From the lower esophagus to the lower rectum four fundamental layers comprise the wall of the digestive tube: mucosa, submucosa, muscularis propria (externa), and adventitia or serosa (see figure at right). However, this basic plan is modified to varying degrees in the different segments of the digestive tube in keeping with the performance of special functions. After learning the basic plan of the tube, complete understanding involves the systematic analysis of these modifications segment by segment.

**ESOPHAGUS**

The esophagus is a transition organ connecting the pharynx (voluntary skeletal muscle) with the stomach (involuntary smooth muscle). Not surprisingly this transition is reflected in the histology of the organ. For example, in the human esophagus, the upper third contains mostly skeletal muscle; the middle third, a mixture of skeletal and smooth muscle; the lower third, only smooth muscle.

The lumen is lined by nonkeratinized stratified squamous epithelium. The submucosa is well developed and contains mucous type glands. The muscularis externa consists of skeletal muscle in the upper part and smooth muscle in the lower. This appears as two layers (inner circular and outer longitudinal) surrounded by an adventitia.

**DIGESTIVE TRACT**

**DRAWING OF THE STOMACH**
STOMACH

The stomach has a mucosa, submucosa, muscularis externa and serosa. Surface mucous cells line the mucosa. There are no goblet cells. The mucosa has infolding, the gastric pits and gastric glands. The parts of gastric glands are isthmus, neck, and base. In the glands, chief cells and parietal cells can be distinguished from each other since the chief cells show a cytoplasmic basophilia. Enteroendocrine cells are also present in the basal part of the glands, but can be positively identified only with the use of appropriate immunochemical markers. Be aware of the many endocrine/paracrine substances these cells secrete. The gastric glands of the pyloric antrum are different from those of the fundus/body of the stomach. They are much deeper and contain mostly mucous secreting cells. The surface epithelium sits on a thin lamina propria which is separated from the submucosa by a muscularis mucosa. There are no glands in the submucosa of the stomach. The muscularis of the stomach is usually described as three-layered: inner oblique, middle circular, outer longitudinal. However, in sections the distinction is often difficult to make.

SMALL INTESTINE (duodenum, jejunum, ileum)

The epithelium lining the small is comprised of columnar epithelium with goblet cells. There is a prominent striated border. The mucosa is thrown into large folds (villi) which contain strands of smooth muscle (from the muscularis mucosa), large central lymphatic vessels (lacteals) and blood capillaries. There are intestinal glands (crypts of Lieberkühn) that are confined to the lamina propria. Paneth cells may be identified toward the base of the intestinal glands. These cells contain refractile granules that occupy most of their cytoplasm. These granules consist of several anti-microbial compounds and other compounds that are known to be important in immunity and host-defense. There are also enteroendocrine cells. At the base of the glands, there are abundant mitotic figures to replace the epithelial lining. In the duodenum there are submucosal (Brunner’s) glands. They open into the basal parts of the intestinal glands in the lamina propria after penetrating the muscularis mucosa and secrete an alkaline mucus to help neutralize stomach acid.

The lamina propria of the small intestine is more abundant than in the stomach and that it contains diffuse aggregations of lymphocytes and plasma cells. In places, lymphocytes can be seen passing through the epithelium into the lumen of the gut. Particularly in the ileum, there are lymphoid nodules, some containing germinal centers. There is a well-developed muscularis mucosa separating the mucosa from the submucosa. You may find some ganglion cells and nerve fibers in the submucosa (the submucosal plexus).

The two layers of the muscularis externa are well developed. Between the two layers you should be able to identify the myenteric plexus. This consists of autonomic nerve fibers, postganglionic parasympathetic nerve cell bodies and nuclei of Schwann cells.

There is an adventitia consisting of connective tissue around the retroperitoneal parts of the intestines, while the intraperitoneal parts (such as the jejunum and ileum) have a serosa lined by mesothelium.
In the ileum that is an increased number of goblet cells in the lining epithelium. In many areas this takes the shape of lymph nodules, some with germinal centers, in the submucosa. Large aggregates of nodules are known as Peyer’s patches and in some places they may become so abundant that they become grossly visible. The villi are not as well developed in the ileum as in the jejunum and the intestinal glands are shallower than in the jejunum.

LARGE INTESTINE (cecum and appendix, colon, rectum)

The large intestine is covered by columnar epithelium with numerous goblet cells. There are straight, unbranched, tubular intestinal glands but there are NO villi.

The mucosa includes a prominent lamina propria and muscularis mucosa, which separates the mucosa from the submucosa. The muscularis externa has an incomplete outer longitudinal layer, called taeniae coli.

The appendix has dense aggregations of lymphoid tissue, nodular and non-nodular. Heaviest infiltrations extend from the lamina propria into the submucosa.
**CHECK LIST**

Understand the four parts of the digestive tract, i.e., esophagus, stomach, small bowel and large bowel, based on the morphology of the four fundamental layers of the tract:
- mucosa
- epithelium
- lamina propria (with large numbers of lymphoid cells)
- muscularis mucosae
- submucosa (extensive blood supply)
- submucosal (Meissner’s) nerve plexus
- muscularis externa (propria)
- circular muscle (inner)
- longitudinal muscle (outer)
- oblique muscle (in stomach)
- myenteric (Auerbach’s) nerve plexus
- adventitia
- serosa (visceral peritoneum)

**Esophagus:**
- submucosal mucous type glands
- type of muscle in the muscularis propria - striated or smooth?

**Stomach:**
- smooth lumen surface with gastric pits leading to gastric glands
- mucous glands in the cardiac and pyloric parts of the stomach
- gastric glands in the fundus and body containing
  - mucous neck cells
  - parietal (oxyntic) cells
  - chief (zymogenic) cells
  - enteroendocrine (argentaffin) cells

**Small intestine:**
- plicae (seen in gross anatomy lab) and extensive villi
- lacteals
- intestinal glands (crypts of Lieberkühn) opening between the bases of the villi
- Paneth cells in base of crypts, prominent distally

**Duodenum**
- high ratio of epithelial absorptive cells to goblet cells
- submucosal (Brunner’s) mucous glands

**Jejunum**
- ratio of absorptive cells to goblet cells decreasing

**Ileum**
- goblet cells abundant compared to absorptive cells
- extensive lymphoid nodules (Peyer’s patches)

**Large intestine (colon):** smooth luminal surface with openings to glands
- glandular goblets cells more abundant than in ileum.

**Appendix:** studied in lymphoid/immunology lab.
DIGESTIVE GLANDS

SALIVARY GLANDS

All of the salivary glands are of the exocrine type and have ducts that drain into the oral cavity. The major paired glands are parotid, submandibular, and sublingual, in order of size. There are also many minor, unnamed seromucous glands within the oral cavity mucosa that add their secretion to that of the major ones to form saliva. (see the drawing to the right)

PANCREAS

The pancreas is a large, serous-type exocrine digestive gland (~ 9” long) that drains into the duodenum (2nd part) via the major pancreatic duct (Wirsung) and often a minor duct (Santorini). The structure of an acinus is shown to the right. It also contains endocrine gland tissue in the form of tiny, scattered islets (of Langerhans).

LIVER

The liver is the second largest organ of the body and the largest gland, weighing about 3.5 kg. It is basically a compound tubular serous gland but is highly modified in mammals. Secretory acini are replaced by cellular plates that branch and anastomose. It has a very profuse blood supply, about 75% coming from the portal vein, the remainder from the hepatic artery. In terms of multiplicity of functions the liver is hard to beat. Its parenchymal cells, the hepatocytes, produce both exocrine and endocrine secretions. You should be familiar with the basic structure and components of the liver lobule:

The “classic liver lobule” has a central vein in the center. Situated in the interlobular connective tissue, mostly at angles, are portal triads, where branches of the portal vein, hepatic artery, and bile duct and often a lymphatic vessel can be found.

Hepatocytes appear cuboidal in section (actually most are 14-sided cells) and are arranged in plates that are one cell thick, usually separated by blood sinusoids. Many cells are binucleate and some have an unusually large nucleus. Bile canaliculi are sandwiched between hepatocytes. Bile is secreted by the hepatocyte and this bile will make its way through these canaliculi into bile ductules (“canals of Hering”) and then into the interlobular bile ducts in the portal triad.
The **hepatic sinusoids** are lined by highly fenestrated endothelial cells and phagocytic **Kupffer cells** ("fixed macrophages").

**GALLBLADDER**

The mucosa of the gallbladder consists of a **simple columnar epithelium** with a well-developed brush border. Contiguous cells are joined by elaborate tight junctions. The function of the epithelium is water transport, i.e., bile concentration. There is a very evident **lamina propria** but no muscularis mucosa nor submucosa. The **muscularis** is in irregular bundles and does not show the inner circular and outer longitudinal arrangement found in the gut. External to the muscularis is some moderately dense connective tissue. The gallbladder has **no** villi, **no** crypts, **no** muscularis mucosa and **no** goblet cells in its epithelium.

**CHECK LIST**

**SALIVARY GLANDS:** Be able to distinguish the parotid gland from the submandibular gland. **Identify:**

- serous secreting cells
- serous demilunes
- myoepithelial cells
- mucous secreting cells
- intralobular ducts
- intercalated ducts-striated
- secretory ducts
- interlobular ducts

**PANCREAS:** Understand that the pancreas has both exocrine and endocrine components. **Identify:**

- secretory acini
- intercalated ducts
- islets of Langerhans
- zymogenic vesicles in acinar cells
- centroacinar cells
- interlobular ducts
- basophilia of acinar cell cytoplasm
- EM ultrastructure of acinar cells

**LIVER:** Understand the concept of the liver lobule and its relationship to blood flow through the liver parenchyma. **Identify:**

- plates of hepatocytes
- EM ultrastructure of hepatocytes
- bile canaliculi
- central vein
- hepatic sinusoids
- space of Disse
- Kupffer cells
- portal triad
- hepatic artery
- portal vein
- bile duct

**GALLBLADDER:** Know the microscopic anatomy and be able to distinguish it from organs of the digestive tract. **Identify:**

- columnar epithelial cells with an apical brush border
- absence of goblet cells
- lamina propria

- absence of submucosa (no muscularis mucosa)
- relatively sparse single muscularis layer
URINARY SYSTEM

The basic unit of gross structure of the kidney is the lobe. Whereas the kidney of the rat or rabbit consists of only one lobe (unilobar) that of the human consists of many lobes (6-16), i.e., it is multilobar.

A renal lobule (see the figure, below) is defined by one collecting duct (black) and includes all the nephrons, which ultimately drain into it. That collecting duct runs in a medullary ray in close parallel association with the loops of Henley of its associated nephrons. Consequently the medullary ray marks the center of the lobule. (Keep in mind that medullary rays and renal lobules are features of the renal cortex). The interlobular arteries tend to be located midway between two medullary rays, so they are found near the lateral margins of the lobules. However, the interlobular arteries DO NOT define the lateral margins of the lobule.
The medulla is subdivided into **renal pyramids**, each along with overlying cortex the basic unit of a **renal lobe**. The base of the pyramid is contiguous with the cortex; the apex is oriented toward the pelvis and projects into a **minor calyx**. Note how the cortex extends down around the sides of the pyramid. These cortical extensions between pyramids are denoted as the **renal columns** (of Bertin).

In the hilar region, the minor calyx cups around the apex (**papilla**) of a pyramid. You may see **papillary ducts** (of Bellini) opening into the calyx at the papillary apex (**area cribrosa**). In addition to the calices and renal pelvis, the **renal sinus** is packed with white adipose tissue as well as the **renal artery, vein and associated nerves**.

**Arterial Supply to the Kidney**

The drawings above depict the parts of the **renal vascular system**. The arteries include: (a) **interlobar**, between adjacent pyramids, (b) **arcuate**, at corticomedullary boundary, (c) **interlobular**, midway between neighboring medullary rays, (d) **afferent and efferent arterioles** of the renal corpuscles. These latter vessels usually cannot be differentiated from each other with ease. There are also **capillary plexi** surrounding tubules in the cortex and medulla that are fed respectively by the efferent glomerular arteriole and the **vasa recta**. The arteries are accompanied by corresponding veins.

**Tubular system.**

The renal corpuscles consist of a **glomerulus** and a **capsule (of Bowman)**. The **parietal epithelial** layer of the glomerular capsule is comprised of simple squamous epithelium encasing the glomerular capillaries and visceral epithelium (see figure to the right).

The visceral epithelium is comprised of podocytes, which are separated from one another by filtration slits. There is a thick basement membrane between the
capillary endothelium and the podocytes. The mesangial cells also exist in this space. They are phagocytic and help maintain the basement membrane.

At the vascular pole of the renal corpuscle, the afferent and efferent arterioles of the glomerulus enter and leave (respectively). The macula densa is created when a segment of distal convoluted tubule abuts the vascular pole and contacts the proximal convoluted tubule. At this location, there is a thickening of the epithelium that, together with the macula densa makes the juxtaglomerular apparatus (JG cells, extraglomerular mesangium).

The urinary pole of the renal corpuscle is the location of origin of the proximal convoluted tubule. This tubule, which is comprised of cuboidal epithelium with a brush border, is continuous with the parietal epithelium of the renal corpuscle.

Calices, Pelvis and Ureter:

The ducts that open onto the papilla discharge into minor calices. These aggregate into major calices and then to the renal pelvis in the hilar region of the kidney. This entire system is lined with urothelium.

The ureter is very distensible. In the undistended ureter the mucosa tends to be thrown into folds. Note that the ureter has a lamina propria, but no submucosa. The muscularis (all smooth muscle) is extensive and interfaced with connective tissue, and the orientation of the muscle bundles is rather haphazard. In general, there tends to be an inner longitudinal and an outer circular layer. The ureter has an adventitial outermost layer.

The urinary bladder has a lamina propria (dense inner and less dense outer layers), no submucosa and a thick outer muscular layer (smooth muscle) in which bundles of fibers go in all directions. The urothelium allows for distension (see the figure).

Diagrams of the luminal surface of urothelial cells in the bladder. The upper drawing is the surface of a distended bladder; the lower drawing is that of a relaxed bladder. The plasma membrane is thickened to form plaques. In the relaxed bladder the plaques are invaginated into the cell, thus reducing the size of the lumen of the bladder. In the distended bladder the plaques are smooth and part of the surface increasing the capacity of the bladder lumen.
CHECK LIST

KIDNEY: Understand the basic concept of the renal lobe at the gross and microscope level, including the vascular branches that contribute to the architecture of a renal lobe. In addition, be able to define:
- cortex
- medullary pyramid
- renal columns (of Bertin)
- interlobar artery
- intralobular artery
- (major calyx)
- medulla
- renal papilla and papillary ducts (of Bellini)
- area cribrosa
- arcuate artery
- afferent arteriole
- (minor calyx)

Be able to identify the tissue structures contained in a nephron. Have a general understanding of the function(s) of each morphological part.

In the cortex, be able to identify:
- medullary ray (continuous into medulla)
- cortical labyrinth
- renal corpuscle
- glomerulus
  - Bowman’s capsule: parietal layer & visceral layer
  - urinary space (filtration cavity)
  - vascular pole: afferent & efferent arterioles
  - juxtaglomerular apparatus - macula densa
  - urinary pole
  - mesangial cells
  - podocytes - foot processes, slit diaphragm.
- proximal convoluted tubule - distal convoluted tubule
- collecting tubule
- EM of tubules listed above

In the medulla, be able to identify:
- descending or ascending thick limb of Henle’s loop
- thin limb of Henle’s loop
- collecting ducts
- vasa recta

URETER: Identify:
- urothelium
- terminal bars

BLADDER: Identify:
- distended urothelium - relaxed urothelium
- detrusor smooth muscle layer