I. Small intestine

The small (diameter) intestine in humans is approximately 6 meters in length and is divided into 3 anatomical regions, from proximal to distal: duodenum, jejunum and ileum.

The small intestine performs multiple digestive functions that include (1) neutralization of the acidic chyme passed from the stomach (duodenum), (2) enzymatic and biliary digestion of fats, carbohydrates and proteins, and (3) absorption of nutrients and water. In addition to its digestive functions, the small intestine provides immune surveillance by means of M.A.L.T. Like the gaster (stomach), its endocrine and exocrine functions are largely restricted to digestion.

Anatomical subdivisions

The duodenum is approximately twelve "fingers" long and receives chyme released from the stomach at the pyloric sphincter. The diagnostic feature of the duodenum is the presence of glands within the submucosa called (drum roll, please) duodenal (Brunner's) glands. These branched glands secrete an alkaline mucous that neutralizes the gastric chyme. In addition to enzymes released from the mucosa, digestion in the duodenum is assisted by 2 accessory digestive organs: (1) The gall bladder which stores bile secreted by the liver and releases it to the duodenum where it emulsifies fat permitting the lipases to do their work; and (2) the pancreas whose exocrine glands secrete enzymes that are also released to the duodenum.

The next segments of the small intestine are the jejunum followed by the ileum. Chyme passes from the ileum into the large intestine at the ileocecal junction. Histologically, the jejunum and ileum are largely indistinguishable and functionally are primarily absorptive. Lymphoid aggregates (mucosal associated lymphoid tissue, MALT) can occur anywhere along the mucosa of the small intestine but are particularly common in the ileum; where large numbers (30-40) of lymphatic nodules aggregate to create macroscopically visible Peyer's patches.

Lumen topology

All regions of the small intestine have 3 features that serve to increase the surface area (SA) of the lumen for absorption: (1) The plica circularis are circular folds comprised of mucosa and submucosa; (2) the villi are finger-like projections of mucosa; and (3) microvilli cover the apical surface of the epithelial lining cells (enterocytes). These features combine to increase the total SA 600-fold.

Histological structure of the small intestine

Like all organs within the gastrointestinal tract the wall of the small intestine is formed by 4 superimposed tunics or coats: mucosa, submucosa, muscularis, and serosa/adventitia.
The mucosa forms villi and intestinal glands. The villi are hair-like projections consisting of a connective tissue core (lamina propria) covered by a simple columnar epithelium (enterocytes; also called absorptive cells) interspersed with goblet cells. The microvilli covering the enterocytes create an apical striated border in LM. The intestinal glands (crypts of Lieberkühn) are simple tubular glands extending to the muscularis mucosae and opening at the base of the villi; their epithelium is similar to the villi but also contains stem cells, Paneth cells and enteroendocrine cells (see below).

The lamina propria of the mucosa is a loose connective tissue (CT) containing the usual cast of suspects: Fibroblasts, capillaries, lymphatics, and immune cells (wandering leukocytes and macrophages). There are 3 things to note in the lamina propria: (1) The blood capillaries drains to the hepatic portal system rather than the systemic caval system; (2) the presence of large, blind-ended, lymphatic capillaries called lacteals that function in fat absorption (see below); and (3) the presence of smooth muscle bundles oriented along the long axis of the villi. This smooth muscle is thought to move the villi about (stirred surface concept).

The muscularis mucosa is bi-laminar with a thin, inner circular layer and a thin outer longitudinal layer. Its contraction is thought to mix the lumenal contents.

The submucosa consists of an irregular CT containing blood and lymph vessels and submucosal (Meissner’s) plexus. Located in the submucosa of only the duodenum are the duodenal (Brunner’s) glands. These glands contain zymogen and mucous secreting cells. The alkaline secretion of these glands acts to (1) neutralize the acidic chyme released from the gaster and (2) raise the pH of the chyme for pancreatic enzyme activation. Their contents are released via the intestinal glands (crypts of Lieberkühn).

The muscularis is typical with an inner circular and outer longitudinal layer of smooth muscle to provide peristalsis. The myenteric (Auerbach’s) plexus can be observed between the layers.

The adventitia / serosa is similarly unremarkable.

Epithelial cells of the small intestine

There are 6 types of epithelial cells found lining the lumen and forming the glands of the small intestine: enterocytes (columnar absorptive cells), goblet cells, M-cells, Paneth cells, stem cells, and enteroendocrine cells.

The enterocytes are the major cell type of the villi and the upper regions of the intestinal glands. These are primarily absorptive cells and any secretions are related to absorption. They are columnar cells with a basal nucleus. Their apical (lumenal) surface is covered with microvilli to which are anchored digestive enzymes. The enterocytes absorb water, sodium, fats, sugars and amino acids. Both active and passive transport are used to move nutrients from the lumen, through the cell and released into the extracellular space. These are also exocrine cells; those of the villi secrete enzymes which anchor in their own microvilli to aid in absorption/digestion (e.g., enterokinase) whereas those of the intestinal glands secrete water and electrolytes to replace that absorbed by the villi.

Goblet cells are unicellular mucous glands with a basal nucleus and apical mucous cup. They have scant microvilli at their apex. They secrete an acid glycoprotein that protects and lubricates the epithelia. They are found in both villi and intestinal glands and their frequency increases from the duodenum to the ileum.

M (microfold) cells are specialized epithelial cells found covering the lumenal surface of the sporadic lymphatic masses (M.A.L.T.s) that are found in the intestine. These cells are squamous-like in shape and their apical surface is covered with microfolds rather than microvilli. They function as antigen-presenting cells: Microorganisms and macromolecules from the lumen are taken up by the M-cells via
endocytosis, transported through the cell, and secreted basally to the extra-cellular space where T-lymphocytes await. The basal lamina below the M-cells is discontinuous allowing for close lymphocyte proximity.

The enteroendocrine cells of the intestine are morphologically identical to those in the gaster and rest of the intestinal tract, and thus difficult to identify in H&E sections. They are concentrated in the lower portion of the intestinal glands. The several types of cells secrete their products into the lamina propria and affect other local cells (paracrine) and distant cells (endocrine) associated with digestion (see but don’t memorize TABLES 16.1 and 16.2 in your text).

Paneth cells are located at the base of the intestinal glands and contain eosinophilic granules. These granules are lysozymes (anti-bacterial enzymes) that along with the cells phagocytic ability permit them to regulate the bacterial flora of the small intestine.

Stem cells are undifferentiated cells that give rise to the other cells types of the epithelium. They are concentrated in the lower half of the intestinal glands.

III. Enterocyte digestion and absorption

The 3 major nutrients absorbed by the small intestine are triglycerides, proteins and carbohydrates.

In the lumen triglycerides are broken down into simpler molecules and are kept emulsified by the bile salts. These molecules pass into the apical region of the enterocytes where they are packaged into chylomicrons and are transported into the lateral inter-cellular space. The chylomicrons migrate through the basement membrane into the lamina propria and enter either (1) the capillaries of the hepatic portal system or (2) lacteals.

Also in the lumen, proteins are digested enzymatically by gastric and pancreatic enzymes into amino acids and small peptides. These smaller molecules are absorbed by the enterocytes by means of specific transporters in the microvilli, transported thru the cell and released thru the basement membrane to enter the capillaries of the hepatic portal system.

Enzymatic digestion of carbohydrates begins in the oral cavity and continues in the small intestine by pancreatic enzymes. Enzymes bound to the microvilli of the enterocytes further degrade the carbohydrates into simple sugars (fructose, galactose, and glucose). These monosaccharides are first actively transported into the cell from the lumen and then actively transported out into the intercellular space where they enter the capillaries of the hepatic portal system.

III. Portal systems

In most tetrapods, including humans, there are 3 types of venous circulatory systems: (1) pulmonary, (2) systemic (caval), and (3) portal. The pulmonary venous system returns oxygenated blood from the lungs to the heart. The caval venous system is responsible for returning blood to the heart. A portal venous system consists of two capillary beds connected by valve-less veins. In humans, there are two major portal systems, (1) the hepatic portal system and (2) the hypothalamo-hypophyseal portal system. The latter plays an important part of the endocrine system.

The hepatic portal system transports nutrients from the gastrointestinal (GI) tract to the liver. Capillary beds in the gastrointestinal tract and its accessory organs (gall bladder, pancreas and spleen) drain via veins to the hepatic sinusoids which are the capillary beds of the hepatic parenchyma. Thus, this system carries (1) nutrients and toxins absorbed from the GI tract, (2) blood cells and their digested products from the spleen and (3) endocrine secretions from the pancreas and the enteroendocrine cells.
of the GI tract. The only nutrients absorbed by the GI tract not to pass through the liver are the chylomicrons absorbed by the lacteals.

IV. Large intestine

The large (diameter) intestine in humans is approximately 1.5 meters in length and comprises the end of the digestive tract. Functionally it is the site of (1) water and ion (electrolyte) absorption and (2) fermentation by symbiotic bacteria. The microfauna of the gut tract is the subject of ongoing research and the number of species and the products they produce (biotin, vitamin K, etc.) expands continuously. We will use vitamin K as an example. Primarily in the large intestine but also along the terminal ileum of the small intestine, several species of bacterial release the vitamin K precursors known as menaquinones. These molecules are absorbed by the absorptive epithelial cells and transported to the liver in chylomicrons where they are converted into vitamin K.

Anatomical subdivisions

The large intestine is divided into 4 regions, from proximal to distal: Cecum (a blind pouch), colon (divisible into ascending, transverse, descending, sigmoid), rectum and anal canal. The large intestine receives chyme from the small intestine at the ileo-colic (or ileo-cecal) junction. After passing through the large intestine, the unabsorbed digesta and dead bacteria are excreted from the anal canal as feces.

Grossly the large intestine exhibits 3 diagnostic features, which can sometimes be observed histologically: (1) The teniae coli are 3 localized thickenings of the longitudinal layer of the tunica muscularis that run the length of the cecum and colon; (2) the haustra coli are sacculations of the tube between the teniae; and (3) the omental appendices are small peritoneal projections filled with fat.

The vermiform appendix is an inconstant diverticulum attached to the cecum. It is a secondary lymphatic organ thought to assist in controlling and maintaining the intestinal microflora of the gut.

Histological structure

Like all organs within the gastrointestinal tract, the wall of the large intestine is formed by 4 superimposed tunics or coats: Mucosa, submucosa, muscularis externa, and serosa/adventitia. The lining of the lumen of the large intestine is smooth (no villi) and is perforated by the openings of the intestinal glands.

The mucosa forms the smooth lining surface and the intestinal glands (crypts of Lieberkühn) and is covered by a simple columnar epithelium. The intestinal glands are simple tubular glands that extend to the muscularis mucosae. Stem cells are found at the bottom of the glands. The remainder of the epithelium (lining and glands) is comprised of colonocytes (also called columnar absorptive cells), goblet cells and enteroendocrine cells. The enteroendocrine cells in the large intestine are the same as those that occur elsewhere in the gut tract but occur in lesser number. The colonocytes are a simple columnar epithelial cell similar in morphology to the enterocytes. They function to absorb water and electrolytes. The goblet cells ( unicellular mucous glands) predominate in the intestinal glands; their secretion serving to lubricate the lumen to facilitate waste elimination. On the surface, the colonocytes and goblet cells exhibit a reciprocal distribution with the proportion of goblet cells increasing distally along the tract.

The lamina propria of the large intestine has the same basic components as that of the small intestine except (1) it lacks lacteals and (2) MALTs are more common. Similarly, the muscularis mucosae shows no changes.

The submucosa and adventitia/serosa are unremarkable. As mentioned above, the outer longitudinal layer of the muscularis externa gives rise to the teniae coli.
IV. The enteric nervous system – a 3rd division of the autonomic nervous system

The enteric nervous system (ENS) innervates the lower esophagus, gastrointestinal tract, pancreas and gallbladder. It is composed of 3 elements: (1) Sensory neurons that monitor the tension of the gut wall and the chemical environment of the gut tract; (2) motor neurons that control the muscles of the gut wall, the muscles of the vasculature, and the secretory activity of the mucosa, and (3) interneurons that provide communication between (1) and (2). Thus the enteric nervous system stands in marked contrast to the sympathetic and parasympathetic systems which, as you recall, are simple two (motor) neuron systems.

The neurons of the ENS are found in two interconnected ganglionic plexi: (1) the submucosal [neural] plexi and (2) the myenteric [neural] plexi. [A nervous plexus (pl. plexi) is a network of nerves and nerve cell bodies; plexi containing neurons are referred to as ganglionic plexi; those without neurons are referred to as aganglionic plexi.] In addition to the two ganglionic plexi, there are numerous smaller, aganglionic plexi in the mucosa, muscularis and adventitia/serosa of these organs.

While the ENS can functionally autonomously, its activity can be modified by both the sympathetic and parasympathetic autonomic nervous systems. Interestingly, the enteric ganglia receive projections from pre-ganglionic parasympathetic neurons but post-ganglionic sympathetic neurons. Innervation from the sympathetic and parasympathetic systems provides (1) a second level of control over digestion and (2) a mechanism to over-ride intrinsic enteric activity in times of emergency or stress (e.g., fight or flight).