**Digestive Tract:**

**General Structure of the Digestive Tract.**

The entire gastrointestinal tract has four main layers: the **mucosa, submucosa, muscularis,** and **serosa.**

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| 1-The **mucosa** comprises an **epithelial lining;** an underlying **lamina propria** of loose connective tissue rich in blood vessels, lymphatics, lymphocytes and smooth muscle cells, sometimes also containing glands; and a thin layer of smooth muscle called the **muscularis mucosae** usually separating mucosa from submucosa. The mucosa is frequently called a **mucous membrane.**  2-The **submucosa** contains denser connective tissue with many blood and lymph vessels and the **submucosal plexus** of autonomic nerves. It may also contain glands and lymphoid tissue.  3-The thick **muscularis** is composed of smooth muscle cells that are spirally oriented and divided into two sublayers. ***i)***In the internal sublayer (closer to the lumen), the orientation is generally circular; in the external sublayer, it is mostly longitudinal. ***ii)*** In the connective tissue between the muscle sublayers are blood and lymph vessels, as well as another autonomic **myenteric nerve plexus**. ***iii)***This and the submucosal plexus together comprise the local **enteric nervous system** of the digestive tract, containing largely autonomic neurons functioning independently of the central nervous system (CNS).  4-The **serosa** is a thin layer of loose connective tissue, rich in blood vessels, lymphatics, and adipose tissue, with a simple squamous covering epithelium (**mesothelium**. In places where the digestive tract is not suspended in a cavity but bound to other structures, such as in the esophagus , the serosa is replaced by a thick **adventitia**, consisting of connective tissue containing vessels and nerves, lacking mesothelium.  **The main functions of the digestive tract's epithelial lining are to**:  1- Provide a selectively permeable barrier between the contents of the tract and the tissues of the body,  2- Facilitate the transport and digestion of food,  3- Promote the absorption of the products of this digestion,  4-Produce hormones that affect the activity of the digestive system,  5-Produce mucus for lubrication and protection.  6-produce antibodies are mainly immunoglobulin A (IgA) and are secreted into the intestinal lumen bound to a secretory protein produced by the epithelial cells. |

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| **Oral Cavity:**  The oral cavity (is lined with stratified squamous epithelium, keratinized or nonkeratinized, depending on the region. 1-The keratin layer protects the oral mucosa from damage during masticatory function and is best developed on the gingiva (gum) and hard palate. The lamina propria in these regions has many papillae and rests directly on bony tissue. 2-Nonkeratinized squamous epithelium covers the soft palate, lips, cheeks, and the floor of the mouth. Surface cells are shed continuously and replaced by progeny of stem cells in the basal epithelial layer. 3-The lamina propria has papillae similar to those in the dermis of the skin and is continuous with a submucosa containing diffuse small salivary glands. 4-The soft palate also has a core of skeletal muscle and lymphoid nodules. In the **lips**, there is also striated muscle and a transition from the oral nonkeratinized epithelium to the keratinized epithelium of the skin . |

**Tongue****:**

1-The tongue is a mass of striated muscle covered by a mucous membrane whose structure varies according to the region. The muscle fibers cross one another in three planes and are grouped in bundles separated by connective tissue. 2-Because the connective tissue of the lamina propria penetrates the spaces between the muscular bundles, the mucous membrane is strongly adherent to the muscle. The mucous membrane is smooth on the lower surface of the tongue. 3-The tongue's dorsal surface is irregular, covered anteriorly by a great number of small eminences called **papillae.** 4-The posterior third of the tongue's dorsal surface is separated from the anterior two thirds by a V-shaped groove, the **terminal sulcus**. Behind this boundary is the root of the tongue, whose surface shows the many bulges of the lingual tonsils and smaller collections of lymphoid nodules .

**Papillae:**

 The numerous papillae on the anterior portion of the tongue are elevations of the mucous membrane that assume various forms and functions. Four types are recognized .

1- **Filiform papillae** are very numerous, have an elongated conical shape, and are heavily keratinized, which gives their surface a gray or whitish appearance. Their epithelium lacks taste buds and their role is mechanical in providing a rough surface that facilitates food movement during chewing.

2- **Fungiform papillae** are less numerous, lightly keratinized, and mushroom-shaped with connective tissue cores and scattered taste buds on their upper surfaces. They are irregularly interspersed among the filiform papillae.

3- **Foliate papillae** are poorly developed in adults, but consist of parallel ridges and furrows on the sides of the tongue, with taste buds.

4- **Vallate** (or circumvallate) **papillae** are the least numerous and largest lingual papillae, and have over half the taste buds on the human tongue. With diameters of one to three mm, seven to twelve circular vallate papillae normally form a V-shaped line just before the terminal sulcus.

**Gingiva:**

  1-The **gingiva** is a mucous membrane firmly bound to the periosteum of the maxillary and mandibular bones . It is composed of stratified squamous epithelium and lamina propria with numerous connective tissue papillae. 2-A specialized part of this epithelium, named **junctional epithelium,** is bound to the tooth enamel by means of a cuticle resembling a thick basal lamina. 3-The epithelial cells are attached to this cuticle by numerous hemidesmosomes. Between the enamel and the epithelium is the **gingival sulcus,** a groove up to 3 mm deep surrounding the neck .

**Esophagus:**

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| 1-It is a muscular tube whose function is to transport food from the mouth to the stomach. It is lined by nonkeratinized stratified squamous epithelium with stem cells scattered throughout the basal layer . 2-In the submucosa are groups of small mucus-secreting glands, the **esophageal glands,** secretions of which facilitate the transport of foodstuffs and protect the mucosa. In the lamina propria of the region near the stomach are groups of glands, the **esophageal cardiac glands**, which also secrete mucus. 3-In the proximal third of the esophagus the muscularis is exclusively skeletal muscle like that of the tongue. 4-The middle third contains a combination of skeletal and smooth muscle fibers and in the distal third the muscularis contains only smooth muscle. 5-Also, only the most distal portion of the esophagus, in the peritoneal cavity, is covered by serosa. The rest is enclosed by a layer of loose connective tissue, the adventitia, which blends into the surrounding tissue. |

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| **Stomach:**  The stomach, like the small intestine, is a mixed exocrine-endocrine organ that digests food and secretes hormones. It also produces a gastric lipase that digests triglycerides . Gross inspection reveals four regions: **cardia, fundus, body,** and **pylorus** . The fundus and body are identical in microscopic structure so that only three histologically distinct regions are recognized. The mucosa and submucosa of the empty stomach have longitudinally directed folds known as **rugae**, which flatten when the stomach is filled with food. The wall in all regions of the stomach is made up of all four major layers. |

**Mucosa****:**

1- at the esophago-gastric junction, the mucosa of the stomach consists of a simple columnar **surface epithelium** that invaginates into the lamina propria, forming **gastric pits** . Emptying into the gastric pits are branched, tubular glands characteristic of the stomach region (cardiac, gastric, and pyloric). 2-Stem cells for the entire epithelial lining of the stomach are located in the upper regions of these glands near the gastric pits. 3-The vascularized **lamina propria** that surrounds and supports these pits and glands contains smooth muscle fibers and lymphoid cells. Separating the mucosa from the underlying submucosa is a layer of smooth muscle, the **muscularis mucosae** .

 4- The luminal surface of the stomach has numerous small circular or ovoid invaginations of the epithelial lining . These are the openings of the gastric pits. The epithelium covering the surface and lining the pits is a simple columnar epithelium, the cells of which produce a protective mucus layer. 5- Glycoproteins secreted by the epithelial cells are hydrated and mix with lipids and bicarbonate ions also released from the epithelium to form a thick, hydrophobic layer of gel with a pH gradient from almost 1 at the luminal surface to 7 at the epithelial cells. 6-The mucus firmly adherent to the epithelial surface is very effective in protection, while the superficial luminal mucus layer is more soluble, partially digested by pepsin and mixed with the luminal contents. 7-Hydrochloric acid, pepsin, lipases, and bile in the stomach lumen must all be considered as potential endogenous aggressors to the epithelial lining. Surface epithelial cells also form an important line of defense due to their mucus production, their tight intercellular junctions, and ion transporters to maintain intracellular pH and bicarbonate production. 8-A third line of defense is the underlying circulatory bed, which provides bicarbonate ions, nutrients, and oxygen to the mucosal cells, while removing toxic metabolic products. The rich vasculature also favors the rapid healing of superficial wounds to the mucosa.

**Cells of the gastric glands:**

1- **Mucous neck cells** are present in clusters or as single cells between parietal cells in the necks of gastric glands . They are irregular in shape, with the nucleus at the base of the cell and the secretory granules near the apical surface. Their mucus secretion is less alkaline and quite different from that of the surface epithelial mucous cells.

2-**Parietal cells** are present mainly in the upper half of gastric glands, with fewer in the base. ***i)***They are large rounded or pyramidal cells, each with one central spherical nucleus and cytoplasm that is intensely eosinophilic due to the high density of mitochondria . ***ii)*** Parietal cells secrete both **hydrochloric acid (HCl)** and **intrinsic factor**, a glycoprotein required for uptake of vitamin B12 in the small intestine. ***iii)*Carbonic anhydrase** produces H2CO3 which dissociates in the cytoplasm into H+ and HCO3+ . ***vi)***The active cell also releases K+ and Cl– and the Cl– ions combine with H+ to form HCl. ***v)***Secretory activity of parietal cells is stimulated both through cholinergic nerve endings (parasympathetic stimulation) and by histamine and a polypeptide called **gastrin,** both secreted by local enteroendocrine cells.

3-**Chief (zymogenic) cells** predominate in the lower region of the tubular glands and have all the characteristics of protein-synthesizing and -exporting cells. ***i)***The cytoplasmic granules contain the inactive enzyme **pepsinogen. *ii)*** This precursor is rapidly converted into the highly active proteolytic enzyme **pepsin** after being released into the acid environment of the stomach. Pepsins are aspartate endoproteinases of relatively broad specificity. ***iii)*** In humans chief cells also produce the enzyme lipase and the hormone leptin.

4-**Enteroendocrine cells** : ***i)***Different enteroendocrine cells secrete a variety of hormones, almost all short polypeptides . ***ii)***In the fundus **enterochromaffin cells (EC cells)** are found on the basal lamina of gastric glands and secrete principally **serotonin (5-hydroxytryptamine)**. ***iii)***In the pylorus and lower body of the stomach other enteroendocrine cells are located in contact with the glandular lumens, including **G cells** which produce the polypeptide **gastrin**. Gastrin stimulates the secretion of acid by parietal cells and has a trophic effect on gastric mucosa.

5-**Stem cells** are few in number and found in the neck region of the glands. ***i)***They are low columnar cells with basal nuclei and divide asymmetrically Some of the daughter cells move upward to replace the pit and surface mucous cells, which have a turnover time of 4–7 days. ***ii)***Other daughter cells migrate more deeply into the glands and differentiate into mucous neck cells and parietal, chief, and enteroendocrine cells. ***iii)*** These cells are replaced much more slowly than are surface mucous cells.

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| **Oth****er Layers of the Stomach:**  1-The **submucosa** is composed of connective tissue containing blood and lymph vessels; it is infiltrated by lymphoid cells, macrophages, and mast cells. 2-The **muscularis** is composed of smooth muscle fibers oriented in three main directions. The external layer is longitudinal, the middle layer is circular, and the internal layer is oblique. Rhythmic contractions of the muscularis serve to mix ingested food and chyme with the secretions from the gastric mucosa. At the pylorus, the middle layer is greatly thickened to form the **pyloric sphincter.** 3-The stomach is covered by a thin **serosa.** |

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| **Small Intestine:**  The small intestine is the site of terminal food digestion, nutrient absorption, and endocrine secretion. The processes of digestion are completed in the small intestine, where the nutrients (products of digestion) are absorbed by cells of the epithelial lining. The small intestine is relatively long—approximately 5 m—and consists of three segments: **duodenum, jejunum,** and **ileum.**  **Mucous Membrane****:**  1- the lining of the small intestine shows a series of permanent circular or semilunar folds ,consisting of mucosa and submucosa , which are best developed in the jejunum. Intestinal **villi** are mucosal outgrowths (epithelium plus lamina propria) and project into the lumen.  2- In the duodenum they are leaf-shaped, but gradually assume fingerlike shapes moving toward the ileum. Villi are covered by a simple columnar epithelium of **absorptive cells** and **goblet cells**. |

3-Between the villi are small openings of short tubular glands called **intestinal crypts** or **crypts of Lieberkühn**. The epithelium of each villus is continuous with that of the intervening glands, which contain differentiating **absorptive and goblet cells, Paneth cells, enteroendocrine cells, and stem cells that give rise to all these cell types.**

**A**- **Enterocytes**: ***i)*** the absorptive cells, are tall columnar cells, each with an oval nucleus in the basal half of the cell . At the apex of each cell is a homogeneous layer called the **striated** (or **brush**) **border**. ***ii)***When viewed with the electron microscope, the striated border is seen to be a layer of densely packed **microvilli**. Microvilli greatly increase the area of contact between the intestinal surface and the nutrients, a function also of the plicae and villi, which is an important feature in an organ specialized for absorption.  ***iii)***Enterocytes absorb the nutrient molecules produced by digestion. Disaccharidases and peptidases secreted by these cells and bound to the microvilli hydrolyze the disaccharides and dipeptides into monosaccharides and amino acids that are easily absorbed through active transport. ***iv)*** Digestion of fats results from the action of pancreatic lipase and bile. In humans, most of the lipid absorption takes place in the duodenum and upper jejunum .

**B-Goblet cells****:** are interspersed between the absorptive cells. ***i)***They are less abundant in the duodenum and more numerous in the ileum. ***ii)*** These cells produce glycoprotein mucins that are hydrated and cross-linked to form mucus, whose main function is to protect and lubricate the lining of the intestine.

**C-Paneth cells**: ***i)***located in the basal portion of the intestinal crypts below the stem cells, are exocrine cells with large, eosinophilic secretory granules in their apical cytoplasm . ***ii)***Paneth cell granules undergo exocytosis to release lysozyme, phospholipase A2, and hydrophobic peptides called defensins, all of which bind and breakdown membranes of microorganisms and bacterial walls. ***iii)*** Paneth cells have an important role in innate immunity and in regulating the microenvironment of the intestinal crypts.

**D**-**Enteroendocrine cells: *i)*** are present in varying numbers throughout the length of the small intestine, secreting various peptides and representing part of the widely distributed **diffuse neuroendocrine system** . ***ii)***stimulation these cells release their secretory granules by exocytosis and the hormones may then exert paracrine (local) or endocrine (blood-borne) effects. ***iii)***Polypeptide-secreting cells of the digestive tract fall into two classes: a "closed" type, in which the cellular apex is covered by neighboring epithelial cells and an "open" type, in which the apex of the cell has microvilli and contacts the lumen. ***iv)***Peptides produced have both endocrine and paracrine effects, which include the control of peristalsis, regulation of secretions necessary for food digestion, and the sense of being satiated after eating.

**E-M** (**microfold**) **cells: *i)*** It is specialized epithelial cells in the ileum overlying the lymphoid follicles of Peyer patches. these cells are characterized by the presence of basal membrane invaginations or pockets containing many intraepithelial lymphocytes and antigen-presenting cells. ***ii)*** M cells selectively endocytose antigens and transport them to the underlying macrophages and lymphocytes, which then migrate to lymph nodes where immune responses to foreign antigens are initiated. ***iii)*** M cells thus serve as sampling stations where material in the lumen of the gut is transferred to immune cells of the MALT in the lamina propria. ***iv)***The basement membrane under the M cells is porous, facilitating transit of cells between the lamina propria and the pockets of M cells.

**Lamina Propria through Serosa****:**

1-The lamina propria of the small intestine is composed of loose connective tissue with blood and lymph vessels, nerve fibers, and smooth muscle cells. The lamina propria penetrates the core of each intestinal villus, bringing with it microvasculature, lymphatics, and nerves . 2-Smooth muscle fibers inside the villi are responsible for their rhythmic movements, which are important for efficient absorption. The muscularis mucosae also produces local movements of the villi and plicae circulares.  3-The proximal part of the duodenum has, primarily in its submucosa but extending into the mucosa, large clusters of branched tubular mucous glands, the **duodenal** (or **Brunner**) **glands**, with small excretory ducts opening among the intestinal crypts . 4-The product of the glands is distinctly alkaline (pH 8.1–9.3), which neutralizes chyme entering the duodenum from the pylorus, protecting the mucous membrane and bringing the intestinal contents to the optimum pH for pancreatic enzyme action. 5-In the ileum both the lamina propria and submucosa contain the lymphoid nodule aggregates known as **Peyer patches,** an important component of the MALT. 6- The muscularis is well developed in the small intestine, composed of an internal circular layer and an external longitudinal layer, and is covered by a thin serosa with mesothelium .

**Large Intestine:**

**1-The** **mucosal** membrane with no folds except in its distal (rectal) portion and no villi . ***i)*** The mucosa is penetrated throughout its area by tubular intestinal glands lined by goblet and absorptive cells, with a small number of enteroendocrine cells . ***ii)***The absorptive cells or **colonocytes** are columnar and have short, irregular microvilli . ***iii)*** Stem cells for the epithelium of the large bowel are located in the bottom third of each gland. ***iv)***The large intestine is well suited to its main functions: absorption of water, formation of the fecal mass from undigestible material, and production of mucus that lubricates the intestinal surface.

 2-**The lamina propria** is rich in lymphoid cells and in lymphoid nodules that frequently extend into the **submucosa**. The richness in MALT is related to the large bacterial population of the large intestine. 3-**The muscularis** comprises longitudinal and circular strands, but differs from that of the small intestine, with fibers of the outer layer gathered in three longitudinal bands called **taeniae coli** . 4-**The serosa**, which is characterized by small, pendulous protuberances of adipose tissue.

**Appendix:**

1-the **appendix** is an evagination of the cecum. It is characterized by a relatively small and irregular lumen, shorter and less dense tubular glands, and no taeniae coli. 2- it has no function in digestion, the appendix is a significant component of the MALT, with abundant lymphoid follicles in its wall .