Instructor's Answer Key

Chapter 18: The Digestive System

Answers to Test Your Understanding of Concepts and Principles

1. During the *cephalic* phase, parasympathetic fibers from the vagus nerve stimulate gastric secretion. Chief cells are stimulated to release pepsinogen while parietal cells are stimulated through ACh binding to muscarinic receptors to secrete HCl. The major mechanism for HCl secretion is indirect, through the vagus nerve stimulation of ECL cells and subsequent secretion of histamine, which in turn stimulates parietal cells to secrete HCl. During the *gastric* phase, secretion of acid and pepsin is stimulated in response to two factors: (1) distension of the stomach by the volume of chyme; and (2) the chemical nature of the chyme. The presence of partially digested protein in the stomach lumen stimulates the chief cells to secrete pepsinogen and the G cells to secrete the hormone, gastrin. Gastrin, then is recirculated back to stimulate more pepsinogen and more HCl secretion (indirectly) creating a positive feedback loop. Fat inhibits acid secretion and glucose has no effect. As the pH of gastric juice drops, so does the secretion of gastrin and HCl release (perhaps mediated by the release of somatostatin from D cells). During the *intestinal* phase, both neural reflexes from the duodenum in response to stretch and osmolality and a chemical hormone (enterogastrone, such as GIP) secreted by the duodenum appear involved in the inhibition of gastric secretion following a meal. [Note: This question is also answered in the Student Study Guide.]

2. Most of the enzymes of pancreatic juice are released into the duodenum in inactive forms (zymogens). The brush border enzyme called enterokinase converts the inactive trypsinogen in pancreatic juice to active trypsin. Trypsin is a proteolytic enzyme that cleaves off parts of other inactive enzymes, thus activating the other enzymes of pancreatic juice. Since the pancreatic enzymes are generally inactive within the acini of the pancreas, there is less danger of these enzymes promoting self-digestion of the pancreas.

3. Peptic ulcers are erosions of the mucous membranes of the stomach or duodenum produced by the action of HCl. Bicarbonate in pancreatic juice serves to neutralize the acidic chyme arriving from the stomach to the duodenum. This helps to prevent the acidic chyme from producing duodenal ulcers, and creates an alkaline environment within the small intestine that is needed for optimal activity of pancreatic juice and brush border enzymes. Excessive gastric acid secretion, however, may negate the buffering effect of the bicarbonate and result in the production of a duodenal ulcer. The stomach, by contrast, is normally adapted to withstand the acidic chyme that is always present in the gastric lumen, and thus gastric ulcers are not produced unless the normal barriers to gastric self-digestion are broken down (as in prolonged exposure to nonsteroidal anti-inflammatory drugs, like aspirin) or excess gastrin is produced (as in Zollinger-Ellison syndrome). Peptic ulcers may also be caused by a bacterium, Helicobacter pylori, which explains why antibiotics help in the treatment of ulcers.

4. The gastric mucosa is protected from self-digestion by several barriers in addition to the demonstrated impermeability of the plasma membranes of parietal and chief cells to gastric acid. These barriers include the alkaline (with bicarbonate) mucous layer of the stomach, the tight junctions between adjacent gastric epithelial cells, and the rapid renal of the gastric epithelium and several protective effects provided by prostaglandins produced by the gastric mucosa. Ulcers develop in the stomach when these barriers are broken down, or in the case of excessive acid secretion.

5. The acini of the pancreas produce pancreatic juice and secrete this product into the pancreatic duct, which carries it to the duodenum. Pancreatic juice is thus an exocrine secretion. Within the pancreas, islands of cells called the islets of Langerhans secrete their products into the blood rather than the duct system. These products are biologically active compounds (insulin and glucagon)—hormones—and thus these islands of tissues within the pancreas are endocrine structures. Tying of the pancreatic duct will prevent the exit of the exocrine secretions of digestive enzymes but will not prevent the endocrine secretions of the pancreas. Since the digestive enzymes cannot be secreted, they may "break up," leak from the acini and digest various portions of the pancreas.

6. (a) Gallstones block the excretion of conjugated bilirubin in the bile, thus resulting in the accumulation of this conjugated bilirubin in the blood. (b) A high rate of red blood cell destruction results in excessive conversion of heme to free bilirubin. This free bilirubin accumulates in the blood and tissues, causing jaundice. (c) Liver disease also results in the presence of high concentrations of free bilirubin, because the diseased liver cannot conjugate the bilirubin and excrete it in the bile. Since phototherapy converts free bilirubin to a water-soluble form that can be excreted in the bile, it would be an effective treatment of jaundice for cases (b) and (c). A person with gallstones, however, cannot excrete the bilirubin, so the jaundice caused by gallstones could not be treated effectively with phototherapy.

7. Before fat can be digested, it must be emulsified so that the surface area is increased. Fat digestion occurs at the surface of the droplets by pancreatic lipase, colipase, and phospholipase A. These enzymes hydrolyze the lipids to liberate free fatty acids and monoglycerides. The free fatty acids, monoglycerides, and lysolecithin products of digestion form "mixed micelles" then move into the intestinal epithelial cells and are synthesized into triglycerides and phospholipids. Triglycerides and phospholipids form particles called *chylomicrons*, which are secreted into the lymphatic capillaries of the intestinal villi. Absorbed lipids then pass through the lymphatic system, eventually entering the venous blood by way of the thoracic duct.

8. Chylomicrons are particles made by the intestinal epithelium, composed of lipid and protein that function to deliver lipids of dietary origin to body cells. Very-low density lipoproteins (VLDLs) are assembled from cholesterol and triglycerides made by the liver and combine with other apolipoproteins. VLDLs serve to deliver endogenously produced triglycerides to body cells. Low-density lipoproteins (LDLs) are formed from the intravascular removal of triglycerides from VLDL particles and serve to deliver endogenous cholesterol to various organs, the liver, and blood vessels. High-density lipoproteins (HDLs) originate from the liver and intestine and help return excess cholesterol from various organs to the liver and steroid-producing glands.

9. The submucosal (Meissner's) and myenteric (Auerbach's) plexuses within the wall of the intestine contain 100 million neurons (~ the same number as the spinal cord). These include preganglionic parasympathetic axons; the ganglion cell bodies of postganglionic parasympathetic neurons; postganglionic sympathetic axons; and afferent (sensory) neurons. Like the CNS, these plexuses also contain interneurons and contain more glial cells (like the CNS, resembling astrocytes) than neurons. For this reason these combined plexuses are sometimes described as the enteric nervous system, or "enteric brain." Many of the sensory neurons within the intestinal plexuses send impulses via the vagus nerve to the CNS. These are *extrinsic afferents* that are involved in regulation of the autonomic nervous system. Other sensory neurons are *intrinsic afferents* with cell bodies locally in the myenteric of submucosal plexuses and synapse with the interneurons in the wall of the intestine. This allows for local or "short" reflexes that operate within the GI tract. There are several intestinal reflexes that control the GI tract both locally and extrinsically. These include the gastroileal reflex, the ileogastric reflex, and the intestino-intestinal reflex.

10. The liver, the largest internal organ, is composed of functional units called lobules. Liver lobules consist of plates of hepatic cells separated by open capillary sinusoids. Blood flows from the periphery of each lobule where the hepatic artery and portal vein empty, through the sinusoids and then out the central vein. The liver cells (hepatocytes) of the lobules can remove hormones, drugs, and other biologically active molecules from the blood by (1) excretion of these compounds in the bile; (2) phagocytosis by Kupffer cells that line the sinusoids; and (3) chemical alteration of these molecules within the hepatocytes. For example the liver has the enzymes needed to convert ammonia into less toxic urea molecules, enzymes to convert toxic porphyrins into bilirubin, and those required to convert toxic purines into uric acid. The liver also has enzymes that convert nonpolar molecules (steroid hormones and drugs) into more polar (more water soluble) forms by hydroxylation and by conjugation with highly polar groups that can be more easily excreted by the kidneys into the urine or the bile.

Answers to Test Your Ability to Analyze and Apply Your Knowledge

1. Pancreatectomy would have the most profound effect on digestion since most digestion is accomplished by the large number of pancreatic enzymes that are secreted with pancreatic "juice" along the pancreatic duct and into the duodenum. These pancreatic enzymes are secreted in inactive zymogen forms that become activated into powerful, hydrolytic enzymes upon their arrival in the small intestine. Since pepsin is the only enzyme of the stomach, gastrectomy has little effect on digestion. Similarly, cholecystectomy has little effect because the gallbladder only stores and concentrates bile for release when fats are present in the duodenum. After gall bladder removal the liver continues to make and release bile into the duodenum, whose role in the emulsification of fats has been curtailed.

2. The GI tract has developed a number of adaptations to increase surface area for absorption or to increase contact between food and digestive enzymes. First, the small intestine mucosa and submucosa layers fold into large pleats, known as plicae circulares. More surface area is provided by smaller microscopic folds of the mucosa, called villi, and more still from foldings of the apical plasma membrane of epithelial cells, called microvilli. In addition to surface area, the intestinal smooth muscle contractions and motility assist in exposing food to the digestive enzymes. Peristalsis, segmentation, and pendular action all help churn or mix GI contents. Finally, emulsifying agents in bile prepare lipids for the digestive action of lipase enzymes by first splitting larger fat globules with less surface exposure into smaller fat droplets (micelles) with greater surface exposure.

3. In the cephalic phase, the vagus nerve stimulates both the G cells to secrete the hormone, gastrin (from G cells) and the ECL cells of the gastric mucosa to secrete histamine. The histamine, in turn, acts as a paracrine regulator molecule to stimulate the parietal cells to secrete HCl into the stomach lumen. Furthermore, gastrin has an endocrine role in stimulating ECL cells directly to secrete histamine, and thus HCl secretion from the parietal cells. Furthermore, the presence of partially digested protein fragments, especially the amino acids phenylalanine and tryptophan, serve as paracrine stimulators of the G cells that, in turn, secrete gastrin, resulting in greater gastric acid secretion. Since gastric acid secretion is stimulated by histamine released from the ECL cells, people with peptic ulcers can be treated with drugs that block histamine action. Such drugs, like Tagamet and Zantac, inhibit acid secretion by specifically blocking the H_2 histamine receptors on the ECL cells of the gastric mucosa.

4. Guanylin is a recently discovered paracrine regulator produced by the ileum and the colon. Guanylin acts on the intestinal epithelial cells to produce cyclic GMP (cGMP) second messengers that, in turn, promote the secretion of Cl^- and water into and to inhibit Na^+ absorption from the lumen. This action leads to normal salt and water loss from the body in feces. Certain *Escherichia coli* bacteria produce heat-stable enterotoxins that cause traveler's diarrhea. The bacterial enterotoxins act by stimulating the same receptors on the apical membranes of the intestinal epithelial cells that are activated by guanylin. By mimicking the normal action of guanylin, the enterotoxins stimulate the increase in intestinal Cl^- and water secretion into the intestine and produce diarrhea.

5. The oral glucose results in a more powerful insulin secretion from the pancreatic islets of Langerhans because the presence of glucose in the digestive tract stimulates the release of two hormones, both of which stimulate insulin secretion. The first hormone is *gastric inhibitory peptide* (GIP), which is released from the intestinal mucosa when glucose arrives. Because of GIP's action to stimulate insulin secretion when glucose is present, a name change has been proposed to fit the acronym – *glucose-dependent insulinotropic peptide*. The second hormone is *glucagon-like peptide-1* (GLP-1), one of a family of peptides produced by the intestine that structurally resembles the hormone glucagon (secreted by the alpha cells of the pancreatic islets) and also is a very potent stimulator of insulin secretion. In this way, these two hormones stimulate the pancreas to "anticipate" a rise in blood glucose by secreting insulin even *before* the glucose has been absorbed into the blood.