Al muthanna University **Pharmacy college**
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SMALL INTESTINE

The small intestine is is divided into three functional segments: duodenum, jejunum, and ileum. The majority of macronutrient, vitamin, and mineral absorption occurs in the small intestine. Absorption of the nutrients facilitated by the increase in epithelial surface area by villi and microvili.

Motility

Intestinal motility function is propels chyme along the intestines via peristalsis addition allows for mixing of enzymes and other secretions from the pancreas and gallbladder. The type of motility in it is segmentation "back-and-forth" mixing movement in the small intestine between adjacent segments. it is initiated via slow waves, but more frequent (12waves/min)than in the stomach, with the parasympathetic nervous system increasing this rate, and the sympathetic nervous system decreasing it.

Migrating motor complexes (MMCs): are additional contractions which are initiated in the stomach and continue on through the small intestine regulated by motilin. Aid in clearing residual contents during the fasting state.

Intestinal secretions: include

-1Mucus: is important for the lubrication of the chyme for intestinal protection and so that peristaltic contractions can better propel the chyme.

-2Hormones: a number of endocrine cells in the intestines secrete the hormones cholecystokinin)CCK), secretin, and glucose-dependent insulinotropic peptide.

Carbohydrate digestion and absorption

Carbohydrates provide a substantial energy substrate for metabolism. Carbohydrates come in many forms (e.g., starch, dietary fiber, disaccharides, and monosaccharides), but they must be broken down into monosaccharides before they can be transported across the intestinal lumen.

.1Starch: Starch is classified as linear chained (amylose) or branch chained (amylopectin). The glucose bonds that form in linear configuration are α 1,4 bonds, whereas those in the branched configuration are α 1,6 bonds. Pancreatic amylase breaks α 1,4 bonds. The products of the amylase reaction are maltose, maltotrose, glucose oligosaccharidases, and -limit dextrin.

.2Dietary fiber: Dietary fiber can be divided into soluble (e.g., pectin) and insoluble (e.g., cellulose .(dietary fiber contains bonds that human enzymes cannot break down in the small intestine. Because

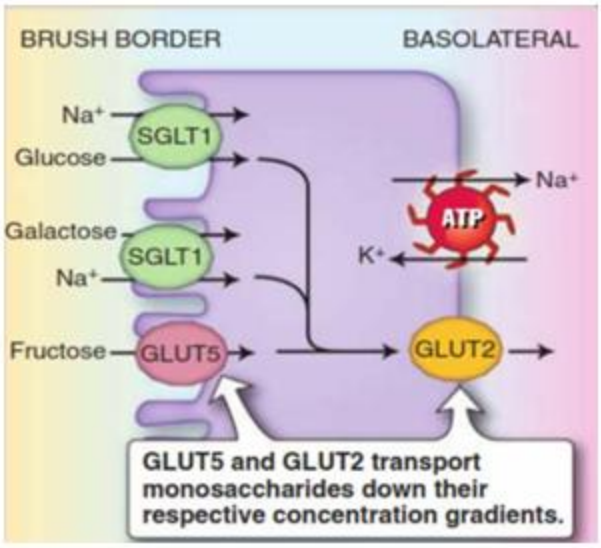
Cellulose contains linear β 1,4 glucose bonds so that dietary fiber cannot be adequately digested. Increased fecal bulk provides some beneficial effects, such as increased intestinal motility and increased frequency of defecation.

.3Disaccharides and oligosaccharides: Disaccharides are derived from the breakdown of starch and from direct dietary sources(e.g., sucrose and lactose). They are broken down into monosaccharides by membrane-bound disaccharidases. The disaccharidases can be specific for a substrate such as lactase, or work on multiple substrates ، such as sucrase and isomaltase. Being membrane bound allows for a close association between enzyme products and absorption transporters. For example, lactose breakdown into glucose and galactose is facilitated by lactase which is located close to cotransporters)SGLT(1 for the products'absorption.

Enzyme	Substrate(s)	Product(s)
Gluco-amylase	Maltose and maltotriose	Glucose
Isomaltase	α-Limit dextrins, maltose, and maltotriose	Glucose
Lactase	Lactose	Glucose and galactose
Sucrase	Maltose, maltotriose, and sucrose	Glucose and fructose

.4Monosaccharides: such as glucose, fructose, and galactose, are transported across the apical and basolateral membranes of small intestine enterocytes. Because monosaccharides are hydrophilic ، transporters are needed to move these nutrients across these membranes.

a. Apical membrane transport: Glucose and galactose are transported across the apical membrane by SGLT1, a Na -glucose cotransporter. The Na+-K + ATPase provides a low Na+ environment within the enterocyte to allow for Na+ to be used as a driving force for the movement of glucose across the apical membrane. Fructose is transported by GLUT 5)glucose transporter.(



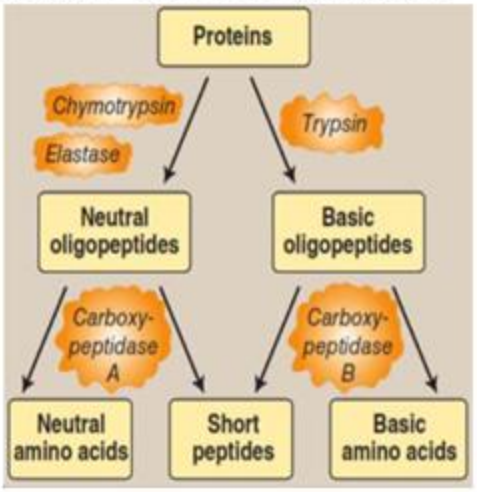
b. Basolateral membrane transport: transport of monosaccharide across the basolateral membrane from the inside of the enterocyte to the interstitium is facilitated by GLUT2 and GLUT5 transporters . GLUT2 transports both glucose and galactose, and GLUT5 transports fructose across the basolateral membrane. These nutrients can then diffuse into the portal circulation to be carried to the liver.

D. Protein digestion and absorption

Proteins also can be used for energy production in a fed state, proteins are primarily used as building blocks for reassembly into other proteins. A small amount of proteins and peptides are absorbed via phagocytosis across the apical membrane of enterocytes and specialized mucosal

immune, or M, cells. Protein digestion begun in the stomach through the action of pepsin is then continued by several other proteases secreted in the small intestine:

.1Luminal proteases: the majority of proteins are broken down into amino acids and oligopeptides by endopeptidases enzymes (trypsin, chymotrypsin, and elastase(for facilitate absorption. The oligopeptides, peptides normally 6 or fewer amino acids in length. Exopeptidases) carboxypeptidase A and B) cleave off single amino acids from oligopeptides.



.2 Apical peptidases: Apical peptidases (also termed brushborder peptidases) break down small peptides and oligopeptides into individual amino acids.

Absorption:

A. Apical transport dipeptide, tripeptide, and amino acid:

-1Amino acids are transported across the apical membrane via different classes of amino acid cotransporters.

-2Di- and tripeptides are transported across the apical membrane by an H+-oligopeptide cotransporter (PepT1).they are then broken down by cytosolic peptidases into individual amino acids.

B. Basolateral amino acid transport: Individual amino acids are transported across the basolateral membrane without the need for cotransport. Many different amino acid transporters are located on the basolateral membrane and provide specificity.

Lipid digestion and absorption

Fats are calorically denser than carbohydrates and proteins and a substantial energy substrate for metabolism. Lipid absorption does not require the same transporter machinery because lipids are hydrophobic and can diffuse across the apical membrane. Lipids must be solubilized to ensure adequate mixing with enzymes.

Lipid digestion begins in the mouth and stomach with lingual and gastric lipase. The vast majority occurs in the small intestine. Assisting with lipid digestion, liver-derived bile salts surround and emulsify lipids so that lipase and colipase can interact with the lipid.

-1Pancreatic lipase is the active enzyme that digests triglycerides into fatty acids and monoacylglycerols.

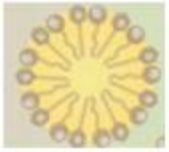
-2Colipase functions to position and stabilize pancreatic lipase.

-3Cholesterol esterase(carboxyl ester hydrolase:(digested the dietary cholesterol esters into cholesterol and fatty acids.

-4Phospholipase A2: breaks down phospholipids into fatty acids and lysolecithin.

Absorption:

.1Free fatty acids: Fatty acid length determines rate of absorption and assimilation. This length distinction is partly related to solubility. The longer the fatty acid, the less soluble it is in an aqueous environment.



a. Long-chain fatty acids are concentrated into micelles in the small intestine lumen. Micelles is hydrophilic portions face outward toward the water, and hydrophobic portions face the center. This allows lipids to enter contact with the apical membranes of enterocytes, the micelle begins to disperse due to a pH change. Long-chain fatty acids are freed and can either diffuse directly across the apical membrane or be transported by fatty acid binding proteins. These binding proteins speed absorption across the apical membrane. In the cytosol, long-chain fatty acids are attached to monoacylglycerols and diacylglycerols to form triglycerides within the enterocyte. triglycerides are packaged in apoprotein vesicles called chylomicrons.

Chylomicrons are then exocytosed through the basolateral membrane into the interstitial space. From the interstitial space, chylomicrons do not enter the circulation because of capillary fenestration size restrictions but, rather, move into the lymphatic system for transportation.

b. **Medium-chain fatty acids** (6–12 carbons long) are more soluble in water than are long-chain fatty acids. This allows them to cross the apical membrane by moving through the cytosol without the need to be repacked into a chylomicron. It can cross the basolateral membrane into the interstitial space and then into the portal circulation.

c. **Short-chain fatty acids:** are less than 6 carbons in length. These fatty acids are absorbed and assimilated in a manner similar to that of medium-chain fatty acids.

-2**Monoacylglycerols and glycerols:** Monoacylglycerol is packaged in micelles and moves across the apical membrane through passive diffusion. In the enterocyte, monoacylglycerols are combined with long-chain fatty acids to form triglycerides and are secreted in chylomicrons.

-3Glycerol is absorbed directly across the enterocyte. After glycerol exits the basolateral membrane of the enterocyte into the interstitial space, it can then diffuse directly into the portal circulation.

-4Cholesterols: Cholesterol esters are also packaged in micelles and released just prior to the enterocyte. Cholesterol esters appear to both diffuse through and be transported across the apical membrane.

One of these transporters is NPC1L1 (Niemann-Pick C1 like1), the pharmacologic blockade of which decreases cholesterol uptake and lowers circulating levels of cholesterol in some patients. In the enterocyte, cholesterol esters are esterified, packaged into chylomicrons, and secreted.

Lysolecithins: Phospholipids are also packaged in micelles, released just prior to the enterocyte ، and move across the apical membrane through passive diffusion. In the enterocyte, phospholipids are esterified into lysolecithin, packaged into chylomicrons, and secreted into the interstitial space to be picked up by the lymphatic system.

Vitamins: Fat-soluble vitamins are incorporated in micelles and absorbed similar to long-chain fatty acids and packaged in chylomicrons. Water-soluble vitamins, with the exception of vitamin B12, are absorbed by Na+ cotransport. Vitamin B12 is absorbed in a four-step process:

First, vitamin B12 is liberated from dietary proteins.

Second, vitamin B12 binds to haptocorrin released from G cells.

Third, pancreatic secretions cause the release of haptocorrin which is how intrinsic factor binds vitamin B12. Intrinsic factor is released from parietal cells.

Fourth the intrinsic factor/vitamin B12 complex is absorbed by phagocytosis in the ileum.

Vitamin	Solubility	Function	Deficiency
Biotin	Water	Metabolism	Unknown
Folate	Water	Metabolism; blood cells	Anemia
Niacin	Water	Metabolism; blood cells	Pellagra
Pantothenic acid	Water	Metabolism	Unknown
Riboflavin	Water	Metabolism	Cheilosis
Thiamin	Water	Metabolism	Beriberi
Vitamin A	Fat	Antioxidant; vision; proteins	Blindness
Vitamin B6	Water	Metabolism; blood cells	Anemia
Vitamin B12	Water	Metabolism; blood cells	Anemia; nerve damage
Vitamin C	Water	Collagen; antioxidant	Scurvy
Vitamin D	Fat	Proteins	Rickets; osteomalacia
Vitamin E	Fat	Antioxidant	Anemia
Vitamin K	Fat	Blood cells	Poor clotting

Minerals: Divalent ions)Ca2+, Mg, 2+Fe2+, Cu2+, and Zn2+) are absorbed in the small intestine.

Mineral	Functions
Calcium	Bone and teeth; cell excitability; blood clotting
Chloride	Cell excitability
Copper	Enzyme cofactor; collagen
Iron	Metabolism; oxygen binding; collagen
Iodine	Hormone synthesis
Magnesium	Metabolism
Phosphorus	Bone and teeth; energy storage; cell signaling
Potassium	Cell excitability
Sodium	Cell excitability
Zinc	Enzyme cofactor

Water absorption

The small intestine is the site of the majority of water absorption, nearly .%80The majority of this absorption occurs via osmosis because of the apical transport of NaCl from the intestinal lumen.

The large intestine

is comprises the cecum; ascending, transverse, descending, and sigmoid colon; rectum; and anus. The large intestine plays a lesser role in digestion compared to the small intestine but is intricately

involved in ion and water absorption.

Motility:

Prime functions of the large intestine. There are three main movement patterns in the large intestine:

-1Segmentation (haustra) contract smaller segments which are seen as the beadlike appearance of the large intestine. This contractions increase the opportunity for contact between the luminal contents and intestinal epithelium, thereby allowing ion and water removal.

-2Peristalsis

3- Mass movement contractions.

Both peristalsis and mass movement contractions perform propel chyme forward. A massive peristaltic wave that results in a significant chyme movement along the large intestine.

Ileocecal sphincter: The ileocecal sphincter prevents backflow from the large to small intestine.

Ileum distention and irritation ⟶ initiates ileum peristalsis and relaxes the sphincter.

cecum distention and irritation ⟶ inhibits peristalsis and contracts the sphincter.

This response is known as the gastroileal reflex and is likely controlled by gastrin and CCK.

Anal sphincters: The anus comprises two sphincters:

-1The internal sphincter is composed of smooth muscle.

-2The external sphincter is composed of skeletal muscle that is under somatic control innervated by the pudendal nerve.

Defecation: is a multistep process involving both sphincters as well as both enteric and somatic regulation. Peristaltic waves from the large intestine forces feces from the rectum toward the anus and then voluntarily relax the external sphincter in order to pass the feces.

Absorption:

.1Electrolytes: Na + and water are absorbed via endothelial Na^+ channels in the distal colon. The capacity for water absorption can be increased twofold during hypohydrated states (e.g., when there is an aldosterone-mediated increase in Na transport that allows for more water to be osmotically absorbed). Cl^- crosses, the apical membrane by Cl^--$HCO3^-$ exchangers. K^+ is passively secreted in the distal colon. Active secretion can also occur by the insertion of apical K^+ channels in the large intestine with increased concentration of aldosterone or certain second messengers.

.2Short-chain fatty acids: Short-chain fatty acids are transported across the apical membrane to be used by colonic epithelial cells as an energy substrate.