

Chapter 2

Form and Function: The Physiological Implications of the Anatomy of the Gastrointestinal System

2.1 Introduction

The digestive system consists of a series of organs and glands that process ingested food by physical and chemical means to provide the body absorbable nutrients and to excrete waste products. In humans, this system includes the alimentary canal, and associated glands which run from the mouth to the anus, plus the hormones and enzymes which assist in digestion. The digestive system is considered in light of its major roles, not only with respect to nutrient exchange but also in regard to its support of other bodily activities and maintenance of homeostasis.

2.2 Digestive System Requirements: Form Meets Function

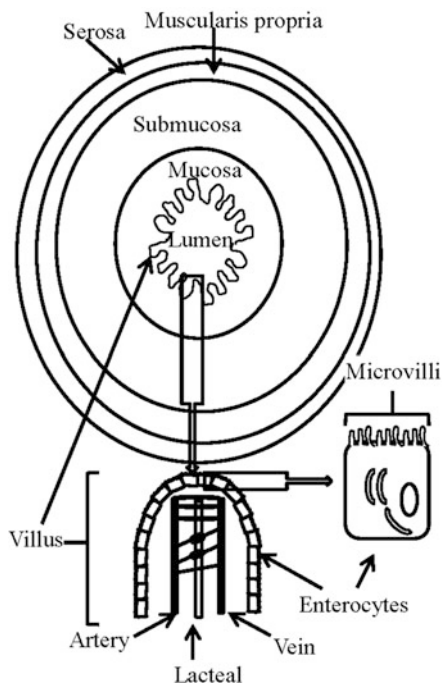
2.2.1 *Absorptive and Secretory Mucosa*

The gut wall comprises four concentric layers as you move from the lumen toward the outer surface: (1) mucosa, (2) submucosa, (3) muscularis propria, and (4) serosa (Fig. 2.1).

The inner surface of the intestines is arranged into longitudinal folds (*plicae circulares* or *Kerckring folds*), which in turn give rise to finger-like projections called *villi* (Fig. 2.1). Epithelial cells and mucus secreting *goblet cells* cover the surface of the villi. The mucus secreted by the goblet cells helps to lubricate food stuffs and facilitate movement in the intestinal tract. The *apical surface* of the villi gives rise to *microvilli*, which increase the absorptive surface area (Fig. 2.1). When viewed with a light microscope, the microvillar surface has a *brush border* appearance. Cells located toward the tips of the villi absorb intestinal contents and those located at the base of the villi or crypts secrete fluids and electrolytes.

The intestinal mucosa is designed to absorb nutrients and fluids via two main paths: (1) a *transcellular path* in which the substance must cross the apical or brush

Fig. 2.1 Cross section of the gut wall highlighting the four concentric layers from the lumen toward the outer surface. The insets show details for a villus and the microvilli on an enterocyte (absorptive intestinal cell) on the villus



border of the intestinal cell, enter into the cell, and then exit the cell across the basolateral border and (2) a *paracellular path* where substances cross *tight junctions* between adjacent intestinal cells, through the intercellular spaces and into the blood (Fig. 2.2). Mechanisms of absorption and secretion will be discussed in later chapters. As you will see, the GI tract muscles, nerves, and vasculature ultimately act to facilitate the functions of the absorptive and secretory mucosa.

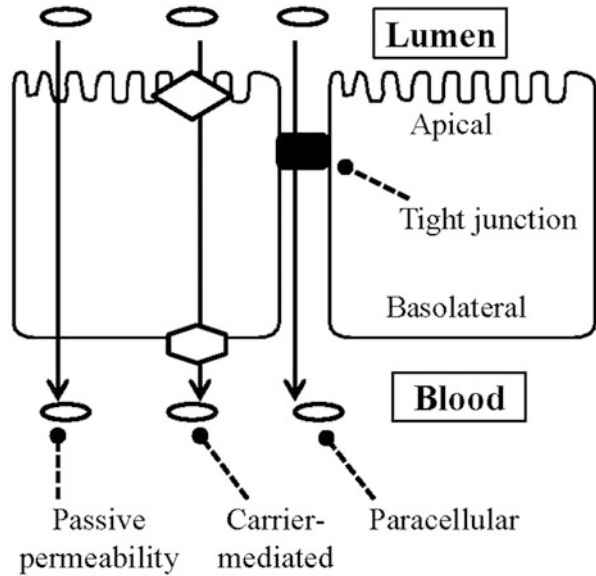
Reality check 2-1: A tennis superstar has recently been diagnosed with Sjogren's disease, a chronic autoimmune disease in which a patient's white blood cells attack his/her moisture-producing glands. What type of an effect would you expect concerning swallowing during a long hot match during the US Open? What would you expect if he/she later is overwhelmed with emotion after a tremendously difficult victory?

2.2.2 Muscles

In general, form and function of the human body are closely related. Nature tends to select features which provide survival advantage.

The following layers are seen in a typical cross section of the gut wall when viewed from the outer surface toward the inward surface: (1) serosa, (2) longitudinal muscle, (3) circular muscle, (4) submucosa, and (5) mucosa (Fig. 2.1).

Fig. 2.2 Mechanisms of nutrient absorption in the small intestine. The transcellular pathway may involve either passive permeability (*left*) or carrier-mediated transport (*middle*) from the apical surface at the lumen side or the basolateral surface at the blood side. The paracellular pathway (*right*) crosses tight junctions between adjacent cells



The *muscularis mucosae* consists of sparse bundles of smooth muscle fibers located between the *submucosal plexus* and the *lamina propria*. The smooth muscle present in the muscularis mucosae is responsible for movement in the mucosal layer of the gut wall. The pressure necessary to propel luminal contents down the GI tract in the process of *peristalsis* actually comes from circular muscle contraction above a point of distension and concurrent relaxation of this muscle layer below the luminal contents (Fig. 2.3). Contraction of the longitudinal muscle during this process shortens the distance over which the circular muscle contraction has to travel in order to move the contents forward.

Whereas striated muscle contraction is under conscious control, smooth muscle contraction is involuntary. Imagine a GI tract under complete conscious control. For peristalsis to move a food bolus along the entire gut one would have to consciously initiate and maintain the effort. That would literally require a lot of thought and would be very inefficient. Fortunately, gut wall smooth muscles have some unique properties which enable them to perform their principal functions. The smooth muscle cells contain actin and myosin filaments in an arrangement which is not as ordered as the sarcomeres of skeletal muscle. Intestinal muscle cells do not actually appear “smooth” when viewed under a light microscope (Fig. 2.4a); they simply lack the striations seen in skeletal muscle (Fig. 2.4b) and, therefore, have a more uniform appearance.

The GI tract comprises unitary smooth muscle which has a high degree of electrochemical coupling between adjacent cells because of the presence of many gap junctions. Because of this special arrangement, stimulation of one cell causes the group of connected cells to contract simultaneously as a *syncytium*. Some smooth muscles (e.g., those found in the esophageal body, small intestine, and

Fig. 2.3 Peristalsis. Distention of the GI lumen triggers a myenteric reflex that causes circular contraction proximal to the site of distention and dilation distal to the site of distention. These contractions, termed peristalsis, move the bolus forward, triggering another myenteric reflex, and so on

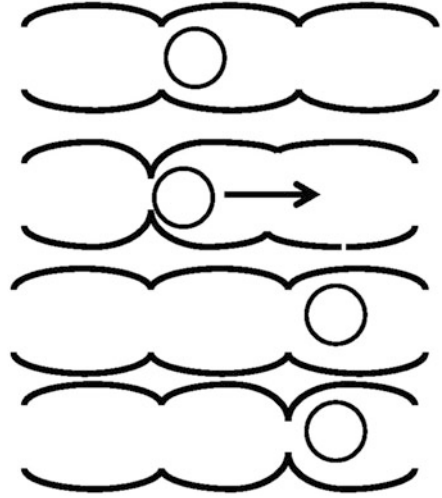
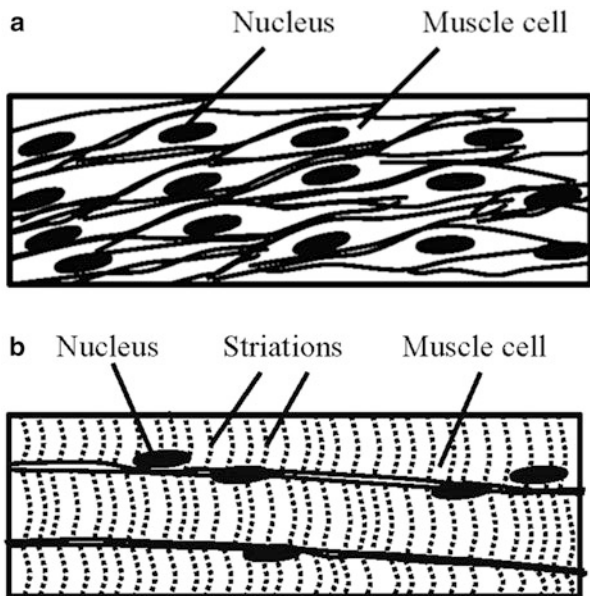


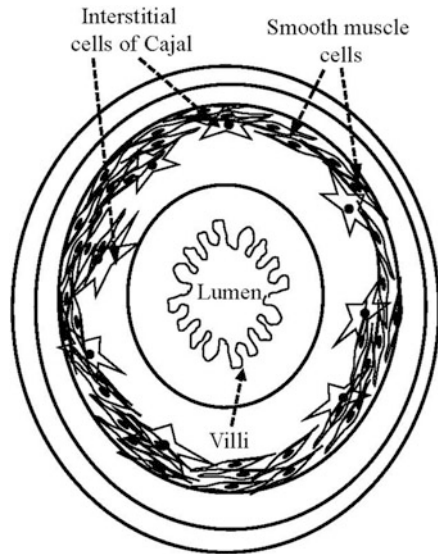
Fig. 2.4 Comparison of structure of muscle. (a) Structure of smooth muscle: spindle-shaped with single nuclei. (b) Structure of skeletal muscle: striated and multinucleated



gastric antrum) contract and relax in a few seconds (phasic contractions). Smooth muscles found in the *lower esophageal sphincter* (LES), ileocecal valve, and anal sphincters may contract over minutes or hours (tonic contractions). The type of contraction is determined by the smooth muscle cell and is independent of neural or hormonal input.

Unitary smooth muscle exhibits slow waves (i.e., spontaneous pacemaker activity) and represents undulations of 5–15 mV in the smooth muscle membrane

Fig. 2.5 Interstitial cells of Cajal and their processes form multiple connections with adjacent smooth muscle cells



potential. These periodic membrane depolarizations and repolarizations are major determinants of the phasic nature of GI smooth muscle contraction. The rate of slow waves and subsequent rhythmic contractions is 3 per minute in the stomach, 12 per minute in the duodenum, and 9 per minute in the terminal ileum. Slow wave activity is due to ionic currents initiated via the interactions of the *interstitial cells of Cajal* (ICCs) with smooth muscle cells (Fig. 2.5). Slow wave generation involves the cyclic opening of calcium channels during depolarization and the opening of potassium channels subsequently during repolarization. Spike potentials are true action potentials which are superimposed on slow waves. When the resting membrane potential of the GI smooth muscle becomes more positive than approximately -40 mV, then spike potentials occur and smooth muscle contraction is initiated (Fig. 2.6a).

In phasically active muscles, stimulation induces a rise in intracellular calcium, which induces phosphorylation of the light chain of myosin (Fig. 2.6b). ATP splits and the muscle contracts as the phosphorylated myosin interacts with actin. When calcium concentration decreases, myosin is dephosphorylated and relaxation occurs. In tonically active muscles, contraction can be maintained at low levels of phosphorylation and ATP utilization. Intestinal smooth muscle action potentials are largely mediated by the inward movement of Ca^{2+} rather than Na^+ . This difference has important ramifications with regard to the classes of pharmacologic agents that can suppress intestinal motility (e.g., calcium channel blockers like verapamil) without significantly affecting skeletal muscle function because skeletal (voluntary) muscle contraction is controlled principally by the central nervous system (CNS).

The two major types of movements in the GI tract are (1) peristalsis or *propulsive movements* and (2) mixing or *segmentation movements* (Fig. 2.7). GI peristalsis (anywhere except the skeletal muscle region of the esophagus) requires an intact

Fig. 2.6 Gastrointestinal smooth muscle function. (a) Slow waves with superimposed action potentials. (b) Stimulation of phasically active smooth muscles induces an increase in intracellular calcium that leads to activation of myosin light chain kinase (MLCK) followed by addition of phosphate to myosin with the consumption of ATP. Contraction of smooth muscle occurs when actin and phosphorylated myosin interact. Smooth muscle relaxation occurs following a decrease in intracellular calcium leading to dephosphorylation of myosin

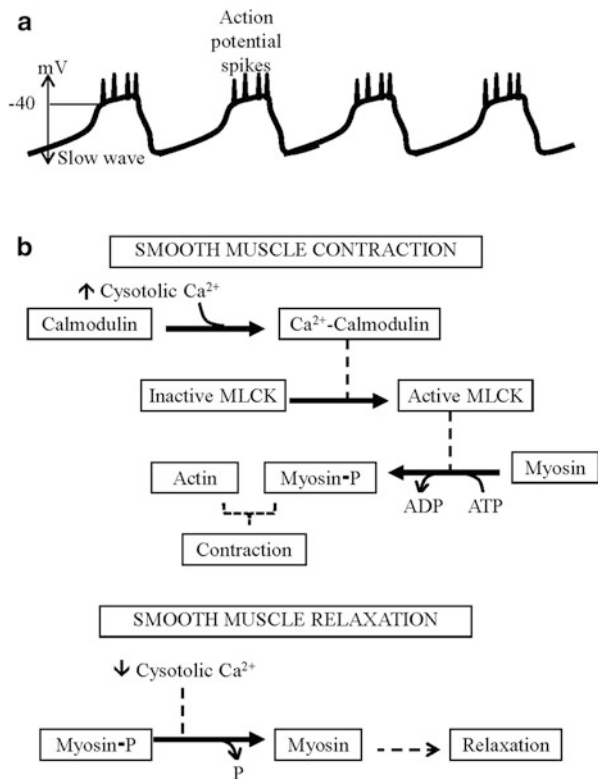
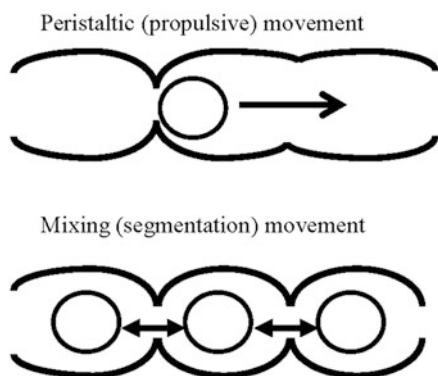


Fig. 2.7 Comparison of peristaltic contractions with mixing contractions in the small bowel. Peristaltic contractions propel the chyme in a caudad direction. Segmentation contractions mix the chyme



and functional myenteric plexus; the contribution to this process made by the respective muscle layers involved is their ability to either contract (above) or relax (below) a point of distension, but this is coordinated by the myenteric plexus and cannot occur in its absence. Physical stretching of unitary smooth muscle may cause smooth muscle excitation but this excitation by itself does not initiate a

peristaltic wave (just a contraction) and, again, this phenomenon cannot be propagated without the coordinating influence of the myenteric plexus. However, once a peristaltic wave is propagated unconsciously, it can be propagated with much greater efficiency which frees our brains to ponder other weighty physiology questions. When a bolus of food enters the esophagus, a primary peristaltic wave of contraction of esophageal muscle passes from the oral to the gastric end. If this primary wave does not cause the bolus to exit from the esophagus, then a secondary peristaltic wave occurs in an attempt to move the food bolus. The LES must be able to relax for the food bolus to exit the esophagus. In addition, the LES must remain a competent sphincter in order to prohibit the reflux of gastric contents into the esophagus.

The relationships between the myenteric plexus, GI smooth muscle, and coordinated motor activity are crucial to understanding the pathophysiological basis of certain motility disorders of the intestines. Patients with primary disorders of small intestinal motility may appear to have intestinal obstruction due to decreased or absent motility and bowel distention. Patients with idiopathic intestinal pseudo-obstruction have a derangement of smooth muscle cells that results in delayed transit or transient ileus or apparent paralysis. Metabolic abnormalities, e.g., the depletion of potassium or administration of drugs such as anticholinergics, decrease neural transmission via the *enteric nervous system* (ENS) resulting in decreased small intestinal motility.

Factors that control colonic motility are not completely understood. However, as is the case in the stomach and small intestine, the following factors are involved in the control of colonic motility: (1) ICCs, (2) properties of smooth muscles, (3) the ENS, and (4) locally released or circulating chemicals. *Hirschsprung's disease* is a developmental disorder of the ENS characterized by an absence of ganglion cells in the distal colon. The enteric neurons in the distal colon and internal anal sphincter seem to be predominantly inhibitory because when they are destroyed or absent the colon is tonically contracted resulting in decreased colonic motility and constipation. Surgical removal of the diseased segment allows normal colonic contractions to occur.

Reality check 2-2: Scleroderma is a rare, progressive connective tissue disease that involves hardening and tightening of the skin and supportive tissues that normally provide the supportive framework for your body. What type of esophageal dysmotility findings would you expect?

Connecting-the-Dots 2-1

A 54-year-old male comes to the emergency room complaining of right lower quadrant abdominal pain. Preoperatively he was diagnosed with acute appendicitis. At operation an inflamed and perforated diverticulum of the cecum was found. The surgeon performed a cecostomy (surgically constructed drainage procedure of the cecum). After 3 weeks the cecostomy

(continued)

still did not function. During this time, the patient lost large volumes (5–7 L) of gastric secretion daily. Glucose, physiological saline, and plasma were given via IV. Also during this period he developed bloating, constipation, and nausea—all symptoms of decreased intestinal motility. At the end of the 3 weeks, the patient's peripheral reflexes were nearly absent but he was not paralyzed. The patient's serum chloride was 81 mmol/L (normal: 95–108). What was the likely factor that caused the decreased intestinal motility and the mechanism that led to this complication?

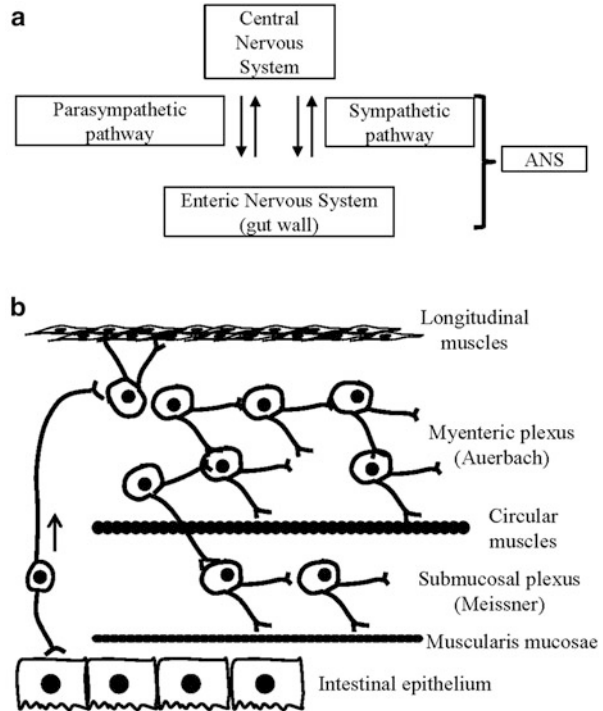
2.2.3 *Gastrointestinal Smooth Muscle Tonic Contractions*

Some GI smooth muscles may undergo tonic contractions as well as, or instead of, rhythmical contractions. Tonic contractions are not associated with the basic electrical rhythm of the slow waves. Tonic contractions occur continuously, often increasing or decreasing in intensity and frequently lasting for several minutes or hours. Tonic contractions may be caused by continuous repetitive spike potentials or by hormones or other factors which cause continuous partial depolarization of smooth muscle membrane without giving rise to action potentials. Continuous movement of Ca^{2+} into the cell interior via a mechanism other than changes in the membrane potential is another cause of tonic contraction in GI smooth muscle. Examples of smooth muscle digestive system sphincters include the LES, the pyloric sphincter at the gastric emptying point, the ileocecal valve, and the internal anal sphincter which is a thickening of the inner circular muscle layer.

2.2.4 *Nervous Innervation: General Features*

While the brain-gut axis modulates intestinal function, the bulk of the afferent–efferent activity occurs via intrinsic rather than extrinsic innervation. The GI system is similar to the cardiovascular, endocrine, and respiratory systems because it can function without the need for conscious control. The autonomic nervous system (ANS) includes the ENS, which constitutes the intrinsic innervation of the gut and the sympathetic and parasympathetic divisions which provide extrinsic innervation to the intestine (Fig. 2.8a). The ENS consists of the *myenteric (Auerbach's) plexus* and the *submucosal (Meissner's) plexus* (Fig. 2.8b). Auerbach's plexus is located between the inner circular and outer longitudinal muscle layers which control gut wall motility. Meissner's plexus lies in the submucosa and controls secretion and blood flow. The enteric plexuses comprise nerve cell bodies, axons, dendrites, and nerve endings. The neuronal processes of the

Fig. 2.8 The autonomic innervation of the gastrointestinal system and the structure of the enteric wall. (a) General overview showing the relationships of the CNS (central nervous system) and ANS (autonomic nervous system) with the ENS (enteric nervous system). (b) Interaction of the myenteric and submucosal plexuses with smooth muscle of the intestinal wall. The myenteric plexus controls gut motility and the submucosal plexus controls secretions and blood flow



enteric plexuses innervate target cells, e.g., secretory, absorptive, and smooth muscle cells, and make connection to sensory receptors and make connections with other neurons both inside and outside the plexus. Hence, integration of various activities can be achieved entirely through the ENS.

The role of neurotransmitters in the ANS: Several neurotransmitters are localized in specific pathways within the ANS. *Acetylcholine (ACh)* is the neurotransmitter found in many of the extrinsic nervous system, preganglionic efferent fibers, and exerts its action on neurons found in the prevertebral ganglia as well as the intrinsic nervous system. *Norepinephrine (NE)* is often found in the postganglionic efferent nerves of the sympathetic nervous system and frequently exerts its effect on the ENS neurons.

Neurotransmitters such as ACh, nitric oxide (NO), vasoactive intestinal peptide (VIP), somatostatin, and serotonin have been localized to interneurons in the ENS. VIP and NO have been found localized to nerves that are inhibitory to the muscle versus ACh and substance P which have been localized to nerves that are excitatory to muscle. An understanding of the neuronal circuits intrinsic to the intestine is helpful in understanding the mechanism of certain GI motility disorders such as Hirschsprung's disease (described above) that primarily affects the rectum and left colon. In the aganglionic segments, NO and VIP neural transmission is ablated resulting in the aganglionic segment's failure to relax and remain contracted. In addition, the extrinsic parasympathetic, cholinergic, and sympathetic adrenergic

innervations remain intact and unopposed further contributing to the aganglionic segment being spastic and unable to support peristalsis. This scenario also explains why the myenteric plexus can concurrently initiate circular muscle contraction above a small intestinal bolus via neurotransmitters ACh and Substance P, while the neurotransmitters VIP and NO can lead to smooth relaxation below the bolus. The repeated sequence of contraction above the bolus and relaxation below the bolus results in peristaltic contractions that help to move the bolus down the intestinal tract.

As discussed in a later chapter, VIP released from submucosal secretomotor neurons actually acts as an excitatory neurotransmitter when it stimulates crypt cell secretion via a cyclic AMP-dependent pathway. Thus, a neurotransmitter is just that and its classification as excitatory or inhibitory is simply a function of the structure onto which it is released and/or the receptor-second messenger system that it then affects.

Reality check 2-3: *Hirschsprung's* disease is a condition characterized by a lack or deficiency of ganglion cells in the myenteric plexus in the sigmoid colon. Consequently, strong peristaltic motility cannot occur in this diseased area of the large intestine. What type of change in bowel diameter would you expect above the level of the diseased aganglionic segment and why?

2.2.5 Gastrointestinal Blood Supply

The GI blood supply consists of a series of parallel circuits that allow blood to be diverted away or directed to specific areas without altering the entire blood supply to the gut as a whole (Fig. 2.9). The splanchnic circulation refers to all organs fed by the celiac (stomach), superior mesenteric (right colon, part of transverse colon, and small intestine), and inferior mesenteric (left colon) arteries. The blood from these organs then collects into the portal vein to drain to the liver. One-third of the total blood volume in a resting person is distributed in the splanchnic circulation. Hence, the splanchnic circulation has a reservoir function greater than any other body region.

Absorption of nutrients takes place in the small intestine. The superior mesenteric artery comes from the aorta to supply the jejunum and ileum (Fig. 2.9) via a series of intercommunicating arcades which travel through the mesentery. Small arteries penetrate the intestinal wall and ultimately supply the capillary network of the intestinal villus tip. In close proximity to the arterial capillary, the venous capillary blood leaves the villus and returns via the intestinal veins and corresponding superior mesenteric vein (Fig. 2.10).

The splenic vein joins with the superior mesenteric vein to form the portal vein which will drain to the liver sinusoids where the reticuloendothelial and hepatic cells absorb and temporally store up to three quarters of all absorbed nutrients. The majority of fat-based nutrients are absorbed into the intestinal lymphatics and then directed to the circulating blood by the thoracic duct, bypassing the liver. The hepatic veins deliver blood from the liver to the vena cava and ultimately to the right atrium.

Fig. 2.9 Splanchnic circulation. Several arteries carry blood from the aorta to the stomach, spleen, pancreas, small intestine, and large intestine. The blood from these organs collects in the portal vein that drains into the liver

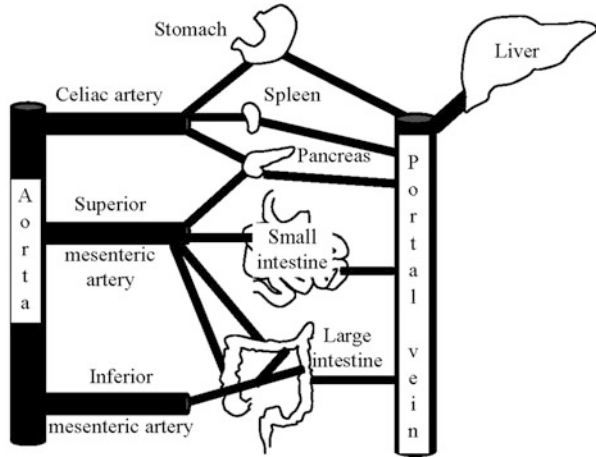
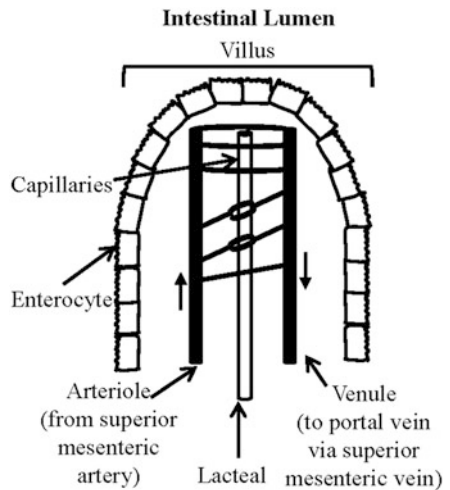


Fig. 2.10 Microcirculation to intestinal villi



Reality check 2-4: A 76-year-old retired GI physiology professor is undergoing emergency abdominal angiography because of massive lower GI bleeding. You observe a blush of contrast spurting from a rent in the superior mesenteric artery. Which portion of the patient’s colon should be resected?

2.2.6 Recall Points

Digestive System Requirements

- Absorptive and secretory mucosa
- Muscles (inner circular, outer longitudinal)
- Nervous innervation (intrinsic, extrinsic); blood supply

2.3 Gastrointestinal Regulation: Brain–Gut Axis

The *brain–gut axis* is the regulatory system which controls GI functions and includes the interconnection of the central nervous system (CNS; brain and spinal cord), the ENS, and the enteroendocrine cells (see Fig. 2.8).

Afferent sensory neurons with their cell bodies in the submucosal or myenteric plexus transmit information from the GI tract to the brain for processing. Intrinsic efferent axons carry neural information from the CNS to the ENS. Extrinsic efferent axons carry neural information to the ANS.

2.3.1 Neural Control of GI Function

2.3.1.1 Intrinsic Nervous Control

ENS: The ENS is located within the wall of the GI tract from the esophagus to the anus. It is primarily responsible for regulating movement within the GI tract and secretion. It consists of both the myenteric (Auerbach’s) plexus and the submucosal plexus (see Figs. 2.1 and 2.8).

The myenteric plexus is the outer plexus that lies between the longitudinal and circular muscle layers (Fig. 2.1) and primarily controls gut motor activity. Stimulation of the myenteric plexus increases gut wall tonic contraction, intensity of rhythmical contractions, rate of the rhythm of contraction, and velocity of conduction of excitatory waves along the gut wall resulting in more rapid movement of peristaltic waves. Some of the neurons of the myenteric plexus secrete inhibitory neurotransmitters (e.g., VIP), which inhibit intestinal sphincter muscles. Inhibition of the pyloric sphincter enables food to leave the stomach with less resistance. If the ileocecal valve is inhibited, small intestinal contents can empty into the colon with reduced resistance. When the circular muscle is stimulated to contract, the gut diameter is reduced. The length of the gut is shortened when the longitudinal muscle contracts.

The submucosal plexus receives sensory signals from mechanoreceptors and chemoreceptors in the GI tract and controls secretion and blood flow within the inner wall of the gut.

2.3.1.2 Neural Control of GI Function: Extrinsic Nervous Control

Parasympathetic Nervous System: The vagus nerve (cranial nerve X) and the pelvic nerve supply parasympathetic innervation to the GI tract. Both of these nerves contain efferent (motor) and afferent (sensory) fibers. The vagus nerve supplies the upper GI tract. The innervations include the striated muscle in the upper third of the esophagus, the wall of the stomach, the small intestine, and the

right colon. The vagus nerve provides extrinsic innervation to esophageal striated muscle that is necessary for contractile activity in the skeletal muscle portion. However, it does not serve the same function in the smooth muscle region where the myenteric plexus regulates this activity. Vagovagal reflexes are sensory-motor reflexes carried in the vagus nerve. The lower GI tract, including the striated muscle of the external anal canal, transverse, descending, and sigmoid colon, is innervated by the pelvic nerve.

The parasympathetic nerves are characterized by long preganglionic fibers which synapse in ganglia located in the wall of the GI tract within the myenteric or submucosal plexuses. The parasympathetic postganglionic neurons are classified as either cholinergic or peptidergic.

ACh, the neurotransmitter released from cholinergic neurons, leads to an increase in GI motility and secretions. Peptidergic neurons release one of several different peptides. VIP, when released from the postganglionic peptidergic neuron, results in a decrease in the constriction of GI tract sphincters.

Sympathetic Nervous System: The preganglionic fibers of the sympathetic nervous system originate in the thoracic and lumbar segments of the spinal cord and are generally shorter than those of the parasympathetic nervous system. The preganglionic nerve fibers of the sympathetic nervous system exit in the spinal nerves and in general form synapses in a paired chain of ganglia, which lay outside the GI tract. There are four sympathetic ganglia which serve the GI tract: celiac, superior mesenteric, inferior mesenteric, and hypogastric. These sympathetic postganglionic fibers synapse on ganglia in the myenteric and submucosal plexuses or directly innervate smooth muscle, secretory, or endocrine cells. They are adrenergic and secrete norepinephrine, which causes a decrease in GI tract motility and secretions but an increase in the constriction of GI sphincters.

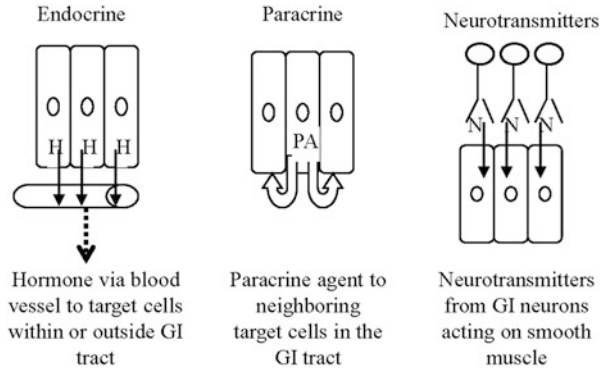
Reality check 2-5: What would you expect to happen to gastrointestinal peristalsis in an individual who is given Atropine (an anticholinergic medication)? Why?

Reality check 2-6: You are evaluating a patient who has suffered a complete C4 cervical cord transection after a motor vehicle accident. What type of bowel movement alteration would you expect and why?

2.3.2 *Regulatory Function of Gastrointestinal Peptides*

Endocrine (hormones), paracrine agents, and neurotransmitters are peptides that regulate functions in the GI tract (Fig. 2.11). Hormones are peptides secreted by GI endocrine cells into the portal circulation which then pass through the liver and enter the systemic circulation. The hormones are delivered to the receptors of their target cells that may lie within or outside the GI tract. For example, gastrin belongs to the hormone family gastrin–cholecystokinin and is secreted by the G cells of the stomach in response to stomach distention, peptides, and gastrin-releasing peptide (GRP) (Table 2.1). Gastrin secretion results in increased stomach motility, secretion

Fig. 2.11 Comparison of endocrine, paracrine, and neurotransmitter functions



of acid, and increased growth of gastric mucosa. *Cholecystinin (CCK)*, also belongs to the hormone family Gastrin–CCK and is secreted by the I cells of the duodenum and jejunum in response to fat, amino acids, and small peptides entering the duodenum. CCK secretion stimulates pancreatic enzyme and bicarbonate secretion and leads to contraction of the gallbladder and relaxation of the sphincter of Oddi. CCK also stimulates exocrine pancreas growth and inhibits stomach emptying.

Secretin, a member of the hormone family secretin–glucagon, is secreted by S cells lining the duodenum. Secretion of secretin in the duodenum is stimulated by H^+ as well as by the presence of fatty acids. Release of secretin leads to increased pancreatic and biliary secretion of bicarbonate. Secretin inhibits gastric H^+ secretion as well as the trophic effect of gastrin on the gastric mucosa. VIP is a peptide with close structural homology to secretin. Like secretin, VIP secretes pancreatic bicarbonate which inhibits gastric acid secretion. *Gastric inhibitory peptide (GIP) aka glucose-dependent insulinotropic peptide*, a member of the hormone family secretin–glucagon, is secreted by duodenal and jejunal mucosal cells. GIP is the only GI hormone that is secreted in response to the three types of nutrients (fats, carbohydrates, and amino acids). GIP stimulates insulin secretion by the beta cells of the pancreas and inhibits gastric acid secretion.

Paracrines are agents released from endocrine cells of the GI tract that diffuse into the interstitial fluid and affect neighboring target cells that possess receptors for the agent. Hence, they act locally and do not enter the systemic circulation. *Somatostatin* and *histamine* are the primary GI paracrine agents. Endocrine cells of the GI mucosa secrete somatostatin in response to decreased luminal pH. Somatostatin strongly inhibits release of most GI hormones and inhibits gastric H^+ secretion. Aside from its paracrine function, somatostatin is secreted by the hypothalamus and by the delta cells of the islets of Langerhans in the pancreas. Histamine is secreted by enteroendocrine cells in the GI mucosa especially in H^+ secreting areas of the stomach. Histamine stimulates gastric acid secretion by activation of parietal cell H_2 -type receptors.

Table 2.1 Regulatory functions of peptides secreted by enteroendocrine cells

Hormone	Location produced	Action
Cholecystokinin (CCK)	Peptide hormone produced by I cells in the duodenum and to a lesser extent the jejunum in response to fats, small peptides, and amino acids in the intestine. Release inhibited by somatostatin	Main effect is the contraction of smooth muscle of the gall bladder with increased bile production/secretion and production/secretion of pancreatic enzymes to promote digestion. Along with secretin, regulates rate of stomach emptying and inhibits gastrin release from G cells in the stomach
Enteroglucagon	Mainly terminal ileum and colon from the prohormone proglucagon	Decreases production of gastric acid by parietal cells and smooth muscle contraction (motility) of the stomach, thereby decreasing gastric emptying
Gastrin	Produced by G-cells in response to presence of undigested proteins, vagal stimulation, distension of the antrum of the stomach, and gastrin-releasing peptide. Inhibited by pH <4 and somatostatin	Stimulates HCl, pepsinogen and intrinsic factor secretion from parietal cells, pepsinogen by chief cells as well as histamine release from enterochromaffin-like cells. Also increases stomach motility (i.e., smooth muscle contraction) and growth of gastric mucosa
Gastric inhibitory peptide (GIP) aka glucose-dependent insulinotropic peptide	Peptide hormone produced in mucosal cells of the duodenum and jejunum. Stimulated by fats, carbohydrates, and amino acids	Decreases gastric acid release by parietal cells as well as smooth muscle contraction (motility) of the stomach. Also increases insulin secretion by pancreatic beta cells and fatty acid metabolism (e.g., milk digestion) by activating lipoprotein lipase
Histamine	Primarily by acid secreting cells of the stomach	Stimulates gastric acid secretion by activation of parietal cell H ₂ -type receptors
Motilin	Peptide made mainly in the duodenum and jejunum. Secretion stimulus unknown	Increases smooth muscle contraction (fundus, antrum, and gall bladder). Also, stimulates secretion of somatostatin, pancreatic peptide, and pepsinogen
Secretin	Produced by the S-cells in the duodenum. Secretion stimulated by acid or fatty acids in the duodenum	Increased secretion of water and bicarbonate as well as insulin from the pancreas and bile from the liver. Inhibits production of gastrin to reduce

(continued)

Table 2.1 (continued)

Hormone	Location produced	Action
		acidity (pH) entering the duodenum. Lowered pH maximizes activation of pancreatic enzymes secreted into this part of the small intestine. Also enhances secretion of pepsin as well as glucagon, pancreatic polypeptide, and somatostatin
Somatostatin	Produced in endocrine cells of the stomach, intestines, and pancreas	Decreases release of gastrin, CCK, secretin, motilin, VIP, GIP, and enteroglucagon, decreasing stomach secretion and contraction
Vasoactive intestinal peptide (VIP)	Peptide hormone produced in digestive tract and brain	Causes relaxation of smooth muscle (LES, stomach, and gallbladder), stimulates pepsinogen secretion, dilutes bile and pancreatic juice, increases bicarbonate production in the pancreas, decreases gastrin-induced gastric acid secretion, and increases water secretion in intestine

Prostaglandins are eicosanoids that exert paracrine effects on gastric mucosal cells resulting in the antagonism of histamine's stimulation of H^+ secretion by activating a G_i protein that inhibits adenylyl cyclase, thereby lowering cyclic AMP. In addition, prostaglandins enhance submucosal microcirculation. Nonsteroidal anti-inflammatory drugs (NSAIDs) inhibit the effect of prostaglandins. Hence, a patient who consumes NSAIDs experiences uninhibited H^+ secretion and a reduction of the submucosal microcirculation that will lead to the retardation in the healing of peptic ulcer. Similarly, the prostaglandins are prosecretory in the intestine. Patients with *inflammatory bowel disease* (IBD) have inflammatory-related secretory diarrhea. When IBD patients take the salicylate-based NSAIDs, they experience an inhibition of their inflammation-related secretory diarrhea.

Let us briefly examine some examples of how paracrine agents and neurotransmitters may interact. By examining the order in which these substances might be released physiologically and their functions, we can better appreciate their interactions. For example, secretin increases duodenal pH by decreasing acid production, slows gastric activities to emptying and mopping up H^+ ions via pancreatic HCO_3^- secretion. This interaction between the effects of secretin upon gastric acid secretion, gastric emptying, and pancreatic bicarbonate secretion all serve to enhance the digestive function. It is useful to consider functional and structural similarities in attempting to better understand the roles played by GI peptides. VIP and secretin

both stimulate pancreatic duct cell HCO_3^- . Interestingly both peptides have nine amino acids that are identical and are classified as members of the secretin family of peptides.

Peptides synthesized in the cell bodies of GI tract neurons are released in response to an action potential in the neuron and act as a neurotransmitter. ACh and NE, two major neurotransmitters, are released into and by the ENS. ACh, secreted by cholinergic neurons, causes contraction of GI wall smooth muscle and the relaxation of GI tract sphincters. In addition, ACh secretion increases salivary, gastric, and pancreatic secretions. NE, secreted by adrenergic neurons, causes relaxation of gut wall smooth muscle as well as contraction of GI sphincters and increased salivary secretion. VIP secretion by neurons of the myenteric and submucosal plexuses results in relaxation of gut smooth muscle. VIP (like secretin) potently stimulates duct cell HCO_3^- secretion, but exerts only a minimal effect on acinar cell enzyme secretion (CCK produces the opposite effect with respect to these cell types). VIP also increases intestinal and pancreatic secretions. *GRP* secretion by neurons of the gastric mucosa increases gastrin secretion. *Substance P* is secreted along with ACh and leads to GI smooth muscle contraction and increased salivary secretion. *Enkephalins* (endogenous opioid peptides) are secreted by mucosal and smooth muscle neurons and cause contraction of gut smooth muscle and decreased intestinal secretion. Opiates in general raise GI smooth muscle tone by suppressing the release of intrinsic inhibitory neurotransmitters thus allowing the inherent excitability of GI smooth muscle to be expressed.

Given that the ENS is called “the little brain” (Fig. 2.8) because it contains all of the neurotransmitters found in the CNS (with the exception of histamine and epinephrine) it would seem much more likely that there will be a region- and function-specific release of a variety of substances that extend well beyond the traditional postganglionic parasympathetic and sympathetic neurotransmitters of simply ACh or NE. For example, in the colon about 70 % of neurally mediated epithelial secretion is atropine resistant, suggesting a major role for at least one other neurotransmitter in this process other than ACh.

Intrinsic Primary Afferent Neurons (IPANs) are neurons that have their cell bodies in the gut wall and whose sensitive endings are in the lamina propria, beneath the mucosal epithelium, in the muscle. 5-Hydroxytryptamine (5-HT) is a potent IPAN stimulant released from mucosal enterochromaffin-like cells that acts as an intermediate in enteric reflexes. When the mucosa is mechanically stimulated, 5-HT is released to elicit motility reflexes. Upon administration of 5-HT antagonists, the motility reflexes will be inhibited.

Kinins are peptides that split from kininogens in areas of inflammation and facilitate the changes in the vasculature associated with inflammation. Kinins also serve as activators of neuronal pain receptors.

2.3.3 *Recall Points*

Requirements of Gastrointestinal Regulation via Brain–Gut Axis

- Neural control
 - Intrinsic control (ENS)
 - Extrinsic control (parasympathetic and sympathetic nervous systems)
- GI hormones and peptides

Reality check 2-7: Endoscopic retrograde cholangiopancreatography (ERCP) is a procedure performed to diagnose and treat problems of the liver, gallbladder, bile ducts, and pancreas (e.g., gallstones, ductal leaks, and obstruction due to strictures or cancer). ERCP combines the use of a lighted and flexible tube called an endoscope and X-rays. Hence, the physician can see inside the stomach and duodenum and inject the bile and pancreatic ducts with dye which can be seen on X-ray. You are trying to locate where the bile duct enters into the duodenum during an ERCP in a patient who has a gallbladder. Why would the intravenous injection of CCK be helpful?

2.4 Nutrient Exchange

2.4.1 *Requirements for Nutrient Exchange*

The primary function of the digestive tract is the absorption of nutrients. To accomplish its mission, food must be reduced to more easily absorbable units. The digestive tract contains special anatomical features, which enhance the absorption of nutrients. Most absorption of nutrients occurs in the small intestine that measures ~22 ft. The small intestinal mucosa gives rise to Kerckring folds, which in turn give rise to the villi and microvilli. The end result is a 500–600 % increase in absorptive surface area. Absorption through the GI mucosa takes place primarily via active transport, diffusion, and solvent drag (Fig. 2.2).

2.4.2 *Absorption Basics*

Seven to eight L of water are absorbed iso-osmotically by diffusion in the small intestine. Imagine if the GI tract did not keep the luminal contents isotonic. In the case of hypertonic GI contents, water would be pulled into the lumen resulting in an increase in water content and attendant diarrhea. In addition, with water being transported from the plasma to the chyme when hyperosmotic solutions are present in the lumen, intravascular fluid depletion would occur possibly causing

hypoperfusion of tissues and organs as well as hypotension. Conversely, in the case of hypotonic GI contents, water would tend to migrate from the lumen into the interstitium thus impeding effective absorption of nutrients. The consequences of the GI tract not maintaining the luminal contents isotonic would be disastrous for whole body homeostasis.

Food molecules of various tonicities travel from the stomach to the small intestine. The GI tract amazingly maintains the isotonicity of the luminal contents, and extracellular and intravascular fluids. Isotonicity is achieved by the special functions performed by different portions of the digestive tract. The stomach secretes HCl but only absorbs a relatively small amount of it. Most absorption of fluids and food stuffs takes place in the small intestine. Small amounts of water are absorbed in the stomach. Both ethanol and aspirin are actually absorbed in the stomach because they are sufficiently water and lipid soluble in this environment to passively diffuse down a concentration gradient and across the gastric mucosa. The colon is involved in the absorption of salt and water. In addition, short chain fatty acids produced by bacteria can be passively absorbed across the colonic mucosa.

The *enterogastric reflex* regulates gastric emptying to ensure that large hypertonic loads are not continuously expelled into the duodenum since this would draw water across the relatively leaky small intestinal mucosa into the gut lumen from the circulation. As the chyme migrates into the first portion of the duodenum, H⁺ ions are absorbed in exchange for Na⁺ ions. In addition, iron is selectively absorbed in the duodenum. The pancreas and Brunner's glands secrete sodium bicarbonate to neutralize the gastric HCl.

Reality check 2-8: Patients with lactose intolerance lack the small intestinal brush border enzyme lactase, which breaks down lactose (milk sugar) into glucose and galactose that are smaller and are absorbed by enterocytes that prevent them from exerting osmotic effects in the lumen. Why do lactose intolerant patients present with diarrhea?

The chyme that reaches the jejunum may contain polysaccharides, triglycerides, and polypeptides, which are quickly digested to smaller molecules that are frequently osmotically active. To maintain isotonicity, special jejunal mechanisms permit the simultaneous absorption of water, electrolytes, and nutrients. If there is an inefficient absorption of water from the gut lumen, then diarrhea will occur. In contrast, excessive absorption of water across the gut lumen will result in constipation. The ileum and colon share the ability to absorb both water and electrolytes actively against big concentration gradients. The ileum is the main site for the absorption of vitamin B12 and bile salts secreted into the intestinal lumen. More details concerning sites and mechanisms of absorption and digestion may be found in other chapters of this book and other texts.

2.4.3 Gut Activity and Metabolic Factors Effect upon Intestinal Blood Flow

The splanchnic circulation includes the blood flow through the gut plus the spleen, pancreas, and liver. Under normal resting conditions, the splanchnic vasculature receives 20 % of the cardiac output and up to 40 % after a meal. During the absorption of a meal, the increase in blood flow is localized to the most active areas. Within the GI tract, blood flow is regulated lengthwise along the canal (segmental control) and between the different gut wall layers (transmural control). Both segmental and transmural controls are determined by tissue activity. Increased blood flow during increased GI activity is probably due to a combination of many factors. During digestion, several vasodilators (CCK, VIP, gastrin, and secretin) are released from the intestinal mucosa. These peptide hormones also have controlling influences on certain secretory and motor activities in the gut. Some GI glands release kallidin and bradykinin, two kinins. These kinins are very potent vasodilators and cause most of the mucosal vasodilatation that accompanies secretion. Decreased oxygen tension in the gut wall can lead to a fourfold rise in adenosine, a powerful vasodilator which could account for much of the increased blood flow.

2.4.4 Role of Immune System Cells

Immune system cells are found near the microcirculatory vessels of the GI organs. Inflammatory stimuli cause mast cells to gather around vessel smooth muscle walls and then degranulate, consequently releasing the vasoactive paracrine agents (serotonin and histamine). Prostaglandins, cytokines, leukotrienes are released by other immunologic cells.

2.4.5 Parasympathetic and Sympathetic Control of GI Blood Flow

Parasympathetic nerve stimulation to the stomach and lower colon increases local blood flow simultaneously with increased glandular secretion. The increased blood flow occurs secondary to the increased glandular secretion. Sympathetic stimulation directly decreases blood flow to the splanchnic vasculature due to intense vasoconstriction of the arterioles.

2.4.6 *Countercurrent Blood Flow in the Intestinal Villus*

The arterial and venous flows in intestinal villi are in opposite directions and the arterioles and venules are in close apposition. When blood initially flows into a villus, oxygen concentration is high in the arterioles but low in the venules. Hence, much of the oxygen diffuses from the arterioles to the venules (down a concentration gradient) without being carried in the blood to the villi tips. Therefore, the arterial blood oxygen content falls as the blood approaches the villus tip. Normally, this shunting of oxygen from arterioles to venules in the villi does not present a problem. However, in instances of severe reduction of blood flow to the gut, this countercurrent loss of oxygen directly contributes to the susceptibility to ischemic death of the villus. In response to ischemic injury, the intestinal villi may disintegrate and become blunted with significant decreases in intestinal absorption.

Case in Point 2-1

Chief Complaint: Diarrhea.

History: A 25-year-old man presents with fatigue and is found to have iron deficiency anemia. He has experienced episodes of intermittent mild diarrhea for many years, previously diagnosed as irritable bowel syndrome and lactose intolerance. He has no current significant gastrointestinal symptoms.

Physical Exam: Pallor and several oral aphthous ulcers. Abdominal examination is normal. The rest of the exam is unremarkable.

Labs:

Hematocrit 28 % (normal: 41–50 %), decreased mean corpuscular volume.

Leukocytes (white blood cells) $8 \times 10^3 \mu\text{L}^{-1}$ (normal: $3.8\text{--}10.8 \times 10^3$).

Chemistry panel and liver function tests/amylase and lipase are normal.

Stool guaiac negative for occult blood.

Recent esophagogastroduodenoscopy and colonoscopy—remarkable for celiac disease (condition in which patients have abnormal small intestinal mucosa that reverts to normal when treated with a gluten-free diet and relapse when gluten is reintroduced).

Assessment: On the basis of these findings, why does this patient experience diarrhea, bloating, and abdominal discomfort after consuming a peanut butter sandwich on whole wheat bread?

2.4.7 *Recall Points*

Requirements of GI Nutrient Exchange

- Most absorption takes place in the small intestine.
- Absorption occurs via active transport, diffusion, and solvent drag.
- GI tract works to maintain isotonicity of luminal contents and extracellular and intracellular fluids.

2.5 Summary Points

- The structural anatomy of the digestive system is very closely related to the physiological requirements of nutrient exchange and GI regulation.
- Signals via various receptors in the digestive system help to modulate control of motility, digestion, and absorption.
- The smooth muscle of the GI tract being unitary smooth muscle has a high degree of electrochemical coupling due to many gap junctions. Hence, the sheets or layers of smooth muscle cells contract simultaneously and act as a syncytium.
- The unitary smooth muscle exhibits characteristic slow waves or pacemaker activity.
- The characteristic pattern of slow waves determines the pattern of action potentials, which in turn establishes the frequency of contraction of the unitary smooth muscle in an organ.
- The brain–gut axis includes both an automatic and voluntary element. The digestive system can function without conscious control, by virtually having a brain of its own (ENS). Function of the digestive system can be modified by the extrinsic nervous system (parasympathetic and sympathetic nervous systems) and by GI hormones and peptides.
- Parasympathetic innervation promotes digestion and absorption by stimulating GI motility and secretions.
- Sympathetic innervation slows digestive processes by decreasing motility and secretions.
- The ENS, located in the wall of the GI tract from the esophagus to anus, consists of the myenteric plexus and the submucosal plexus.
- The myenteric or Auerbach’s plexus primarily controls gut motor activity.
- The submucosal or Meissner’s plexus controls secretion and blood flow within the inner wall of the gut.
- The GI peptides (e.g., hormones, paracrine agents, and neurotransmitters) regulate functions in the GI tract.
- Hormones secreted by GI enteroendocrine cells ultimately enter the systemic circulation for delivery to their target cells.
- Paracrines, released from GI tract endocrine cells, diffuse a short distance in the interstitial fluid to affect neighboring target cells.

- Neurocrines, synthesized in GI neurons, act as neurotransmitters.
- The splanchnic circulation includes blood flow through the gut, spleen, pancreas, and liver and receives between 20 and 40 % of the cardiac output.
- Most absorption of nutrients occurs in the small intestine. The colon absorbs salt and water. In addition, short chain fatty acids produced by bacteria can be passively absorbed across the colonic mucosa. Small amounts of water are absorbed in the stomach.
- Absorption through the GI mucosa occurs primarily via active transport, diffusion, and solvent drag.
- The majority of nonfat, water soluble nutrients are absorbed from the GI tract via the portal vein and temporally stored in the liver.
- The majority of fat-based nutrients are absorbed into the intestinal lymphatics and then directed to the circulating blood by the thoracic duct, bypassing the liver.
- During the absorption of a meal, increased blood flow localizes to the most active areas.
- During vigorous exercise, the arterioles of the GI tract experience intense vasoconstriction and decreased blood flow as a result of sympathetic stimulation.

2.6 Review Questions

- 2-1. A 30-year-old dental hygienist has been diagnosed with Scleroderma, an infiltrative connective tissue disorder that leads to increased fibrosis of the esophageal wall and LES incompetence. An esophageal motility study is performed. Which of the following conditions will she exhibit?
- A. Decreased heartburn symptoms by assuming a supine position
 - B. Heartburn symptoms untreatable with medication
 - C. More efficiently clear refluxed gastric acid
 - D. Reduced heartburn symptoms by remaining upright for at least 2 h after a meal
- 2-2. A 75-year-old man is taking an anticholinergic medication called benztropine mesylate (Cogentin) for Parkinson's disease. Which of the following will this patient experience?
- A. Constipation due to decreased gut motility
 - B. Diarrhea due to decreased gut motility
 - C. Diarrhea due to increased gut motility
 - D. No change in his gut motility
- 2-3. A 55-year-old patient with Zollinger–Ellison syndrome (ZES) presents to the emergency department complaining of abdominal pain and diarrhea. ZES is a disorder of gastric acid hypersecretion and severe peptic ulcer diathesis due to markedly elevated levels of gastrin from a non-beta-cell endocrine neoplasm.

Which of the following will happen to his gastric mucosal lining and acid production as a consequence of this syndrome?

- A. Mucosal lining and acid production will remain the same
 - B. Mucosal lining will atrophy with decreased acid production
 - C. Mucosal lining will atrophy with increased acid production
 - D. Mucosal lining will increase in thickness with increased acid production
- 2-4. A Marine on foot patrol in Iraq has just been informed that an improvised explosive device (IED) is about to explode. As he runs for cover, which of the following changes would you expect to occur in his gastrointestinal blood flow?
- A. Vasoconstriction of the splanchnic arterioles with redirection of the blood flow toward the somatic muscles
 - B. Vasoconstriction of the splanchnic arterioles with redirection of the blood flow toward the gut
 - C. Vasodilatation of his somatic arteries with redirection of blood flow toward the gut
 - D. Vasodilatation of the splanchnic arterioles with blood flow toward the gut
- 2-5. An 89-year-old woman with severe congestive heart failure complains of dull, aching chest pains when she consumes a large meal. Which of the mechanisms is the most likely cause of her ischemic chest pain?
- A. Vasoconstriction of the splanchnic arterioles with the blood flow directed toward the heart
 - B. Vasoconstriction of the splanchnic arterioles with the blood flow directed toward the gut
 - C. Vasodilatation of the coronary arteries with blood directed away from the gut
 - D. Vasodilatation of the splanchnic arterioles with blood directed away from the coronary circulation toward the gut

2.7 Answer to Case in Point

Case in Point 2-1: To address this question first consider how the structure of the digestive system is affected by the patient's celiac disease. Ingestion of gluten in celiac disease patients leads to the production of autoantibodies and T lymphocytes to produce cytokines that damage enterocytes. Hence, exposure to gluten, the cereal protein to which the patient's small intestinal mucosa was sensitive, led to decreased absorption of fluids and nutrients due to atrophy of the mucosal lining and decreased absorptive surface area and its effects on other nutrient exchange mechanisms. Excessive amounts of unabsorbed fluids would have contributed to the patient's bouts of diarrhea. In addition, a large loss of fluids and nutrients would

have also resulted in decreased weight and energy. Diminished absorption of duodenal iron would lead to iron deficiency anemia and fatigue. Mucosal atrophy and interference with the absorption of bile salts in the terminal ileum would result in fat malabsorption. Another mechanism contributing to the patient's diarrhea would be the effect of unabsorbed bile salts entering the colon when the relevant transporters are lost along the epithelium of the terminal ileum. In addition, effacement of the terminal ileal mucosa would contribute to vitamin B12 deficiency and an erythrocyte deficiency, pernicious anemia. By adhering to a gluten-free diet, the patient's intestinal mucosa was allowed to return to a more normal state. Hence, effective and efficient fluid and nutrient exchange was reestablished.

2.8 Answer to Connecting-the-Dots

Connecting-the-Dots 2-1: The patient's loss of peripheral reflexes coupled with decreased intestinal motility is indicative of hypokalemia. Indeed the patient's serum potassium measured at the time of the chloride measurement was just 2.3 mmol/L (normal 3.5–5). Potassium diminished, like the chloride, because of the large loss of gastric secretion. The decline in blood potassium, and hence in extracellular spaces of muscle, alters the potassium electrochemical gradient that is essential for normal nerve function. The role of potassium is to repolarize the cell membrane to its resting state after the action potential has passed. The hypokalemia leads to hyperpolarization of the resting membrane potential thus requiring a greater than normal stimulus to initiate a new action potential. This increased demand leads to loss of reflexes and can even cause paralysis. Administration of potassium chloride to the patient allowed the cecostomy to begin functioning and muscle function also returned to normal.

2.9 Answers to Reality Checks

Reality check 2-1: Sjögren's syndrome is a chronic autoimmune disease in which white blood cells attack their moisture-producing glands. Today, as many as four million Americans live with this disease. We would expect the tennis superstar to experience a dry mouth and decreased lubricating secretions in the GI tract. In addition, she would probably show a decreased ability to produce tears in the face of an emotional victory.

Reality check 2-2: Patients with scleroderma involving the esophagus experience difficulty swallowing solids and liquids due to hardening of the connective tissues. This scenario greatly compromises esophageal peristalsis and the propulsion of boluses toward the stomach. In addition, due to fibrotic infiltration of the LES, patients also experience gastroesophageal reflux.

Reality check 2-3: Hirschsprung's disease results from a lack of ganglion cells of the involved colonic segment. In this case, the aganglionic sigmoid colon does not relax and causes an obstruction. One would expect dilation of the colon above the level of the sigmoid colon.

Reality check 2-4: The superior mesenteric artery supplies blood to the right and part of the transverse colon. These would be the areas under consideration for colonic resection.

Reality check 2-5: Parasympathetic innervation to the gastrointestinal tract is supplied by the vagus and pelvic nerves. The parasympathetic postganglionic neurons are classified as cholinergic or peptidergic. ACh is the neurotransmitter released from cholinergic neurons which lead to an increase in GI motility and secretions. Atropine is an anticholinergic agent. Therefore, you would expect a patient receiving atropine to experience a decrease in peristalsis and secretions.

Reality check 2-6: Complete transection of the spinal cord at the C4 level would cause a major alteration in the brain–gut axis. Spinal cord injury damages nerves that allow a patient to control bowel movements. Above the T-12 level, the patient may lose the ability to feel when the rectum is full and requires emptying. In addition, the anal sphincter remains tight. In these patients, when the rectum is full a defecation reflex occurs and the bowel empties. Hence, patients with spinal cord injuries above T-12 lose volitional bowel control and suffer from constipation. In contrast, patients with a spinal cord injury below the T-12 level experience a weakened defecation reflex and decreased anal sphincter strength. This results in a flaccid bowel and incontinence.

Reality check 2-7: CCK injection leads to gallbladder contraction, sphincter of Oddi relaxation, and the secretion of bile into the duodenal lumen. When the endoscopists see the bile enter the duodenum that alerts them to search in that area for the ampulla which communicates with the bile duct.

Reality check 2-8: Patients with lactose intolerance lack the lactase brush border enzyme. Therefore, the lactose cannot be broken down to the smaller molecules of glucose and galactose which are absorbed by enterocytes. Their normal absorption prevents them from exerting osmotic effects in the lumen. When lactose cannot be absorbed in its parent form, it presents a large osmotic load that draws water into the gut lumen if it is not broken down by the enzyme lactase.

2.10 Answers to Review Questions

2-1. **D.** Scleroderma is an infiltrative connective tissue disorder, which in this case results in decreased esophageal peristalsis and an incompetent LES. These combined defects will lead to gastroesophageal reflux of stomach acid. In general, when a patient waits for 2 h after consuming a meal, the gastric contents should empty to some degree. Therefore, a smaller volume of gastric contents versus none would be available for reflux. In addition, the clearance of the refluxate will be aided by gravity when the patient is upright.

- 2-2. **A.** Benzotropine mesylate (Cogentin) is an anticholinergic medication. In general, cholinergic innervation leads to increased gut motility. Therefore, when given an anticholinergic medication, the patient should experience decreased gut motility and constipation.
- 2-3. **D.** ZES is a disorder of gastric acid hypersecretion and severe peptic ulcer diathesis due to hypersecretion of gastrin from non-beta-cell endocrine neoplasm. Gastrin secretion results in increased stomach acid production, increased thickness of the stomach mucosal lining, and increased stomach motility. Thus, in a ZES patient with hypergastrinemia, one would expect both stomach acid secretion and stomach mucosal lining to be increased.
- 2-4. **A.** The vigorous exercise induced by running away from an explosive device results in sympathetic nervous stimulation to the gut. The GI tract arterioles experience intense vasoconstriction and decreased blood flow which would direct blood flow away from the gut and toward the somatic muscles to aid in flight.
- 2-5. **D.** During the absorption of a meal, the increase in blood flow is localized to the most active areas in the gut. When this elderly patient consumes a large meal, blood is shifted away from her systemic circulation toward her splanchnic circulation. In a patient with a poor cardiac pump, even a relatively small diversion of blood flow would result in lower blood flow to the heart and ischemic cardiac pain.

Suggested Reading

- Costanzo LS. Physiology. 4th ed. Philadelphia: Saunders; 2010. Chapter 8, Gastrointestinal Physiology; p. 327–78.
- Fenoglio-Preiser CM, Noffsinger AE, Stemmermann GN, Lantz PE, Isaacson PG. Gastrointestinal physiology. 3rd ed. Philadelphia: Lippincott Williams & Wilkins; 2008. Chapter 1, General features of the gastrointestinal tract and evaluation of specimens derived from it; p. 1–10.
- Janson LW, Tischler ME. The big picture: medical biochemistry. New York: McGraw Hill; 2012. Chapter 11, The digestive system; p. 149–66.



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