This lecture will present the histology of the small and large intestines, including the rectum and the anal canal.

These are the resources for text reading and practical lab exercises that will complement this lecture.

This is the vocabulary of terms related to the content of this lecture.
Learning Outcomes

After completing a study of this lecture and working through the related laboratory exercise, you should be able to:

- describe and explain the general plan of histological organization of the intestines.
- describe, give the name and location of and explain how specialized structures at the tissue and cellular level increase the surface area of the intestine about 500 times more than a smooth bore tube.
- describe and differentiate between the mucosa of the small and large intestines.
- identify and distinguish between the duodenum, jejunum and colon histologically.
- describe the histology, the location of and give the function of intestinal absorptive cells, goblet cells, Paneth cells and stem cells.
- describe, give the location of, and the function of Auerbach’s and Meissner’s plexi.
- describe and give the location of Taeniae Coli.
- compare the histology of the appendix, rectum and anal canal.

Lecture Topics

- Gross Anatomy and Histological Organization of the Intestines
  - Small Intestine
    - Surface Area Amplification Structures
      - The Enteroocyte: the intestinal absorptive cell
      - The Goblet Cell
      - The Paneth Cell
    - Digestion and Absorption
      - Renewal of Intestinal Cells
      - Peyer’s Patch
      - Auerbach’s and Meissner’s Nerve Plexi
      - Parasites
  - Large Intestine
  - Appendix
  - Rectum, Anal Canal and Anus
  - Precancerosus Colon Polyp and Adenocarcinoma of the colon
- Quiz

The small intestine is divided into three structural parts: 1) the duodenum approximately 10 inches in length, 2) the jejunum approximately 8 feet in length and 3) the ileum approximately 12 feet in length. The colon consists of ascending, transverse and descending parts and is about 5 feet long. The diameter of the small intestine averages 1 inch compared to 2.5 inches for the colon. Although the small intestine is much longer than the large intestine (typically around 3 times longer), it gets its name from its comparatively smaller diameter. As a simple tube the length and diameter of the small intestine would have a surface area of only about 0.5 m². However, special structures that you learn about like villi, microvilli and folds of the mucosa increase the surface area about 500 times greater than a smooth bore tube would have. The surface area of the small intestine is on the order of 200 square meters (the size of a tennis court).
This drawing will serve to present an overview of the gastrointestinal tract from stomach to large intestine. The surface epithelial lining from the stomach to the anal canal is simple columnar. The stomach and intestines are bound to the posterior abdominal wall by a mesentery. The two layers of mesothelium split when the mesentery reaches the intestines and surrounds them. This mesothelial layer and a small amount of connective tissue beneath constitute a serosa, which in the case of the stomach and intestines is the visceral peritoneum. The liver and pancreas are accessory glands to the intestinal tract and their secretions enter the intestinal lumen via a major duct that passes through the wall of the duodenum. Throughout the stomach and intestines Auerbach’s and Meissner’s plexus are present. The duodenum is characterized by having villi and submucosal glands (this and the esophagus are the only two locations from esophagus to the anus where submucosal glands are present). The remainder of the small intestine, the jejunum & ileum, have villi. Special folds of the mucosa called plica circularis are located mostly in the small intestine with a few folds in the colon. These folds add to the surface area of the lumen of the intestine. The ileum is characterized by having villi in the mucosa and large masses of lymphatic nodules in the mucosa and submucosa (Peyer’s Patches). Finally the colon is characterized by having no villi – only mucosal simple tubular glands with a dominate presence of goblet cells.

The small intestine is designed at several levels to provide a large surface area for food undergoing digestion to have maximal contact with the surface epithelial cells for absorption. First the small intestine is very long, including the duodenum, a total of nearly 21 feet. Second, the mucosa, including all three layers, is folded with the submucosa at the core. These folds are called Plicae Circulars (singular – plica circularis). Observe that the jejunum has the largest number of folds per unit length and this is the segment of the small intestine where most of the amino acids, fatty acids, glycerol, glucose and other nutrients are absorbed.
Plica circularis
fol of the mucosa

Submucosa supports the plicae

Villi and Intestinal Glands

This drawing illustrates the fact that the plicae circularis are folds of the intestinal mucosa with the submucosa occupying the core of the folded mucosa. Another term for a plica circularis is valve of Kerckring.

The blue ovals outline plicae circularis that illustrates the submucosal support of these structures in a histological section.

A villus is a fold of the epithelium with the lamina propria as the core. The muscularis mucosa lies at the base of the villus. Villi project into the lumen and they are shaped like fingers. The villi in turn have a complex of capillaries (left drawing), a central lacteal (lymphatic capillary-middle drawing) & bands of smooth muscle (right drawing) that have contractile properties helping to keep nutrient molecules stirred up with the digestive enzymes between the villi by an alternating action of shortening and lengthening. A longitudinal section through a villus is shown on the right. The villus is covered with a simple columnar epithelium and the epithelium encloses the lamina propria as seen in the cross-section below. Villi are on the average 0.5 mm wide and range between 0.5 – 1.5 mm long. There are approximately 40 villi per square centimeter in the duodenum and jejunum and less in the ileum – about 10 villi per square centimeter. The intestinal glands are located between the villi. Intestinal glands are simple (no branching ducts) tubular (secretory cells arranged as a tube) glands.
Histology of the Large & Small Intestines

The duodenal mucosa is organized into villi and intestinal glands. The submucosa contains Brunner’s Glands (mucous glands). This enlarged view of Brunner’s glands displays the mucous cells of Brunner’s glands that secrete mucus into the lumen of the duodenum. They produce a highly alkaline secretion which helps to neutralize the acid contents coming from the pyloric region of the stomach. The only other area of the GI tract where you will find submucosal glands is in the esophagus. Villi are long projections into the lumen of the intestine. This enlargement illustrates several villi, one of which is labeled. Each villus is covered by simple columnar epithelium with a mix of absorptive cells with many microvilli and goblet cells. Beneath the epithelium is a core of loose connective tissue containing fibroblasts, lymphocytes, plasma cells, blood vessels and a lymphatic capillary (a lacteal). Intestinal glands are simple tubular glands that are included as a part of the mucosa, not the submucosa. They are mucosal glands. Details of villi and intestinal glands are presented in the following slides.

Between villi the epithelium forms downward projected tubes that form simple tubular glands. These are the intestinal glands (also called the crypts of Lieberkuhn because they resemble a crypt and Dr. Lieberkuhn long ago discovered them). Paneth cells lie at the base of the gland. They are exocrine cells with prominent eosinophilic granules which contain lysozyme. Presumably this helps to keep the bacterial flora in check in the lumen. Regenerative or stem cells are also located in these simple tubular glands. They differentiate into all the other cell types, including the intestinal absorptive cell (simple columnar cells covering the villus that contain many microvilli). Enteroendocrine cells are present and they secrete a variety of peptides. Goblet cells are interspersed among the absorptive cells lining the villi. They appear in the duodenum & increase in number as you move along the GI tract. They secrete mucus that lubricates the lining of the GI tract. Absorptive cells (also called enterocytes) are tall columnar cells which have numerous microvilli (3,000/cell) on their luminal surface (striated border). Glucose, amino acids, lipids and other molecules resulting from digestion of food are taken into the body by these cells.
The arrows point to the bright red granules of the Paneth cells in the intestinal gland (crypt of Lieberkuhn). The granules contain mostly lysozyme which aids in keeping the bacterial flora in check in the lumen of the intestine. How can you differentiate a Paneth cell from a mast cell (both have bright red granules)? Ans: Paneth cells are always in the intestinal epithelium while mast cells are in the lamina propria. Mast cells have their nucleus located in the center of the cell.

The enterocyte, also referred to as the surface or intestinal absorptive cell, has multiple functions. Amino acids, glucose, fatty acids and glycerol are absorbed through the apical cell membrane. The apical cell membrane has very tiny projections called microvilli. When viewed in the light microscope as the image below and left, the microvilli density is so great that the apical end of the cell has a border that has been referred to as a striated border (because at a 100x magnification you can just make out lines between the microvilli so it appears striated). (some texts call this a brush border, more commonly brush border refers to the border of the proximal tubule cells of the kidney) If the border is magnified and examined with an electron microscope you can easily see the individual microvilli that are 1 – 2 microns long. These microvilli increase the surface area of the tip of each absorptive cell 200 times over a cell with no microvilli of the same dimensions. Observe that each absorptive cell is attached to others around it by a junctional complex that includes very tight junctions so that molecules cannot pass between the cells; they must pass through the absorptive cell. If the microvilli are enlarged further it is seen that there is a very complex glycocalyx (a complex of molecules anchored in the cell membrane and projecting into the lumen). This helps to trap enteropeptidases that work to carry out the final breakdown of peptides into amino acids.
The Goblet Cell

Goblet cells are interposed between the absorptive cells covering the villi. They synthesize and release mucus in cycles. They increase in density from the duodenum to the colon where they are dominant in the epithelium of the colon intestinal glands with only a few absorptive cells bordering the lumen. Mucus or mucins are a family of high molecular weight, heavily glycosylated proteins. Goblet cells store mucus until the cell is greatly distended so that the dimension of the cell above the nucleus is wider than the width at the nucleus and below. When the goblet cell is full of mucus it is shaped like a ‘goblet’ hence the name. Unlike stomach surface lining cells that also produce mucus, but continuously, goblet cells expel their gorge of mucins all at once. In the drawing note the mucus plug. At some point this plug is lost and the mucus just pours out onto the epithelial surface.

Digestion & Absorption

This is a view of the mucosa of the small intestine and part of the submucosa. Villi and intestinal glands play critical roles in the absorption of glucose, lactose, fructose, amino acids and fatty acids. These two figures illustrate the process of breaking down glycogen and proteins into molecules that can be absorbed by the cells lining the small intestine. Glycogen digestion begins in the oral cavity with the amylase enzyme content of the saliva. Protein digestion begins in the stomach by the action of hydrochloric acid and pepsin. Lipids ingested in the form of triglycerides are acted upon by lipases secreted into the small intestine by the pancreas. As illustrated in this figure, triglycerides are broken down into monoglycerides (glycerol) and fatty acids. The fatty acids are bound to special carrier proteins that actively transport the fatty acids across the apical cell membrane of the absorptive cell. Once the fatty acids and monoglycerides are in the cytoplasm of the absorptive cell they are recombined into triglycerides unique to humans. The cell then coats the triglycerides in small amounts forming what are called chylomicrons that range from 1 – 3 microns in diameter. These pass out of the absorptive cell into the lamina propria where they go into lymphatic capillaries called lacteals. They are carried through increasingly larger lymphatics until they are emptied into the venous system. From there when they reach either the liver or adipose tissue the triglyceride is freed from its protein coat by lipoprotein lipase the triglyceride is taken up by liver cells or adipocytes.

What you should recall from this slide is that sugars, proteins and lipids undergo their final digestion in the small intestine and they are taken into the body by the intestinal absorptive cells of the villi.
Renewal of Intestine Cells

This slide illustrates the location of regenerating cells in the wall of the intestine gland. These cells provide replacement cells for all of the cell types in the intestinal gland and the epithelial covering of the villi. The next slide will show this cycle of stem cell – specific cell types – loss of cells at the tip of the villi.

Intestinal Epithelial Cell Renewal

This scheme illustrates the life and renewal of the intestinal epithelial cells of the villus and the intestinal gland. All of the mitosis occurs in the population of cells in the wall of the intestinal gland, not at the base of the gland where Paneth cells reside. Observe how the new cells migrate up over the villus pushing older cells that undergo apoptosis and are shed at the tip of the villus. It only takes a maximum of 3 – 4 days for a new cell generated by mitosis from a stem cell in the intestinal gland to migrate to the tip and be shed. In other words the life of an intestinal epithelial cell that covers the villus is approximately 4 days. This is very important because these cells work very hard and wear out quickly.

Ileum Peyer’s Patches

Peyer’s patches are unique to the ileum. They are large groups / masses of lymphatic nodules that occupy the mucosa and submucosa in the wall of the ileum opposite the attachment of its mesentery. Special cells in the epithelial lining call M cells overlie the Peyer’s patches. They have microfolds at their apical surface rather than microvilli. They take up microorganisms and macromolecules from the lumen in endocytotic vesicles. The M cell is an antigen presenting cell. The antigen is presented to T cells that activate B cells that are cloned in the lymphatic nodules. B cells transform into plasma cells, which secrete secretory IgA that passes into the lumen of the intestine to interact with the antigen. This is similar to the role that plasma cells play in the salivary glands.
The GI tract is controlled by the autonomic nervous system (sympathetic/parasympathetic). Nerve plexi are located in two regions: the myenteric plexus (Auerbach’s) is situated between the layers of smooth muscle in the muscularis externa layer and the Meissner's plexus is located in the submucosa.

Peristalsis is a radially symmetrical contraction of muscles which propagates in a wave down the muscular tube to propel the contents of the intestinal tract toward the anus. The plexi of nerve fibers that extend from cells bodies of parasympathetic neurons in ganglia located in Auerbach’s myenteric plexus innervate the smooth muscle of the muscularis externa. The rhythmic stimulation by these nerves causes the coordinated wave-like contracting and relaxing that propels digesting food and the feces in the colon. One developmental abnormality results in the absence of the neurons and their processes of the myenteric plexus in the colon. This leads to the disease known as Hirschsprung’s disease. Hirschsprung disease is a disease of the large intestine that causes severe constipation or intestinal obstruction. Constipation means stool moves through the intestines slower than usual. Bowel movements occur less often than normal and stools are difficult to pass. Some children with HD can’t pass stool at all, which can result in the complete blockage of the intestines, a condition called intestinal obstruction. People with HD are born with it and are usually diagnosed when they are infants. Less severe cases are sometimes diagnosed when a child is older. An HD diagnosis in an adult is rare.
The colon begins at the end of the ileum at the ileocecal junction and extends to the anus. It is about 5 feet long. The colon consists of 4 parts: 1) the ascending colon (A), 2) the transverse colon, 3) the descending colon, and 4) the sigmoid colon (S-shaped). The enlargement on the left shows the detail of this junction. Observe that the appendix extends out of the cecum. The appendix (also vermiform appendix) is a worm-like structure (vermiform is a Latin adjective used to denote this shape). The cecum of humans is small and rudimentary; however, in animals that are herbivores the cecum is very large. The large intestine differs most obviously from the small intestine in that it is much wider and that the longitudinal layer of the muscularis externa is reduced to 3 strap-like structures known as the taenia coli as will be illustrated.

There are no villi in the colon but it is rich in goblet cells & GALT. The mucosa has absorptive cells bordering the lumen, but the intestinal glands are lined with nearly 100% goblet cells. There are no glands in the submucosa that consists of loose connective tissue that may contain a variable amount of adipose tissue with blood vessels, nerves, and lymphatics. In the mucosa and often projecting into the submucosa there is often lymphoid tissue that is diffuse or in aggregates that may contain lymphatic nodules (GALT). The muscularis externa consists of an inner layer of smooth muscle that is oriented circularly and an outer layer of longitudinally oriented smooth muscle. In the colon, this outer longitudinal layer of the muscularis externa is organized into three thickened bands with the region between the bands being very thin. The three thickened bands are called the Taeniae Coli. Taenia is from a Greek word meaning band or ribbon. Coli means colon. When these bands contract they create a series of puckers in the intestinal wall called haustra. These are little sacculations. The action of the inner and outer longitudinal muscle of the muscularis externa helps to compact the feces. Finally the outer wrapping of the colon is a serosa.
Here we see the many goblet cells in the intestinal glands of the colon mucosa and the surface cells that are absorptive. The detail of the submucosa reveals loose connective tissue, adipose tissue, blood vessels and a lymphatic nodule with a germinal center. The muscularis externa consists of an inner layer of smooth muscle that is oriented circularly and an outer layer of longitudinally oriented smooth muscle. An enlargement of the muscularis externa and the serosa reveals their detail. In this specimen the inner circular layer smooth muscle cells are sectioned in a plane parallel to their longitudinal axis as verified by this enlargement. Observe the myenteric plexus of Auerbach consisting of autonomic nerve cell bodies and processes between the inner and outer muscle layers. The outer longitudinal layer of smooth muscle cells are sectioned at right angles to their longitudinal axis (cross-sectioned). From this information you can determine whether this specimen, when prepared for microscopy, is a longitudinal or cross-section. So, which is it? It is a cross-section because the outer longitudinal oriented layer of the muscularis shows cross-sectional profiles of the smooth muscle cells. This can be determined for any segment of the small and large intestines. When a pathologist is cutting in a specimen to be examined the usual procedure is to cut a length of the intestine and then section it longitudinally because that provides more of a sample for inspection in the microscope. If this were that kind of section, the outer muscle cells would show longitudinal profiles.

Because there are no villi in the colon, all the lining cells are in the glands. The same cells are found here as in the small intestine except you will note that there are no enzyme producing cells for digestion. The ratio of goblet cells to lining cells is very high. The absorptive cells are only located at the lumen surface. These cells participate in the absorption of water that helps to compact the feces.
Histology of the Large & Small Intestines

Appendix

Fewer, shorter glands
Numerous lymphoid follicles
No taeniae coli

RECTUM - ANAL CANAL - ANUS

- Rectum
  - Histology is similar to colon
  - Simple columnar epithelium with mucosal glands

- Anal Canal
  - Epithelium transitions from simple columnar to stratified squamous non-keratinized
  - Hemorrhoidal veins in the lamina propria

Hemorrhoidal vein plexus in the lamina propria of the anal canal

- Rectal ampulla

The rectum (from the Latin rectum intestinum, meaning straight intestine) is the final straight portion of the large intestine terminating in the anus. The rectum has a mucosa similar to the colon – simple columnar epithelium at the surface with tubular intestinal mucosa glands containing many goblet cells. The submucosa, muscularis externa and serosa are also similar to the colon. The human rectum is about 12 cm long. Its caliber is similar to that of the sigmoid colon at its commencement, but it is dilated near its termination, forming the rectal ampulla. Just beyond the rectal ampulla, the mucosa is folded forming the anal columns. The mucosa continues as in the rectum, however, at a certain line called the pectinate line, the epithelium begins to transition from simple columnar to stratified squamous non-keratinized epithelium. In the transition zone for a short segment the epithelium is stratified columnar. At the end of the anal canal is an opening, the anus. At this point the epithelium becomes slightly keratinized and then merges with the skin epidermis that is characteristically keratinized. Observe the large veins in the lamina propria of the anal canal. These are the internal hemorrhoidal veins that frequently become so distended that they cause the mucosa to protrude into the lumen reducing its diameter. They can rupture to cause temporary bleeding. The rectum acts as a temporary storage site for feces. As the rectal walls expand due to the materials filling it from within, stretch receptors from the nervous system located in the rectal walls stimulate the desire to defecate. If the urge is not acted upon, the material in the rectum is often returned to the colon where more water is absorbed. If defecation is delayed for a prolonged period, constipation and hardened feces results. When the rectum becomes full, the increase in intrarectal pressure forces the walls of the anal canal anal apart, allowing the fecal matter to enter the canal. The rectum shortens as material is forced into the anal canal and peristaltic waves propel the feces out of the rectum. The internal and external sphincter allows the feces to be passed by muscles pulling the anus up over the exiting feces.
The Rectum and Anal Canal

This slide illustrates the epithelial histology at the pectinate line where the epithelium transitions from simple columnar epithelium to stratified squamous non-keratinized epithelium.

Precancerous Colon Polyp

A precancerous colon polyp is formed as a result of ‘out of control’ cell division of colon epithelial cells. The normal colon epithelium is indicated between the two dotted lines. In the precancerous polyp image the normal colon is also indicated between two dotted lines. The polyp formed by the proliferation of epithelial cells is located within the circle. You can see that the polyp is connected to the normal part of the colon by a stalk. This is what a physician is looking for when a colonoscopy is performed. If found during a colonoscopy, a wire loop is placed around the polyp and it is excised as a biopsy and submitted to a pathologist for examination. At this stage the polyp is a neoplastic growth. It is benign because it is still contained within the epithelial layer of the colon.

Adenocarcinoma of the Colon

Adenocarcinoma is a cancer the cells of which are derived from gland cells. In this case, the cells of the intestinal glands. The cancer term prefix is -adeno- because the cells were derived from gland cells and –carcinoma- because the cells were derived from epithelial gland cells. On the left is presented the normal epithelial lining of the colon where you can see many empty spaces that are actually single cells called goblet cells. On the right you see abnormal epithelial lining cells that no longer have empty spaces but are solid and are deeply stained. In the insets on the right and left, compare the normal epithelium on the left to the cancerous epithelium on the right. You can see in the adenocarcinoma specimen that there are no goblet cells, the cells are darkly stained and the nuclei occupy more area in the cells. Finally, this cancer is malignant because the cancer cells have migrated through the basement membrane into the connective tissue as evidenced by the cells within the encircled region.
Summary

- This lecture began with a presentation of the general plan of organization of the wall of the intestines.
- The small intestine was presented with explanations and illustrations of the difference between plicae circulares, villi and microvilli. The cells of the intestinal gland were presented and how they are renewed by stem cells dividing in the crypts of Lieberkuhn.
- The histology of the colon was presented that included illustrated examples of colon polyps and adenocarcinoma of the colon.
- The histology of the appendix, rectum and anal canal were presented emphasizing their similarities and differences.