ANAT D502 – Basic Histology

Digestive System I - Upper tract
Revised 10.8.15

Reading assignment: Chapter 16: Digestive System I: Oral Cavity and Associated Structures; pay special attention to Folders 16.1, 16.2 (American system only), 16.3 and 16.4 (Clinical Correlations).

Chapter 17: Digestive System II: Esophagus and Gastrointestinal Tract; pay special attention to Folders 17.1, 17.2, 17.6 and 17.7 (Clinical Correlations)

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I. Introduction to Digestive System

Digestion is the breakdown of food substances into simpler molecules. The digestive (or alimentary) system in humans is comprised of a tubular gut providing for a one-way flow of food particles. Digestion is entirely extracellular with the unabsorbed food excreted as feces. Different segments of the digestive tract are specialized for different digestive functions. This system provides two advantages: (1) Digestion is continuous (due to one-way flow different portions can perform their different functions simultaneously) and (2) there is no limit on the size of food that can be ingested (due to mastication, i.e. as long as the object can be rendered into bite size pieces, it’s ingestible (e.g., a whale)).

There are 4 mechanisms of digestion. (1) Mechanical reduction occurs in the oral cavity (mastication) and stomach (gastric peristalsis). (2) Acid digestion which occurs in the stomach. Here hydrochloric acid is used to break up large food items into smaller pieces by dissolving intercellular substances. The acid also serves as an immunological barrier and to activate gastric enzymes (e.g., pepsinogen to pepsin). (3) Enzymatic digestion uses enzymes to cleave specific molecules. Digestive enzymes are produced by the salivary glands, stomach, small intestine and pancreas. (4) Fermentation occurs in the colon and distal ileum and involves the use of symbiotic microorganisms (bacteria and protozoans) that give off by-products useful to the host (e.g., vitamin K).

II. Overview of the digestive system

The digestive system consists of consists of (a) the digestive tract (containing intrinsic glands embedded in wall of tract) and (b) the accessory (extrinsic) digestive glands.

The digestive tract is a tubular passageway that extends from mouth opening to anus and is divisible into the following regions:
oral cavity - contains teeth, tongue and palate
pharynx - muscular sac connecting oral cavity to esophagus
esophagus
gastrointestinal tract; divided into 3 regions
  gaster (stomach)
  small intestine
  large intestine
The accessory digestive glands are extrinsic glands located outside walls of digestive tract and connect to the lumen of the GI tract via long ducts. The three principle sets of glands are as follows:
  extrinsic salivary glands - empty into oral cavity
  liver and gall bladder - empties into small intestine
  pancreas - empties into small intestine

III. Oral cavity – site of mechanical and enzymatic digestions

The oral cavity contains the teeth, tone and palate. It is the site of mastication which is the mechanical reduction of food particles. The entire oral cavity except for the crowns of the teeth is lined by oral mucosa.

A. Oral mucosa

Definitions:

mucosa – mucous membrane; a mucous tissue lining consisting of an epithelium, a lamina propria and, in the digestive tract only, a layer of smooth muscle (muscularis mucosa)
mucus – the clear, viscid secretion of mucous membranes, consisting of mucin, epithelial cells, leukocytes and various inorganic salts suspended in water.

Aside from the skin and lining of ducts and vessels, most of the linings of the body are formed by a mucosa. The mucus is produced by cells within the lining epithelium (e.g., goblet cells) and/or by glands intrinsic or extrinsic to the walls of the organs.

The oral mucosa consists of a stratified squamous epithelium over a lamia propria. It varies in its degree of keratinization between regions (and individuals) and species (run your finger over the tongue and internal cheek of your pet cat or goat, if you dare). In humans, most regions are non-keratinized but others are lightly (parakeratinized) or fully keratinized (e.g., gingiva, hard palate, dorsum of tongue).

Similarly the surface of the mucosa is variable. The mucosal surface may be smooth (gums, hard palate) or covered with papillae of varying size.

Moisture (saliva) is provided two sets of glands: (1) Intrinsic salivary glands that are located in the submucosa, and (2) extrinsic salivary glands that lie external to the oral cavity (e.g., parotid, submandibular, sublingual).

Saliva both moistens the food for transport and initiates enzymatic digestion of carbohydrates with its amylase.

B. Tongue – muscular and sensory organ occupying base of oral cavity

The tongue is a muscular organ with both motor and sensory functions (somatic and special). Mechanically, its muscles assist in mastication, oral transport (movement of the bolus through the oral cavity) and deglutition (passage of the bolus into the esophagus). It contains two sets of skeletal muscles, both innervated by the hypoglossal nerve (CN XII): (1) the extrinsic tongues muscles that are responsible for excursions and (2) the intrinsic tongue muscles which produce changes in shape. Owing
to the lack of skeletal elements within the tongue, the intrinsic tongue muscles function as a muscular hydrostat.

In addition to abundant somatic sensory innervation (pain, touch, temperature), the tongue also possesses the special sensory component of taste (gustation). Gustation is provided by sensory organs called taste buds (more below) which are associated with specific types of papillae.

The oral mucosa covering dorsum of tongue is keratinized (protection) and folded into four types of lingual papillae.
(1) Filiform papillae are found over the entire surface and consist of elongate, conical shapes. They lack taste buds.
(2) Fungiform papillae are interspersed over the anterior 2/3 surface. As their names suggest they are mushroom-shaped and can contain taste buds on their upper surface.
(3) Foliate papillae are found along the lateral edges of the tongue and appear as ridge-like structure with taste buds along their sides.
(4) Circumvallate papillae are found posteriorally. They are few in number but large with numerous taste buds along their sides.

Other structures within the tongue include the lingual salivary glands and lingual tonsils. The lingual salivary glands are intrinsic salivary glands located primarily adjacent to taste buds, their secretion serving to continually “wash” away the food material from these sensory organs. An example is von Ebner’s glands which are acini of seromucous cells associated with the circumvallate papillae. The lingual tonsils are an example of persistent MALT and consist of sporadic, diffuse lymphatic tissue in the submucosa along the posterior edge of the tongue.

The taste buds are the sensory organs that provide gustatory sensation. In the tongue they are associated with fungiform, foliate and circumvallate papillae. They appear histologically as oval, pale-staining bodies extending through the epithelium and terminating in an apical taste pore. They are comprised of three cell types: (1) Neuroepithelial cells are sensory cells. They contain taste receptors in their apical microvilli and synapse with afferent axons at their base; (2) Supporting cells which serve an unknown function; and (3) basal cells which are the stem cells for the other two types.

There are to date five documented taste stimuli that have corresponding taste receptors on the microvilli of the neuroepithelial cells: Sweet, salty, bitter, acid and umami. Note that most taste buds contain multiple types of receptors; thus the localization of specific tastes to specific regions of the tongue has no basis in anatomy and might be viewed as suspect (As in watch out and don’t step in the “suspect”).

C. Teeth – mineralized organs used to mechanically reduce food items

i. Structure

The teeth are mineralized organs which are used to mechanically reduce foods items. The crown of the tooth projects into the oral cavity and consists of a dentin core covered by enamel. The root of the tooth projects into a socket of alveolar bone and consists of a dentin core covered by cementum. The pulp cavity lies in the center of the tooth surrounded by dentin; its nerves and blood vessels enter via the apex of the root. The periodontal ligament anchors the cementum to the surrounding alveolar bone.

Dental tissues

The tooth contains three specialized mineralized tissues. The enamel is the most highly mineralized tissue in the body consisting of 95% hydroxyapatite (HAP), 4.5% water, and less than 0.5% organic matrix. The HAP crystals are arranged into keyhole-shaped rods which span thickness of enamel layer. Enamel is formed by cells called ameloblasts which degenerate after the matrix has mineralized. The organic matrix contains remnants of the developmental enamel matrix proteins (amelogenins, ameloblastins, enamelines and tuftelins).
Dentin forms the core of both the crown and root. It is more mineralized than bone (70% HAP) and its organic matrix contains mostly type I collagen, dentin phosphoprotein and sialoprotein. Dentin is formed by odontoblasts which line interior surface of dentine. Dentin contains dentine tubules which are occupied by odontoblastic processes that span thickness of dentin (see below).

Cementum is similar to bone in mineral and matrix composition (65% HAP) but its matrix is avascular and mostly acellular. Cementum is formed appositionally by cementocytes adjacent to the periodontal ligament. Collagen fibers projecting from the cementum penetrate the alveolar bone and anchor the tooth (Sharpey’s fibers).

The pulp forms the interior of the tooth and contains odontoblasts and fibroblasts in a loose connective tissue. Afferent nerves and blood vessels that supply the pulp enter though an apical foramen.

The periodontal ligament functions both to anchor the tooth and in proprioception. The ligament contains collagen and elastic fibers, fibroblasts, nerves and vessels. Sharpey’s fibers (collagen) link the cementum to the adjacent alveolar bone. Nerve endings within the ligament are thought to function in modulating bite force. The alveolar bone which surround the tooth root is regular bone; it resorbs when the tooth is lost.

The gingiva or gums has two components: (1) a keratinized oral mucosa which covers the alveolar bone and (2) a junctional epithelium which adheres to the cementum of the tooth via hemidesmosomes, sealing off the periodontal ligament from pathogens.

ii. Tooth Development

Tooth development is a classic example of an organ that arises though epithelial-mesenchymal interaction (others include glands, hair, scales, feathers, etc.). Tooth development starts with the bud stage in which an in-growth of the oral epithelium (the future enamel organ) induces a condensation of mesenchymal cells (the future dental papilla).

In the cap stage the enamel organ begins forming as the cells along the dental papilla differentiate into the inner enamel epithelium (IEE). In the bell stage the dental papilla adjacent to the IEE differentiates into odontoblasts inducing the adjacent IEE cells to form ameloblasts. The enamel organ begins to separate from the oral epithelium and further differentiates to form the outer enamel epithelium and stellate reticulum.

During the appositional stage the odontoblasts secrete a thin pre-dentin layer which stimulates the ameloblasts to secrete enamel matrix. As secretion continues the predentin slowly mineralized, to dentin creating a tri-laminar structure of enamel, dentin and predentin.

Following formation of the enamel crown, the cells of the enamel organ die. Continued growth of the root (dentin and cementum) results in the tooth penetrating the oral cavity in an event called eruption.

Histology of the appositional phase

In a section through a tooth bud in the appositional phase, tight junctions of the ameloblasts and odontoblasts seal off the tooth bud to create a micro-environment for mineralization. The columnar odontoblasts move inward toward the pulp cavity secreting matrix and trailing a cytoplasmic process which becomes the odontoblast process of the dentin tubule. These processes are thought to convey the sensation of heat/pain to the pulp nerves experienced on trips to the dentists. The columnar ameloblasts move outwardly secreting matrix proteins and calcium phosphates that become mineralized soon after secretion.

iii. Tooth morphology
Humans possess a heterodont dentition, that is, they have teeth of different shapes and sizes. The shape of the crown and root varies with function and four classes are defined from mesial to distal:

1. Incisors have single roots and spatula shaped crowns for cutting (incising).
2. Canines have single roots and single-cusped crowns for puncturing.
3. Premolars have 1+ root and 2+ cusped crowns for grinding.
4. Molars have 2+ roots and 3+ cusped crowns also for grinding.

Human dentitions are diphyodont, that is, two sets of dentition erupt during their lifetime. The dental formula is the number of teeth per class per quadrant, from mesial to distal: incisors, canine, premolar and molars. Thus, the deciduous (primary) dentition has a dental formula 2:1:2 / 2:1:2 (maxillary / mandibular). Similarly the succedaneous (secondary) dental formula is 2:1:2:3 / 2:1:2:3 (maxillary / mandibular).

IV. Organization of esophagus and gastrointestinal tract

The esophagus and gastrointestinal tract share a common architecture based upon 4 concentric coats (or tunica); starting from the lumen these coats are the mucosa, submucosa, muscularis externa and adventitia / serosa. The different regions of the tract differ in their expression of these layers, particularly the mucosa.

The mucosa protects, absorbs and secretes. It is comprised of 3 layers: epithelium, lamina propria and muscularis mucosae. The epithelium lines the lumen and separates the external environment of the lumen from the tissues of the body. It is the site where nutrients are absorbed and mucous, hormones, antibodies and digestive molecules are secreted. The lamina propria is a loose connective tissue beneath the epithelium containing capillaries, lymphatics, lymphocytes and occasionally smooth muscle. It may also contain glands (mucosal glands). The muscularis mucosae is a layer of smooth muscle marking the external boundary of the mucosa.

The submucosa is an irregular connective tissue containing blood and lymph vessels, submucosal (Meissner’s) plexi (ganglia and nerve fibers), and in some regions glands (e.g., duodenum).

The muscularis is typically a concentric, bi-laminar arrangement of smooth muscle (inner concentric layer and outer longitudinal; ICOL). The myenteric (Auerbach’s) plexus lies between the two muscle layers. Sphincters are formed by thickenings of the muscularis externa at junctions along the digestive tract (e.g., pyloric, ileocecal, anal). The enteric nervous system induces rhythmic contractions of the muscularis to produce peristalsis which propels the food through the lumen.

The adventitia contains loose CT, blood and lymph vessels and nerves. The peritoneum is the mucous sac that surrounds the abdominal (peritoneal) cavity; the sac consists of a mesothelium and underlying loose CT. When the adventitia of an organ protrudes against the peritoneum, it becomes
partly covered by the mesothelium (a simple squamous epithelium) and is referred to as a serosa. That is, a serosa is simply an adventitia with a mesothelial covering, specifically the visceral peritoneum.

V. Esophagus:

The esophagus is a muscular tube connecting the pharynx to the gaster (stomach). During deglutition the bolus (ball of masticated food) passes through the pharynx to enter the esophagus.

The mucosa of the esophagus is lined by a stratified squamous epithelium; the muscularis mucosa is small and inconstant. Distally, adjacent to the cardiac region of the gaster, esophageal cardial glands can be found within the mucosa. These branched tubular glands secrete a slightly alkaline mucus which neutralizes any refluxed gastric juices.

The submucosa of the esophagus consists of irregular connective tissue. Submucosal glands are concentrated in the proximal (cranial) half of the esophagus in the submucosal tunic and consist of compound tubulo-alveolar glands that secrete a slightly acid mucus to lubricate the lumen.

The muscularis is bi-laminar with an inner concentric and outer longitudinal arrangement. Remarkably and atypically, the type of muscle forming the muscularis externa changes from skeletal muscle proximally to smooth muscle distally. The adventitia is unremarkable.

VI. Gaster [stomach]

The gaster (stomach) performs multiple functions. During feeding, it serves to store food and slowly release its contents to the small intestine. Simultaneously, mechanical, enzymatic and acid digestion results in a substance referred to as chyme. Absorption of nutrients is limited and inconsequential. The stomach’s endocrine (Tables 17.1 and 17.2) and exocrine secretions are largely restricted to digestion.

Grossly, the gaster can be divided into four regions: cardia, fundus, body and pyloris. Histologically, only three regions are defined on the basis of the gastric glands: pyloric, fundic (which includes the body) and cardiac. Internally the lining (mucosa and submucosa) consists of multiple longitudinal folds called rugae which permit expansion of the lumen in an accordion-like manner to accommodate Hoosier-sized meals.

The mucosa of the stomach contains a lining epithelium perforated by gastric pits that lead to branched tubular glands. The composition of the glands varies with the region (fundic, pyloric, cardiac; see below). Surface mucous cells line the surface and the gastric pits. These are simple columnar cells that secrete thick, viscous mucus that protects the lining from the acidic chyme. The lamina propria of the mucosa is scant but the muscularis mucosa is well developed.

The submucosa is dense irregular connective tissues containing blood and lymph vessels and the submucosal plexus. It is infiltrated with lymphocytes, macrophages, mast cells and plasma cells.

The muscularis is traditionally described as having three layers. However, these layers are indistinct due to the varying orientation of the smooth muscle fibers. [This arrangement of fibers is typical of all organs which must undergo expansion and contraction, e.g., urinary bladder, uterus.] The myenteric plexus is contained within this layer. The serosa is unremarkable.

A. gastric or fundic glands – simple branched tubular glands

Again, the 3 histological regions of the gaster differ primarily in the composition of their mucosal glands.

Fundic (or gastric) glands are found in the fundus and body of the stomach. These are branched tubular glands that open into the gastric pits: they are comprised of an isthmus, neck and fundus. The
fundus usually divides into 2-3 branches. Five types of cells can be found within the gland: **stem, mucous neck, parietal, enteroendocrine, and chief.**

**Mucous neck cells** are similar to the mucous lining cells but are shorter and produce a thinner mucous. The **parietal cells** are also found in the neck of the gland and appear histologically as large, round or pyramidal cells with a central nucleus and intensely eosinophilic cytoplasm. These cells produce hydrochloric acid which serves in acid digestion, pepsin activation and as a bacteriostat. The acid is formed extra-cellularly by active transport of H+ and Cl- ions into the misnamed intracellular canalicus. The cytoplasm of these cells is rich in mitochondria (ATP) and carbonic anhydrase, the enzyme which produces H+. The cells also produce and secrete intrinsic factor (glycoprotein) which binds to vitamin B12 and is important in B12 absorption in the ileum.

**Chief (zymogenic) cells** are found in the **fundus** of the gland. Histologically these appear as cuboidal to round cells with intense basophilic granules in the cytoplasm. These granules contain pepsinogen (inactive) which is converted to pepsin (a protease) by gastric acid. These cells also secrete lipase.

**Stem** cells are found in the **isthmus** of the gland; they divide and differentiate into the other cell types. The turn-over time for mucous cells is only 3-5 days compared to half a year for the parietal, chief and enteroendocrine cells.

**Enteroendocrine cells** are found throughout the digestive tract. In the stomach they are concentrated in the fundus but are present throughout the gland. They are difficult to identify in H&E sections. They secrete several types of hormones into the lamina propria that act on local (paracrine) and more distant (endocrine) cells associated with digestion. (SEE BUT DON’T MEMORIZE TABLES 17.1 and 17.2).

**B. Gastric cardial and pyloric glands**

The **gastric cardial glands** are branched tubular glands adjacent to the esophageal opening (cardiac region). They are composed of predominately mucous-secreting cells with scattered enteroendocrine cells. They act in conjunction with the esophageal cardiac glands by secreting an alkaline mucous to protect the esophagus from gastric chyme.

The pyloric glands are branched, tubular glands adjacent to the pyloric sphincter (pyloric region). They are composed of predominantly mucous-secreting cells with scattered enteroendocrine cells. They act with the duodenal glands of the small intestine to protect the small intestine from gastric chyme.
12.82a. The general arrangement of the alimentary canal, its mural tunicae and (below) the general histology at the levels indicated (highly diagrammatic). The transverse colon (above right) has been displaced downwards to reveal the duodenum.