Physiology

Gastrointestinal Physiology Answers

Done by : Abdel Al-Mue'z

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1. C) Chewing is important for the digestion of all solid foods. It is especially important for most fruits and vegetables because these foods have an indigestible cellulose membrane surrounding the nutrient portion that must be broken to allow contact with digestive enzymes.

2. D) The three major sources of carbohydrates in the normal human diet include sucrose mainly from sugarcane and sugar beets, lactose from milk, and a wide variety of large polysaccharides collectively known as starches. Although some diets may contain a large quantity of cellulose, this substance cannot be digested by the human gut and is not considered a food. Maltose is a product of the digestion of starch but is not consumed in large quantities in the human diet.

3. D) Triglycerides are digested within the intestinal lumen to monoglycerides and free fatty acids, which are then absorbed directly through the membrane of the intestinal epithelial cells. After entering the epithelial cell, the fatty acids and monoglycerides are taken up by the cell's smooth endoplasmic reticulum where they are mainly used to form new triglycerides that are subsequentl released in the form of chylomicrons through the base of the epithelial cell. The chylomicrons are absorbed by the central lacteal in the villus and transported in lymph through the thoracic lymph duct to the circulating blood. Thus, most triglycerides bypass the portal circulation.

4. . C) Achlorhydria means simply that the stomach fails to secrete hydrochloric acid; it is diagnosed when the pH of the gastric secretions fails to decrease below 4 after stimulation by pentagastrin. When acid is not secreted, pepsin also usually is not secreted; even when it is, the lack of acid prevents it from functioning because pepsin requires an acid medium for activity. Thus, protein digestion is impaired.

5. D) Pepsinogen is the precursor of the enzyme pepsin. Pepsinogen is secreted from the peptic or chief cells of the gastric gland (also called the oxyntic gland). To be converted from the precursor form to the active form (pepsin), pepsinogen must come in contact with hydrochloric acid or pepsin itself. Pepsin is a proteolytic enzyme that digests collagen and other types of connective tissue in meats.

6. C) Under basal conditions, saliva contains high concentrations of potassium and bicarbonate ions and low concentrations of sodium and chloride ions. The primary secretion of saliva by acini has an ionic composition similar to that of plasma. As the saliva flows through the ducts, sodium ions are actively reabsorbed and potassium ions are actively secreted in exchange for sodium. Because sodium is absorbed in excess, chloride ions follow the electrical gradient causing chloride levels in saliva to decrease greatly. Bicarbonate ions are secreted by an active transport process causing an elevation of bicarbonate concentration in saliva. The net result is that, under basal conditions, sodium and chloride concentrations in saliva are about 10% to 15% of that of plasma, bicarbonate concentration is about three-fold greater than that of plasma, and potassium concentration is about seven times greater than that of plasma.

7. A) Although the potassium concentration in saliva is about seven times greater than that of plasma, and the bicarbonate concentration in saliva is only about three times greater than that of plasma, the actual concentration of bicarbonate in saliva is 50 to 70 mEq/L, whereas the concentration of potassium is about 30 mEq/L, under basal conditions.

8. C) The gastrointestinal hormones are secreted from endocrine cells located in the mucosa. The endocrine cells are not clumped together but are dispersed among the epithelial cells, making it virtually impossible to remove surgically the source of any one gastrointestinal hormone. Gastrin is the only listed hormone found in the antrum, but it is also found in the duodenal and to a lesser extent the jejunal mucosa. CCK and secretin secreting endocrine cells are found in the duodenum, jejunum, and ileum. Motilin and GLIP secreting cells are found in the duodenum and jejunum.

9. B) GLIP is the only gastrointestinal hormone released by all three major foodstuffs (fats, proteins, and carbohydrates). The presence of fat and protein in the small intestine stimulates the release of CCK, but carbohydrates do not stimulate its release. The presence of protein in the antrum of the stomach stimulates the release of gastrin, but fat and carbohydrates do not stimulate its release. Fat has a minor effect to stimulate the release of motilin and secretin, but neither hormone is released by the presence of protein or carbohydrate in the gastrointestinal tract.

10. A) CCK is the only gastrointestinal hormone that inhibits gastric emptying under physiological conditions. This inhibition of gastric emptying keeps the stomach full for a prolonged time, which is one reason why a breakfast containing fat and protein "sticks with you" better than breakfast meals containing mostly carbohydrates. CCK also has a direct effect on the feeding centers of the brain to reduce further eating. Although CCK is the only gastrointestinal hormone that inhibits gastric emptying, all of the gastrointestinal hormones with the exception of gastrin are released to some extent by the presence of fat in the intestine.

11. D) GLIP is released by the presence of fat, carbohydrate, or protein in the gastrointestinal tract. GLIP is a strong stimulator of insulin release and is responsible for the observation that an oral glucose load releases more insulin and is metabolized more rapidly than an equal amount of glucose administered intravenously. Intravenously administered glucose does not stimulate the release of GLIP. Neither CCK nor VIP stimulates the release of insulin. GLIP does not stimulate glucagon release, and glucagon has the opposite effect of insulin, that is, it would decrease the rate of glucose clearance from the blood. VIP does not stimulate GLIP release.

12. F) All of these factors can inhibit gastric acid secretion under normal physiological conditions. Gastric acid stimulates the release of somatostatin (a paracrine factor), which has a direct effect on the parietal cell to inhibit acid secretion as well as an indirect effect mediated by suppression of gastrin secretion. Secretin and GLIP inhibit acid secretion through a direct action on parietal cells as well as indirectly through suppression of gastrin secretion. Enterogastrones are unidentified substances released from the duodenum and jejunum that directly inhibit acid secretion. When acid or hypertonic solutions enter the duodenum, a neutrally mediated decrease in gastric acid secretion follows.

13. B) Gastrin stimulates gastric acid secretion, and secretin and GLIP inhibit gastric acid secretion under normal, physiological conditions. It is important to differentiate the physiological effects of the gastrointestinal hormones from their pharmacological actions. For example, gastrin and cholecystokinin (CCK) have identical actions on gastrointestinal function when large, pharmacological doses are administered, but they do not share any actions at normal, physiological concentrations. Likewise, GLIP and secretin share multiple

actions when pharmacological doses are administered, but only one action is shared at physiological concentrations: inhibition of gastric acid secretion.

14. E) The cephalic phase of gastric secretion occurs before food enters the stomach. Seeing, smelling, chewing, and anticipating food is perceived by the brain, which, in essence, tells the stomach to prepare for a meal. Stimuli for the cephalic phase thus include mechanoreceptors in the mouth, chemoreceptors (smell and taste), thought of food, and hypoglycemia. Because the cephalic phase of gastric secretion is mediated entirely by way of the vagus nerve, vagotomy can abolish the response. Antacids neutralize gastric acid, but they do not inhibit gastric secretion. An antigastrin antibody would attenuate (but not abolish) the cephalic phase because this would have no effect on histamine and acetylcholine stimulation of acid secretion. Atropine would attenuate the cephalic phase by blocking acetylcholine receptors on parietal cells; however, atropine does not abolish acetylcholine stimulation of gastrin secretion. A histamine H2 blocker would attenuate the cephalic phase of gastric secretion, but would not abolish it.

15. E) Hirschsprung disease is characterized by a congenital absence of ganglion cells in the distal colon resulting in a functional obstruction. Most cases of Hirschsprung disease are diagnosed in the newborn period. Hirschsprung disease should be considered in any newborn who fails to pass meconium within 24 to 48 hr after birth. Although contrast enema is useful in establishing the diagnosis, rectal biopsy remains the criterion standard. Aganglionosis begins with the anus, which is nearly always involved, and continues proximally for a variable distance. Both the myenteric (Auerbach) and submucosal (Meissner) plexus are absent, resulting in reduced bowel peristalsis and function. The precise mechanism underlying the development of Hirschsprung disease is poorly understood.

16. C) Migrating motility complexes (sometimes called interdigestive myoelectric complexes) are peristaltic waves of contraction that begin in the stomach and slowly migrate in an aboral direction along the entire small intestine to the colon. By sweeping undigested food residue from the stomach, through the small intestine, and into the colon, MMCs function to maintain low bacterial counts in the upper intestine. Bacterial overgrowth syndrome can occur when the normally low bacterial colonization in the upper gastrointestinal tract increases significantly. It should be clear that an absence of MMCs would decrease duodenal motility and gastric emptying. MMCs do not have a direct effect on mass movements and swallowing.

17. C) Gastric emptying is accomplished by coordinated activities of the stomach, pylorus, and small intestine. Conditions that favor gastric emptying include (a) increased tone of the orad stomach because this helps to push chyme toward the pylorus, (b) forceful peristaltic contractions in the stomach that move chyme toward the pylorus, (c) relaxation of the pylorus which allows chyme to pass into the duodenum, and (d) absence of segmentation contractions in the intestine, which can otherwise impede the entry of chyme into the intestine.

18. E) Gastrointestinal smooth muscle undergoes rhythmical changes in membrane potential called slow waves. The slow waves are thought to be caused by variations in the sodium conductance of specialized pacemaker cells, called interstitial cells of Cajal. The discharge frequency of the pacemaker cells and hence the frequency of slow waves is fixed (i.e., does not change) in various parts of the gut. Slow-wave frequency averages about 3 per minute in

the stomach, 12 per minute in the duodenum, 10 per minute in the jejunum, and 8 per minute in the ileum. When a slow wave depolarizes sufficiently, it elicits spike potentials which are true action potentials. In the small intestine, slow waves cannot initiate smooth muscle contraction in the absence of spike potentials; however, slow waves themselves can initiate the contraction of smooth muscle in the stomach. The number of spike potentials associated with a given slow wave is increased by parasympathetic stimulation and decreased by sympathetic stimulation. Therefore, the autonomic nervous system controls gut motility by changing the frequency of spike potentials. Neither gastrin nor secretin has significant effects on gut motility at physiological concentrations.

19. C) The palatopharyngeal folds located on each side of the pharynx are pulled medially forming a sagittal slit through which the bolus of food must pass. This slit performs a selective function, allowing food that has been masticated sufficiently to pass by but impeding the passage of larger objects. The soft palate is pulled upward to close the posterior nares, which prevents food from passing into the nasal cavities. The vocal cords of the larynx are strongly approximated during swallowing, and the larynx is pulled upward and anteriorly by the neck muscles. The epiglottis then swings backward over the opening of the larynx. The upper esophageal sphincter relaxes, allowing food to move from the posterior pharynx into the upper esophagus.

20. C) The gastrocolic reflex occurs when distension of the stomach (gastro) stimulates mass movements in the colon (colic). All of the gut reflexes are named with the anatomical origin of the reflex as the prefix followed by the name of the gut segment in which the outcome of the reflex is observed, that is, the gastrocolic reflex begins in the stomach and ends in the colon. The duodenocolic reflex has a similar function to the gastrocolic reflex. When the duodenum is distended, nervous signals are transmitted to the colon, which stimulates mass movements. The enterogastric reflex occurs when signals originating in the intestines inhibit gastric motility and gastric secretion. The intestino- intestinal reflex occurs when overdistension or injury to a bowel segment signals the bowel to relax. The rectosphincteric reflex, also called the defecation reflex, is initiated when feces enters the rectum and stimulates the urge to defecate.

21. D) When feces enters the rectum, distention of the rectal wall initiates signals that spread through the myenteric plexus to initiate peristaltic waves in the descending colon, sigmoid colon, and rectum all of which force feces toward the anus. At the same time the internal anal sphincter relaxes allowing the feces to pass. In people with transected spinal cords, the defecation reflexes can cause automatic emptying of the bowel because the external anal sphincter is normally controlled by the conscious brain through signals transmitted in the spinal cord.

22. E) Cholecystokinin (CCK) is the only gastrointestinal hormone that inhibits gastric emptying under normal, physiological conditions. CCK inhibits gastric emptying by relaxing the orad stomach, which increases its compliance. When the compliance of the stomach is increased, the stomach can hold a larger volume of food without excess build up of pressure in the lumen. None of the gastrointestinal hormones increase gastric emptying under physiological conditions; however, gastrin, secretin, and GLIP can inhibit gastric emptying when pharmacological doses are administered experimentally.

23. A) Gastrin and CCK do not share any effects on gastrointestinal function at normal, physiological conditions; however, they have identical actions on gastrointestinal function when pharmacological doses are administered. Gastrin stimulates gastric acid secretion and mucosal growth throughout the stomach and intestines under physiological conditions. CCK stimulates growth of the exocrine pancreas and inhibits gastric emptying under normal conditions. CCK also stimulates gallbladder contraction, relaxation of the sphincter of Oddi, and secretion of bicarbonate and enzymes from the exocrine pancreas.

24. D) The act of vomiting is preceded by antiperistalsis that may begin as far down in the gastrointestinal tract as the ileum. Distension of the upper portions of the gastrointestinal tract (especially the duodenum) becomes the exciting factor that initiates the actual act of vomiting. At the onset of vomiting, strong contractions occur in the duodenum and stomach along with partial relaxation of the lower esophageal sphincter. From then on, a specific vomiting act ensues that involves (a) a deep breath, (b) relaxation of the upper esophageal sphincter, (c) closure of the glottis, and (d) strong contractions of the abdominal muscles and diaphragm.

25. E) Essentially all proteolytic enzymes are secreted in an inactive form, which prevents autodigestion of the secreting organ. Enterokinase is physically attached to the brush border of the enterocytes which line the inner surface of the small intestine. Enterokinase activates trypsinogen to become trypsin in the gut lumen. The trypsin then catalyzes the formation of additional trypsin from trypsinogen as well as several other proenzymes (e.g., chymotrypsinogen, procarboxypeptidase, proelastase, and others). Pepsin is first secreted as pepsinogen, which has no proteolytic activity. However, as soon as it comes into contact with hydrochloric acid, and especially in contact with previously formed pepsin plus hydrochloride acid, it is activated to form pepsin.

26. E) The rectum is empty of feces most of the time. When a mass movement forces feces into the rectum, the desire to defecate is initiated immediately. Reflex contraction of the rectum and relaxation of the internal anal sphincter follows. If a person is in a place where defecation is possible (like a bathroom), the external anal sphincter is consciously relaxed and the feces is expelled. It should be clear that mass movements do not cause duodenal peristalsis, gastric retropulsion, or hunger sensations.

27. B) The use of nonsteroidal anti-inflammatory drugs (NSAIDs) may result in NSAID-associated gastritis or peptic ulceration. Chronic gastritis, by definition, is a histopathological entity characterized by chronic inflammation of the stomach mucosa. When inflammation affects the gastric corpus, parietal cells are inhibited, leading to reduced acid secretion. Although diagnosis of chronic gastritis can only be ascertained histologically, the administration of pentagastrin should produce a less than expected increase in gastric acid secretion. Pentagastrin is a synthetic gastrin composed of the terminal four amino acids of natural gastrin plus the amino acid alanine. It has all the same physiologic properties of natural gastrin. Although gastrin and pentagastrin can both stimulate growth of the duodenal mucosa, it should be clear that intravenous pentagastrin would not cause substantial growth in the context of a clinical test. In any case, chronic administration of pentagastrin would not lead to a less than expected growth of the duodenal mucosa. Pentagastrin is not expected to increase gastrin secretion, pancreatic enzyme secretion, or pancreatic growth.

28. E) Vitamin B12 absorption requires intrinsic factor,
which is a glycoprotein secreted by parietal cells in the

stomach. Binding of intrinsic factor to dietary vitamin B12 is necessary for attachment to specific receptors located in the brush border of the ileum. Therefore, ileal resection can lead to vitamin B12 deficiency. Achalasia is a neuromuscular failure of relaxation at the lower end of the esophagus with progressive dilation, tortuosity, incoordination of peristalsis, and often hypertrophy of the proximal esophagus. Atrophic gastritis is a type of autoimmune gastritis that is mainly confined to the acid-secreting corpus mucosa. The gastritis is diffuse and eventually severe atrophy develops. Ileal resection is likely to cause diarrhea, but not constipation. Benign gastric and duodenal ulcers are best classified together as peptic ulcers even though their etiology is different. In both types of ulcer it is acid and pepsin which causes the mucosal damage. Duodenal ulcers are more common.

29. E) The presence of acid, fatty acids, and hyperosmotic solutions in the duodenum and jejunum lead to suppression of acid secretion through a variety of mechanisms. Acid stimulates the secretion of secretin from the small intestine, which in turn inhibits acid secretion from parietal cells. Acidification of the antrum and oxyntic gland area of the stomach stimulates the release of somatostatin, which in turn inhibits acid secretion by a direct action on the parietal cells and an indirect action mediated by suppression of gastrin secretion. The presence of fatty acids in the small intestine stimulates the release of GLIP (glucose-dependent insulinotropic peptide), which inhibits acid secretion both directly (parietal cell inhibition) and indirectly (by decreasing gastrin secretion). Hyperosmotic solutions in the small intestine cause the release of unidentified enterogastrones, which directly inhibit acid secretion from parietal cells. Isotonic solutions have no effect on acid secretion.

30. E) All of the GI hormones are released following a meal and all have physiological effects.

31. A) *H. pylori* is a bacterium that accounts for 95% of patients with duodenal ulcer and virtually 100% of patients with gastric ulcer when chronic use of aspirin or other non-steroidal anti-inflammatory drugs (NSAIDS) are eliminated. *H. pylori* is characterized by high urease activity, which metabolizes urea to NH3 (ammonia). Ammonia reacts with H1 to become ammonium (NH4 1). This reaction allows the bacterium to withstand the acid environment of the stomach. The ammonium production is believed to be the major cause of cytotoxicity because the ammonium directly damages epithelial cells, increasing the permeability of the gastric mucosal barrier. Bile salts and NSAIDS can also damage the gastric mucosal barrier, but these are not directly related to *H. pylori* infection. Pepsin can exacerbate the mucosal lesions cause by *H. pylori* infection, but pepsin levels are not increased by *H. pylori*. It should be clear that gastrin does not mediate the mucosal damage caused by *H. pylori*.

32. B) Neither plasma gastrin levels nor the rate of acid secretion are diagnostic for duodenal ulcer. However, when duodenal ulcer patients are pooled together they exhibit a statistically significant increase in the rate of acid secretion and a statistically significant decrease in plasma gastrin levels. How is this possible? The basal and maximal acid secretion rates of normal subjects range from 1 to 5 mEq/hr and from 6 to 40 mEq/hr, respectively, which overlaps with the basal (2–10 mEq/hr) and maximal (30–80 mEq/hr) acid secretion rates of duodenal ulcer patients. The increase in acid secretion of the average duodenal ulcer patient suppresses the secretion of gastrin from the antrum of the stomach. It should be obvious that endoscopy is diagnostic for duodenal ulcer.

33. C) The various secretagogues, which include acetylcholine, gastrin, and histamine, have a multiplicative or synergistic effect on gastric acid secretion. This means that histamine potentiates the effects of gastrin and acetylcholine, and that H2 blockers attenuate the secretory responses to both acetylcholine and gastrin. Likewise, acetylcholine potentiates the effects of gastrin and histamine, and atropine attenuates the secretory effects of histamine and gastrin. Therefore, in the experiment described, the stimulation of acid secretion by pentagastrin is attenuated by the H2 blocker because of this multiplicative effect of the secretagogues.

34. B) Cholera toxin causes an irreversible increase in cAMP levels in enterocytes, which leads to an irreversible opening of chloride channels on the luminal surface. Movement of chloride into the gut lumen causes a secondary movement of sodium ions through paracellular pathways into the gut lumen. Water follows the osmotic gradient causing a tremendous increase in fluid loss into the gut lumen, which results in severe diarrhea.

35. E) One of the most critical actions of gastrointestinal hormones is their trophic activity. Gastrin can stimulate mucosal growth throughout the gastrointestinal tract as well as growth of the exocrine pancreas. If most of the endogenous gastrin is removed by antrectomy, the gastrointestinal tract atrophies. Exogenous gastrin prevents the atrophy. Partial resection of the small intestine for tumor removal, morbid obesity, or other reasons results in hypertrophy of the remaining mucosa. The mechanism for this adaptive response is poorly understood. Both cholecystokinin and secretin stimulate growth of the exocrine pancreas. GLIP (glucose-dependent insulinotropic peptide) and motilin do not appear to have trophic actions on the gastrointestinal tract

36. A) During a swallow, the orad portion of the stomach and lower esophageal sphincter relax at about the same time. Intraluminal pressures in both regions decrease before the arrival of the swallowed bolus. This phenomenon is called receptive relaxation. Because the orad stomach relaxes with each swallow, the stomach can accept a large volume of food with only a few mm Hg rise in intragastric pressure. Receptive relaxation is mediated by afferent and efferent pathways in the vagus. Receptive relaxation and gastric distensibility are impaired following vagotomy. The palatopharyngeal folds are important for determining whether a bolus of food is small enough to be swallowed. The pharynx and thoracic esophagus undergo peristaltic contractions during swallowing, but they do not undergo receptive relaxation. The upper esophageal sphincter opens during a swallow, but this is not considered to be receptive relaxation.

37. B) Relaxation of the ileocecal sphincter occurs with or shortly after eating. This reflex has been termed the gastroileal reflex. It is not clear whether the reflex is mediated by gastrointestinal hormones (gastrin and cholecystokinin) or extrinsic autonomic nerves to the intestine. Note that the gastroileal reflex is named with the origin of the reflex first (gastro) and the target of the reflex named second (ileal). This method of naming is characteristic of all the gastrointestinal reflexes. The enterogastric reflex involves signals from the colon and small intestine that inhibit gastric motility and gastric secretion. The gastrocolic reflex causes the colon to evacuate when the stomach is stretched. The intestino-intestinal reflex causes a bowel segment to relax when it is overstretched. The rectosphincteric reflex is also called the defecation reflex.

38. E) The defecation reflex (also called the rectosphincteric reflex) occurs when a mass movement forces feces into the rectum. When the rectum is stretched, the internal anal sphincter relaxes and the rectum contracts pushing the feces toward the anus. The external anal sphincter is controlled voluntarily and can be contracted when defecation is not possible. Therefore, when a person feels the urge to defecate, the internal anal sphincter is relaxed, the rectum is contracting, and the external anal sphincter is either contracted or relaxed depending on the circumstances.

39**. D)** Damage to the gastric mucosal barrier allows hydrogen ions to back-leak into the mucosa in exchange for sodium ions. A low pH in the mucosa causes mast cells to leak histamine, which damages the vasculature causing ischemia. The ischemic mucosa allows a greater leakage of hydrogen ions—more cell injury and death—resulting in a vicious cycle. Factors that normally strengthen the gastric mucosal barrier include mucus (which impedes the influx of hydrogen ions), gastrin (which stimulates mucosal growth), certain prostaglandins (which can stimulate mucus secretion), and various growth factors that can stimulate growth of blood vessels, gastric mucosa, and other tissues. Factors that weaken the gastric mucosal barrier include *Helicobacter pylori* (a bacterium that produces toxic levels of ammonium) as well as aspirin, NSAIDS, ethanol, and bile salts.

40. A) Hydrogen ions leak into the mucosa when it is damaged. As the hydrogen ions accumulate in the mucosa, the intracellular buffers become saturated, and the pH of the cells decreases resulting in injury and cell death. The hydrogen ions also damage mast cells causing them to secrete excess amounts of histamine. The histamine exacerbates the condition by damaging blood capillaries within the mucosa. The result is focal ischemia, hypoxia, and vascular stasis. The mucosal lesion is a forerunner of gastric ulcer. Mucus secretion helps to strengthen the gastric mucosal barrier because mucus impedes the leakage of hydrogen ions into the mucosa. Various proton pump inhibitors are used as a treatment modality for gastric ulcer because these can decrease the secretion of hydrogen ions (protons). The tight junctions between cells within the mucosa help to prevent the back-leak of hydrogen ions. Vagotomy was once used to treat gastric ulcer disease because severing or crushing the vagus nerve decreases gastric acid secretion.

41. B) Gastrin has a critical role to stimulate mucosal growth throughout the gastrointestinal system.

42. C) The medical treatment of gastric ulcers is aimed at restoring the balance between acid secretion and mucosal protective factors. Proton pump inhibitors are drugs that covalently bind and irreversibly inhibit the H1/K1 adenosine triphosphatase (ATPase) pump, effectively inhibiting acid release. Therapy can also be directed toward histamine release, that is, H2 blockers, such as cimetidine (Tagamet), ranitidine (Zantac), famotidine (Pepcid), and nizatidine (Axid). These agents selectively block the H2 receptors in the parietal cells. Antibiotic therapy is used to eradicate the *H. Pylori* infection. NSAIDS (nonsteroidal anti-inflammatory agents) can cause damage to the gastric mucosal barrier, which is a forerunner of gastric ulcer.

43. F) It is a common misconception that the pH of the gastric contents is lowest (most acidic) following a meal when acid secretion is highest. Before a meal, when the stomach is empty, the pH of the gastric contents is the lowest and acid secretion is suppressed. Acid secretion is low because (a) the acid stimulates somatostatin release (which has a direct action to decrease secretion of both gastrin and acid), and (b) acid has a direct effect to suppress

parietal cell secretions. When a meal is taken, the buffering effects of the food cause the gastric pH to increase, which allows the various secretagogues to stimulate acid secretion.

44. B) Movement of chloride ions out of cells leads to secretion of fluid by cells. Cystic fibrosis (CF) is caused by abnormal chloride ion transport on the apical surface of epithelial cells in exocrine gland tissues. The CF transmembrane regulator (CFTR) protein functions both as a cyclic AMP-regulated Cl2 channel and, as its name implies, a regulator of other ion channels. The fully processed form of CFTR is found in the plasma membrane of normal epithelia. Absence of CFTR at appropriate cellular sites is often part of the pathophysiology of CF. However, other mutations in the CF gene produce CFTR proteins that are fully processed but are nonfunctional or only partially functional at the appropriate cellular sites.

45. C) Acid acts directly on somatostatin cells to stimulate the release of somatostatin. The somatostatin decreases acid secretion by directly inhibiting the acid secreting parietal cells and indirectly by inhibiting gastrin secretion from G cells in the antrum. Acid is a weak stimulus for CCK release, but CCK does not inhibit (or stimulate) gastrin release. Acid does not stimulate GLIP release. Fatty acids are a weak stimulus for motilin, but motilin does not affect gastrin release. Fatty acids are not thought to stimulate somatostatin release.

46. C) Hirschsprung disease results from the absence of parasympathetic ganglion cells in the myenteric and submucosal plexus of the rectum and/or colon. Congenital aganglionosis begins with the anus, which is always involved, and continues proximally for a variable distance. Both the myenteric (Auerbach) and submucosal (Meissner) plexus are absent, resulting in reduced bowel peristalsis and function. The precise mechanism underlying the development of Hirschsprung disease is unknown. It should be clear that an absence of lymphatic endothelial cells, capillary endothelial cells, or red blood cells would not affect colonic motility. Smooth muscle cells are present in Hirschsprung disease.

47. A) Mass movements force feces into the rectum. When the walls of the rectum are stretched by the feces, the defecation reflex is initiated and a bowel movement follows when this is convenient. Mass movements do not affect gastric motility. Haustrations are bulges in the large intestine caused by contraction of adjacent circular and longitudinal smooth muscle. It should be clear that mass movements in the colon do not affect esophageal contractions or pharyngeal peristalsis.

48. A) Celiac sprue is a chronic disease of the digestive tract that interferes with the absorption of nutrients from food. The mucosal lesions seen on upper GI biopsy are the result of an abnormal, genetically determined, cell-mediated immune response to gliadin, a constituent of the gluten found in wheat. A similar response occurs to comparable proteins found in rye and barley. Gluten is not found in oats, rice, and maize. When affected individuals ingest gluten, the mucosa of their small intestine is damaged by an immunologically mediated inflammatory response, resulting in malabsorption and maldigestion at the brush border. Digestion of fat is normal in celiac sprue because the pancreas which secretes lipase still functions normally. Because celiac sprue causes malabsorption it should be clear that the stool content of carbohydrates, fat, and nitrogen is increased.

49. E) ZES is typically caused by a gastrin-secreting tumor that is located in the pancreas, duodenal wall, or in lymph nodes. The most simple and reliable test for ZES is secretin injection. Secretin inhibits antral gastrin, but it simulates gastrin secretion in patients with ZES (gastrinoma). Two units of secretin per kilogram body weight are injected intravenously. Serum gastrin levels are measured at various times for 30 min after injection. An increase in serum gastrin of more than 200 ng/mL is diagnostic for ZES. The physiological mechanism of the secretin test remains unclear; however, it is the most important diagnostic test to exclude other conditions associated with increased acid secretion. CCK, GLIP, motilin, and pentagastrin have minimal effects on gastrin secretion and are not diagnostic for gastrinoma.

50. A) Intrinsic factor is a glycoprotein secreted from parietal cells (i.e., acid secreting cells in the stomach) that is necessary for absorption of vitamin B12. The patient has a diminished capacity to secrete acid because of chronic gastritis. Because acid and intrinsic factor are both secreted by parietal cells, a diminished capacity to secrete acid is usually associated with diminished capacity to secrete intrinsic factor. Ptyalin, also known as salivary amylase, is an enzyme that begins carbohydrate digestion in the mouth. The secretion of ptyalin is not affected by gastritis. Rennin, known also as chymosin, is a proteolytic enzyme synthesized by chief cells in the stomach. Its role in digestion is to curdle or coagulate milk in the stomach, a process of considerable importance in very young animals. It should be clear that saliva secretion is not affected by gastritis. Trypsin is a proteolytic enzyme secreted by the pancreas.

51. C) Gastrin, acetylcholine, and histamine can directly stimulate parietal cells to secrete acid. These three secretagogues also have a multiplicative effect on acid secretion such that inhibition of one secretagogue reduces the effectiveness of the remaining two secretagogues. Acetylcholine also has an indirect effect to increase acid secretion by stimulating gastrin secretion from G cells. Somatostatin inhibits acid secretion.

52. D) Duodenal ulcer patients have about 2 billion parietal cells and can secrete about 40 mEq H1 per hour. Normal individuals have about 50% of these values. Plasma gastrin levels are related inversely to acid secretory capacity because of a feedback mechanism whereby antral acidification inhibits gastrin release. Thus, plasma gastrin levels are reduced in duodenal ulcer patients. Maximal acid secretion and plasma gastrin levels are not diagnostic for duodenal ulcer disease because of significant overlap with the normal population among individuals in each group.

53. E) A proton pump inhibitor such as omeprazole inhibits all acid secretion by directly inhibiting the H1, K1-ATPase (H1 pump). The parietal cell has receptors for secretagogues such as gastrin, acetylcholine, and histamine. Therefore, antigastrin antibodies, atropine, and histamine H2 blockers can reduce the secretion of acid, but none of these can totally eliminate acid secretion. Antacids neutralize gastric acid once it has entered the stomach, but they cannot inhibit acid secretion from parietal cells.

54. B) Secretin inhibits gastrin release from the antrum of the stomach, but it stimulates gastrin secretion from a gastrinoma. Thus, patients with a gastrinoma have increased serum gastrin levels within 30 min after secretin administration; whereas secretin decreases serum gastrin levels in normal subjects. Secretin injection is the most simple and reliable test for gastrinoma; however, the physiological mechanism of the secretin test is poorly understood. Secretin normally inhibits gastric acid secretion, but it could conceivably increase acid secretion in patients with gastrinoma because of the increase in gastrin secretion that occurs.

Secretin can inhibit gastric emptying when pharmacological doses are given, but this is not diagnostic for gastrinoma. Secretin has a normal physiological effect to stimulate pancreatic HCO32 secretion, which is independent of gastrinoma.

55. D) The discovery of *H. pylori* and its association with peptic ulcer disease, adenocarcinoma, gastric lymphoma,and other diseases make it one of the most significant medical discoveries of this century. In the United States, about 26 million people will suffer from ulcer disease in their lifetime and up to 90% will likely be due to *H. pylori*. *H. pylori* is a gram-negative bacterium with high urease activity, an enzyme that catalyzes the formation of ammonia from urea. The ammonia (NH3) is converted to ammonium (NH41) in the acid environment of the stomach. The ammonium damages the gastric mucosal barrier because it damages epithelial cells. *H. pylori* also increases gastric acid secretion, possibly by increasing parietal cell mass. This combination of increased acid secretion along with damage to the gastric mucosal barrier promotes the development of gastric ulcer. Bile salts can damage the gastric mucosal barrier, but they do not have a clinically significant effect on acid secretion. Epidermal growth factor, gastrin, and mucous strengthen the gastric mucosal barrier.

56. B) Antral peristalsis pushes chyme toward the pylorus and thus promotes gastric emptying. Other factors that promote gastric emptying include (a) decreased compliance of the stomach, (b) relaxation of the pylorus, and (c) an absence of segmentation contractions in the small bowel. Gastric emptying is thought to be slow in eating disorders such as anorexia nervosa, bulimia nervosa, and obesity. Scleroderma is a systemic disease that affects many organ systems. The symptoms result from progressive tissue fibrosis and occlusion of the microvasculature by excessive production and deposition of types I and III collagens. Deposition of fibrous tissues in the pylorus reduces gastric emptying. Gastroparesis (paralysis of the stomach) occurs in about 20% of type I diabetics. The high blood glucose is thought to damage the vagus nerve and thereby reduce gastric emptying.

57. C) Pancreatitis is inflammation of the pancreas. The pancreas secretes digestive enzymes into the small intestine that are essential in the digestion of fats, proteins, and carbohydrates. Reduced secretion of fluid into the pancreatic ducts in cystic fibrosis cause these digestive enzymes to accumulate in the ducts. The digestive enzymes then become activated in the pancreatic ducts (which typically would not occur) and can begin to “digest” the pancreas, leading to inflammation and a myriad of other problems (cysts and internal bleeding). Enterokinase is located at the brush border of intestinal enterocytes where it normally activates trypsin from its precursor, trypsinogen. Trypsin inhibitor is normally present in the pancreatic ducts where it prevents trypsin from being activated, and thus prevents autodigestion of the pancreas. When the ducts are blocked in cystic fibrosis, the available trypsin inhibitor is insufficient to prevent trypsin from being activated. Excessive secretion of CCK does not occur in cystic fibrosis. Gallstone obstruction can lead to pancreatitis (by autodigestion) when the obstruction prevents pancreatic juice from entering the intestine, but this is unrelated to cystic fibrosis.

58. C) The cephalic phase of gastric secretion is mediated entirely by the vagus nerve: vagotomy abolishes the response. The vagus also mediates a significant portion of the gastric phase of gastric secretion. Vagal stimulation increases acid secretion by a direct action of parietal cells as well as by stimulating gastrin secretion. Vagal stimulation increases gastrin secretion by (a) directly stimulating G cells, which secrete gastrin, and (b) inhibiting somatostatin cells from secreting somatostatin, which would otherwise inhibit G cells from secreting gastrin. Gastrin releasing peptide (GRP) is the neurotransmitter released from interneurons that stimulate G cells to secrete gastrin.

59. E) Following a meal, the pH of the gastric contents increases because the food buffers the acid in the stomach. This increase in pH suppresses the release of somatostatin from delta cells in the stomach (hydrogen ions stimulate the release of somatostatin). Because somatostatin inhibits secretion of both gastrin and gastric acid, the fall in somatostatin levels leads to an increase in acid secretion. The increase in acid secretion causes the pH of the gastric contents to decrease. As the pH of the gastric contents decreases, the rate of acid secretion also decreases.

60. C) About 20% of persons older than 65 years have gallstones (cholelithiasis) in the United States, and 1 million newly diagnosed cases of gallstones are reported each year. Gallstones are the most common cause of biliary obstruction. Regardless of the cause of gallstones, serum bilirubin values (especially direct or conjugated) are usually elevated. Indirect or unconjugated bilirubin values are usually normal or only slightly elevated. Only answer C shows a high level of direct bilirubin (conjugated bilirubin) compared to the level of indirect bilirubin (unconjugated bilirubin).

The end