. mucous neck cells

C. parietal or oxyntic cells

D. all of the above

E. chief or zymogenic cells

14. What substance can inhibit hydrochloric acid secretion?

A. Gastrin

B. Enterogastrone and adrenaline

C. Histamine

D. acetylcholine

E. adrenaline

15. What inactive enzymes does stomach produce for proteins digestion?

A. lipase

B. Chymotrypsins

C. ά-amylase

D. Pepsinogens

E. Pepsins

16. The parietal cells in the gastric glands of the pyloric region produce … that binds with Vitamin … to make it more readily absorbed in the ileum.

A. hydrochloric acid; B12

B. mucus; D

C. pepsinogen; D

D. intrinsic factor; B12

E. mucus; C

17. What substance can stimulate hydrochloric acid secretion?

A. Gastrin, Histamine

B. Enterogastrone

C. Histamine

D. adrenaline

E. Sympathetic stimulation

18. The major food digested by gastric secretions is

A. fat

B. starch

C. nucleic acids

D. nucleic acids and fat

E. protein

19. What substances stimulate the secretion of pancreatic juice during gastric phase?

A. Gastrin

B. Enterogastrone

C. Secretin

D. Cholecystokinin

E. Pepsin

20. Secretin, which is produced in duodenum, acts on the pancreas, causing production of pancreatic juice with large amount of:

A. enzymes

B. bicarbonate ions

C. magnesium ions

D. gastrin

E. pepsin

ANSWERS

1	**E**	**8**	**B**	**15**	**D**
2	**C**	**9**	**E**	**16**	**D**
3	**B**	**10**	**D**	**17**	**A**
4	**C**	**11**	**D**	**18**	**E**
5	**B**	**12**	**C**	**19**	**A**
6	**B**	**13**	**E**	**20**	**B**
7	**A**	**14**	**B**		

PRACTICAL SKILLS

Topic: ***Digestion functions of Stomach and Pancreas***

TASK1. **Put information about the Stomach functions in this table.**

#	***Stomach functions***	***your explanation***
1.	Storage function	
2.	Mechanical function	
3.	Digestive function	
4.	Protective function	
5.	Hemopoetic function	
6.	Excretory function	

TASK2. **Two years ago Bob developed cancer and a doctor removed his Pylorus. What happened with Stomach secretory function after that? Write an explanation.**

TASK3. **Put information about the role of gastric enzymes in digestion of various types of food.**

	Food types	***Final products of digestion***
Gastric amylase		
Gastric gelatinase		
Pepsin		
Gastric lipase		
Rennin		

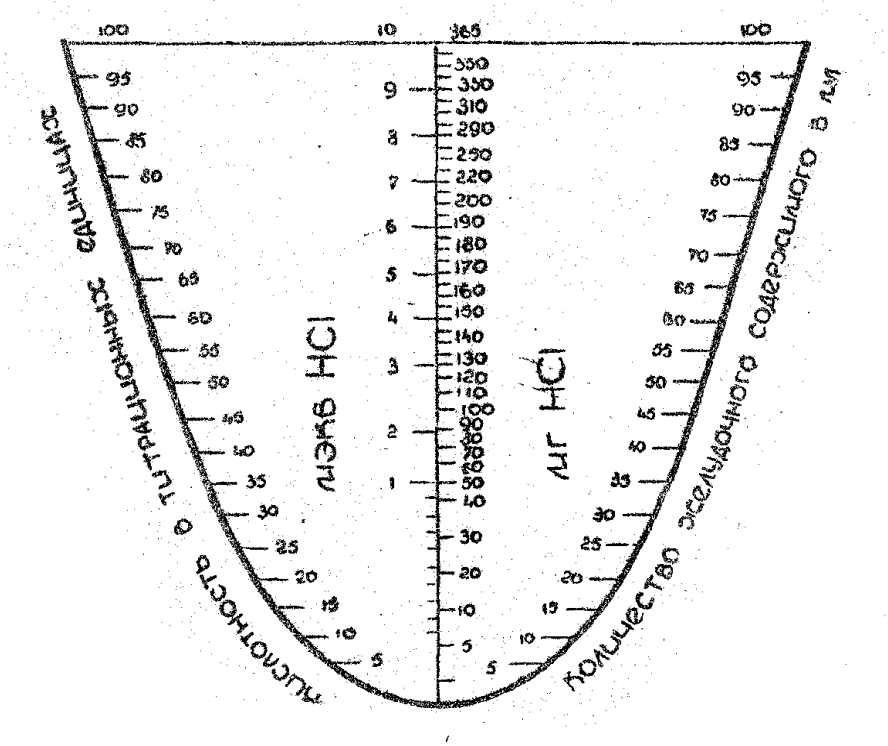
TASK4. **Analysis of Basal Acid Output (BAO) and Maximal Acid Output (MAO) in Gastric juice.**

The specimen is collected over a 2½ hour period. The first 60 minutes, collected in 15-minute intervals is called the Basal Acid Output (BAO). The amount of gastric juice collected from a normal patient will range from 30 mLs to

80 mLs. After chemical stimulation with pentagastrin, histalog, or histamine, the following continuous 60 minutes of 15-minute interval collections is called the Maximal Acid Output (MAO). These four consecutive 15-minute samples are used for the MAO value. Normal values for basal and maximal acid output are as follows:

	BAO mMol/hr	**MAO mMol/hr**	**Typical ratio of BAO to MAO**
man	0-10	7-48	~20%
women	0-6	5-30	~20%
Gastric ulcer	>2	1-20	20%-40%
Gastric cancer	>2	0-20	~20%
Pernicious anemia	0	0	0

TASK5. **Definition the debit of hydrochloric acid in gastric juice by a nomogram.**



Nomogram

Mark volume of gastric juice (ml) in the right branch of this curve. Then mark acidity of this one (T/unit) in the left branch. Connect these two points by a ruler. The point of intersection between the ruler and vertical line of Nomogramm is quantity of hydrochloric acid (ml) .

The amount of hydrochloric acid in gastric juice collected from a normal patient will range from 40 to 150 mg (during the first 60 minutes of gastric secretion) and from 40 to 220 mg (during the second 60 minutes of one).

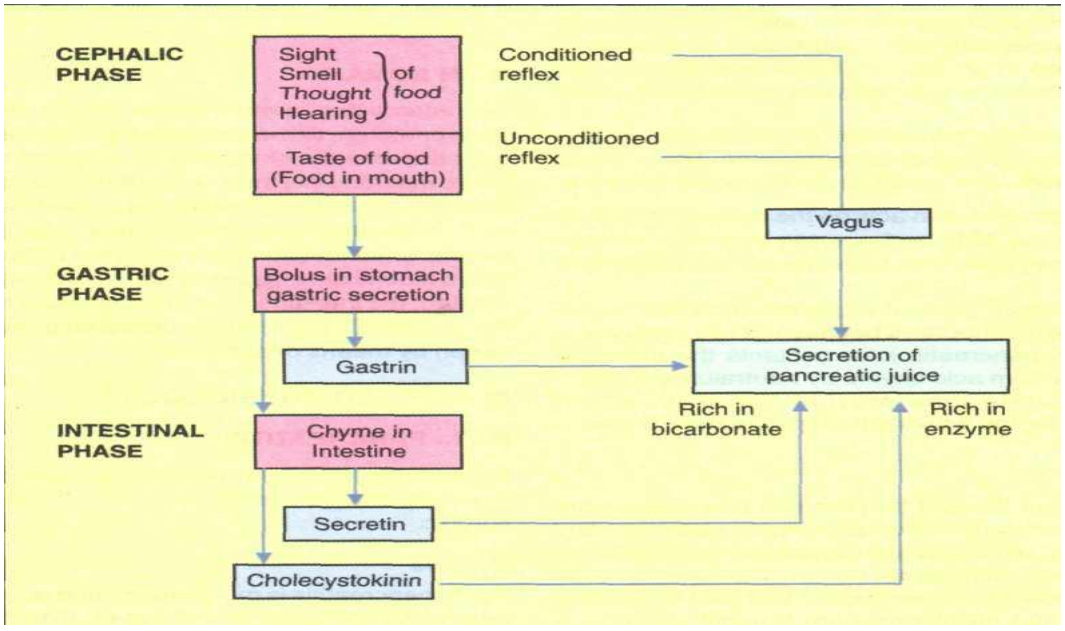
The patient's second portion of gastric juice (90ml) contains about 60 T/unit of acidity. How many mg of hydrochloric acid are there in his specimen? Explain your result and write an explanation.

TASK 6. **Write your explanations for these clinical situations.**

a). The patient has got gastric juice hyper secretion. Why can't he eat a fried meat?

b).The acidity of patient's gastric juice was increased. Can he eat meat-broth?

TASK7. **Draw this figure and write your explanation for this clinical situation. The person's Secretin level was increased. How the Pancreatic juice pH will change in this case?**



Task for initial independent training

Topic: *Digestion functions of Liver, Small Intestine and Colon.*

1. How many ml of bile does liver produce in a healthy person per day?

A. 500- 600 ml

B. 100- 400 ml

C. 800- 1200 ml

D. 1500- 1600 ml

E. 2000- 2500 ml

2.The small intestine contains fingerlike projections called _____, which function is to

A. villi; secret mucus

B. rugae; allow for expansion

C. Crypts of Lieberkuhn; produce mucus, digestive enzymes and hormones

D. villi; increase surface area

E. A and B

3. What substance can increase the release of bile from gallbladder into the intestine?

A. Acetylcholine

B. Gastrin

C. Bile salts

D. Histamine

E. Cholecystokinin

4.Each day about 9 liters of water enter the gastrointestinal tract. By the time the contents leave the large intestine as feces, about _____% of water is reabsorbed.

A. 1

B. 6-7

C. 25

D. 92

E. 99

5. Which proteolytic enzymes does Small intestine produce?

A. Gastrin

B. Enterogastrone

C. Aminopeptidase

D. Maltase

E Cholecystokinin

6. Arrange these sphincters in correct order according the food passage through them:

1. external anal sphincter

2. ileocecal sphincter

3. lower esophageal (cardiac) sphincter

4. pyloric sphincter

A. 1,3,2,4

B. 2,3,4,1

C. 2,1,3,4

D. 3,4,2,1

E. 4,2,1,3

7. Absence of enterokinase in intestinal juice causes deficiency of …….

A. Lipase

B. Trypsin

C. vitamin B12

D. Cholesteryl ester hydrolase

E. Amylase

8. The mucosal lining of the large intestine contains predominantly

A. absorptive cells

B. endocrine cells

C. goblet cells

D. granular cells

E. parietal cells

9. What substances can't Large intestine absorb?

A. Water and Electrolytes

B. Lipids

C. Alcohol

D. Proteins

E. Lipids and Proteins

10. Gastrin secretion is stimulated by

A. duodenal pH greater than 3.

B. secretin

C. cholecystokinin

D. gastric inhibitory polypeptide

E. all of these

11. How many ml of succus entericus does small intestine produce in a healthy person per day?

A. 500- 600 ml

B. 100- 400 ml

C. 800- 1200 ml

D. 1500- 1600 ml

E. 1800ml

12. Cells in duodenum monitor chyme coming from the stomach that has a pH of

1. What would you expect from the duodenal cells to do?

A. release gastric inhibitory polypeptide and cholecystokinin, which inhibits gastric secretions

B. initiate the enterogastric reflex, which increases gastric secretions

C. release secretin, which inhibits gastric secretions

D. release enterogastrone, which inhibits gastric secretions

E. C and D

13. What substance can stimulate the bile secretion from liver?

A. Acetylcholine and Bile salts

B. Gastrin

C. Bile salts

D. Histamine

E. Cholecystokinin

14. Which one of the following hormones is released by both the stomach and small intestine?

A. gastrin and secretin

B. secretin

C. cholecystokinin

D. gastric inhibitory polypeptide

E. gastrin

15. Which enzymes does small intestine produce for sugar digestion?

A. Gastrin

B. Enterogastrone

C. Lactase

D. Maltase and Lactase

E. Cholecystokinin

16. Which one of the following parts of the GI tract has the following characteristics: simple columnar epithelium, muscularis mucosa, Meissner's plexus, two layers of smooth muscle in the tunica muscularis and Peyer's patches of lymph nodules?

A. duodenum

B. jejunum

C. ileum

D. colon

E. rectum

17. Absence of intrinsic factor in the small intestine causes deficiency of …….

A. Lipase

B. Trypsin

C. vitamin B12

D. Cholesteryl ester hydrolase

E. Amylase

18. All of these occur in the large intestine EXCEPT:

A. large numbers of bacteria utilize undigested food

B. fatty acids are absorbed

C. vitamin K is produced

D. sodium and water are absorbed

E. mucus is produced

19. What substances does large intestine absorb?

A. Water, Alcohol , Electrolytes

B. Lipids

C. Alcohol

D. Proteins

E. Electrolytes

20. The major secretory product of the colon is

A. mucin

B. chlorides

C. bicarbonates

D. secretin

E. A,B,C

ANSWERS

1	**C**	**8**	**A**	**15**	**D**
2	**D**	**9**	**E**	**16**	**C**
3	**E**	**10**	**A**	**17**	**C**
4	**D**	**11**	**E**	**18**	**B**
5	**C**	**12**	**E**	**19**	**A**
6	**D**	**13**	**A**	**20**	**E**
7	**B**	**14**	**E**		

PRACTICAL SKILLS

Topic: ***Digestion functions of Liver, Small Intestine and Colon.***

TASK1. **Put information about the functions of Liver in this table.**

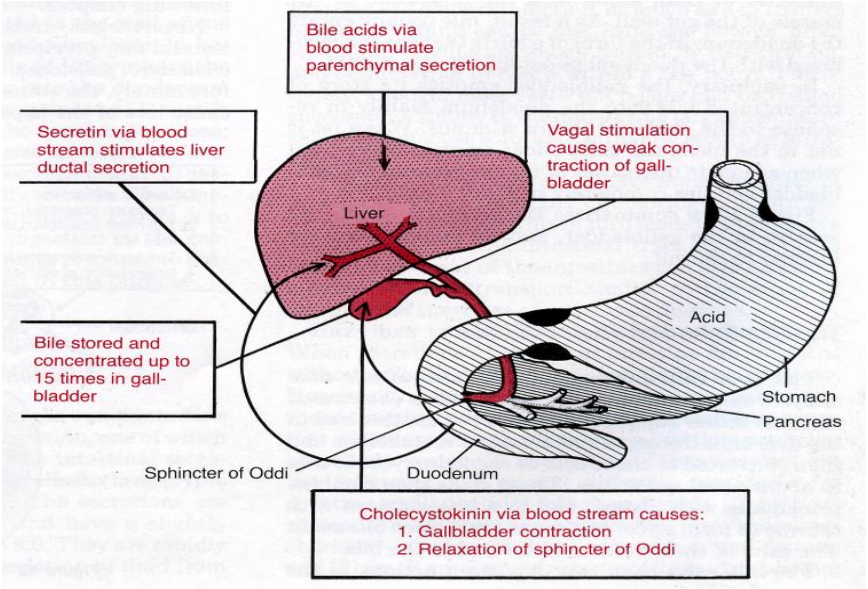
#	***Liver functions***	***your explanation***
1.	Metabolic function**.**	
2.	Storage function	
3.	Synthetic function	
4.	Secretion of Bile	
5.	Excretory function	
6.	Heat production	
7.	Hemopoetic function	
8.	Hemolytic function	
9.	Inactivation of Hormones and Drugs	
10.	Defensive and detoxification functions	

TASK2. **Put information about the Bile functions in this table.**

#	***Bile functions***	***your explanation***
1.	Digestive function**.**	
2.	Absorptive function	
3.	Excretory function	
4.	Laxative action	
5.	Antiseptic action	
6.	Choleretic action	
7.	Maintenance of pH in gastrointestinal tract	
8.	Prevention of Gallstone formation	
9.	Lubrication function	
10.	Cholagogue action	

TASK3. **Study the bile action to fat filtration.** Take two test tubes with funnels. Put filters paper into the funnels. Moisten the first filter with bile but the second one with water. Fill about 1 ml of oil into the each tube. Oil is faster to filter off through the bile layer then through moist paper. Why? **Describe this experiment. Write an explanation**

TASK 4. **Draw this figure**. **Write an explanation about the regulation of Liver secretion and gallbladder emptying.**



TASK5. **Two years ago Den had a gallstone and a doctor removed his gallbladder. What happened with digestion function after that? Write an explanation.**

TASK6. **Put information about the Intestine enzymes role for digestive in this table.**

Enzymes type	***Food types***	***Final products of digestion***
Proteolytic enzymes **:** such as aminopeptidase, dipeptidase and tripeptidase		
Amylolytic enzymes: such as lactase, sucrase, maltase, dextrinase and trehalase		
Lipolytic enzymes: such as intestinal lipase		

TASK7. **Put information about the regulation of succus entericus secretion in this table.**

	type of regulation	**mechanism**	**effect**
1.	**Nervous regulation :**		
a).	Stimulation of parasympathetic nerves		
b).	Stimulation of sympathetic nerves		
c).	The local nervous reflexes		
2.	**Hormonal regulation:**		
a).	cholecysto-kinin		
b).	secretin		
c).	enterocrinin		

TASK 8. **Study the parietal digestion in rat's Intestine.**

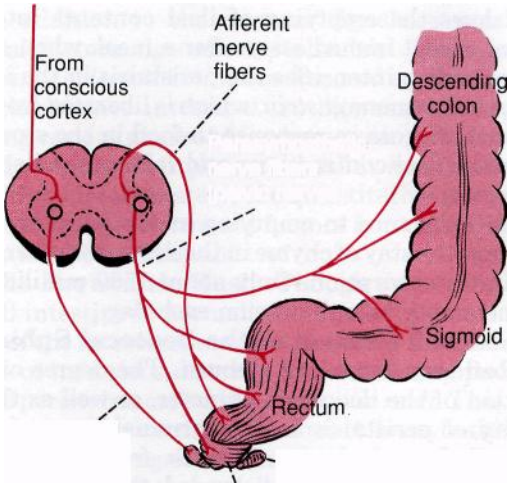
Put about a ml of physiological solution and 0, 5 ml of starch slurry in two test tubes. Add a piece of rat's crushed intestine into the first of the two. Put these test tubes in a thermostat (at 37 ° C) for 20 minutes. Then add about a drop of iodine solution in both ones. Estimate the Amylase activity by color change. **Describe this experiment**. **Write an explanation.**

TASK9.**The person's secretin level was decrease. How can it change the succus entericus secretion?**

TASK10. **Put information about the Colon functions in this table.**

#	***Large intestine functions***	***your explanation***
1.	Digestive function**.**	
2.	Absorptive function	
3.	Formation of feces	
4.	Excretory function	
5.	Secretory function	
7.	Synthetic functions	

TASK 11. **Draw this figure**. **Write an explanation about the afferent and efferent pathways of the parasympathetic mechanism for the defecation reflex.**



External anal sphincter Internal anal sphincter

Tasks for final control

1. Part of the stomach was removed in the patient. What diet should he follow?

A. small meals 6-8 times a day.

B. Major portions 2 times a day.

C. Normal food 3 times a day

D. Eat at night

E. Eat lunch one time a day.

2. In terms of experience "sham feeding" we can learn secretion of:

A. salivary glands

B. stomach in all phases of its secretion

C. stomach in cephalic phase

D. stomach in gastric phase

E. stomach in the intestinal phase

3. The doctor advised the patient, with increased acidity of gastric juice to eat boiled, not grilled meat. Because grilled meat contains substances that stimulate gastric secretion. What is the name of these substances?

A. Fat.

B. Hydrochloric acid.

C. Carbohydrates.

D. Extractives

E. Gastrin.

4. Peripheral sympathetic fibers supplying the parotid gland were stimulated during experiment in an animal. What happened with the secretion of saliva?

A. Saliva was not produced.

B. A little amount of liquid saliva was produced.

C. A little amount of thick saliva was produced.

D. A large amount of liquid saliva was produced.

E. A large amount of thick saliva was produced.

5. What hormonal stimulants of gastric juice in gastric phase of secretion are released?

A. kinins and prostaglandins

B. Histamine and acetylcholine.

C. Enterogastrone and secretin.

D. secretin, CCK-PZ.

E. Histamine and gastrin.

6. Insert the missing words: primary protease in gastric juice is ... which is produced in ...

A. Gastrin, active form

B. Pepsin, inactive form

C. Pepsin, active form

D. Gastrin, inactive form

E. trypsin, inactive form

7. Which of the following substances are natural endogenous stimulators of gastric secretion. Choose the most correct answer:

A. histamine, gastrin, secretin

B. histamine, gastrin, acetylcholine

C. Histamine, hydrochloric acid

D. enterokinase, gastrin, hydrochloric acid

E. Gastrin, hydrochloric acid, secretin

8. The nerve is irritated, which leads to the secretion of large amount of liquid saliva by the parotid gland. What nerve is irritated?

A. N. trigeminus

B. N. sympathicus

C. N. facialis

D. N. vagus

E. N. Glossopharyngeus

9. How does the secretory function of stomach change under the stimulation of H2 (histamine) receptors?

A. secretion of hydrochloric acid and pepsin decreases

B. pepsin secretion increases

C. secretion of hydrochloric acid decreases and pepsin - increases

D. secretion of mucus and pepsin increases

E. secretion of hydrochloric acid increases

10. 150 ml of meat broth was introduced in the stomach of a dog. Concentration of what substance rapidly increases in the blood of animal?

A. Insulin

B. Somatostatin

C. Gastrin

D. Neurotensine

E. VIP

11. The sympathetic nerves to the gastrointestinal tract

A. Reach the wall of the tract in the form of preganglionic fibres.

B. Have preganglionic fibres that liberate a cholinergic transmitter

C. have postganglionic fibres which liberate predominantly NANC (non-adrenergic, non-cholinergic) transmitters.

D. have postganglionic fibres which synapse directly with the muscular fibres of the muscularis externa.

E. have postganglionic fibres which liberate transmitters than generally depolarize the smooth muscle fibres.

12. The gastrointestinal electrical control activity (ECA)

A. originates in the myenteric plexus.

B. is dependent on extracellular Ca++

C. is abolished by atropine.

D. is detectable in the circular but not in the longitudinal muscle fibres.

E. is detectable both during the digestive period and the interdigestive period.

13. The bursts of spike potentials that constitute the gastrointestinal electrical response activity (ERA) are initiative of contractions which

A. have an amplitude that is related to the number of spikes per burst.

B. have an amplitude that is characteristically lower following sympathetic denervation of the tract.

C. have a maximal frequency that is limited by the number of spikes per burst.

D. have a higher maximal frequency in the longitudinal muscle fibres that in the circular muscle fibres at corresponding points along the tract.

E. have a higher maximal frequency in the ileum than in the jejunum.

14. "Deglutition Apnea"

A. gives rise to odynophagia.

B. normally precedes every primary esophageal peristaltic wave.

C. may be induced by intraluminal distension of the esophagus.

D. is seen only in individuals who have abnormal patterns of swallowing.

E. results from activation of inhibitory nerve fibres to the respiratory muscles.

15. With respect to the resting tone of the lower esophageal sphineter (LES), all of the following are correct EXCEPT:

A. It diminishes significantly following section of its vagal innervation.

B. It diminishes significantly following the administration of progesterone.

C. It does not diminish significantly following the administration of ganglionic blocking agents.

D. It increases significantly following the administration of very large (pharmacological) doses of gastrin.

E. It is normally in the range of 10-30 mmHg above intragastric pressure.

16. Before fat molecules are eventually placed into micelles in the lumen of the gastrointestinal (GI) tract, they are digested by pancreatic lipase to form:

A. Glycerol

B. Monoglycerides

C. Free fatty acids

D. A and B

E. A and C

17. The chemical digestion of this class of compounds begins in the small intestine.

A. Carbohydrates

B. Proteins

C. Lipids

D. Nucleic acids

E. Starch

18. Which of the following is true about the enteric nervous system?

A. It is capable of responding independently to stimuli within the gastrointestinal tract.

B. Its function is regulated by the autonomic nervous system.

C. It is sometimes referred to as the "little brain".

D. It uses serotonin as its main neurotransmitter.

E. All of the above.

19. All of the following are secreted by the pancreas into the duodenal region of the small intestine EXCEPT:

A. Bicarbonate

B. Amylase

C. Nuclease

D. Peptidase

E. Intrinsic factor

20. The interstitial cells of Cajal are responsible for:

A. Regulating the osmolality of the kidney interstitial fluid.

B. Secreting secretin into the interstitial fluid of the small intestine.

C. Setting the contractile rhythm of the smooth muscle of the segments of the gastrointestinal (GI) tract.

D. Secreting cholecystokinin into the bloodstream.

E. Secreting the antidiuretic hormone into the bloodstream.

21. Stomach parietal cells are responsible for secreting:

A. Hydrochloric acid (HCl)

B. Pepsinogen

C. Intrinsic factor

D. Bicarbonate (HCO_3^-)

E. A and C.

22. After ingestion of a meal, the pH of gastric fluid is about:

A. 1,5

B. 3,5

C. 5,5

D. 7,5

E. 9,5

23. Which one of the following is consistent with absorption of glucose molecules across the intestinal epithelium?

A. Glucose enters the intestinal epithelial cell through glucose channels in the apical membrane and leaves the cell through the basal membrane by facilitated diffusion.

B. Glucose enters through the apical membrane by facilitated diffusion and leaves through the basal membrane by facilitated diffusion also.

C. Glucose enters the cell through the apical membrane by co-transport with Na^+ and leaves the cell through the basal membrane by facilitated diffusion.

D. Glucose enters the cell through the apical membrane by facilitated diffusion and leaves the cell through the basal membrane by co-transport with Na^+.

E. None of the above.

24. Most of the chemical digestion in the gastrointestinal (GI) tract occurs in the:

A. Mouth

B. Stomach

C. Small intestine

D. Large intestine

E. Colon

25. Most of the water and electrolytes absorbed across the walls of the gastrointestinal (GI) tract is absorbed in this region:

A. Mouth

B. Stomach

C. Small intestine

D. Large intestine

E. Colon

26. Fat digestion begins in this region of the gastrointestinal (GI) tract.

A. Mouth

B. Stomach

C. Duodenum of the Small intestine

D. Jejunum of the Small intestine

E. Large intestine

27. Which one of the following cells in the gastric glands produce pepsinogen?

A. endocrine cells

B. mucous neck cells

C. parietal or oxyntic cells

D. all of the above cells

E. chief or zymogenic cells

28. What substance is able to inhibit hydrochloric acid secretion?

A. Gastrin

B. Enterogastrone and adrenaline

C. Histamine

D. acetylcholine

E. Adrenaline

29. How many ml of pancreatic juice does healthy pancreas produce per day?

A. 500- 800 ml

B. 60- 80 ml

C. 900- 1000 ml

D. 1200- 1500 ml

E. 2000- 2500 ml

30. What kind of substances are produced by accessory cells of stomach?

A. mucoid secretion

B. enzymes of the gastric juice

C. hydrochloric acid

D. mucoid secretion and hydrochloric acid

E. All of the above

31. This substance is an important maturation factor during erythropoiesis and factor of Castle is necessary for the absorption of this one.

A. vitamin B12

B. hydrochloric acid

C. Vitamin B6

D. Vitamin D

E. Pepsinogen

32. This substance causes denaturation and swelling of proteins and in that way facilitates their breakdown by enzymes

A. vitamin B12

B. hydrochloric acid

C. Vitamin B6

D. Vitamin D

E. All of the above

33. Each day about 9 liters of water enter the gastrointestinal tract. By the time the contents leave the large intestine as feces, about _____% of water is reabsorbed.

A. 1%

B. 6-7%

C. 25%

D. 92%

E. 99%

34. Pancreatic juice collected from the pancreatic duct has no effect on proteins because it contains inactive forms of enzymes.

A. Trypsinogen

B. Chymotrypsinogen

C. Trypsinogen and Chymotrypsinogen

D. Pepsinogen

E. Pepsin

35. What factors can arrest the action of pepsin in the duodenum?

A. alkaline content

B. hydrogen ions

C. water

D.acid

E. all of the above

36. What factors can arrest the action of pepsin in the duodenum?

A. bile

B. hydrogen ions

C. water

D. acid

E. all of the above

37. Pancreatic secretion begins …to…minutes after a meal

A. 4,5

B. 5,6

C. 6,7

D. 7,8

E. 2, 3

38. Pancreatic secretion after a meal lasts for … to …hours

A. 1,2

B. 3,4

C. 5,6

D. 6,14

E. 1,7

39. Substances, which increase the secretion of bile from liver, are known as …….

A. Cholemimetic

B. Choleretics

C. Cholagogues

D. Cholelitics

E. all of the above

40. What substances are Choleretic?

A. Acetylcholine

B. Secretin and bile salts

C. CCK-PZ

D. acid chyme in intestine

E. all of the above

41. This substance increases the release of bile from gallbladder into the intestine.

A. Cholemimetic

B. Choleretics

C. Cholagogues

D. Cholelitics

E. all not correct

42. Which of the following is not a macronutrient?

A. Vitamin C

B. Protein

C. Carbohydrates

D. Fats

E. all of the above

43. Water is an important component of the diet because

A. it helps stabilize body temperature

B. it is required for many chemical reactions

C. it helps maintain normal concentrations of wastes and nutrients in the body

D. A and B

E. All of the above

44. What ions can block sugar influx into the epithelial cells?

A. a high concentration of Na+

B. a low concentration of sodium

C. a high concentration of potassium

D. a low concentration of potassium

E. a low concentration of iron

45. The esophageal phase of swallowing is caused by the

A. peristaltic reflex

B. coughing reflex

C. swallowing center

D. enteric reflex

E. all answers are incorrect

46. What can happen with salivation after stimulation of the sympathetic nerve?

A. secretion of small amounts of saliva and a high concentration of organic material

B. secretion of small amounts of saliva

C. secretion of watery saliva

D. a low concentration of organic material

E. a high concentration of organic material

47. Some nerve fibers of Auerbach's plexus accelerate the movements by secreting the excitatory neurotransmitter substances like ……

A. Acetylcholine

B. serotonin

C. substance P

D. Acetylcholine, serotonin, substance P

E. Noradrenalin

48. These nerve fibers cause constriction of blood vessels of gastrointestinal tract.

A. Auerbach's plexus

B. Giza plexus

C. Meissner's plexus

D. Salary plexus

E. Auerbach's plexus and Salary plexus

49. These nerve fibers inhibit the movements of gastrointestinal tract

A. Sympathetic nerve fibers

B. Auerbach's plexus

C. Giza plexus

D. Meissner's plexus

E. Salary plexus

50. These nerve fibers decrease the secretions of gastrointestinal tract

A. Sympathetic nerve fibers

B. Auerbach's plexus

C. Giza plexus

D. Meissner's plexus

E. Salary plexus

51. These nerve fibers accelerate the secretory activities of the glands in the gastrointestinal tract.

A. Sympathetic nerve fibers

B. Auerbach's plexus

C. parasympathetic nerve fibers

D. Meissner's plexus

E. Salary plexus

52. These nerve fibers increase the motility of gastrointestinal tract

A. Sympathetic nerve fibers

B. parasympathetic nerve fibers

C. Auerbach's plexus

D. Meissner's plexus

E. Salary plexus

53. This neurotransmitter is responsible for the activation of the motility of gastrointestinal tract and is secreted by the ……..fibers

A. Acetylcholine, parasympathetic nerve

B. Acetylcholine, Auerbach's plexus

C. Noradrenalin, Auerbach's plexus

D. Noradrenalin, sympathetic nerve

E. Serotonin, Meissner's plexus

54. This neurotransmitter is responsible for the inhibition of the movements of gastrointestinal tract and decrease the secretions of gastrointestinal tract by secreting the neurotransmitter ……..

A. Acetylcholine, parasympathetic nerve

B. Acetylcholine, Auerbach's plexus

C. Noradrenalin, Auerbach's plexus

D. Noradrenalin, sympathetic nerve

E. Serotonin, Meissner's plexus

55. This substance contributes to the curdling of milk, i. e. to the conversion of caseinogen into casein by the pepsins and rennin.

A. vitamin B_{12}

B. hydrochloric acid

C. Vitamin B6

D. Vitamin D

E. trypsin

ANSWERS

1A	9E	17D	25C	33E	41C	50A
2C	10C	18E	26A	34C	42A	51C
3D	11B	19E	27E	35A	44B	52B
4C	12E	20C	28B	36A	45D	53A
5E	13A	21E	29A	37E	46A	54D
6B	14B	22A	30A	38D	47D	55B
7B	15A	23C	31A	39B	48C	
8E	16C	24C	32B	40E	49A	

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