How Well Do You Know Your Gut? Gastrointestinal Anatomy and Physiology: A Review

Cynthia Yoshida, MD, AGAF
Gastroenterologist
Charlottesville, VA

Abstract

Some of the most devastating complications of diabetes mellitus (DM) affect the luminal gastrointestinal (GI) tract and liver. These include: gastroparesis, small bowel bacterial overgrowth, diabetic diarrhea, constipation and non-alcoholic fatty liver disease. This article will review GI anatomy and physiology to aid the reader in understanding the complications discussed in the succeeding articles.

Pancreas

The pancreas is divided into the head/uncinate process (situated within the C loop of the duodenum) and the body and the tail (located directly behind the stomach). The endocrine pancreas secretes hormones (e.g., insulin, glucagon, somatostatin and amylin) directly into the blood whereas the exocrine pancreas secretes digestive enzymes and alkaline pancreatic juice into the small intestine (SI) via the main pancreatic duct.

Endocrine Pancreas

The endocrine pancreas is comprised of over a million islet cells with four distinct cell types: alpha cells (20%) produce glucagon, beta cells (68%) produce insulin and amylin, delta cells (10%) produce somatostatin, and PP cells (2%) produce pancreatic polypeptide.

Glucose homeostasis requires an intricate balance of pancreatic (e.g., insulin, glucagon, amylin) and gut modulators (e.g., glucagon-like peptide (GLP-1), glucose-dependent insulinotropic peptide (GIP), epinephrine, cortisol and growth hormone) that influence multiple target tissues (e.g., muscle, liver, brain, adipose). Circulating glucose derives from: 1) intestinal absorption following a meal; 2) hepatic glycogenolysis; and 3) hepatic/renal gluconeogenesis during fasting. Blood glucose levels peak about 1.5 hours after a meal and after ~4 hours slowly return to fasting levels. Immediately after eating, a rapid release of pre-formed insulin (first-phase insulin) is initiated, increasing insulin levels before a rise in blood glucose. This phase of insulin secretion lasts ~10 minutes. Second phase, newly synthesized insulin is released to maintain blood glucose levels. Plasma half-life averages ~6 minutes; most circulating insulin is cleared rapidly within 10 to 15 minutes by insulinase enzymes in the liver, kidney and muscles.

Glucagon maintains basal glucose concentrations during fasting and exercise by glycogenolysis (during the first 12 hours of fasting) and by gluconeogenesis (with prolonged fasting or exercise). Amylin is secreted simultaneously with insulin after a meal by beta cells. Amylin works with insulin to manage blood glucose via three mechanisms: 1) suppresses postprandial glucagon secretion via centrally mediated vagal efferents, 2) slows gastric emptying to decrease nutrient transport from the stomach to the SI and 3) dose-dependently decreases food intake and body weight. Amylin exerts its actions through central nervous system receptors in the area postrema, which lacks a blood-brain barrier and allows exposure to rapid changes in plasma glucose levels.

Exocrine Pancreas

The pancreas secretes ~1.5 liters of pancreatic juice (bicarbonate, water and digestive enzymes) daily into the duodenum via the pancreatic duct. Pancreatic exocrine secretion is regulated by vagal stimulation, secretin and cholecystokinin (CCK). The latter two gut hormones are produced by duodenal cells when gastric acid, peptides and luminal fatty acids reach the SI. Secretin stimulates pancreatic bicarbonate and hepatic bile secretion. CCK stimulates pancreatic digestive enzyme secretion and bile release from the gallbladder. Pancreatic enzymes include proteases, pancreatic lipase and amylase.

Luminal GI Tract

Luminal GI tract functions include digestion, absorption and defecation. The adult human GI tract is ~ 8 meters long and includes:

- Mouth / oropharynx / cricopharyngeus
- Esophagus, gastroesophageal junction
- Stomach, pylorus
- Small Intestine (duodenum, jejunum, ileum) / ileocecal valve
- Large Intestine (colon) / rectum

Gastrointestinal Motility

GI motility mixes and propagates the food bolus from mouth to rectum. GI contraction involves peristalsis, segmentation and the migrating motor complex. Segmentation mixes food with enzymes and allows for maximal epithelial contact for efficient absorption. Migrating motor complex (between meals) peristaltic wave cycles last 5 to 15 minutes and repeat every 1 to 2 hours to remove excess food and bacteria. Motility is controlled by the vagus nerve. Contractile activity varies by location. It takes 8 to 20 seconds for peristalsis to proceed down the length of the esophagus. Gastric slow waves occur at three cycles per minute and originate from a pacemaker in the body of the stomach. Duodenal contractions occur ~12 cycles/minute. In the colon, non-propagating, mixing contractions occur at 2 to 4 cycles per minute. Mass motor movements (high amplitude propagating contractions usually resulting in defection) are infrequent and occur ~ one to two times a day.

Mouth, Oropharynx, Cricopharyngeus

Chewing increases food surface area and lubricates the bolus with saliva (water, mucins and bicarbonate to maintain pH 6.5-7.5). Salivary amylase initiates the digestion of starch to maltose.

Swallowing is a complex coordination of nerves and muscles that occurs in two phases:

1) Oral phase (one second) — lip closure and anterior to posterior tongue movement pushing food to the oropharynx and
2) Pharyngeal phase (one second) — velum elevation, velopharyngeal port closure (to prevent food from entering the nasal cavity), and initiation of pharyngeal peristalsis

Once the larynx is elevated and closed and the cricopharyngeus (upper esophageal sphincter) relaxes, the bolus passes from the pharynx to esophagus.

Esophagus

The esophagus is a 25-30 cm muscular tube that propagates food from pharynx to stomach. It is lined with non-keratinized stratified squamous epithelium, and submucosal glands secrete mucin, bicarbonate, epidermal growth factor and prostaglandin E2, which protect the mucosa from gastric acid. The gastroesophageal junction is made up of the lower esophageal sphincter (LES) and the skeletal muscle right diaphragmatic crus. Remaining closed at rest and after swallowing, the LES relaxes to allow food to pass into the stomach.

Stomach

The stomach accommodates and stores the meal, triturates food into smaller particles, and controls emptying into the duodenum. When empty, gastric volume is ~50 mL but can expand to ~4 liters. Gastric parietal cells produce 1.5 to 2 liters of acid daily resulting in a pH between 1 to 2; peak basal secretion occurs in the evening. Acid secretion is regulated by neural, paracrine and endocrine factors. Receptors that relay information stimulating gastric antral G cells to secrete gastrin into the bloodstream are stretched by gastric distension with food stimulates. Gastrin stimulates parietal cell secretion of hydrochloric acid, and is inhibited by gastric pH less than 4 and by somatostatin. There are three phases of gastric acid secretion:

1) cephalic phase (30% of gastric acid produced) when food is smelled/tasted
2) gastric phase (60%) after stomach distension and protein digestion
3) intestinal phase (10%) following SI distension.

Vasoactive inhibitory peptide (VIP), CCK and secretin inhibit acid production. Gastric mucosal cells are protected from acid by a mucus gel layer. Patients with frequent vomiting lose excess chloride and acid resulting in profound metabolic alkalosis.

Gastric chief cells secrete pepsinogen which breaks down to active pepsin in acidic conditions. Food-bound vitamin B-12 is released by gastric acid and is bound to R protein (haptocorrin). Pancreatic enzymes cleave B-12-R protein complex in the SI. After cleavage, intrinsic factor (secreted by gastric parietal cells) binds with vitamin B-12. Intrinsic factor is required for absorption of food-bound vitamin B-12 (but not synthetic B-12) in the terminal ileum.

Gastric emptying is controlled by the calorie content of the meal; the stomach delivers ~150 kilocalories per hour to the duodenum. Increased size/energy density of a meal results in increased rates of gastric emptying. Duodenal mucosal receptors for fatty acids (FA), amino acids (AA) and carbohydrates (CHO) regulate neural/humoral feedback mechanisms. GIP, CCK, secretin and enteroglucagon decrease gastric motility. Within the ileum and colon, chyme delays gastric transit ("ileal brake") allowing more time for digestion and absorption. Chyme is delivered to the duodenum at a controlled rate to allow adequate mixing with pancreaticobiliary secretions. Consistency, viscosity, pH, osmolality, lipid and caloric content determine the rate of stomach-emptying. The pylorus controls gastric emptying by selectively allowing rapid passage of liquids and retention of solid particles greater than 2 millimeters in size.

Small Intestine

The small intestine (SI) is ~600 cm long and is comprised of the duodenum (26 cm), jejunum (250 cm) and ileum (350 cm). The term "small" intestine refers to the smaller diameter (3 cm) as compared to the large intestine (7 cm).

With a majority of digestion occurring in the SI, trypsin and chymotrypsin – proteolytic pancreatic enzymes – are secreted into the duodenum to cleave proteins into smaller peptides. Intestinal brush border peptidases (carboxypeptidase, aminopeptidase, dipeptidase) break down di- and tri-peptides into individual AA. Lipid metabolism also occurs in the proximal SI. Pancreatic lipase is secreted into the duodenum and breaks down triglycerides into free fatty acids and monoglycerides. CHO digestion begins in the mouth with salivary amylase; in the SI, pancreatic amylase cleaves CHO into oligosaccharides. Brush border enzymes dextrinase, glucoamylase, maltase, sucrase and lactase further break down oligosaccharides.

Nutrient absorption occurs through finger-like SI mucosal villi. Each villus is covered in microvilli to increase SI surface area (equivalent to a doubles tennis court). Glucose and AA are transported via active transport into the intestinal cells and then into the capillaries. Glycerol and FA enter villi by passive diffusion and are reassembled into triglycerides. They combine with proteins, expelled by exocytosis, then move into the lacteals for transport via the lymphatic system. Most nutrients are absorbed in the jejunum with the following exceptions: 1) iron absorbed in the duodenum, and 2) bile salts and food-bound vitamin B-12 absorbed in the ileum.

The majority of *chemical* digestion occurs in the duodenum, the shortest SI segment. Secretin, released in the duodenum in response to acid gastric chyme, stimulates pancreatic bicarbonate and enzymes (e.g., trypsin, lipase and amylase) secretion. CCK, released by duodenal epithelial cells following fatty stimuli, stimulates the liver and gallbladder to bile release to aid in lipid digestion. Mucus is secreted by Brunner's glands. The majority of *nutrient* absorption occurs in the jejunum whose longer villi and plicae circulares maximize surface area. Jejunal pH remains ~7 to 8. The ileum — the most distal portion of the SI — absorbs residual nutrients that are not absorbed by the jejunum including food-bound vitamin B-12; bile salts are absorbed in the terminal ileum. By regulating the flow of liquid chyme into the colon, the ileocecal valve functions as a one-way valve.

Fluid Secretion in the GI tract

Between 6 to 7 liters of fluid are secreted into the GI tract every day. This includes: saliva (1to 1.5 liters), stomach (1.5 to 2.5 liters), bile (0.5 to 1 liter), pancreas (1 to 1.5 liters), SI (1 to 1.8 liters). Electrolytes and water make up most of the volume of secreted fluids. Ions (hydrogen, potassium, chloride, sodium, bicarbonate) are initially secreted then reabsorbed along the GI tract. Bicarbonate secretion neutralizes gastric acid and prevents degradation of digestive enzymes. Digestive enzymes are secreted by the mouth, stomach, intestines and pancreas. Some (e.g., lactase) are embedded in the SI epithelium. Gastric chief cells secrete pepsinogen which is activated by gastric acid to active pepsin. Bile is made up of bile salts, bilirubin and cholesterol. It is produced in the liver, stored in the gallbladder and released into the duodenum via the common bile duct after a meal. Bile salts facilitate fat absorption by forming hydrophilic emulsion (micelles). Bile salts are reabsorbed in the terminal ileum, returned via the portal vein to the liver, and reused. This enterohepatic circulation handles ~30 grams of bile acids daily. A small amount escapes and is lost in the feces. Mucus is secreted in the stomach, small and large intestine to lubricate and protect the intestinal epithelium.

Colon

The colon is 150 cm in length. The main function of the colon is to absorb the remaining water and electrolytes and to compact and store fecal matter prior to defecation. When chyme enters the colon, greater than 80% of dietary liquid and GI secretions have been absorbed. If water is not absorbed, diarrhea can result, causing dehydration and ion loss. Colonic transit time is ~20 to 25 hours. The colon also absorbs vitamin K which is produced by colonic bacteria.

Dietary fiber is comprised of:
1) soluble (functional/prebiotic) fiber that is fermented by colonic bacteria to form gases and short-chain fatty acids, and 2) insoluble (non-

functional) fiber that bulks/softens stool, absorbs water and shortens transit time. Short-chain fatty acids (acetate, proprionate and butyrate) lower colonic pH and enhance the colonic mucosal barrier. Butyrate nourishes colonocytes.

Fecal matter is composed of 75% water and 25% solids. One-third of the solids are intestinal bacteria, the other two-thirds are undigested materials. Between 300 to 1000 different species of bacteria reside within the colon to make up the intestinal microbiota or "flora." Bacterial fermentation of undigested carbohydrate results in the formation of several gases: nitrogen, carbon dioxide, hydrogen, methane and hydrogen sulfide.

Liver

The liver, the largest solid organ, weighs 1.5 kilograms. Hepatocytes perform over 500 functions and produce over 1000 essential enzymes. The liver's major functions include:

- Bile synthesis — hemoglobin is broken down to bilirubin/biliverdin, which are then combined with bile salts/cholesterol to make bile. The bile then drains from the bile canaliculi into the common bile duct to be temporarily stored in the gallbladder or secreted into the duodenum to aid in fat emulsification.
- Carbohydrate metabolism — gluconeogenesis, glycogenolysis, glycogenesis and the breakdown of many hormones (e.g., insulin, glucagon).
- Lipid metabolism — cholesterol synthesis and lipogenesis.
- Protein synthesis/metabolism — produces albumin, a major blood osmotic protein. The liver also produces blood clotting factors, proteins C and S and antithrombin; and converts lactate to alanine and ammonia to urea.
- Detoxification — metabolizes many toxic substances/drugs (e.g., acetaminophen).
- Storage — glucose (as glycogen), vitamin B-12, iron, copper and vitamin A.
- Immunologic effects — hepatic reticuloendothelial cells clear antigens from the portal circulation so they do not reach the systemic circulation.

Summary

Understanding GI anatomy/physiology is paramount to the management of disease. While this article cannot be all-inclusive, hopefully, it will aid the registered dietitian in understanding the following articles that discuss the GI complications of DM.

Resource List

- Feldman M, Friedman LS, Brandt LJ. *Sleisenger and Fordtran's Gastrointestinal and Liver Disease, Ninth Edition*. Philadelphia, PA: WB Saunders; 2010.
- Yamada T, Alpers DH, Kalloo AN, Kaplowitz N, Owyang C, Powell DW. *Textbook of Gastroenterology, 5th Edition.* Hoboken, NJ: Wiley-Blackwell; 2009.
- Bowen RA, Austgen L, Rouge M. Pathophysiology of the Digestive System. Available at http://www.vivo.colostate.edu/hbooks/pathphys/digestion/. Accessed February 2, 2011.

CPE CREDIT
ANSWER KEY

See the CPE credit self-assessment questionnaire on page 30.

1. b
2. c
3. d
4. d
5. c
6. a
7. b
8. e
9. d
10. c