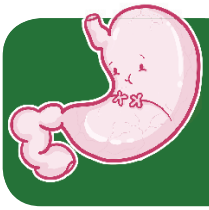

NOTES
DIGESTION & ABSORPTION

DIGESTION & ABSORPTION

- *Digestion:* breakdown of large food molecules into monomers for absorption in gastrointestinal (GI) tract
- Chemical digestion accomplished by enzymes secreted into alimentary canal by glands

Mechanical digestion

- Mastication
  - Mouth ingests food, begins mechanical, chemical digestion (mastication, salivation), initiates propulsion by swallowing
  - Partly voluntary, partly reflexive (e.g. stretch reflexes, pressure inputs)

Deglutition (swallowing)

- Movement of food from mouth to stomach
- *Buccal phase:* voluntary
  - Occurs in mouth
  - Tongue pushes against hard palate forcing food bolus into oropharynx
- *Pharyngeal-esophageal phase:* involuntary
  - Controlled by brainstem swallowing center
  - Cranial nerves (mainly Vagus) activate muscles of pharynx, esophagus
  - Soft palate rises, closes nasopharynx, epiglottis covers larynx, upper esophageal sphincter relaxes → peristalsis moves food through pharynx, esophagus → gastroesophageal sphincter relaxes allowing food to enter

Two absorption pathways

- *Cellular pathway:* substance crosses apical/luminal membrane to enter intestinal epithelial cell, then crosses basolateral membrane to enter into blood
- *Paracellular pathway:* move across tight junctions between intestinal epithelial cells to enter blood
- Absorptive surface maximized by villi, microvilli, folds (folds of Kerckring) in small intestine
  - Most digestion occurs in duodenum, least amount of digestion occurs in ileum (as reflected by length of villi - longest villi in duodenum, shortest in ileum)
  - *Brush border:* surface of microvilli containing digestive enzymes

HYDRATION

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- Total body water
  - Intracellular fluid (inside cells) + extracellular fluid (outside cells—e.g. blood, interstitium)
- Water functions
  - Bodily secretions, digestion, detoxification (urination), thermoregulation (sweating)
- Total body water balanced by intake, elimination

Water intake

- Water ingested in fluid/food form
  - 80% → fluid; 20% → food
- Bloodstream absorption in small, large intestines

Water loss

- Breathing; sweating; urinating, defecating

DEHYDRATION

- Occurs when water loss > water intake
- Causes
  - Vigorous exercise, decreased oral intake, dry air, vomiting, diarrhea, excessive sweating, inability to swallow, diuretics
- Symptoms
  - Thirst, dry mouth/lips, nausea, fatigue, lightheadedness, darkened/decreased urine
- High risk groups
  - *Children:* lower stores of water, ↑ surface area to body mass, thirst sensors not fully developed, depend on caregivers
  - *Elderly:* decreased thirst sensation, medication, chronic diseases affecting kidneys

CARBOHYDRATES & SUGARS

osms.it/carbohydrates-and-sugars

DIGESTION

Mouth

- Begins carbohydrate digestion
- *Enzyme:* salivary alpha amylase
  - Starts starch digestion → dextrins, maltose, maltotriose

Stomach

- Salivary amylase inactivated
- Relatively no breakdown of starch

Small intestine

- Majority of carbohydrate digestion
- Enzymes include
  - *Pancreatic amylase:* digests starch → disaccharides; hydrolyzes interior 1,4-glycosidic bonds in starch yielding disaccharides
  - *Intestinal brush border enzymes:* digest oligosaccharides, disaccharides → lactose, maltose, sucrose → galactose, glucose, fructose; e.g. dextrinase, maltase, glucoamylase, lactase, sucrase

ABSORPTION

- *Primary site of absorption:* small intestine

Pathway of absorption

- *Glucose, galactose:* absorbed into enterocytes via sodium ion cotransport (secondary active transport) → GLUT2 transporter extrudes glucose, galactose across basolateral membrane into blood

- *Sodium-glucose cotransporter (SGLT1):* moves glucose inside enterocytes against electrochemical gradient using ATP created from sodium gradient created by sodium-potassium ATPase on the basolateral membrane
- *Fructose:* absorbed into enterocytes via facilitated diffusion by GLUT5 transporter in apical membrane → GLUT2 transporter extrudes fructose across basolateral membrane into blood; fructose absorption cannot occur against electrochemical gradient
- Monosaccharides leave epithelial cells via facilitated diffusion → enter villi capillaries → hepatic portal vein → liver

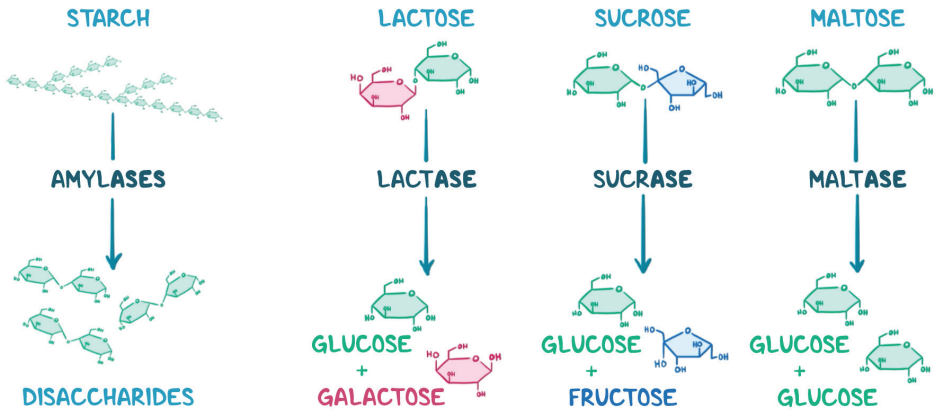

Figure 39.1 Overview of the actions of some of the enzymes involved in carbohydrate digestion.

PROTEINS

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- Proteins can be absorbed in the form of amino acids, dipeptides, or tripeptides (as opposed to carbohydrates)

DIGESTION

- Proteins → large polypeptides → smaller polypeptides/peptides → individual amino acids/dipeptides/tripeptides

Stomach

- *Gastric pepsin (with HCl):* digests proteins → large polypeptides
  - Protein digestion starts with gastric pepsin
  - Secreted by chief cells, activated by low pH
- *Proteases* (endopeptidases, exopeptidases)
  - *Endopeptidases:* trypsin, chymotrypsin, pepsin; hydrolyze interior peptide bonds (pepsin, trypsin, chymotrypsin)
  - *Exopeptidases:* hydrolyze individual individual amino acids from carboxyl end (carboxypeptidases A, B)

Small intestine

- Pancreatic, intestinal brush border enzymes continue digestion
- Pancreatic enzymes
  - *Zymogens:* trypsinogen, chymotrypsinogen, procarboxypeptidase A, B
  - *Active forms:* trypsin, chymotrypsin, carboxypeptidase
  - Enterokinase activates trypsinogen → trypsin → trypsin autocatalyzes itself, activates additional pancreatic zymogens

- Digest large polypeptides → small polypeptides/peptides
- Intestinal brush border enzymes
  - Dipeptidase, aminopeptidase, carboxypeptidase
  - Digest small polypeptides/peptides → amino acids/dipeptides/tripeptides

ABSORPTION

- *Site of absorption:* small intestine

Pathway of absorption

- *Amino acids:* absorbed via cotransport with sodium ions or facilitated diffusion out of epithelial cells → enter villi capillaries → hepatic portal vein → liver
  - Four separate transporters one each for neutral, acidic, basic amino acid
- *Dipeptides, tripeptides:* absorbed into enterocytes via cotransport with protons → broken down into amino acids/transcytosis

NUCLEIC ACID DIGESTION & ABSORPTION

- Nucleic acids → pentose sugars, nitrogen-containing bases, phosphate ions
- *Site of digestion:* small intestine only
- Enzymes
  - Pancreatic ribonuclease, deoxyribonucleases
  - Intestinal brush border enzymes (nucleosidases, phosphatases)
- *Site of absorption:* small intestine
- *Absorption pathway:* active transport into enterocytes by membrane carriers → villi capillaries → hepatic portal vein → liver

FATS

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- Unemulsified triglycerides → monoglycerides/diglycerides, fatty acids
- *Site of digestion:* mouth, stomach, small intestine
- Lipid digestion begins with lingual, gastric lipases hydrolyzing triglycerides → glycerol, fatty acids
  - CCK slows gastric emptying, allowing adequate time for pancreatic enzymes to work
- Pancreatic enzymes (pancreatic lipase, cholesterol ester hydrolase, phospholipase A2), colipase finish digestion in small intestine
  - Bile salts, lysolecithin surround, emulsify dietary lipids to create large surface area for pancreatic enzymes
  - Pancreatic lipase secreted as active enzyme, hydrolyzes triglyceride → monoglyceride + 2 fatty acids
  - Colipase (secreted as inactive procolipase, activated by trypsin) binds to pancreatic lipase protecting it from being inactivated by bile salts

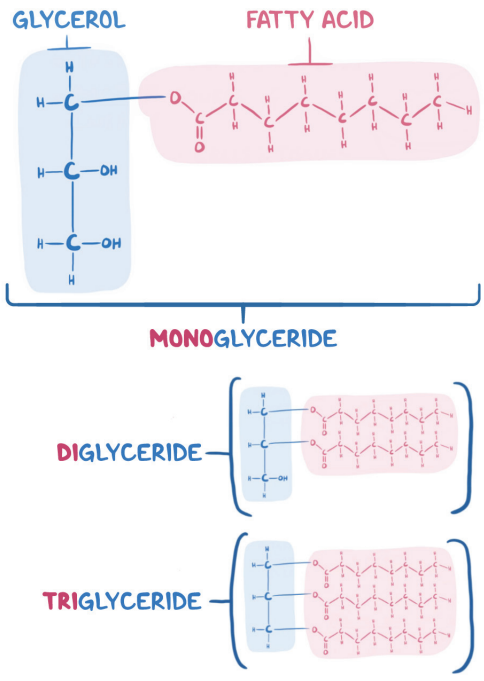

Figure 39.2 Fats are comprised of glycerol backbone and one or more fatty acid chains. A few examples of fats shown above.

- Cholesterol ester hydrolase (secreted as active enzyme) hydrolyzes cholesterol ester → free cholesterol, fatty acids; hydrolyzes triglycerides → glycerol
- Phospholipase A2 (secreted as proenzyme, activated by trypsin) hydrolyzes phospholipids → lysolecithin, fatty acids

- *Final products of lipid digestion:* monoglycerides, cholesterol, glycerol, fatty acids, lysolecithin
  - Since products are hydrophobic (except glycerol),must be solubilized in micelles before transport to enterocyte apical membrane for absorption
  - *Micelles:* products of lipid digestion surrounded by bile salts
- *Site of absorption:* small intestine

Pathway of absorption

- Fatty acids, monoglycerides absorbed via
  - Diffusion
  - Fatty acids, monoglycerides leave micelles → enter epithelial cells → triglyceride formation → chylomicrons formation (fat globules plus surface apoproteins) → chylomicrons enter lacteals → lymph in lacteal transports chylomicrons into systemic circulation
- Apoproteins are essential for absorption of chylomicrons (specifically Apo B)
- Short chain fatty acids diffuse into villi capillaries → hepatic portal vein → liver

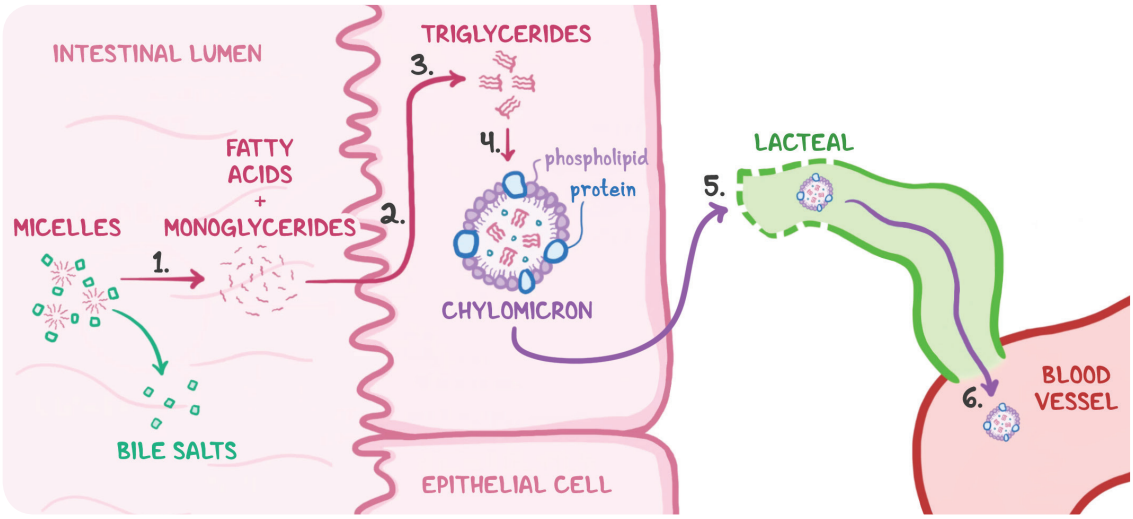

Figure 39.3 Overview of the fat absorption pathway.
1. Fatty acids and monoglycerides leave micelles and
2. enter epithelial cells.
3. They form triglycerides.
4. Chylomicrons containing the fats are then formed.
5. The chylomicrons enter lacteals, and
6. are transported into systemic circulation.

VITAMINS

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- With the exception of vitamin K, which is produced by intestinal bacteria, vitamins are not synthesized in body therefore must be attained by diet

Fat soluble (Vitamins A, D, E, K)

- *Location:* small intestine
- *Mechanism:* incorporated into micelles along with products of lipid digestion, absorbed into enterocytes

Water-soluble (B vitamins, vitamin C, biotin, folic acid, nicotinic acid, pantothenic acid)

- *Location:* ileum
- *Mechanism:* cotransport with sodium (need intrinsic factor) except vitamin B_{12} (cobalamin)
- Vitamin B_{12}
  - Requires intrinsic factor
  - *Pathway:* ingestion → stomach acidity releases B_{12} from its food carrier proteins → free vitamin B_{12} binds to haptocorrin (R proteins) secreted by salivary glands (protects B_{12} from acid degradation) → pancreatic proteases degrade R proteins in duodenum → B_{12} binds to intrinsic factors (secreted by gastric parietal cells) to protect it from pancreatic enzymes → intrinsic factor-B_{12} complex resistant to degradation from pancreatic enzymes → absorbed in ileum

Absorption of calcium

- Active form of vitamin D, 1,25-dihydroxycholecalciferol, required for calcium absorption
- Dietary vitamin D_3 (cholecalciferol) is inactive
- Cholecalciferol → 25-hydroxycholecalciferol (inactive) in liver → 1,25-dihydroxycholecalciferol in kidney by 1alpha-hydroxylase → synthesizes calbindin D-28K (vitamin D-dependent calcium binding protein → promotes calcium absorption from small intestine
- *Decreased by:* oxalic acid, tannins, magnesium, phosphorus, phytates
- *Increased by:* acidic conditions in intestine, vitamin D, estrogen, lactose
- *Location:* small intestine (primarily duodenum)
- *Mechanism:* vitamin D-dependent calcium binding protein

Absorption of iron

- *Location:* small intestine
- *Mechanism:* ferric state (Fe^{3+}) reduced → to ferrous state (Fe^{2+}) → binds apoferritin in enterocytes → transported across basolateral membrane → binds to transferrin in blood → transferrin carries to liver

The absorptive state: hormones

- Digested nutrients enter blood stream from intestines → blood glucose rises → stimulation of pancreatic insulin release → body cells increase glucose uptake reducing blood glucose concentration back to normal
- Hepatocytes
  - Excess glucose → glycogen for storage via glucose-6-phosphate intermediate
  - Amino acids → ketone bodies (converted to acetyl CoA if needed later)
- Myocytes
  - Excess glucose → glycogen for storage via glucose-6-phosphate intermediate
  - Amino acids → actin, myosin → muscle fibers
- Adipocytes store excess lipids increasing fat reserves

INTESTINAL FLUID BALANCE

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- Along with nutrient digestion, GI tract re-absorbs large amounts of fluid, electrolytes (Na^+, Cl^-, HCO_3^-, K^+)
- Small, large intestine together absorb approximately 9L/2.38 gallons daily
  - Diet → 2L/0.44 gallons; pancreatic, biliary, intestinal secretions → 7L/1.85 gallons
  - Approximately 100–200mL /0.03–0.06 gallons) excreted in feces
  - Absorptive mechanisms disrupted → diarrhea (enormous potential body-water, electrolyte loss)

Villi

- Line intestinal epithelial cells
  - *First step:* solute absorbed; *second step:* water follows
  - Fluid absorbed = isosmotic (water, solute absorption: parallel proportions)
  - Similar to renal proximal tubule
  - Absorptive mechanisms vary by intestinal part

Jejunum

- Major site of Na^+ absorption
  - Enters epithelial cell → Na^+-dependent coupled transporters on apical membrane (Na^+-monosaccharide cotransporters (Na^+-glucose/ Na^+-galactose), Na^+-amino acid cotransporters, Na^+-H^+ exchanger)
  - Translocates across basolateral membrane via Na^+-K^+ ATPase
  - H^+ source (for Na^+-H^+ exchanger) = intracellular CO_2 + H_2O → carbonic anhydrase converts to H^+, HCO_3^- → H^+ secreted into lumen → blood absorbs HCO_3^- ("alkaline tide")

Ileum

- Same transporters as jejunum + Cl^--HCO_3^- exchanger on apical membrane
- Cl^- transporter in basolateral membrane
- H^+ secreted into lumen + HCO_3^- secreted into lumen (via Cl^--HCO_3^- exchanger; not absorbed into blood) → Cl^--HCO_3^- exchanger, Na^+-H^+ exchanger → net NaCl movement into cell → net NaCl absorption

Colon

- Apical membrane contains Na^+, K^+ channels
- Net Na^+ absorption + K^+ secretion
- Aldosterone induces Na^+ channel synthesis → ↑ Na^+ absorption, secondary to K^+ secretion

Fluid, electrolyte secretion

- Epithelial cells lining crypts of small intestine → secrete fluid, electrolytes (mucus, lubricating fluids assisting in mixing, digestion) → must also be absorbed more distally
- Electrolyte, fluid secretion route
  - *Small intestine:* paracellular route → "leaky" tight junctions (↓ resistance)
  - *Colon:* cellular route → "tight" tight junctions (↑ resistance)
- Electrolyte, fluid secretion mechanism
  - *Apical membrane:* Cl^- channel
  - *Basolateral membrane:* Na^+-K^+-$2Cl^-$ cotransporter (similar to thick ascending loop of Henle)
  - Na^+, K^+, Cl^- ions move into cells from blood → Cl^- diffuses into lumen via Cl^- channel on apical membrane → Na^+ follows Cl^- passively, paracellularly → H_2O secretion follows NaCl secretion
  - Apical Cl^- channels closed in resting state → opens after various hormones/ neurotransmitters (ACh, VIP) bind
  - Bind to basolateral receptor → activate adenylyl cyclase → ↑ cAMP in crypt cells → cAMP opens Cl^- channels
  - Adenylyl cyclase can be maximally activated in cholera → severe, life-threatening diarrhea