Human Phys PCB4701

Lecture 23: Digestion part 1

Anatomy of Digestive System
Peristalsis
Stomach and Acid Secretion
Liver and Bile Secretion

Pancreas and pancreatic juice
Pancreas and glucose regulation (19.3 & 19.4)
Diabetes
GLP-1 agonists

Analysis of Internal Transport in an Organism:

Movement of chemicals from external environment into the body, and between organs of the body.

Tranported Chemicals can be essential metabolic nutrients (O_2, glucose) or toxic waste products (CO_2, N (urea), heme (bilirubin))

1. What is the internal transport system that carries the chemicals from the exchange surface to target tissues? GI tract, circulation, lymphatics
2. What provides & controls the force to move chemicals through the system? peristalsis, segmentation – muscular contraction of tubes themselves
3. What are the exchange surfaces? intestinal villi, capillaries, lacteals
4. How do the chemicals enter/exit the cells of the exchange surface? transporters for glucose, amino acids:
5. How are the chemicals unloaded by the transport system and taken up by the target cells? glucose transporters, etc in liver, muscle

Functions of Digestive System

Motility:
movement of food through GI tract

Secretion:
exocrine secretion of H_20, HCl, HCO_3–, & enzymes
endocrine secretion of several hormones

Digestion:
breakdown of macromolecules to monomers
hydrolysis by enzymes (amylase/sacchridase; peptidases; lipases)

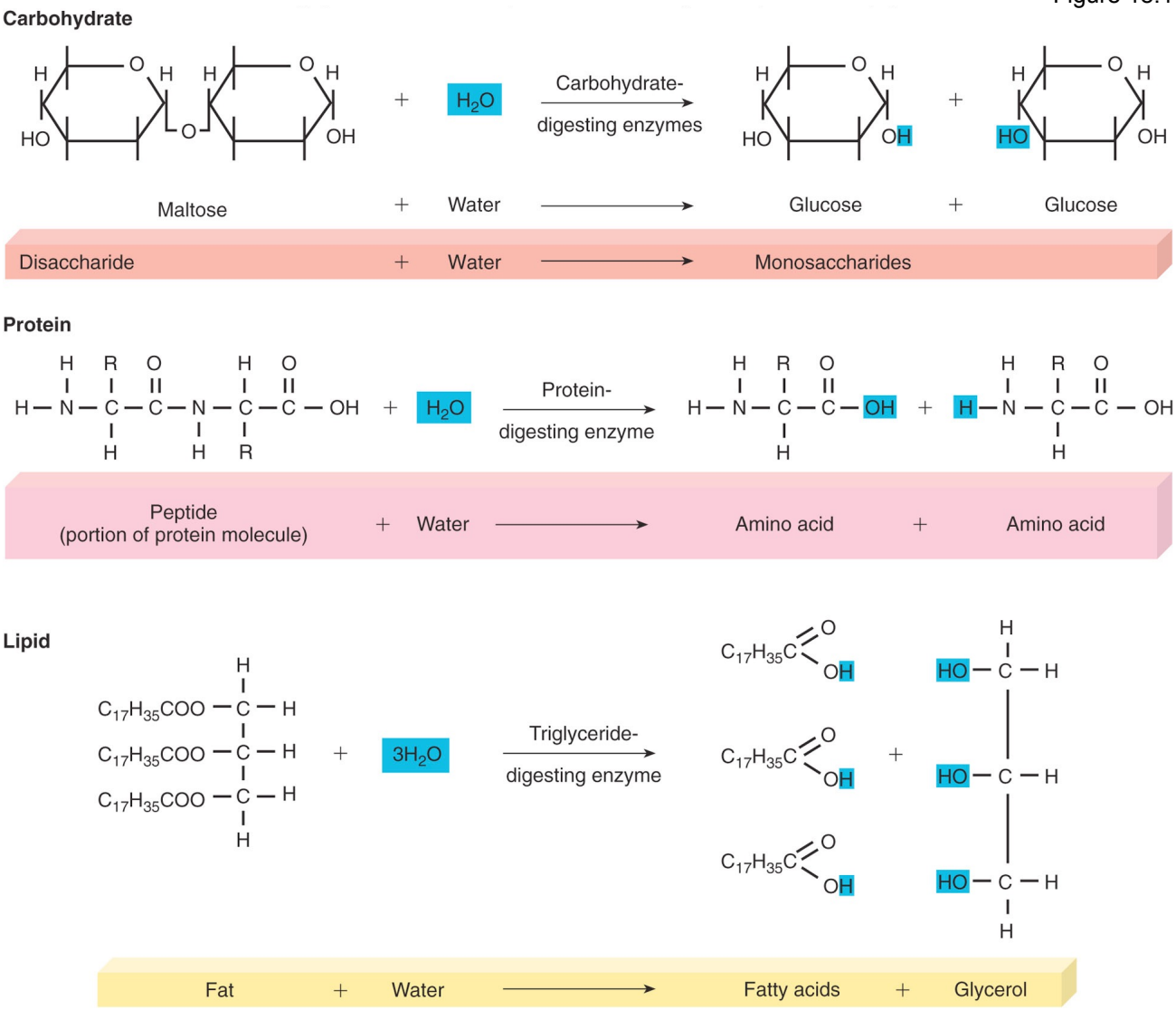
Absorption:
monomers absorbed into blood or lymph;
postabsorptive utilization by tissue or storage (e.g. in liver or fat)

Storage and Elimination

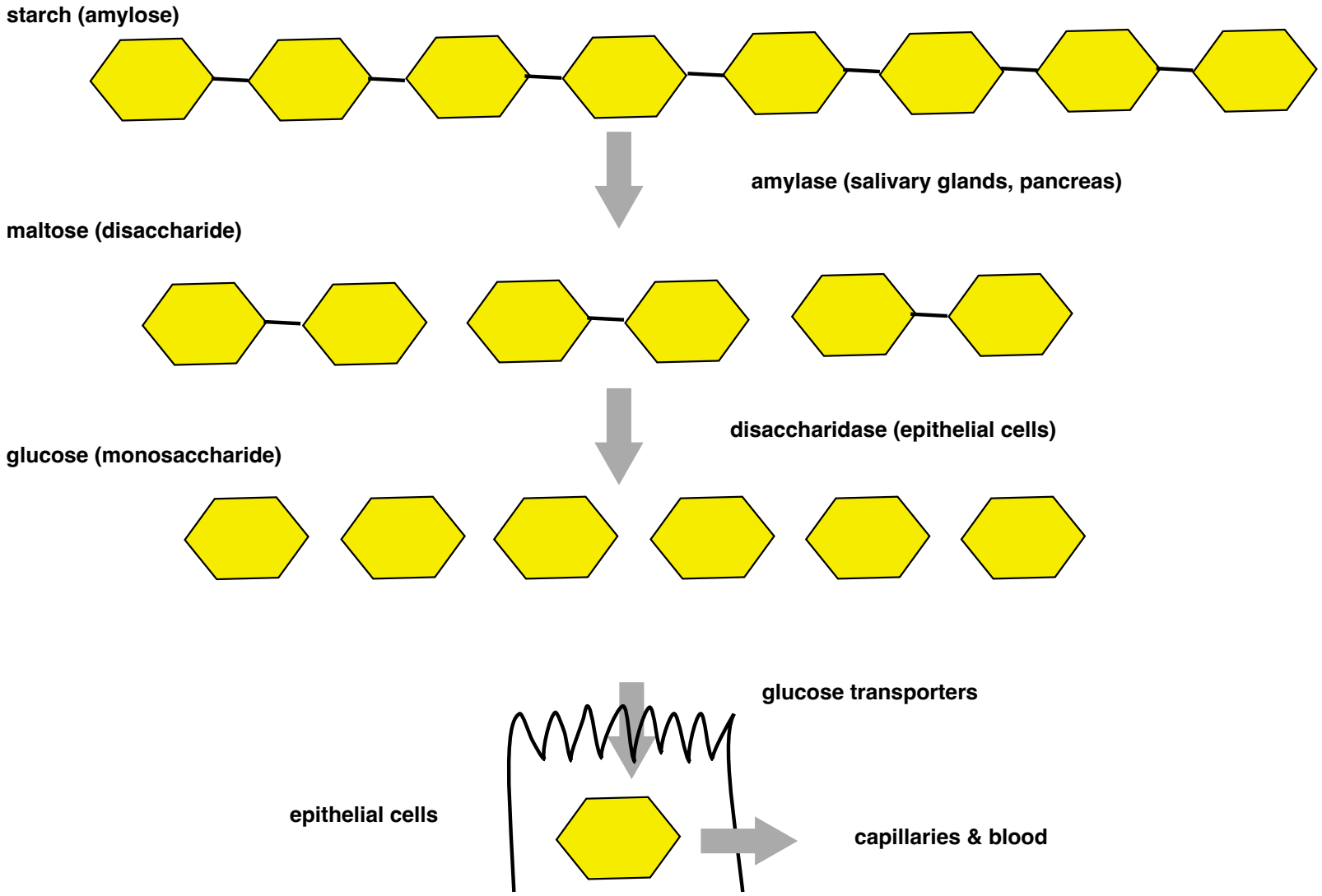
Immune Barrier
because lumen of gut is on "outside" of body

gastrointestinal tract
alimentary canal
gut

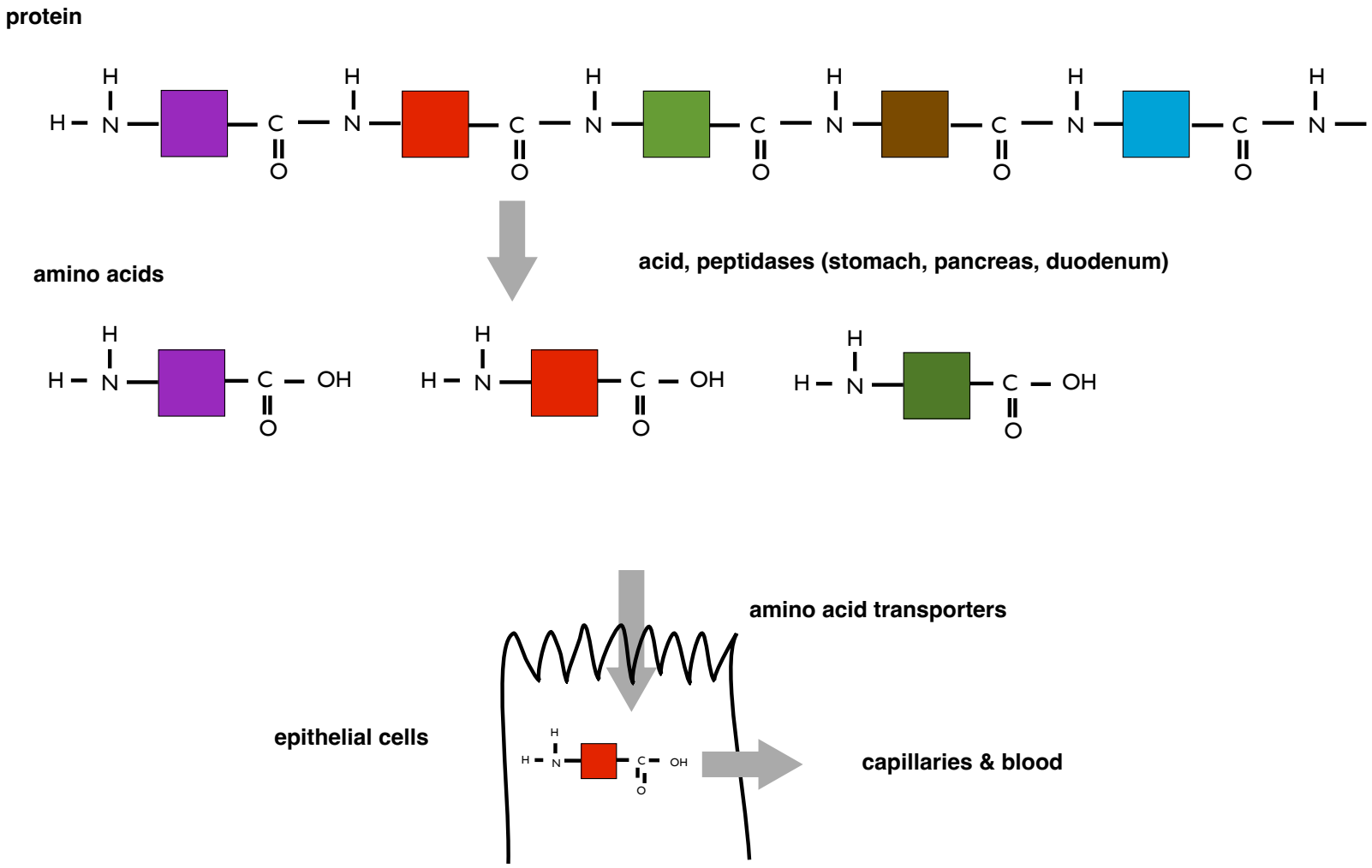
Figure 18.1


Carbohydrate
Carbohydrate-digesting enzymes
Maltose + Water → Glucose + Glucose
Disaccharide + Water → Monosaccharides
Protein
Protein-digesting enzyme
Peptide (portion of protein molecule) + Water → Amino acid + Amino acid
Lipid
Triglyceride-digesting enzyme
Fat + Water → Fatty acids + Glycerol

Carbohydrate digestion



Protein digestion



Lipid

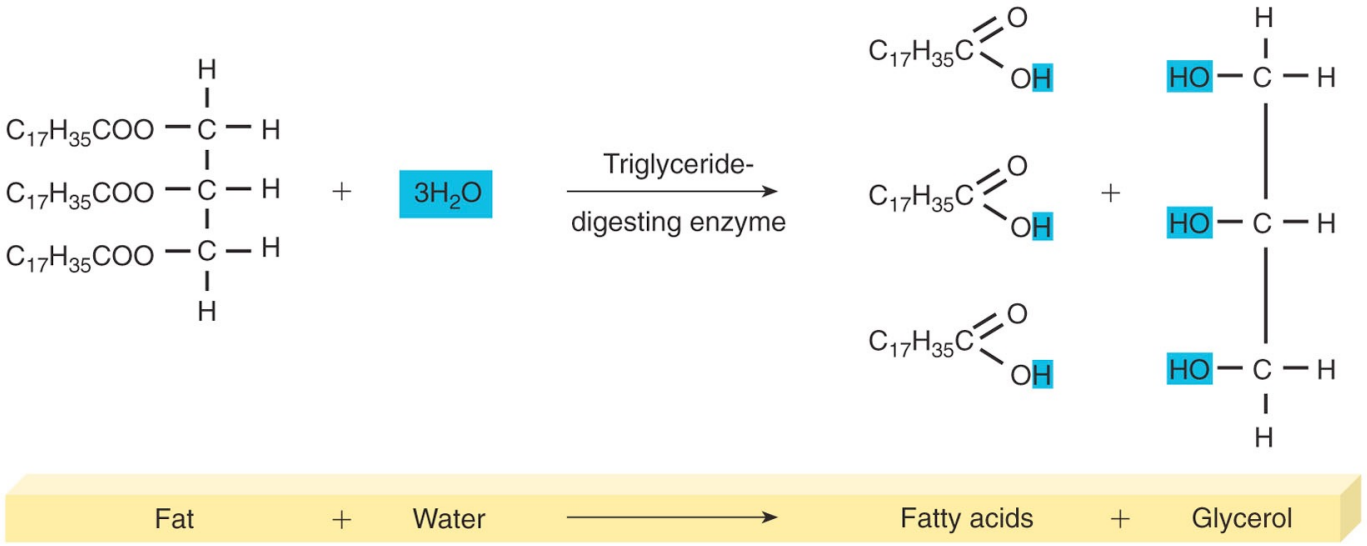
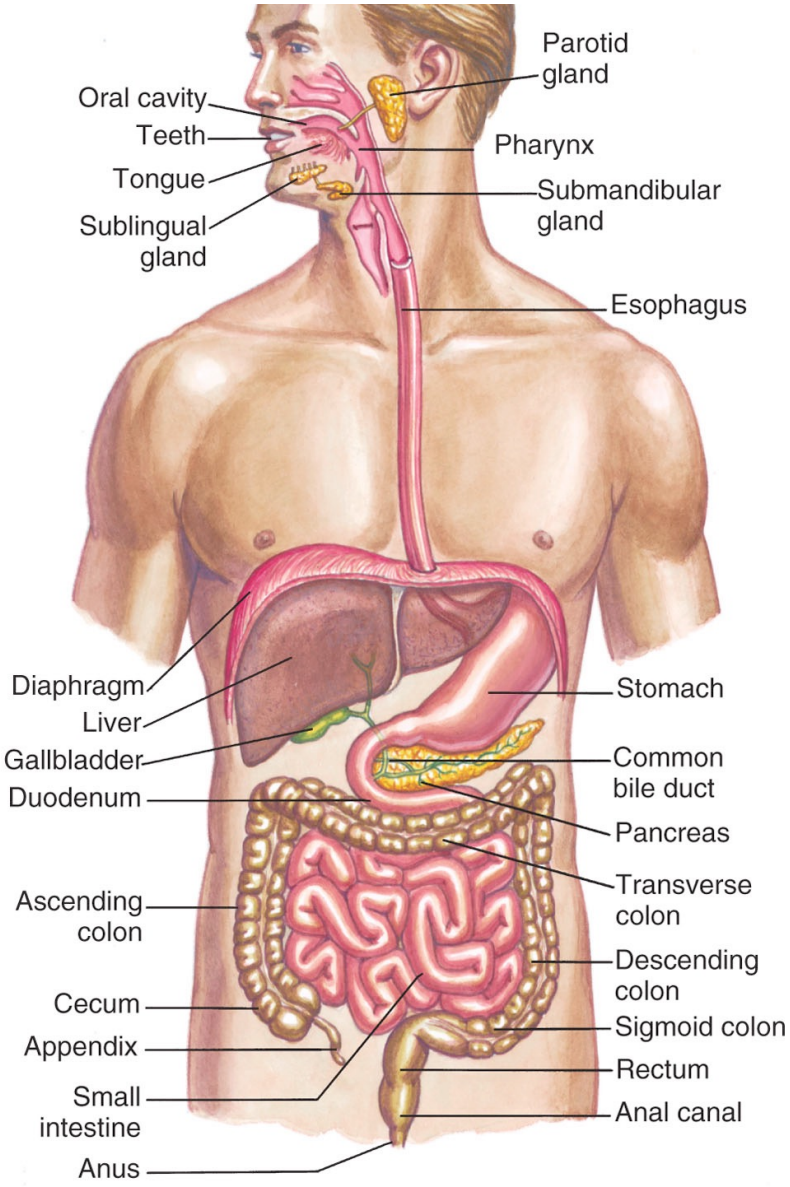
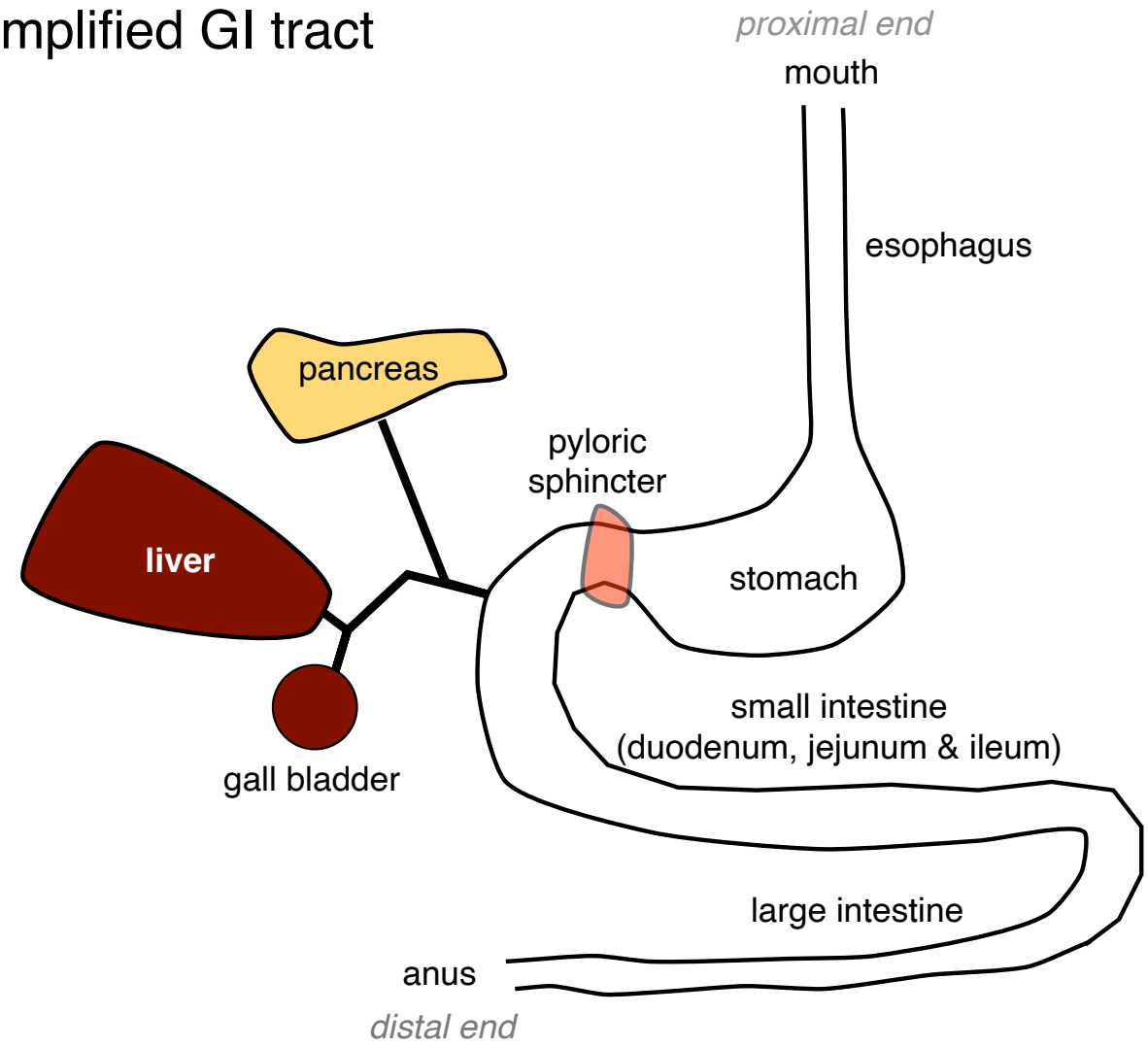

$C_{17}H_{35}COO$
$C_{17}H_{35}COO$
$C_{17}H_{35}COO$
$3H_2O$
Triglyceride-
digesting enzyme
$C_{17}H_{35}C$
OH
HO
Fat
Water
Fatty acids
Glycerol

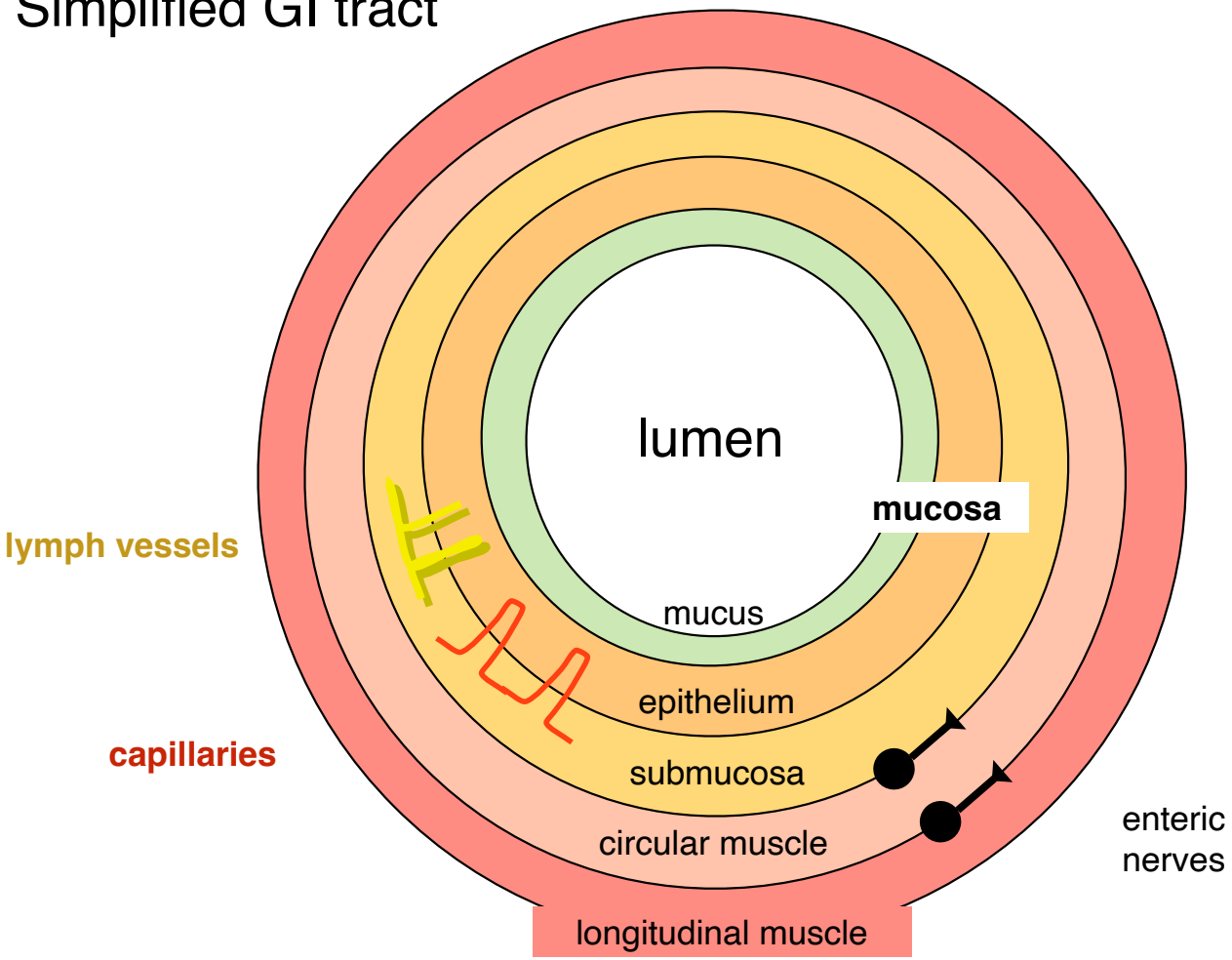
Figure 18.2

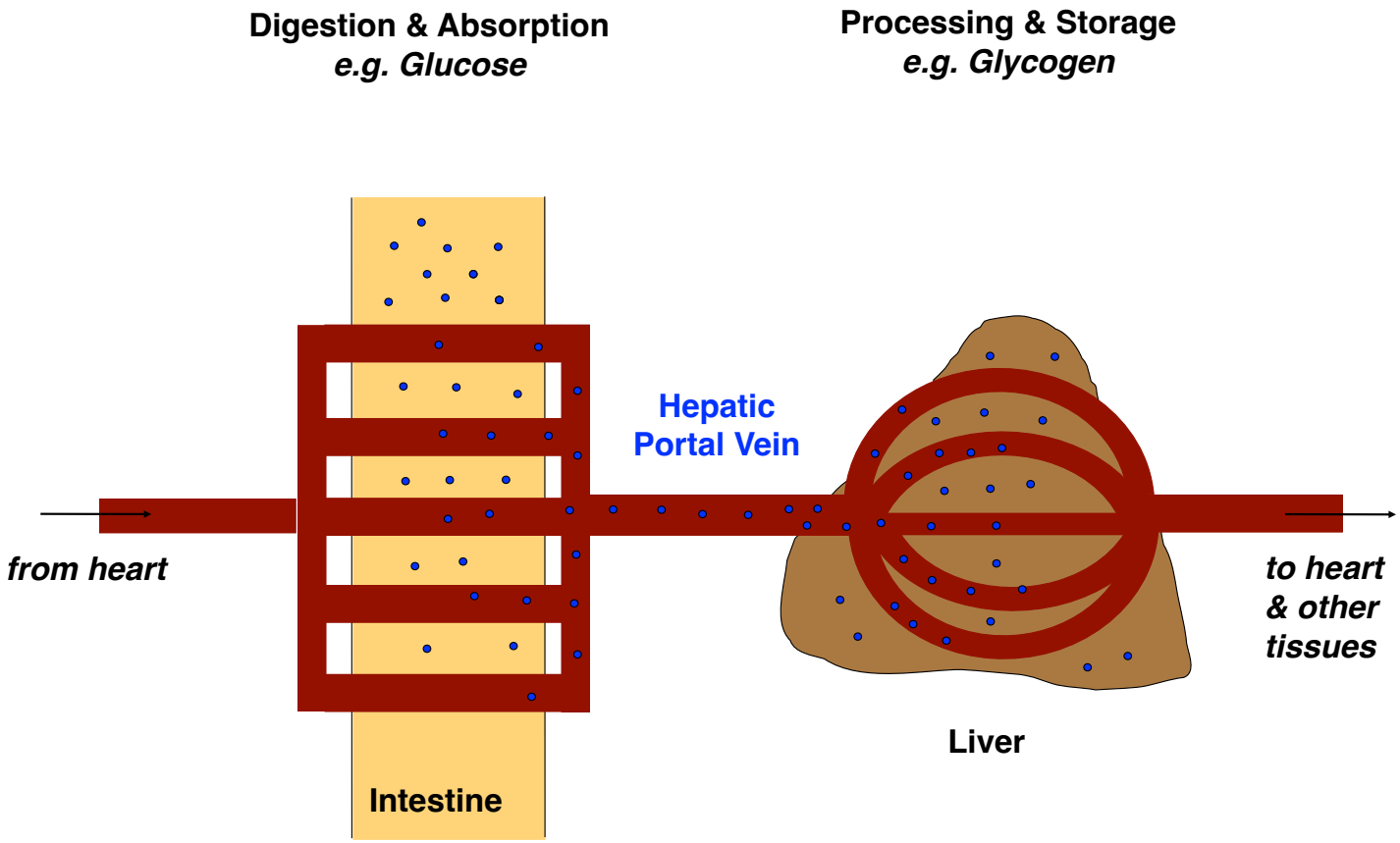

Parotid gland
Oral cavity
Teeth
Tongue
Sublingual gland
Pharynx
Submandibular gland
Esophagus
Diaphragm
Liver
Gallbladder
Duodenum
Stomach
Common bile duct
Pancreas
Transverse colon
Ascending colon
Descending colon
Cecum
Sigmoid colon
Appendix
Rectum
Small intestine
Anal canal
Anus

Simplified GI tract



Simplified GI tract





2 capillary beds for nutrient absorption and storage

Motility: Peristalsis and Segmentation

Peristalsis
Wave of muscular relaxation & contraction in reflex response to stretch of GI wall. Moves food down esophagus and stomach; weaker in intestines.

Segmentation
Rhythmic coordinated contraction of segments of intestine that mixes chyme, mucus, enzymes. Faster at proximal end of intestine; creates pressure that moves food down intestines.

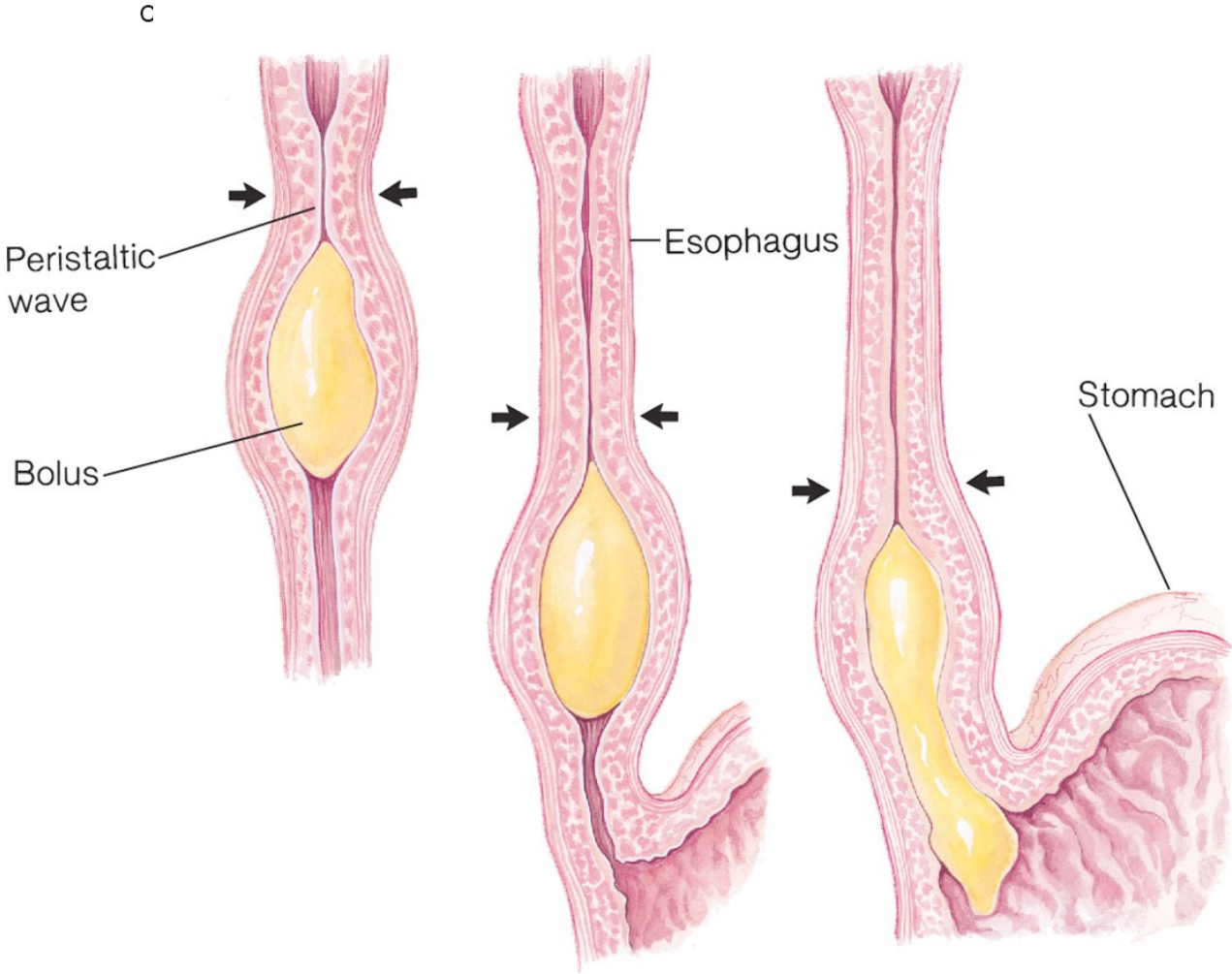
Slow waves are generated by slow pacemaker activity in interstitial cells of Cajal (ICC); depolarizes smooth muscle.

ICC have muscarinic receptors: parasympathetic acetylcholine increases amplitude and duration of slow waves.

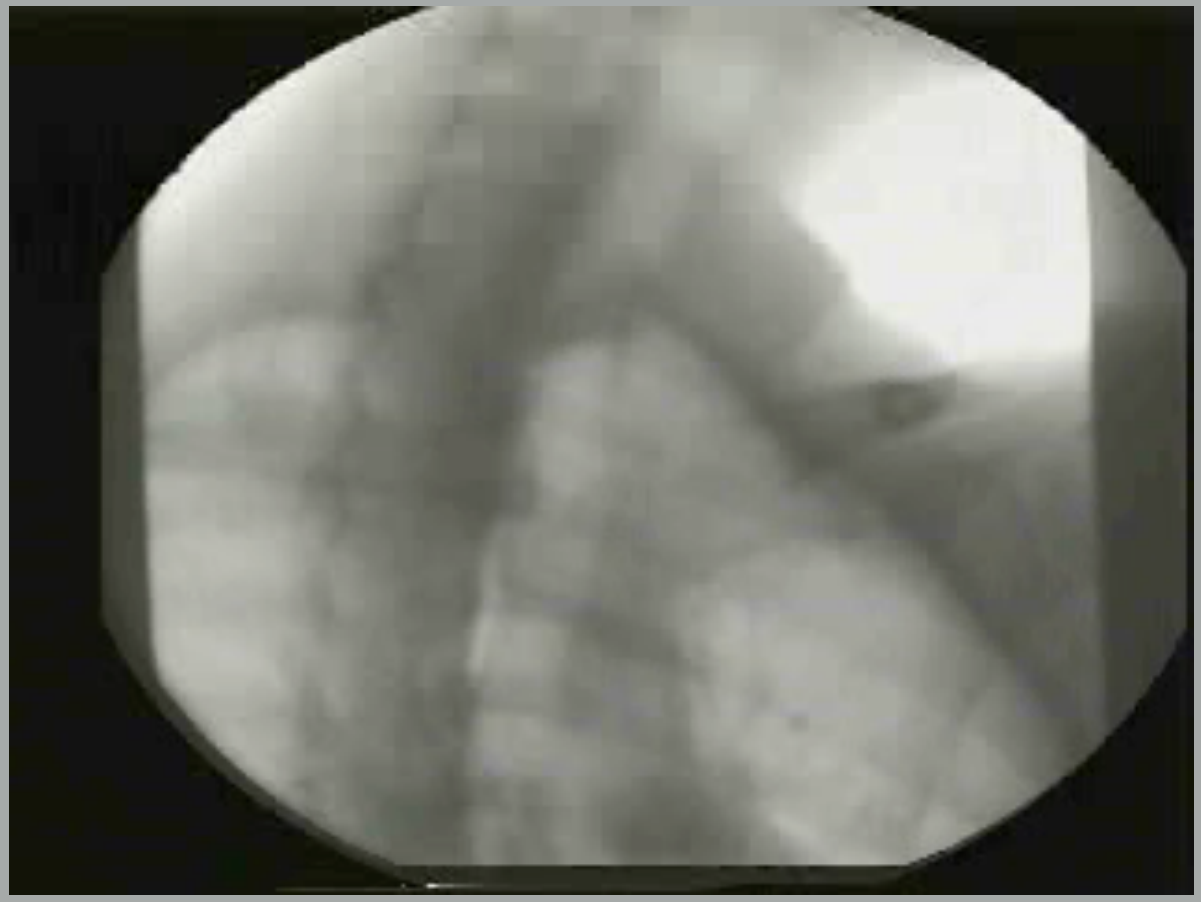
http://www.sciencephoto.com/media/410578/view

Figure 18.4

Peristalsis during swallowing



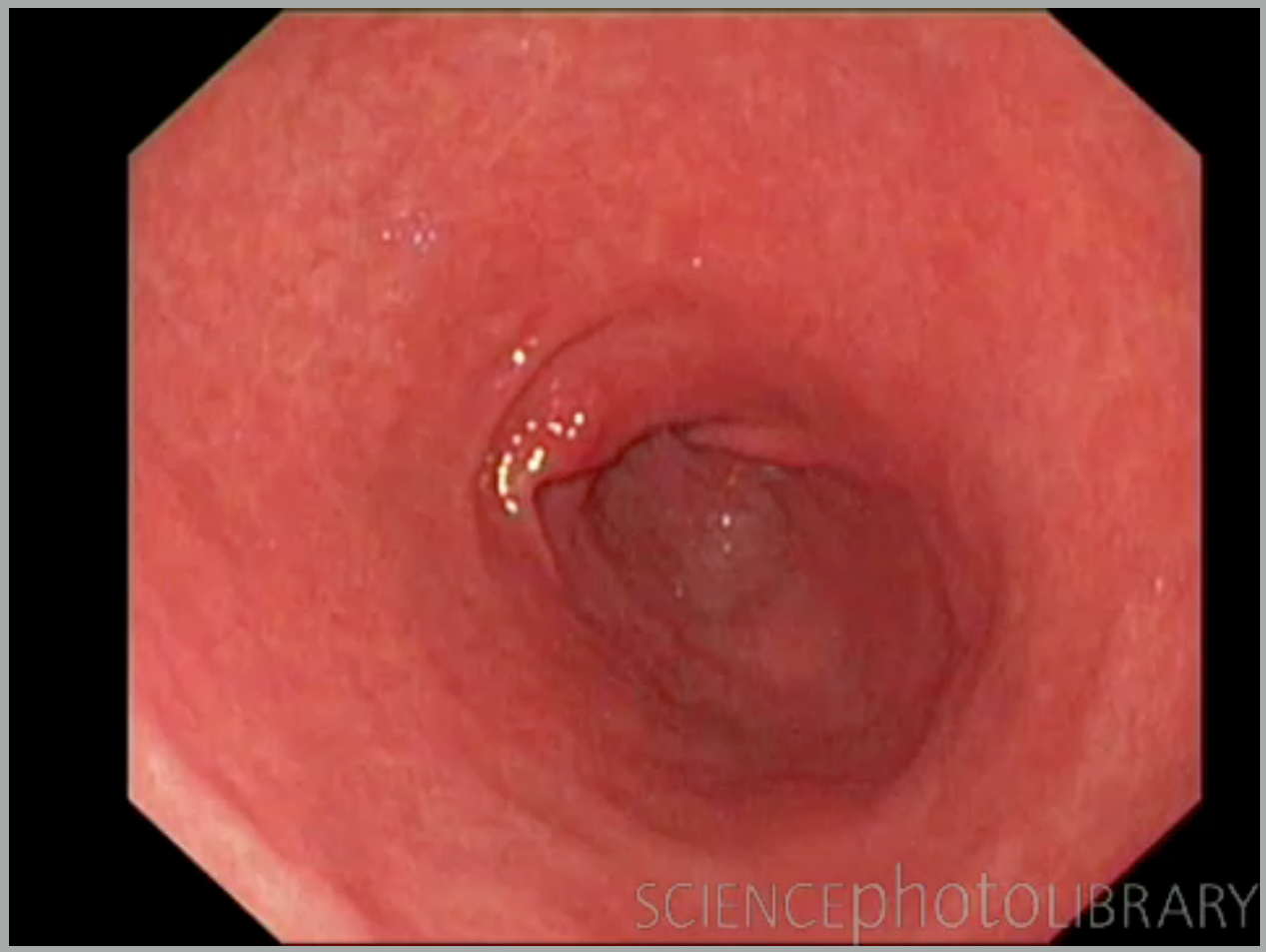
Videofluoroscopy of deglutition and primary peristalsis



The subject swallows a mouthful of barium sulfate, which is then propelled down the esophagus and into the stomach by a peristaltic contraction wave.

Esophageal peristalsis
William G. Paterson
GI Motility online (2006)
doi:10.1038/gimo13

Peristalsis in the stomach, endoscopy



http://www.sciencephoto.com/media/410578/view

Peripheral Nervous System:

Neurons and nerve fibers outside the brain and spinal cord

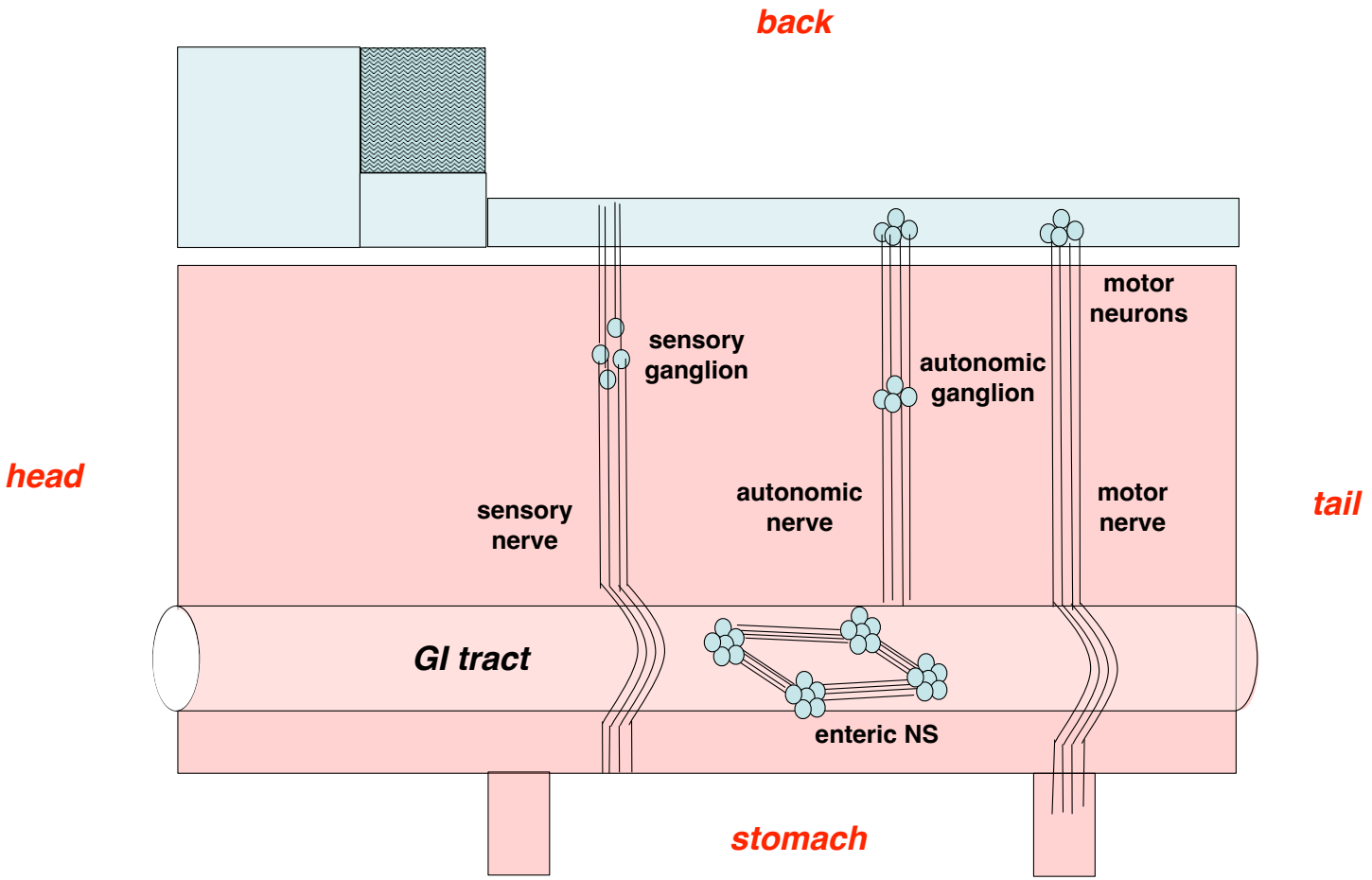
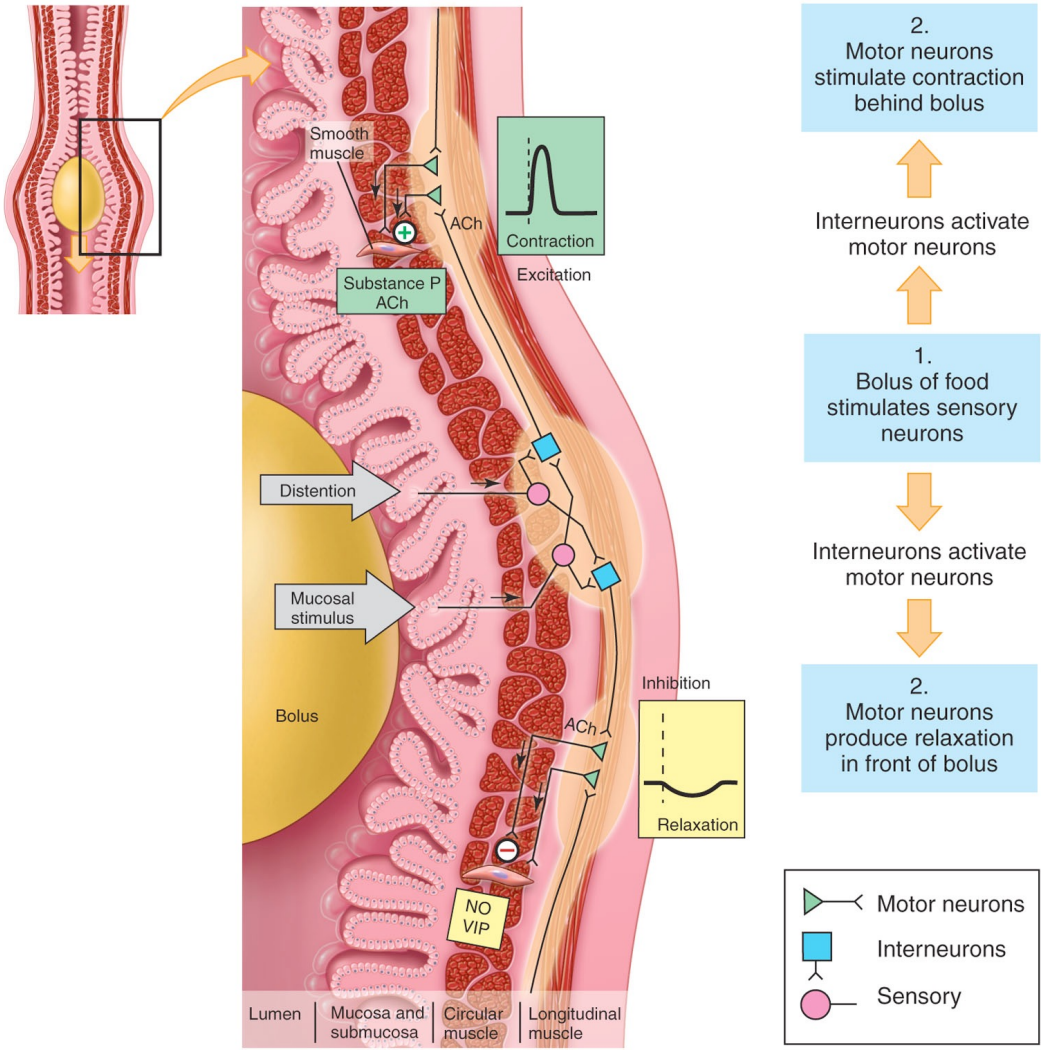
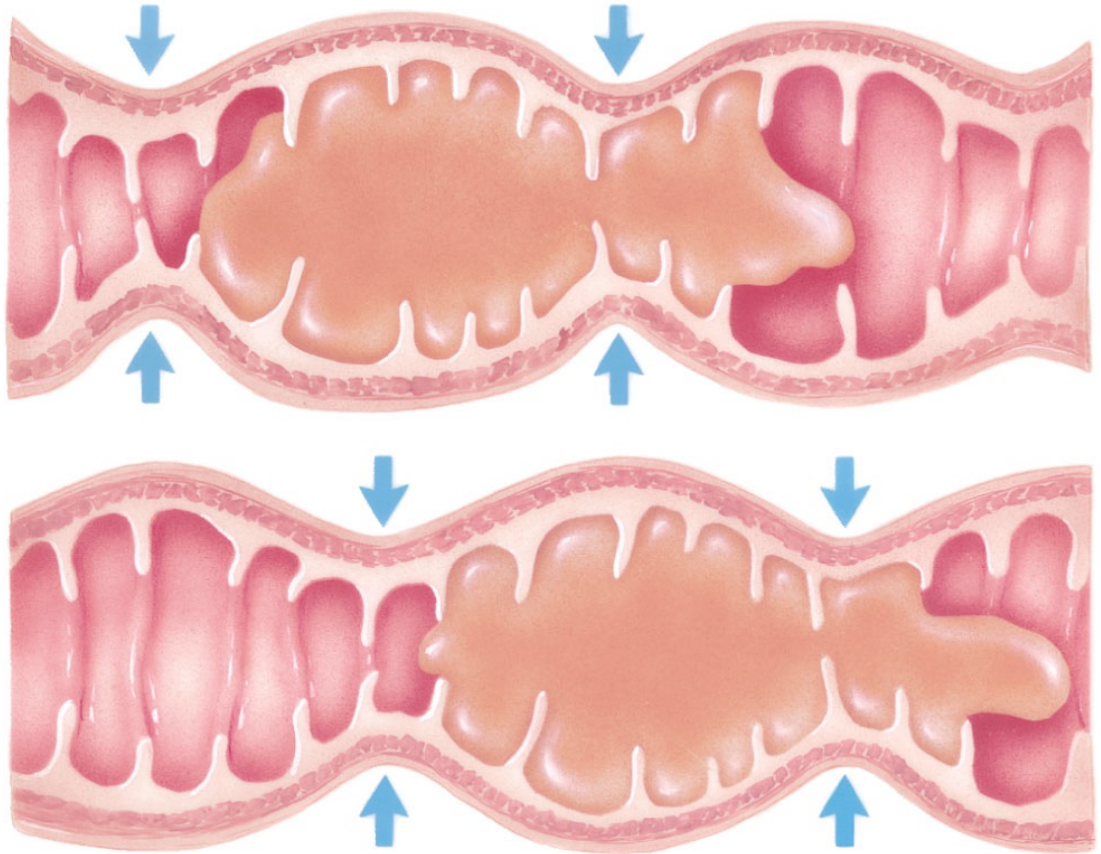


Figure 18.31


Smooth muscle
ACh
Contraction
Excitation
Substance P
ACh
Distention
Mucosal stimulus
Bolus
Inhibition
ACh
Relaxation
NO
VIP
Lumen
Mucosa and submucosa
Circular muscle
Longitudinal muscle
2. Motor neurons stimulate contraction behind bolus
Interneurons activate motor neurons
1. Bolus of food stimulates sensory neurons
Interneurons activate motor neurons
2. Motor neurons produce relaxation in front of bolus
Motor neurons
Interneurons
Sensory

Segmentation

Figure 18.13




Jejunum
© Ehrlein - University of Hohenheim

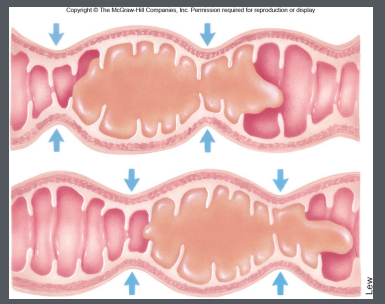

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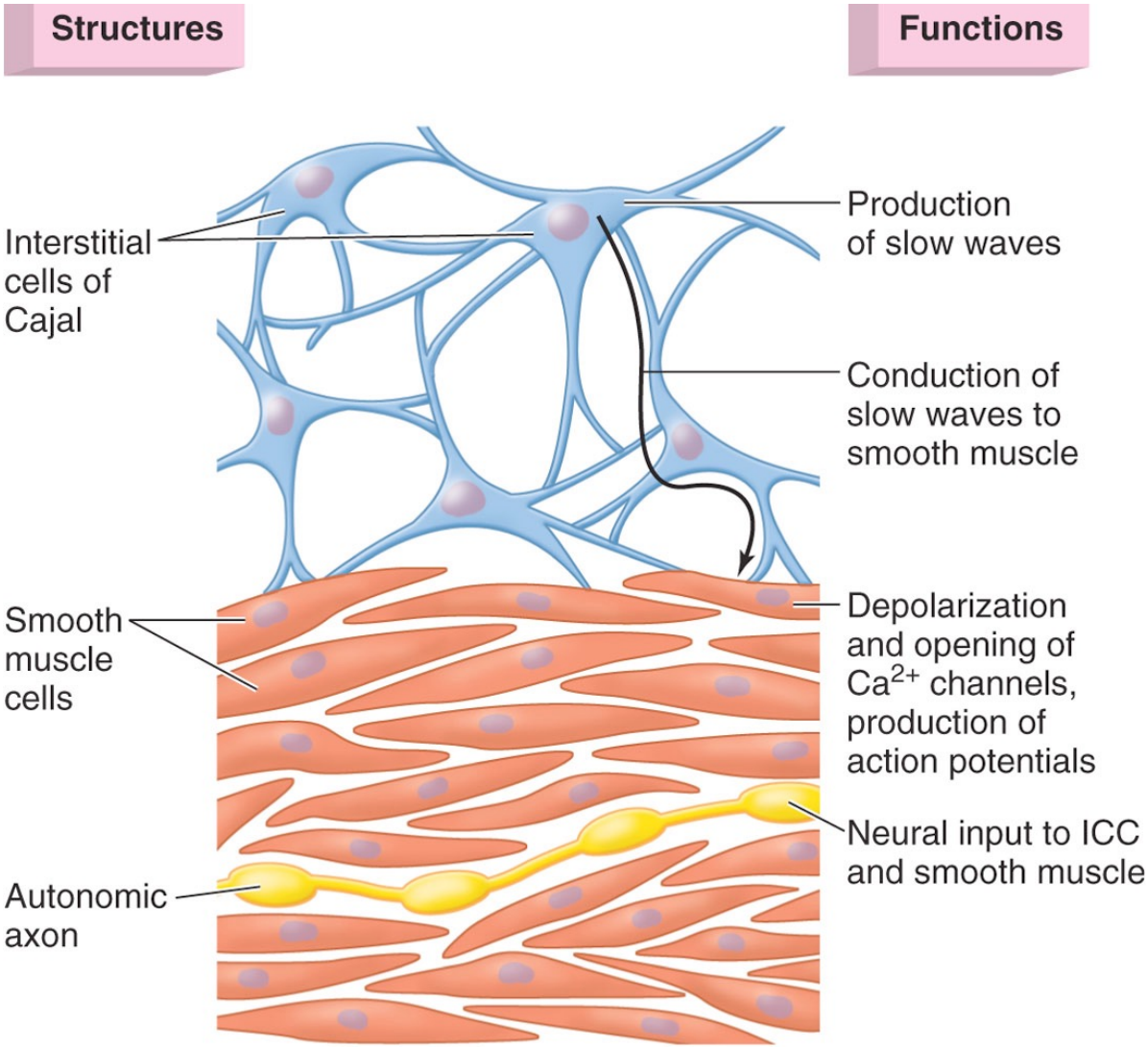
Figure 18.15


Structures
Functions
Interstitial cells of Cajal
Production of slow waves
Conduction of slow waves to smooth muscle
Smooth muscle cells
Depolarization and opening of Ca^{2+} channels, production of action potentials
Neural input to ICC and smooth muscle
Autonomic axon

Pacemaker activity in interstitial cells of Cajal (ICC)

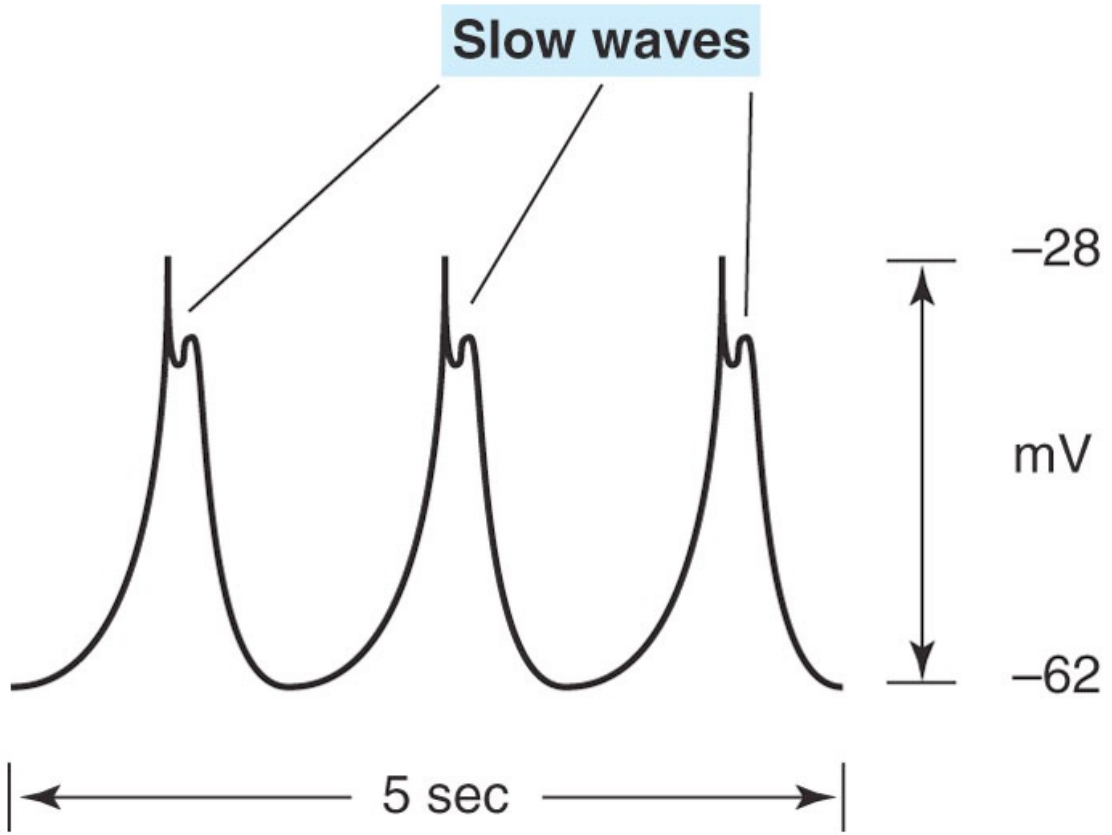


Figure 18.14

Stomach and Acid Secretion

Gastric pits contain **gastric glands**, composed of several cell types including:

parietal cells: secrete **HCl acid**
- carbonic anhydrase converts CO_2 to H^+ & HCO^-_3
- H^+ is pumped into lumen by H^+/K^+ ATPase pump
- HCO^-_3 exchanged for Cl- from blood
- Cl- moves through membrane channel into lumen

chief cells: secrete **pepsinogen** (cleaved to **pepsin**, a peptidase)

enterochromaffin-like (ECL) cells: secrete **histamine** and **serotonin** that stimulate chief cells

G cells: secrete **gastrin** into blood that stimulates ECL cells

Gastric juice is low pH (< 2), with 3 functions:
- kills ingested bacteria
- denatures & starts hydrolysis of ingested proteins
- optimal pH for pepsinogen cleavage and pepsin activity

mucous neck cells & mucosal surface cells: secrete mucus. *Adherent layer of mucus* is high in HCO^-_3 to protect mucosa from HCl acid

Figure 18.5

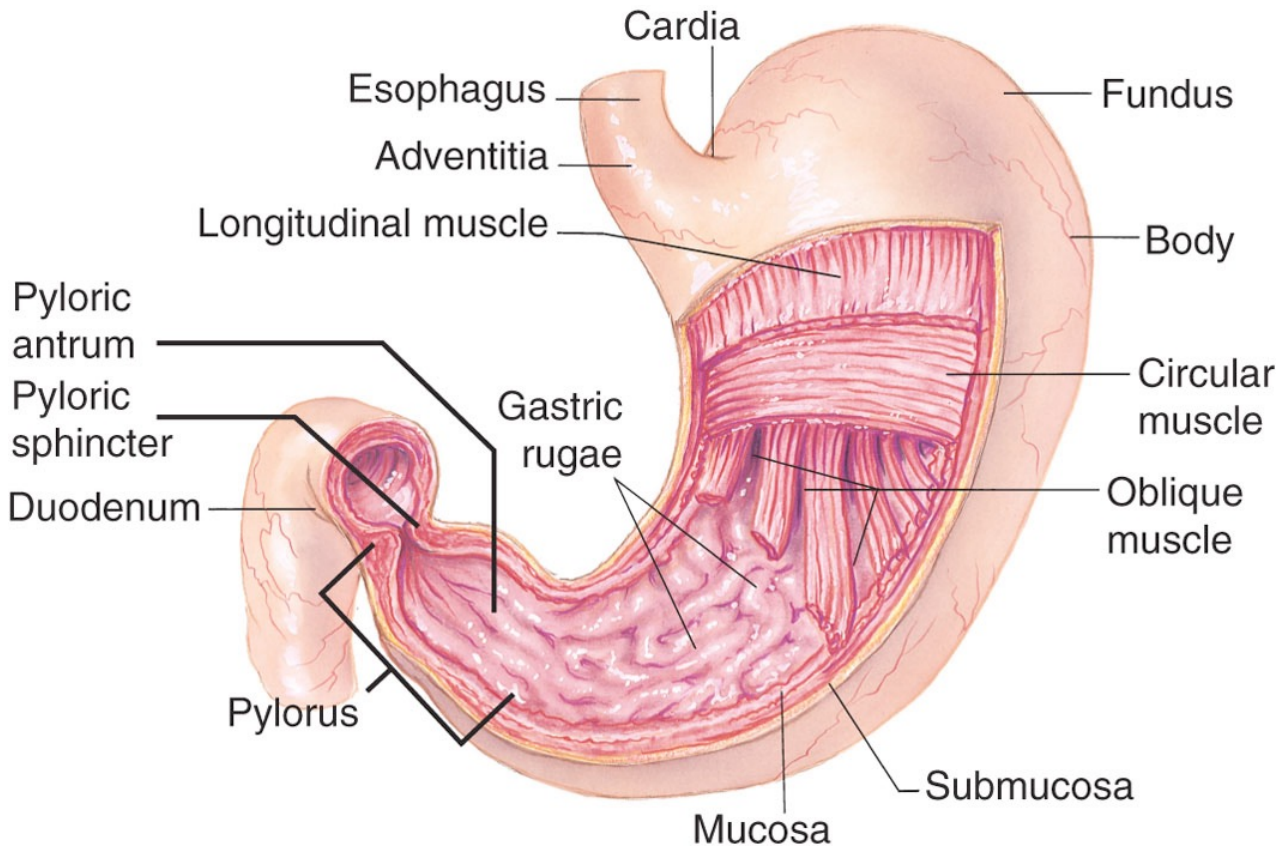

Cardia
Esophagus
Fundus
Adventitia
Longitudinal muscle
Body
Pyloric antrum
Pyloric sphincter
Gastric rugae
Circular muscle
Duodenum
Oblique muscle
Pylorus
Submucosa
Mucosa

Figure 18.6

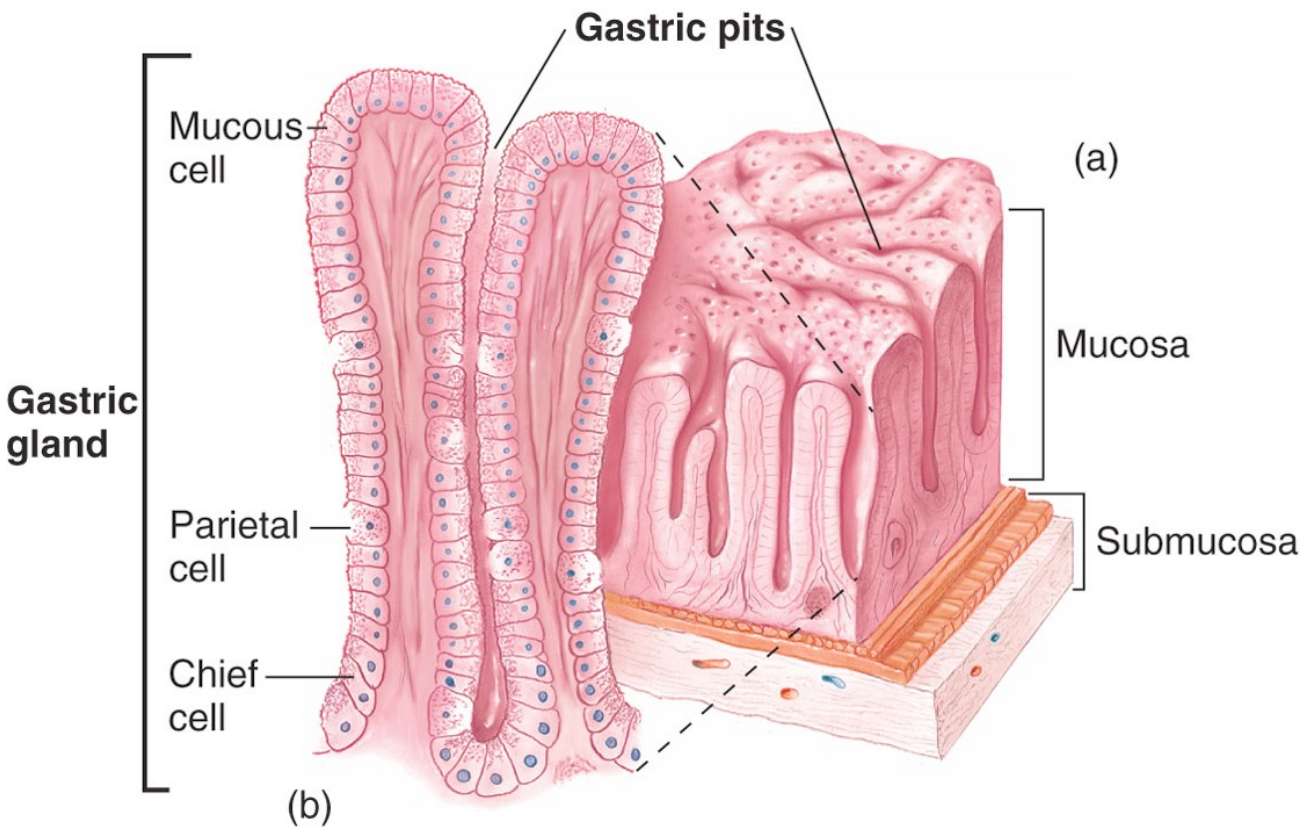

Gastric pits
Mucous cell
Gastric gland
Parietal cell
Chief cell
(b)
(a)
Mucosa
Submucosa

Figure 18.7

Acid Secretion by Parietal Cell in Stomach

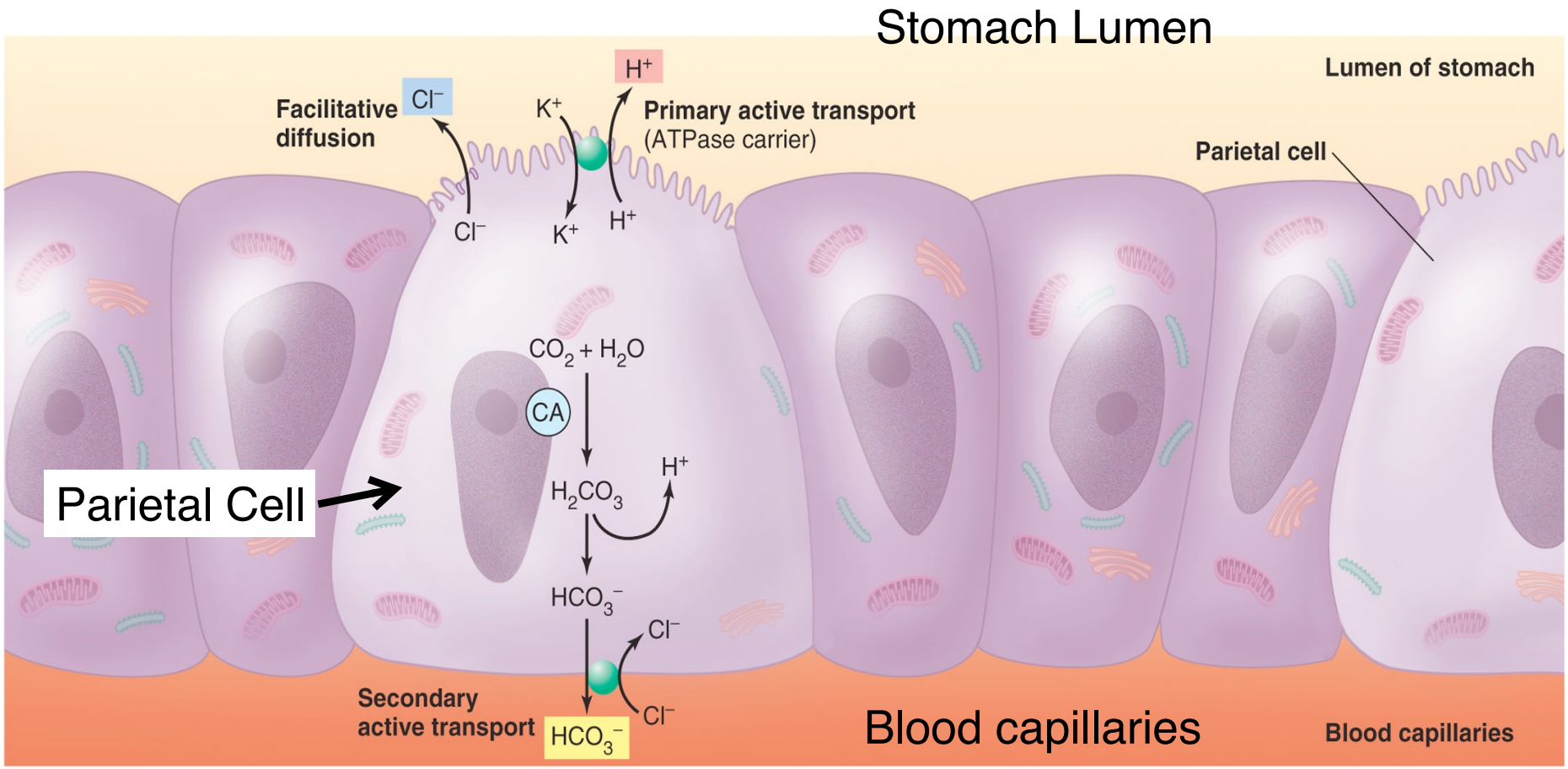
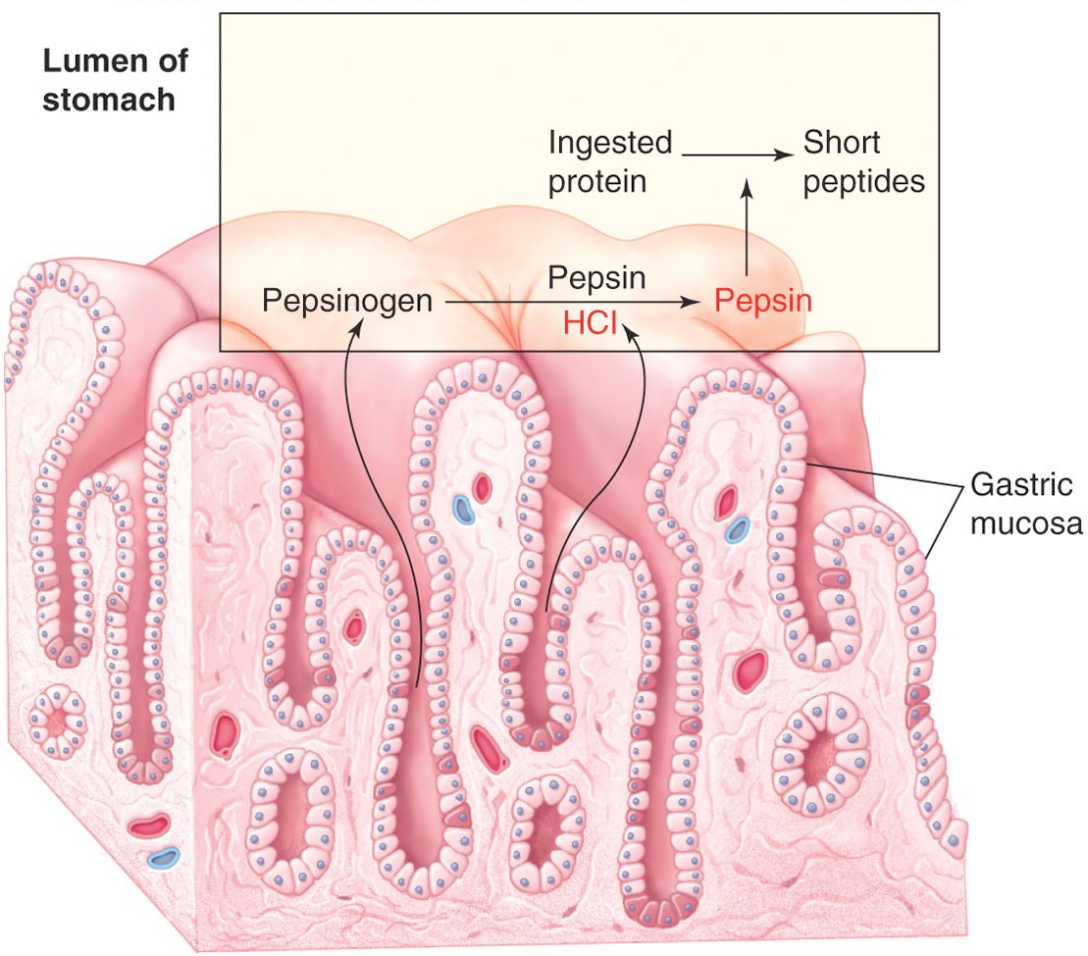


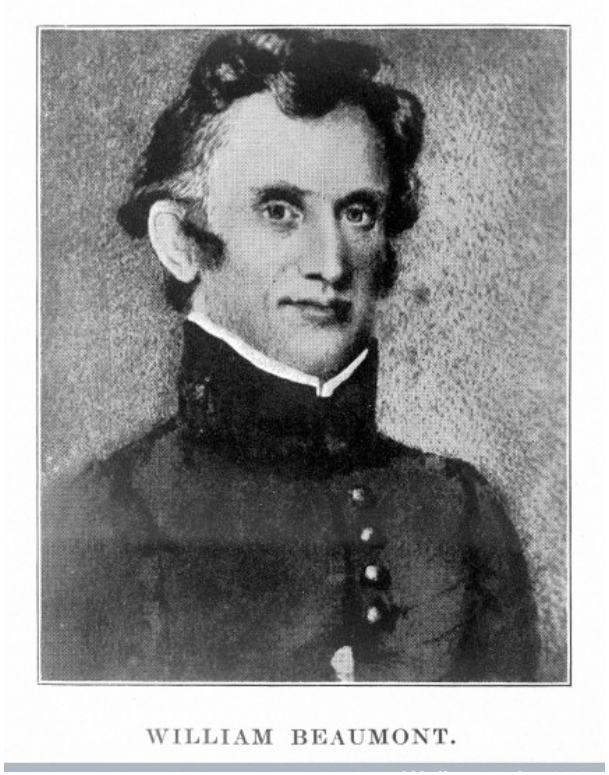
Figure 18.8

Pepsinogen Secretion by Chief Cell in Stomach

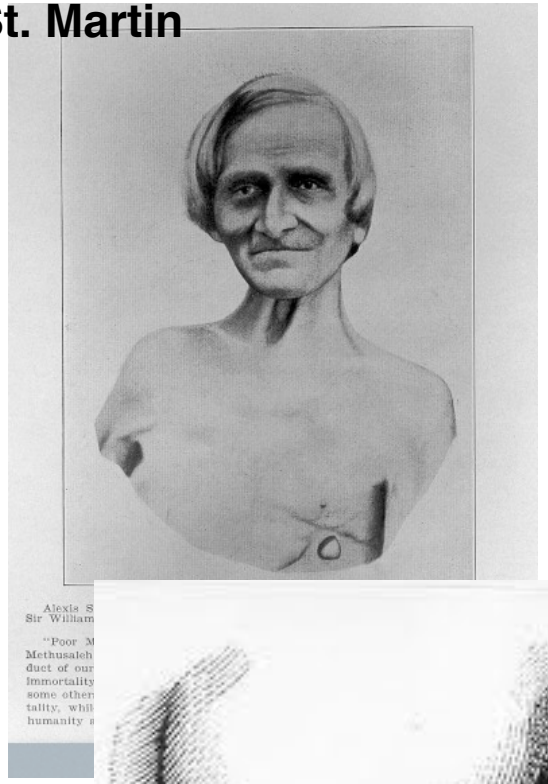


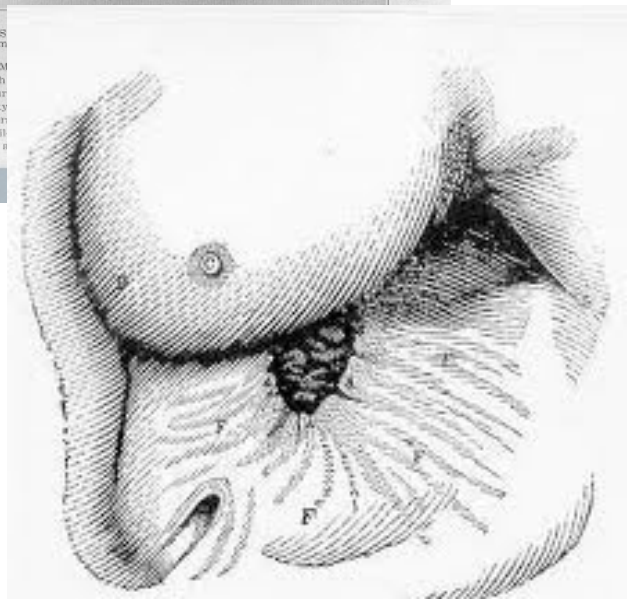
Dr. William Beaumont and Alexis St. Martin

1825 - Mackinaw Island, Michigan
Gunshot wound -> gastric fistula
Used by Beaumont to demonstrate gastric digestion by acid



WILLIAM BEAUMONT.





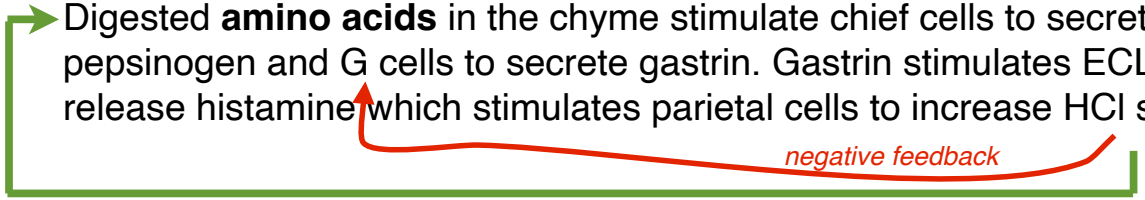
Regulation of Gastric Acid Secretion

Vagus nerve releases acetylcholine onto muscarinic receptors on ECL cells and G cells.

ECL cells release histamine that has paracrine effect on H2 receptors on nearby parietal cells to increase HCl secretion.

Distension of stomach stimulates vagus nerve.

Digested **amino acids** in the chyme stimulate chief cells to secrete pepsinogen and G cells to secrete gastrin. Gastrin stimulates ECL cells to release histamine which stimulates parietal cells to increase HCl secretion.



Fat, amino acids, and distension of the **intestine** inhibit acid secretion and **gastric emptying** (shut the pyloric sphincter to decrease movement of food from stomach to small intestine).

Figure 18.30

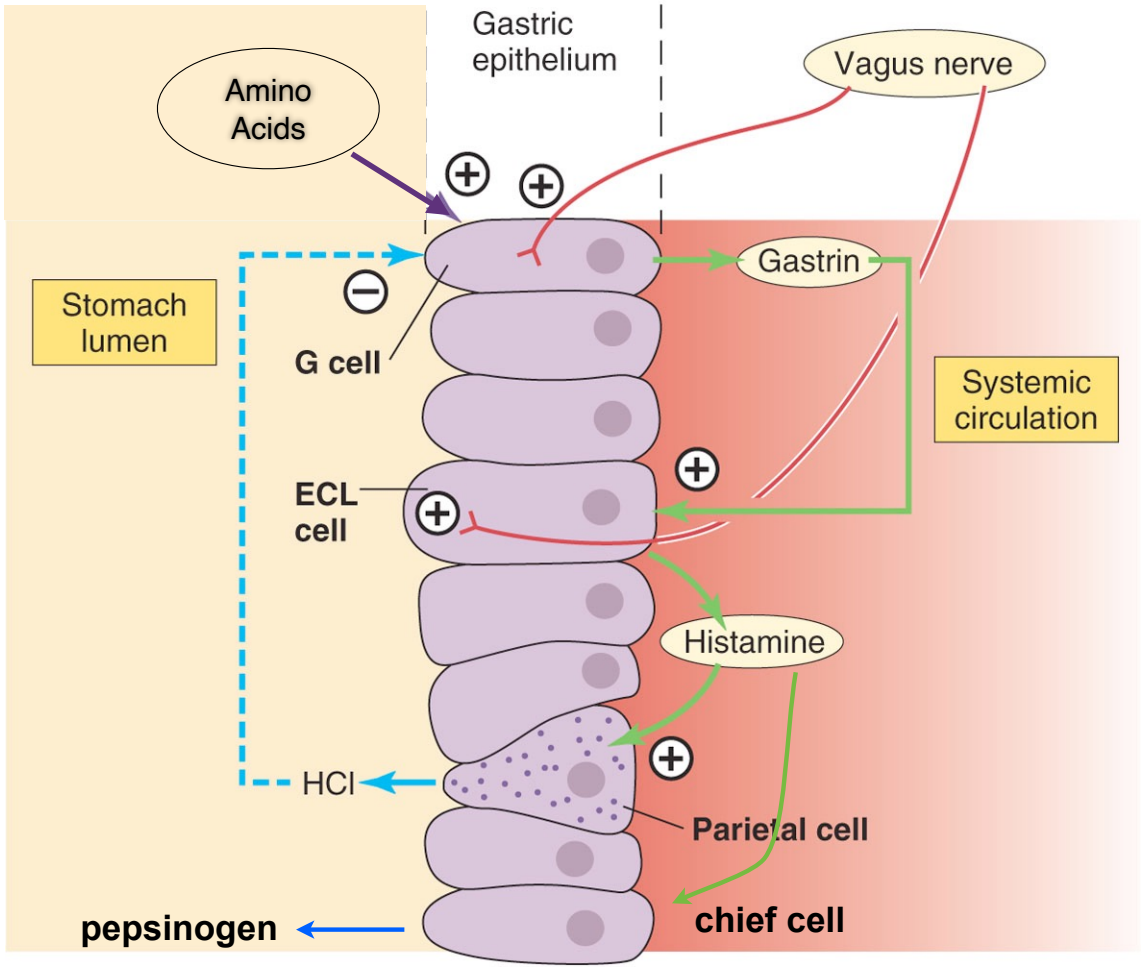

Gastric epithelium
Amino Acids
Vagus nerve
Gastrin
Stomach lumen
G cell
Systemic circulation
ECL cell
Histamine
HCl
Parietal cell
pepsinogen
chief cell

Table 18.6

Table 18.6 | The Three Phases of Gastric Secretion

Phase of Regulation	Description
Cephalic Phase	1. Sight, smell, and taste of food cause stimulation of vagus nuclei in brain 2. Vagus stimulates acid secretion a. Indirect stimulation of parietal cells (major effect) b. Stimulation of gastrin secretion (lesser effect)
Gastric Phase	1. Distension of stomach stimulates vagus nerve; vagus stimulates acid secretion 2. Amino acids and peptides in stomach lumen stimulate acid secretion a. Direct stimulation of parietal cells (lesser effect) b. Stimulation of gastrin secretion; gastrin stimulates acid secretion (major effect) 3. Gastrin secretion inhibited when pH of gastric juice falls below 2.5
Intestinal Phase	1. Neural inhibition of gastric emptying and acid secretion a. Arrival of chyme in duodenum causes distension, increase in osmotic pressure b. These stimuli activate a neural reflex that inhibits gastric activity 2. In response to fat in chyme, duodenum secretes a hormone that inhibits gastric acid secretion

Disorders of Acid Secretion

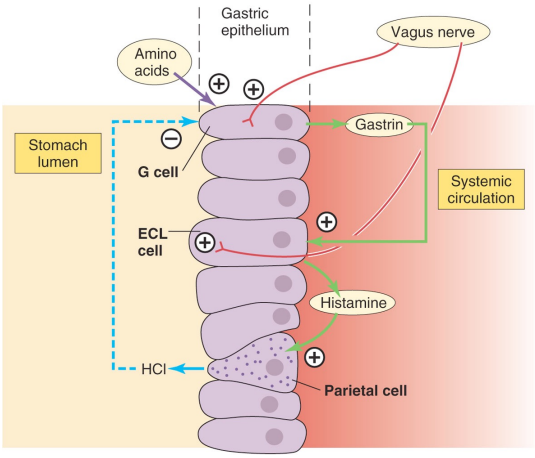
Gastroesophygeal reflux
Reflux of gastric juice into esophagus -> heartburn

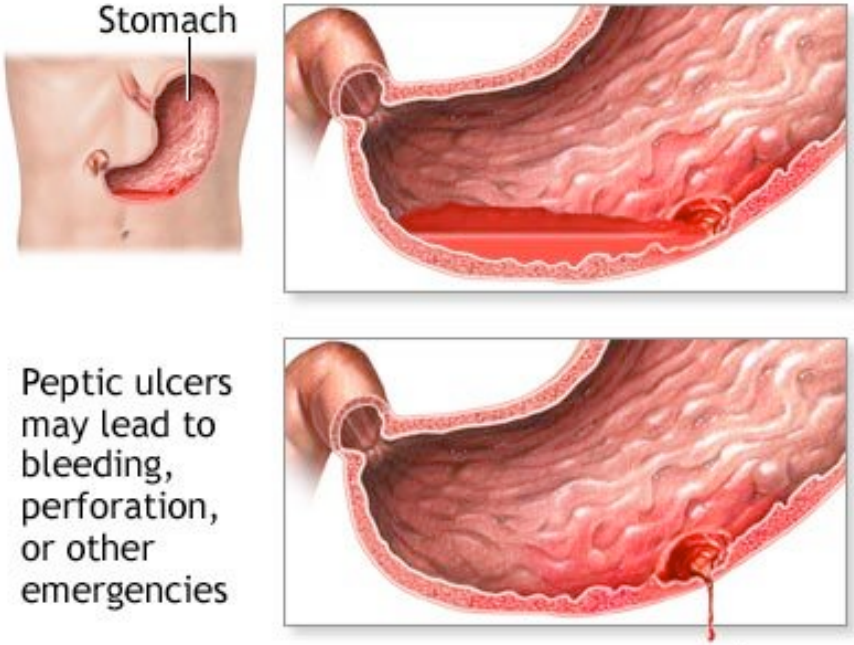
Peptic ulcers
gastric acid erodes mucosa of stomach or duodenum

***Helicobacter pylori* infection:** present in 50% of adults
aspirin: blocks prostaglandins that promote mucus secretion

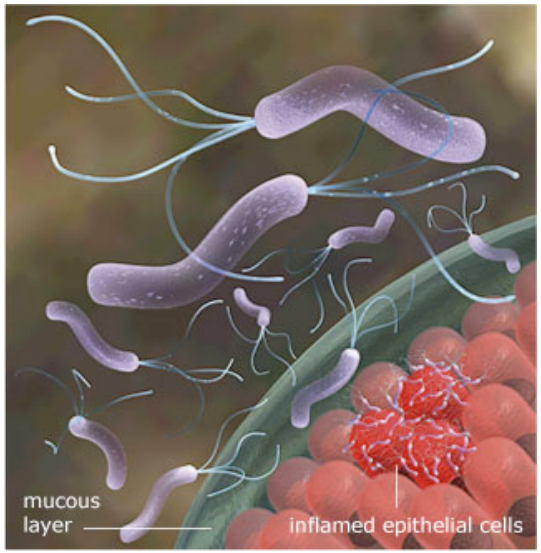
histamine release in response to infection or irritation -> more acid secretion

Treatments
antacids: to temporarily neutralize stomach acid
proton pump inhibitors: Prilosec, Prevacid
H2 Histamine receptor blockers: Tagamet, Zantac
note: antihistamines for allergies block H1 receptors
Antibiotics to suppress H. pylori infection

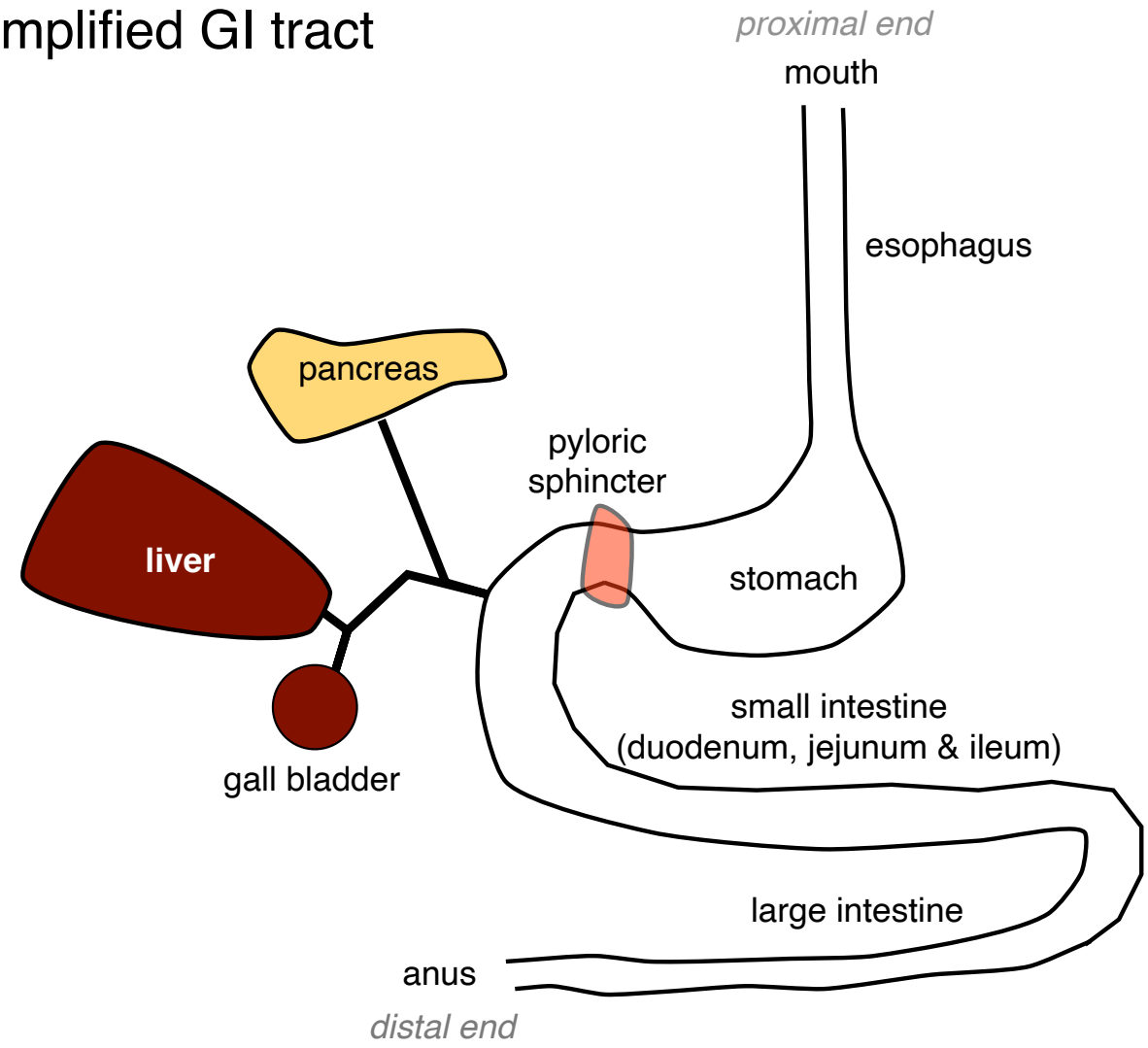




Helicobacter pylori



Simplified GI tract



Small Intestine (duodenum, jejunum, ileum)

Mucosa folded into villi. Each **villus** coated with epithelium cells. Epithelium cells have **microvilli** protrusions into lumen (the brush border).

Large surface area for absorption of nutrients and exposure to digestive enzymes (**brush border enzymes**).

Villi are perfused by **capillaries** to transport water-soluble nutrients (glucose, amino acids) and **lacteal** lymph vessel to transport fat and lipids.

Figure 18.3

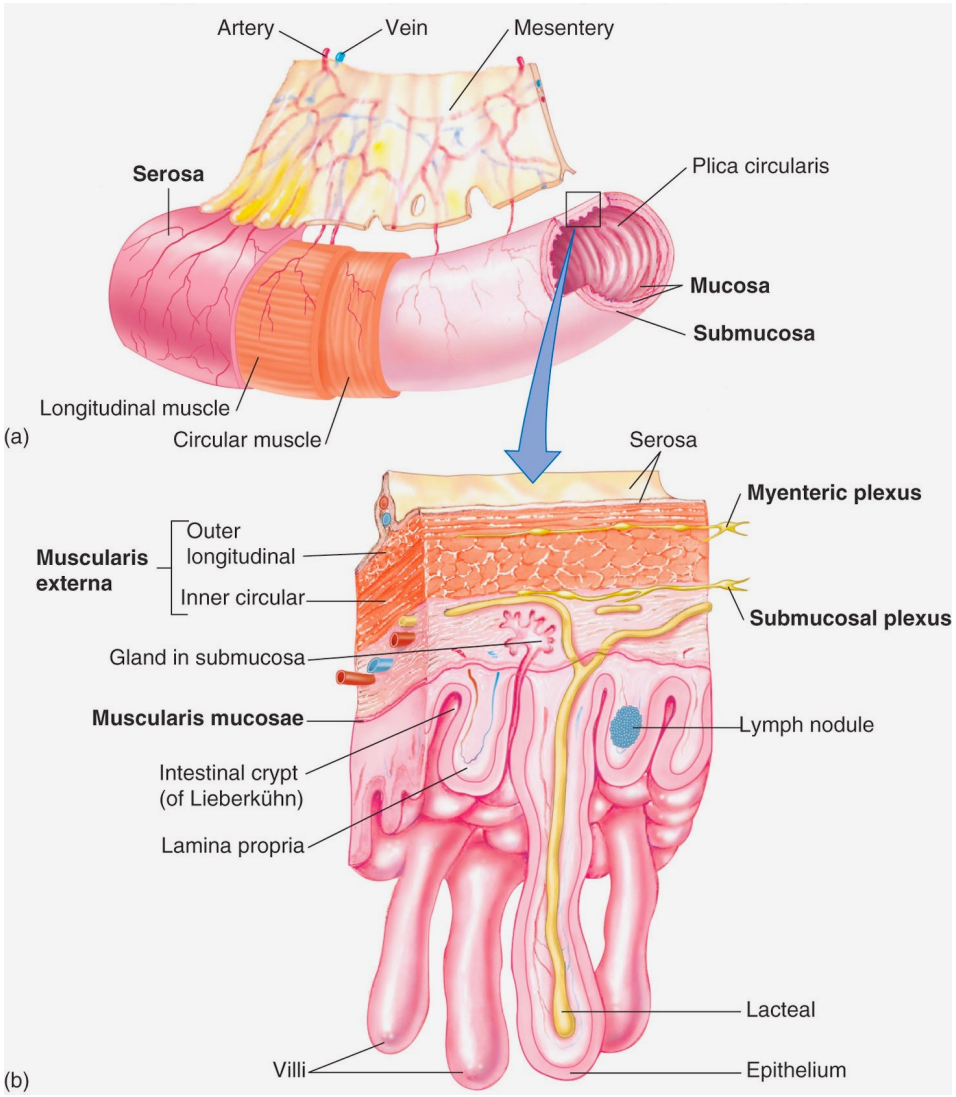

Artery
Vein
Mesentery
Serosa
Plica circularis
Mucosa
Submucosa
Longitudinal muscle
Circular muscle
(a)
Serosa
Myenteric plexus
Muscularis externa
Outer longitudinal
Inner circular
Submucosal plexus
Gland in submucosa
Muscularis mucosae
Lymph nodule
Intestinal crypt (of Lieberkühn)
Lamina propria
Lacteal
Villi
Epithelium
(b)

Figure 18.9

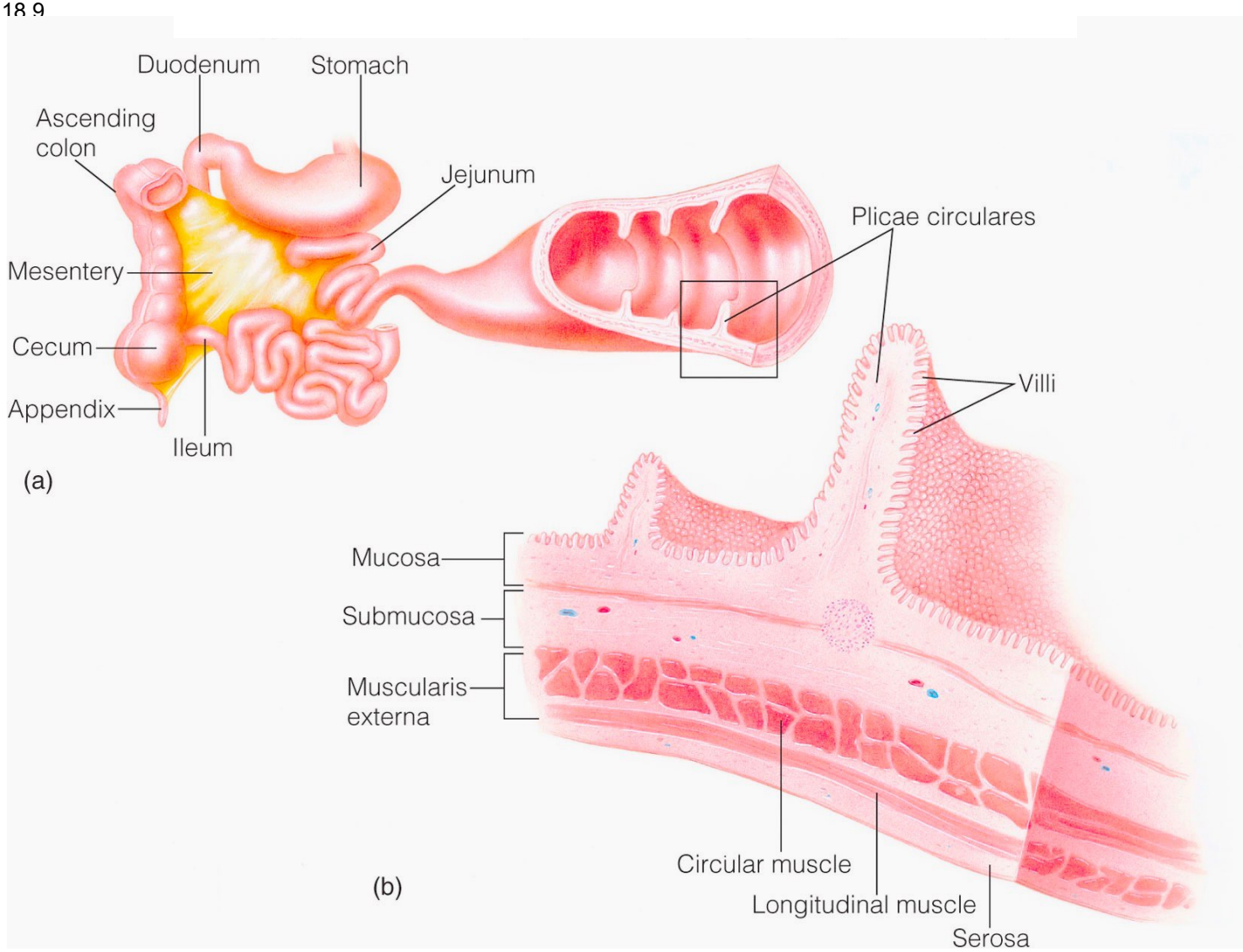
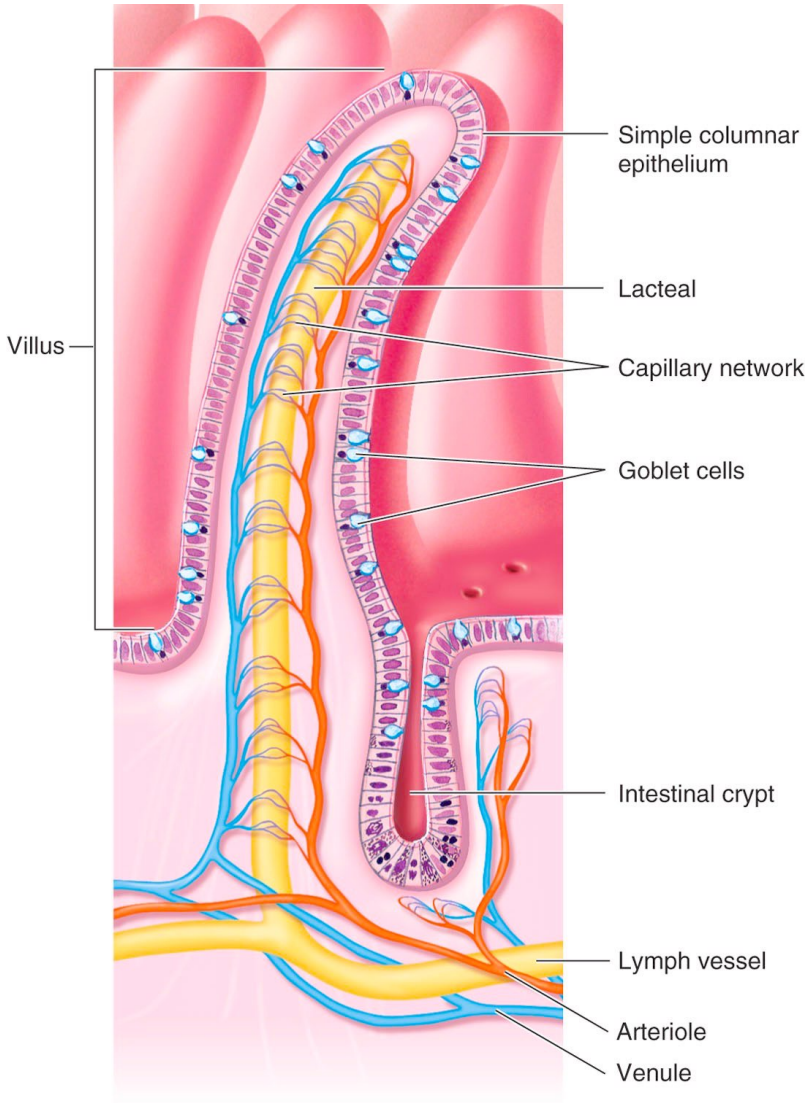
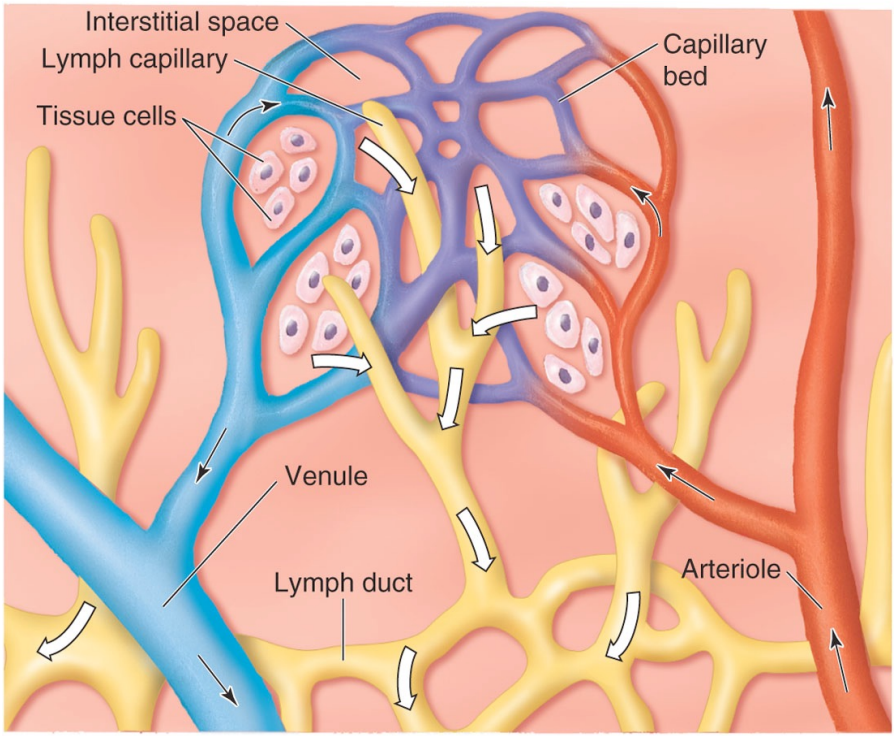

Duodenum
Stomach
Ascending colon
Jejunum
Plicae circulares
Mesentery
Cecum
Appendix
Ileum
(a)
Villi
Mucosa
Submucosa
Muscularis externa
Circular muscle
Longitudinal muscle
Serosa
(b)

Figure 18.10


Villus
Simple columnar epithelium
Lacteal
Capillary network
Goblet cells
Intestinal crypt
Lymph vessel
Arteriole
Venule

Lymphatic System

Figure 13.36



Lymphatic System

Figure 13.37

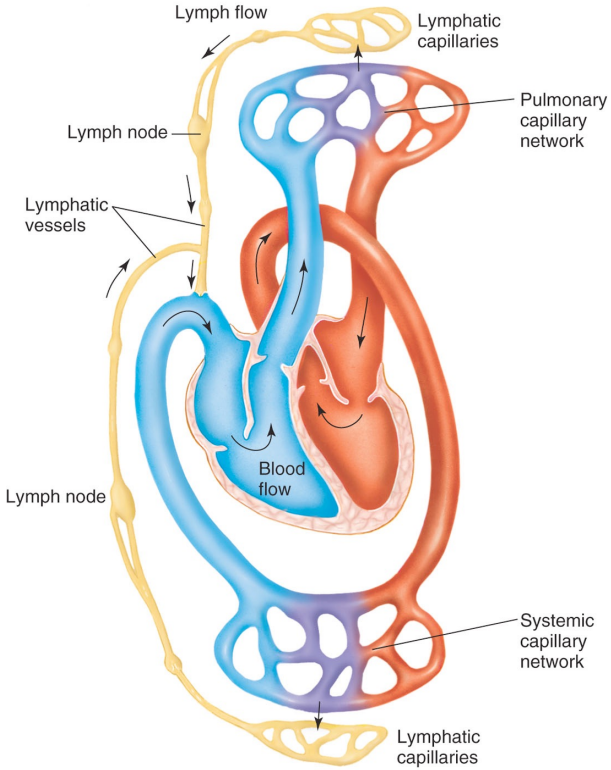


Figure 18.10

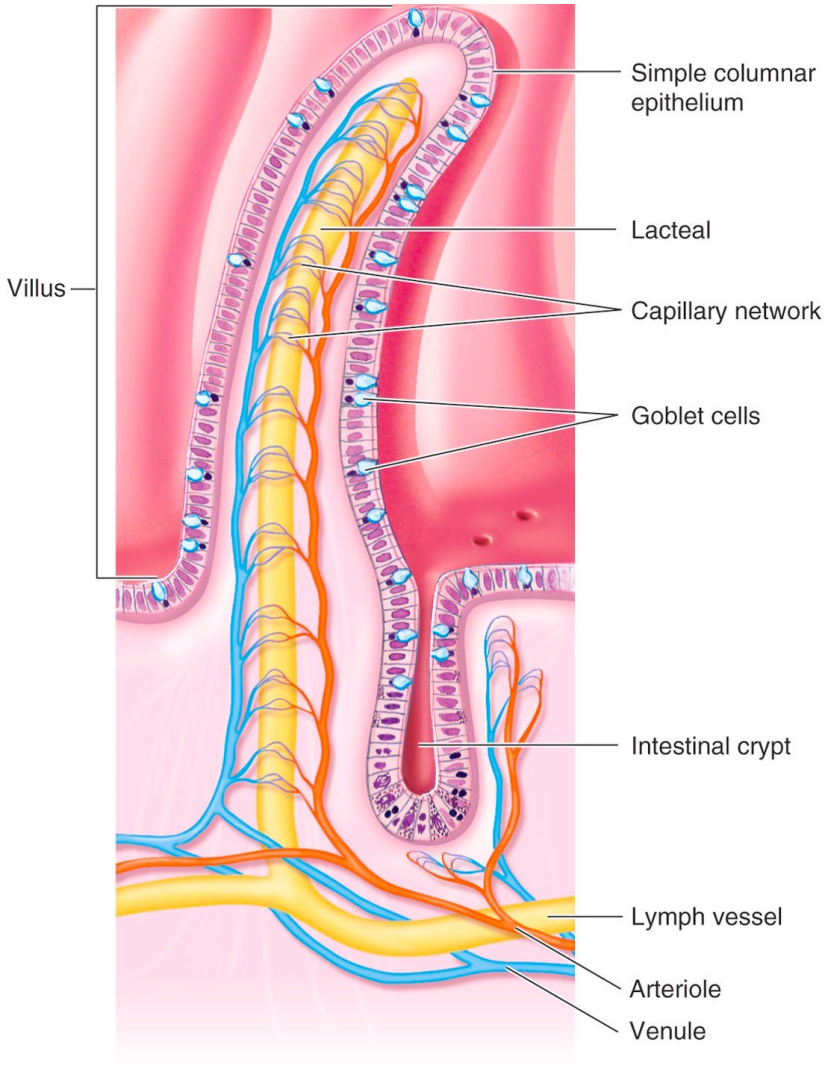
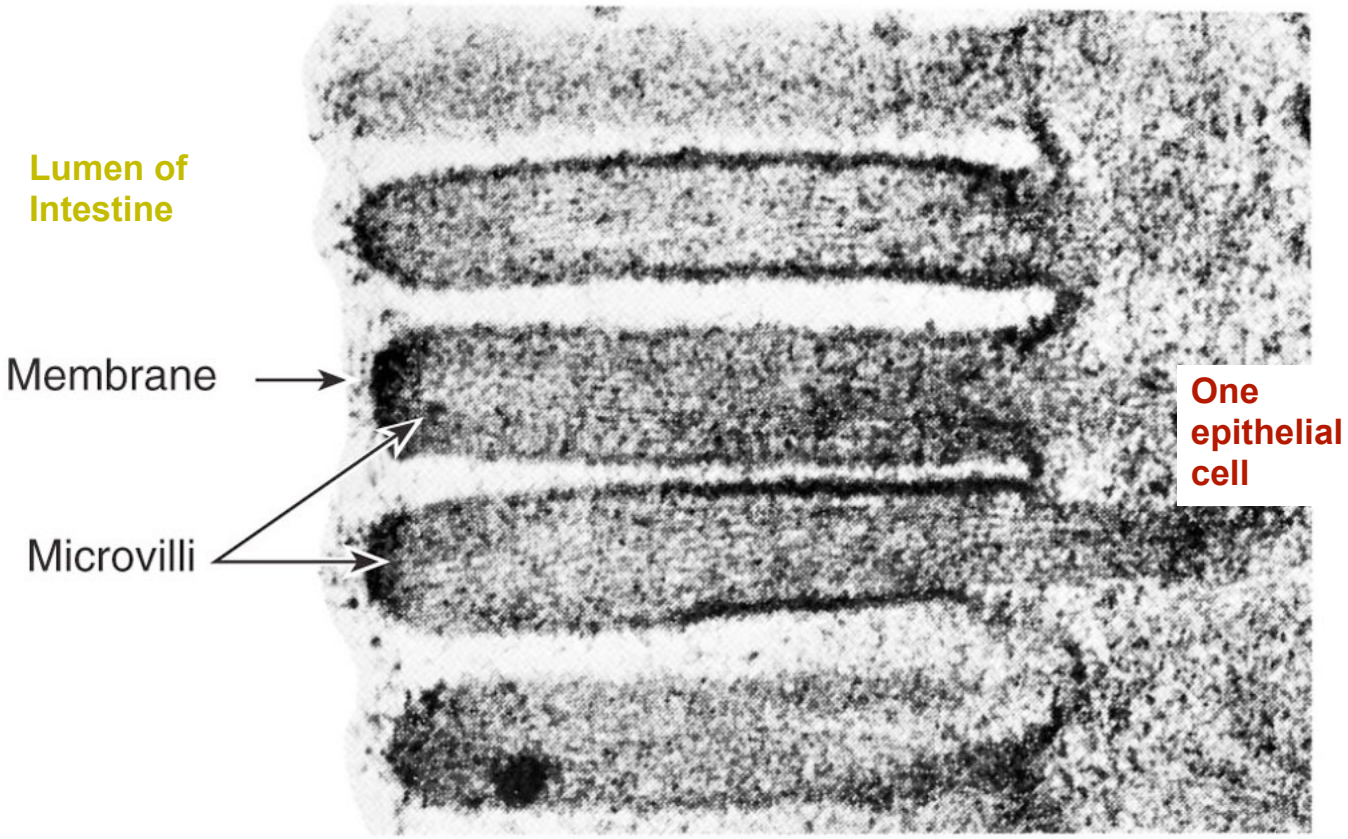

Villus
Simple columnar epithelium
Lacteal
Capillary network
Goblet cells
Intestinal crypt
Lymph vessel
Arteriole
Venule

Figure 18.11


Lumen of Intestine
Membrane
Microvilli
One epithelial cell

Digeston of Macromolecules in Small Intestine

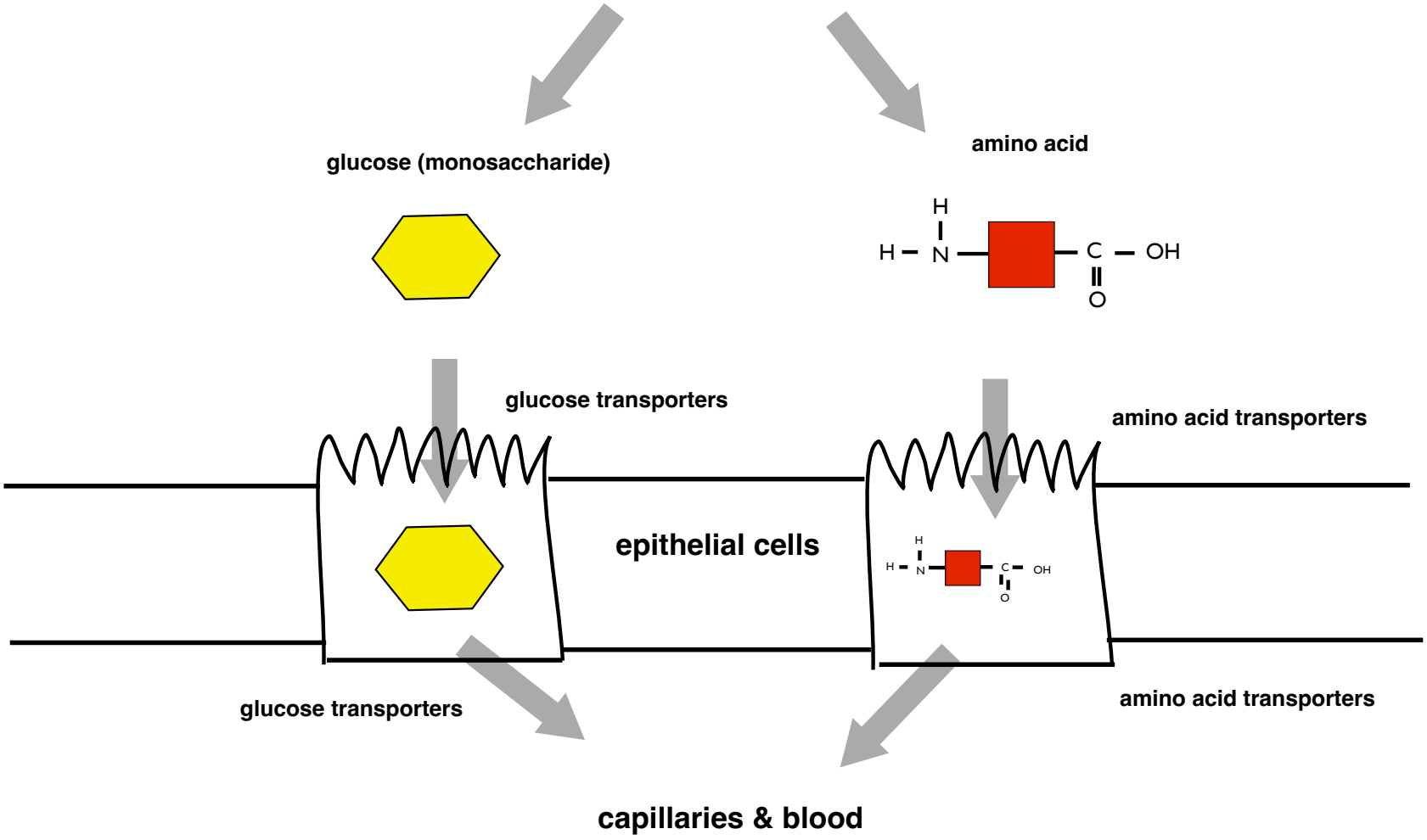


Figure 18.12

Brush Border Enzymes in membrane of Epithelial Cell

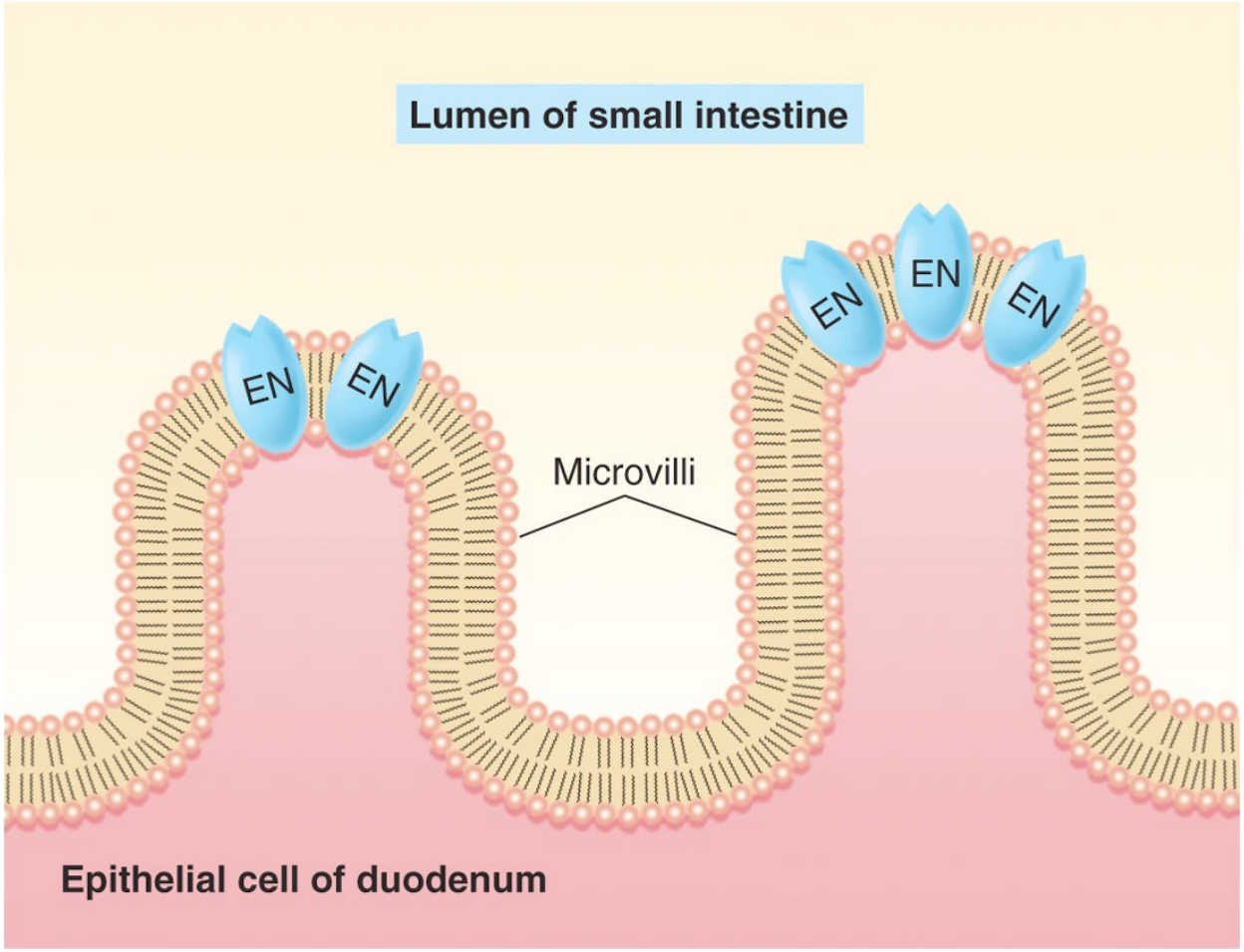


Table 18.1

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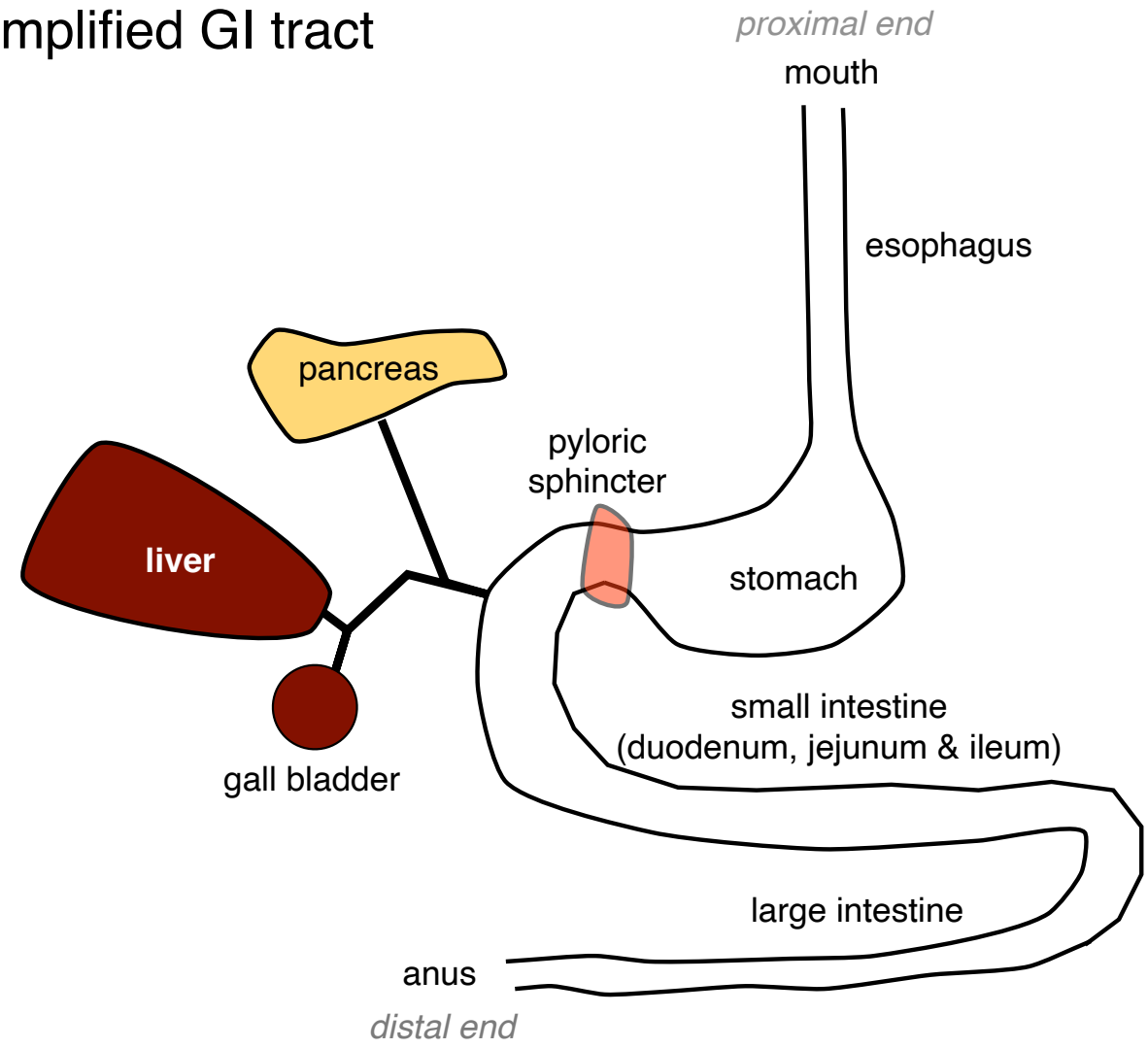
Table 18.1 | Brush Border Enzymes Attached to the Cell Membrane of Microvilli in the Small Intestine

Category	Enzyme	Comments
Disaccharidase	Sucrase	Digests sucrose to glucose and fructose; deficiency produces gastrointestinal disturbances
	Maltase	Digests maltose to glucose
	Lactase	Digests lactose to glucose and galactose; deficiency produces gastrointestinal disturbances (lactose intolerance)
Peptidase	Aminopeptidase	Produces free amino acids, dipeptides, and tripeptides
	Enterokinase	Activates trypsin (and indirectly other pancreatic juice enzymes); deficiency results in protein malnutrition
Phosphatase	Ca^{2+}, Mg^{2+}-ATPase	Needed for absorption of dietary calcium; enzyme activity regulated by vitamin D
	Alkaline phosphatase	Removes phosphate groups from organic molecules; enzyme activity may be regulated by vitamin D

Simplified GI tract



Liver and Pancreatic Secretion into Duodenum

Pancreas secretes bicarbonate and digestive enzymes.

Liver secretes bile (250 - 1500 ml/day) to emulsify fat. Stored in gall bladder. Gall bladder contracts in response to hormone cholecystokinin (CCK), released by duodenum in response to fat.

Bile secreted from common bile duct. Recycled by enterohepatic circulation. Sphincter of Oddi closes bile duct when duodenum is empty.

Bile contains:

phospholipids
cholesterol *(bile -sterol)*

chole - bile
cholecyst - gall bladder
kinin - mover

bilirubin (bile pigment)
derived from heme groups (part of metabolism of hemoglobin)
bacteria convert bilirubin to urobilinogen -> brown/yellow color

bile salts
acid form of cholesterol that **emulsifies** fats to form **micelles**

Bile produced in liver, stored in gall bladder, released into duodenum, recycled by enterohepatic circulation.

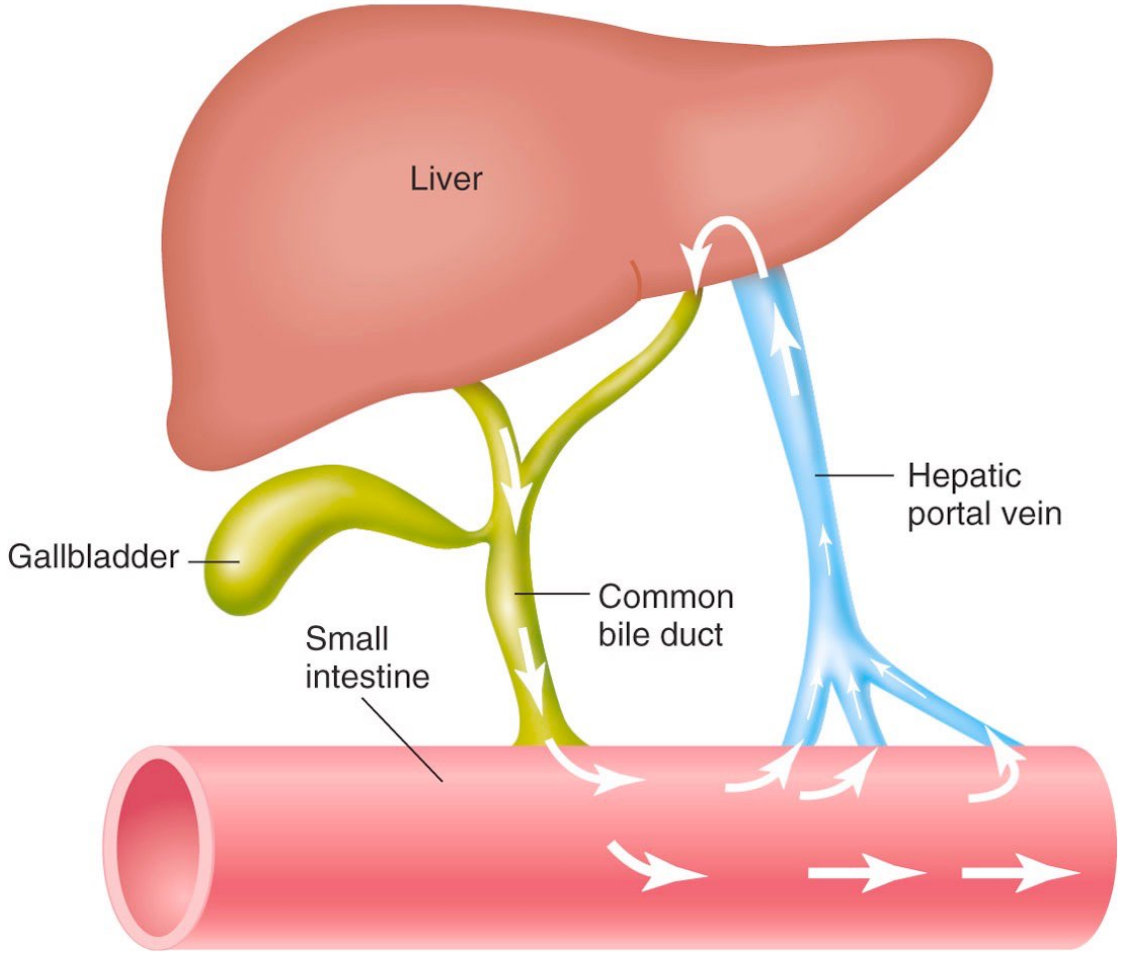
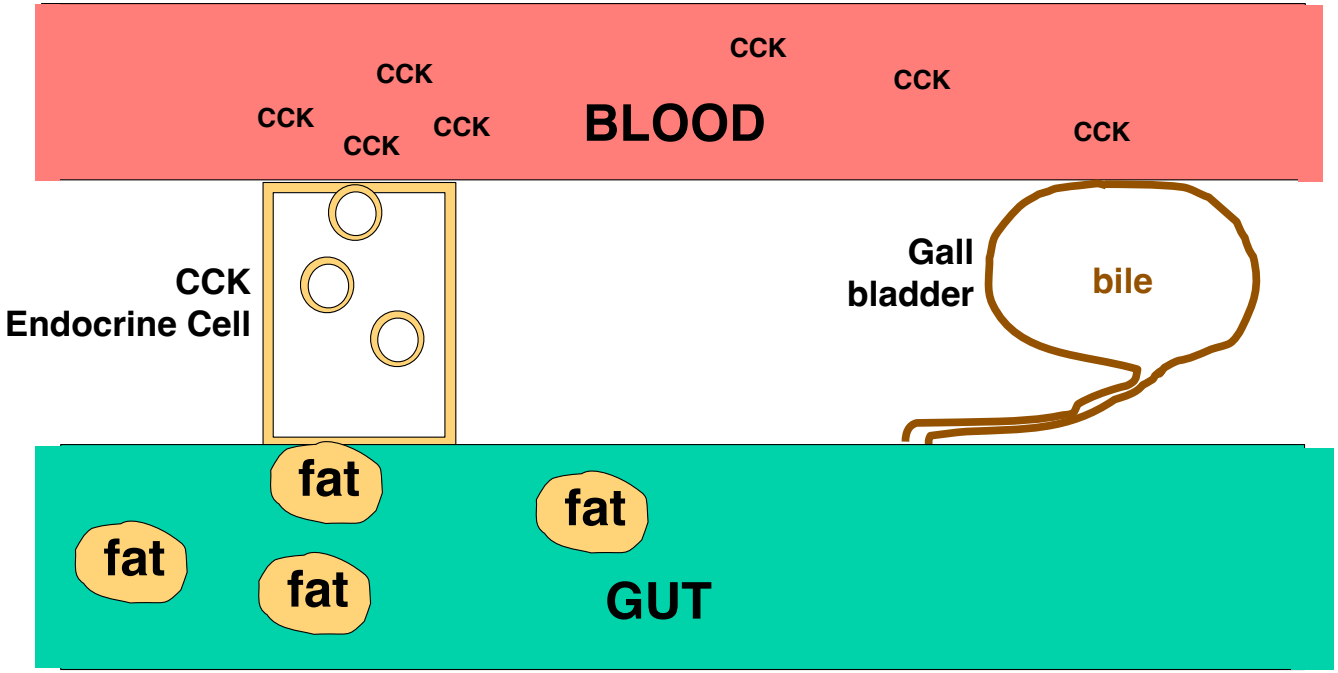


Figure 18.21

Gall bladder contracts in response to hormone cholecystokinin (CCK), released by duodenum in response to fat.

2. CCK reaches gall bladder & causes contraction



1. fat in gut stimulates CCK release into blood

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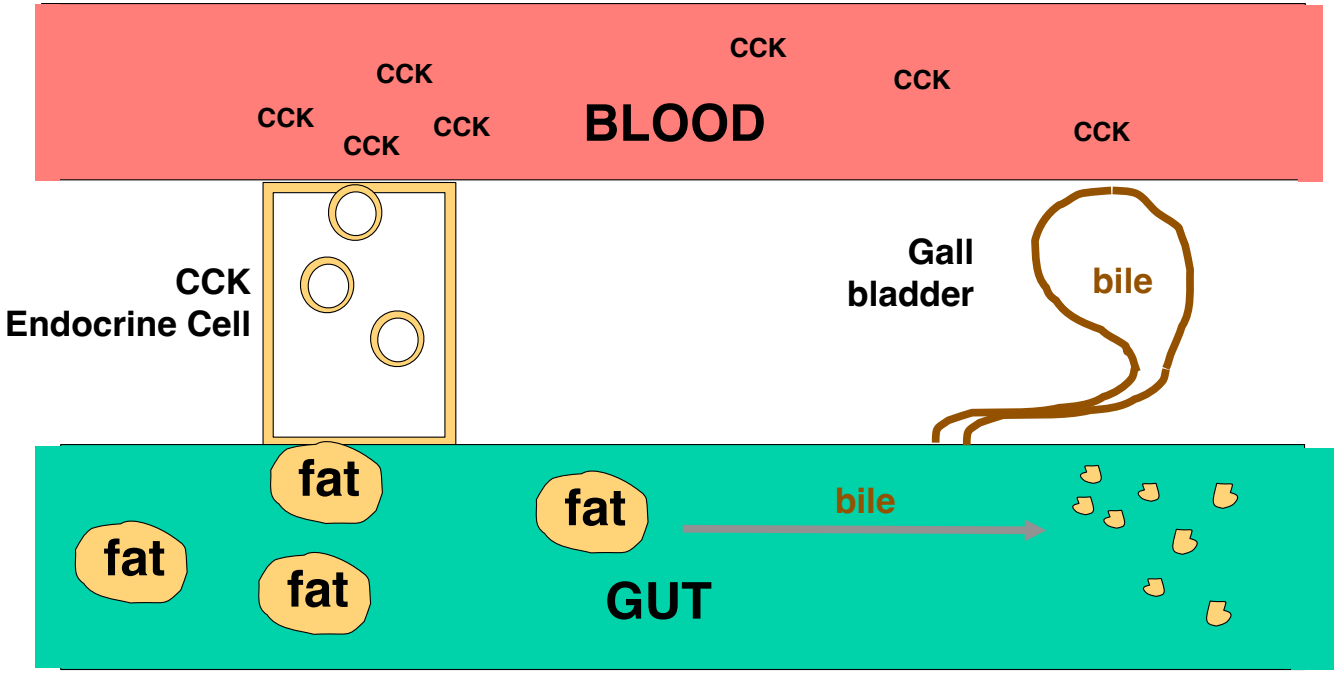


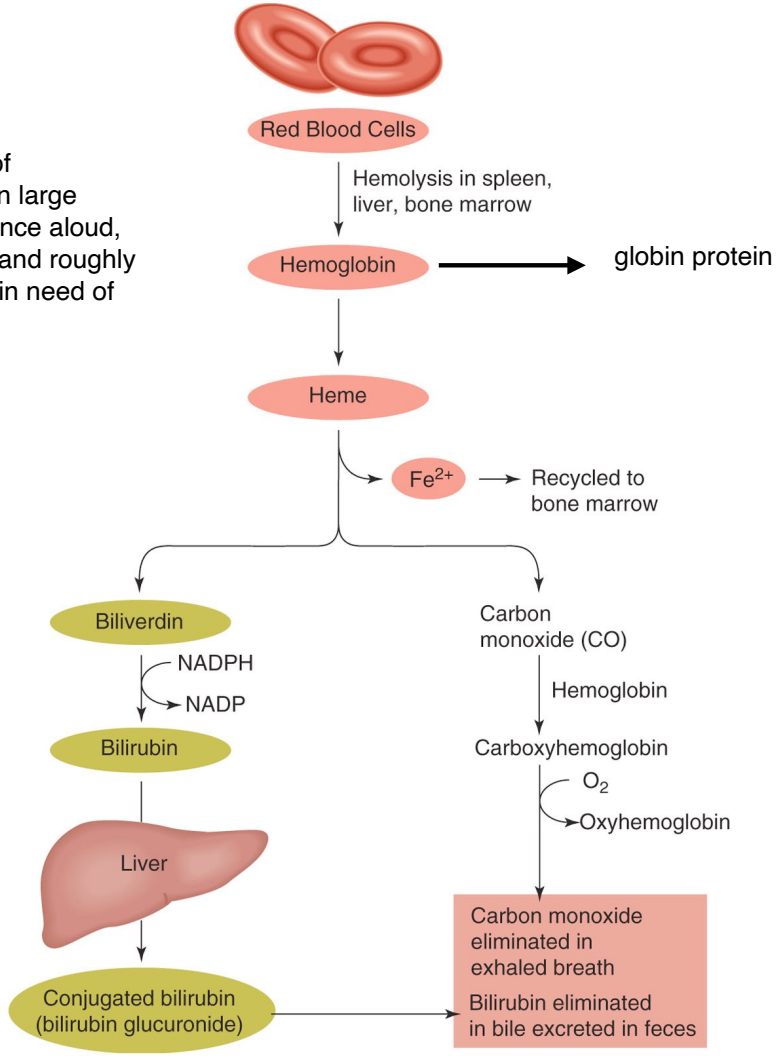
1. fat in gut stimulates CCK release into blood

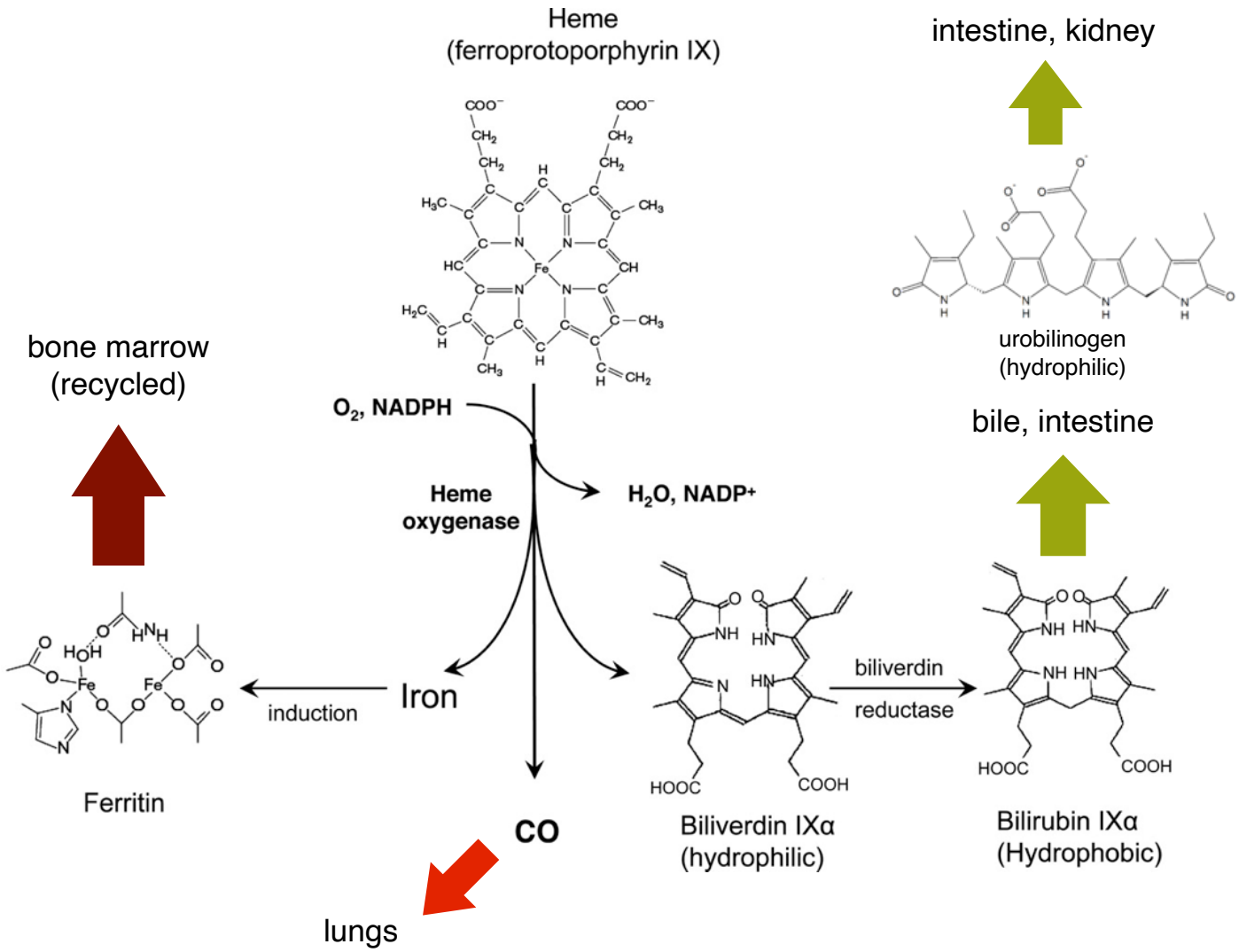
3. bile is secreted into gut to emulsify fat

Figure 18.22

Bilirubin

Bilirubin is a useless and toxic breakdown product of hemoglobin, which also means that it is generated in large quantities. In the time it takes you to read this sentence aloud, roughly 20 million of your red blood cells have died and roughly 5 quintillion (5×10^{15}) molecules of hemoglobin are in need of disposal.





http://pharmrev.aspetjournals.org/content/57/4/585/F2.large.jpg

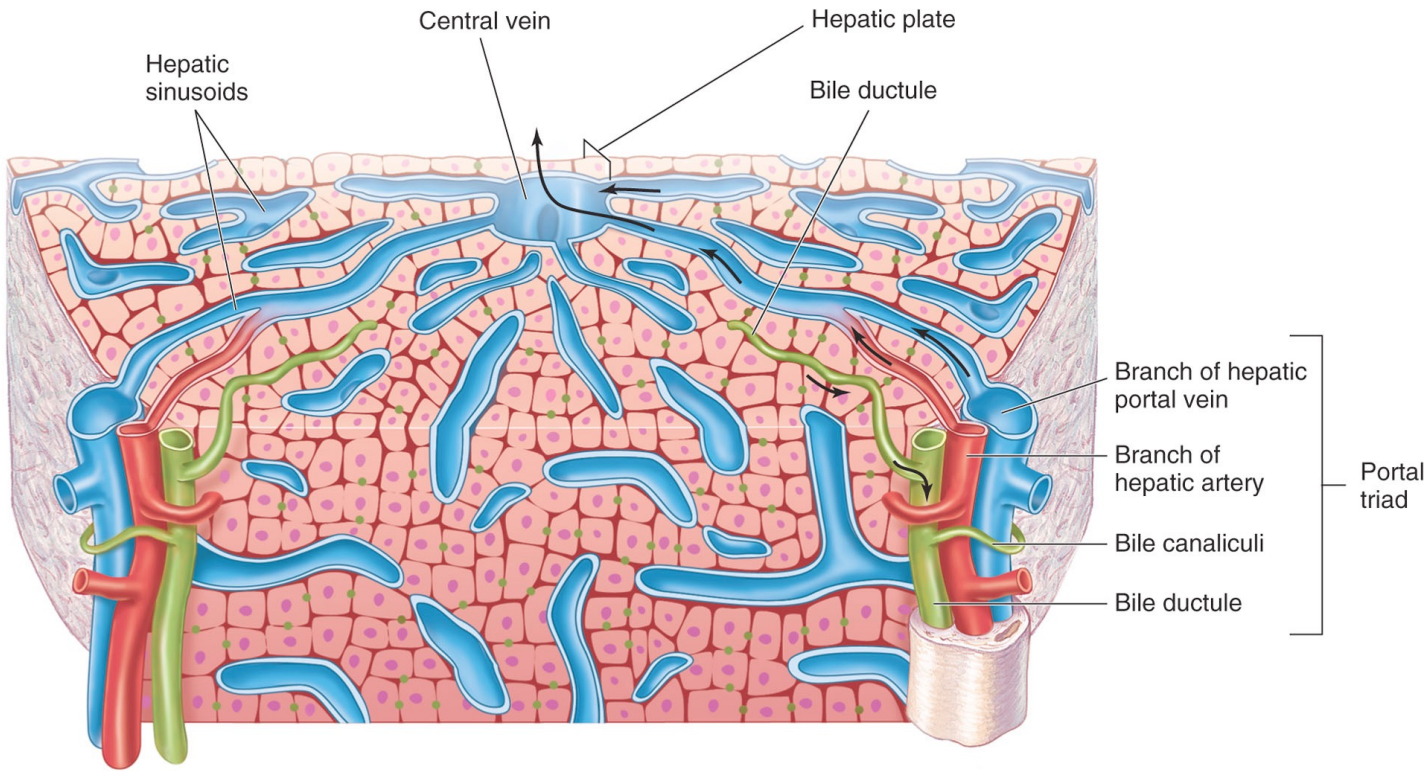

Central vein
Hepatic plate
Hepatic sinusoids
Bile ductule
Branch of hepatic portal vein
Branch of hepatic artery
Bile canaliculi
Bile ductule
Portal triad

Figure 18.19

Figure 18.20

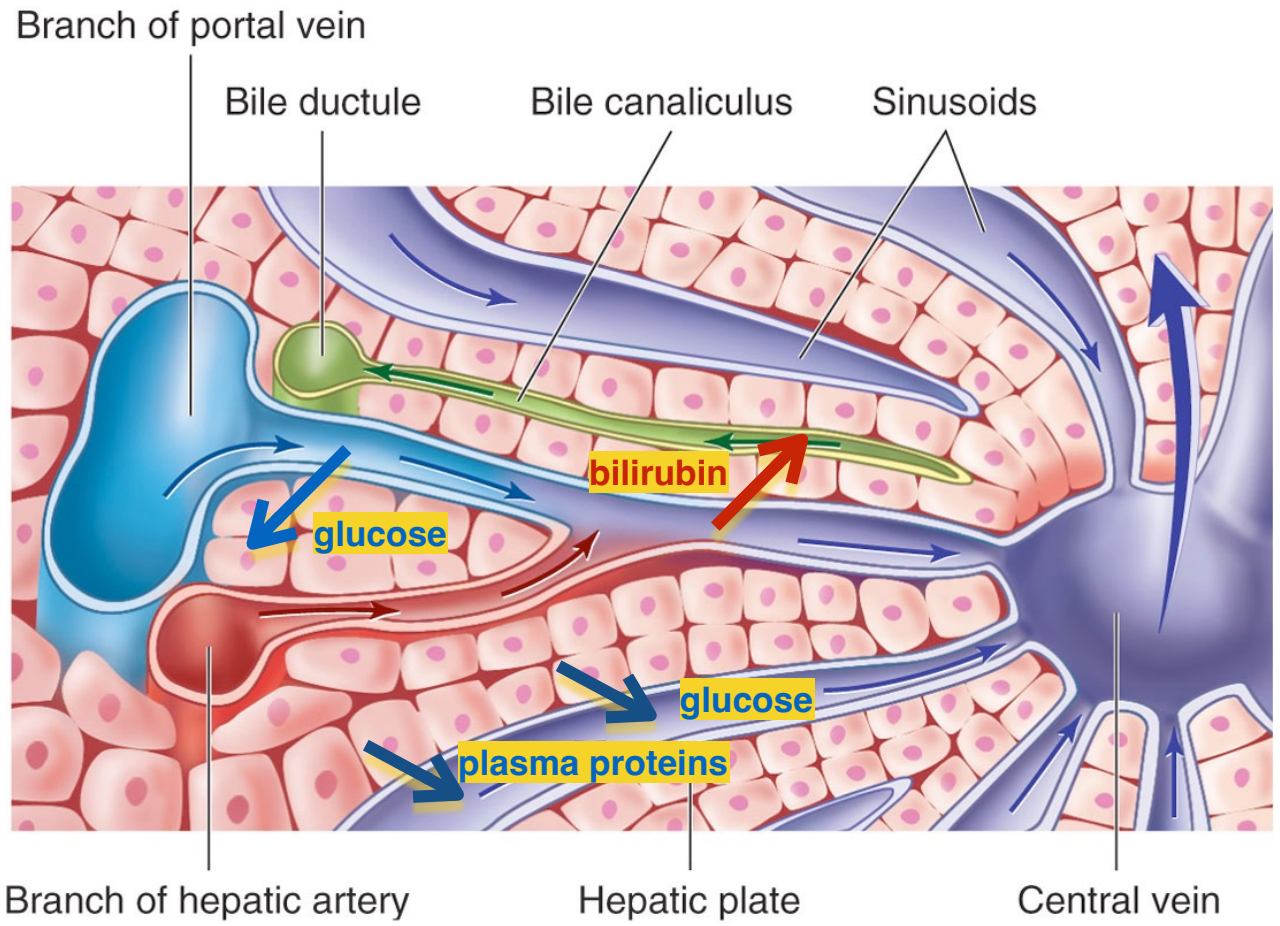

Branch of portal vein
Bile ductule
Bile canaliculus
Sinusoids
bilirubin
glucose
glucose
plasma proteins
Branch of hepatic artery
Hepatic plate
Central vein

Figure 18.23

Enterohepatic Circulation

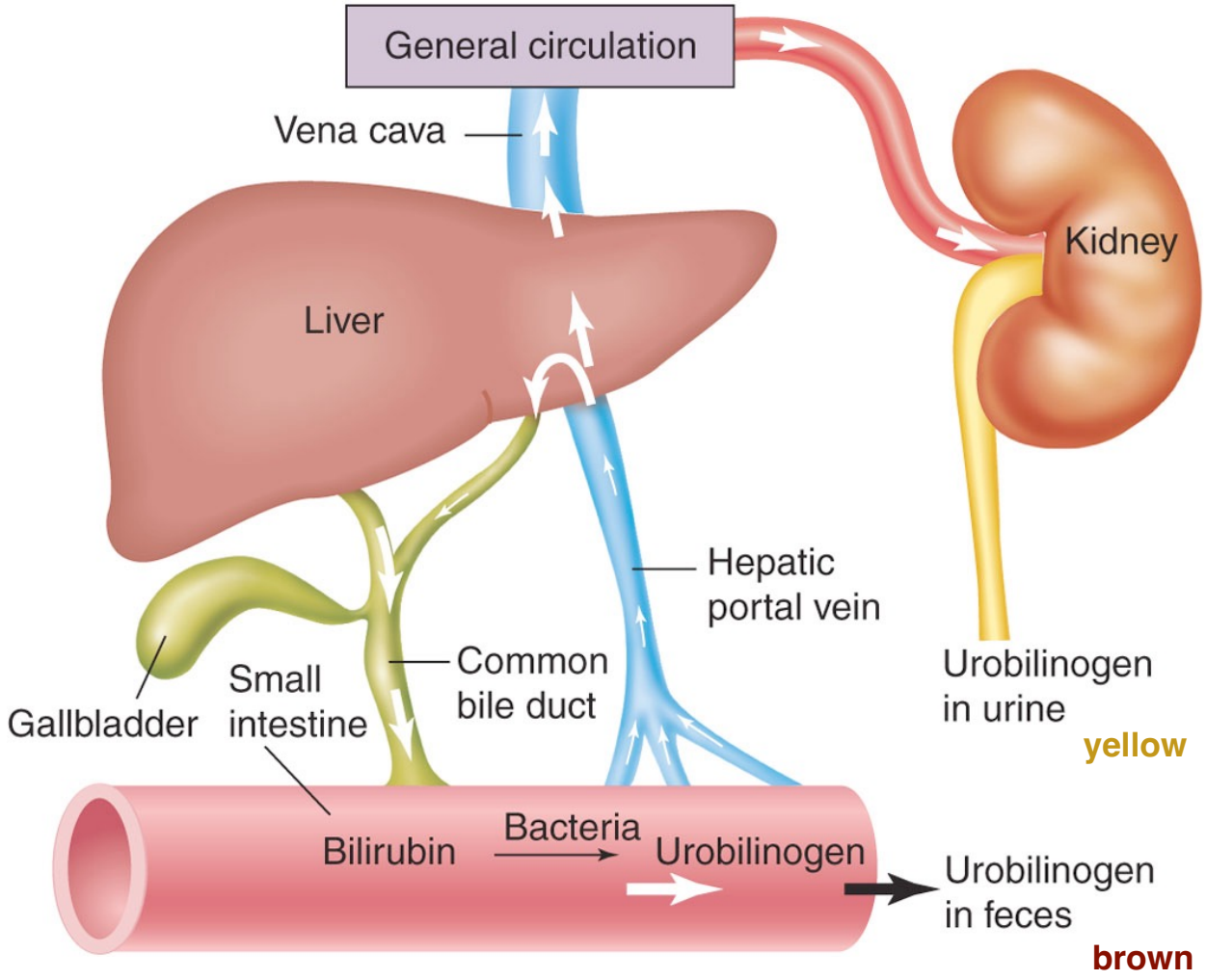
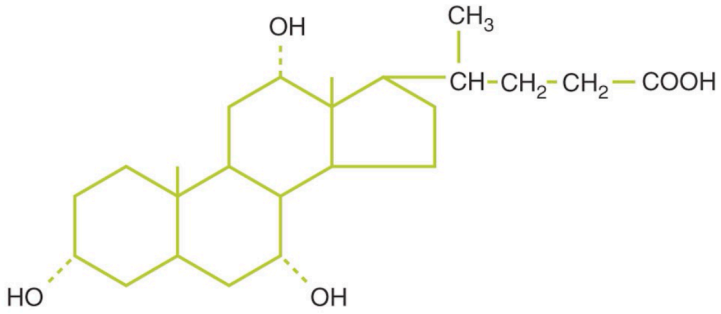


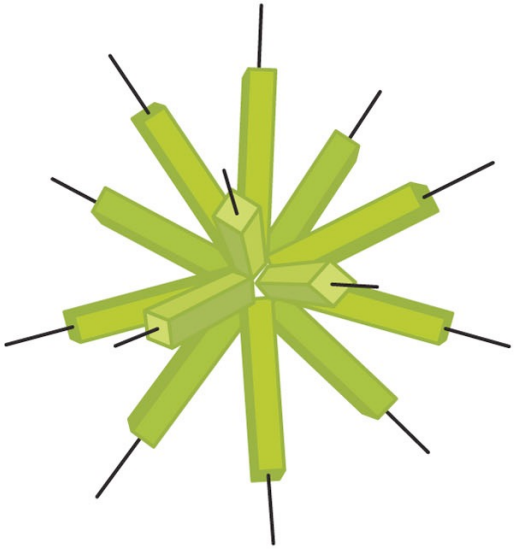
Figure 18.24

bile salts



(a) **Cholic acid** (a bile acid)

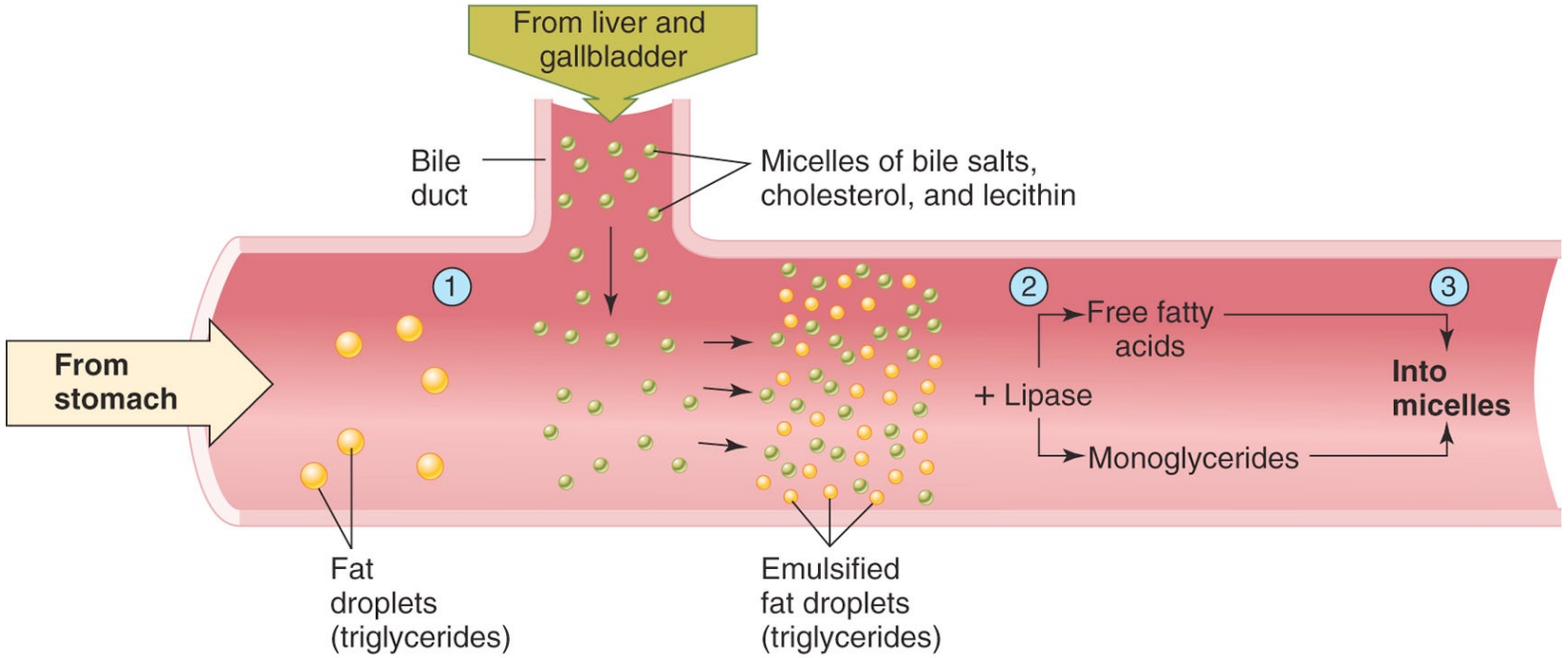
(b) Simplified representation of bile acid



(c) **Micelle** of bile acids

Figure 18.35

bile salts

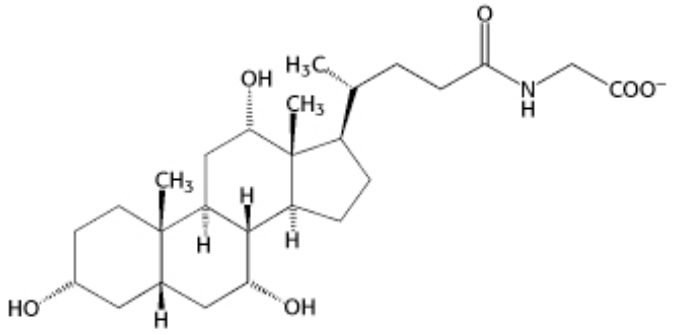


Step 1: Emulsification of fat droplets by bile salts

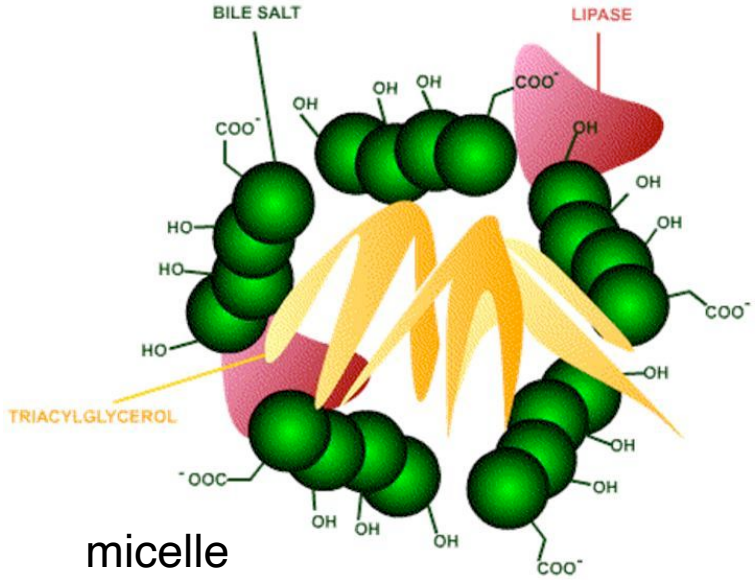
Step 2: Hydrolysis of triglycerides in emulsified fat droplets into fatty acid and monoglycerides

Step 3: Dissolving of fatty acids and monoglycerides into micelles to produce “mixed micelles”

Bile & Lipases



Glycocholate



micelle

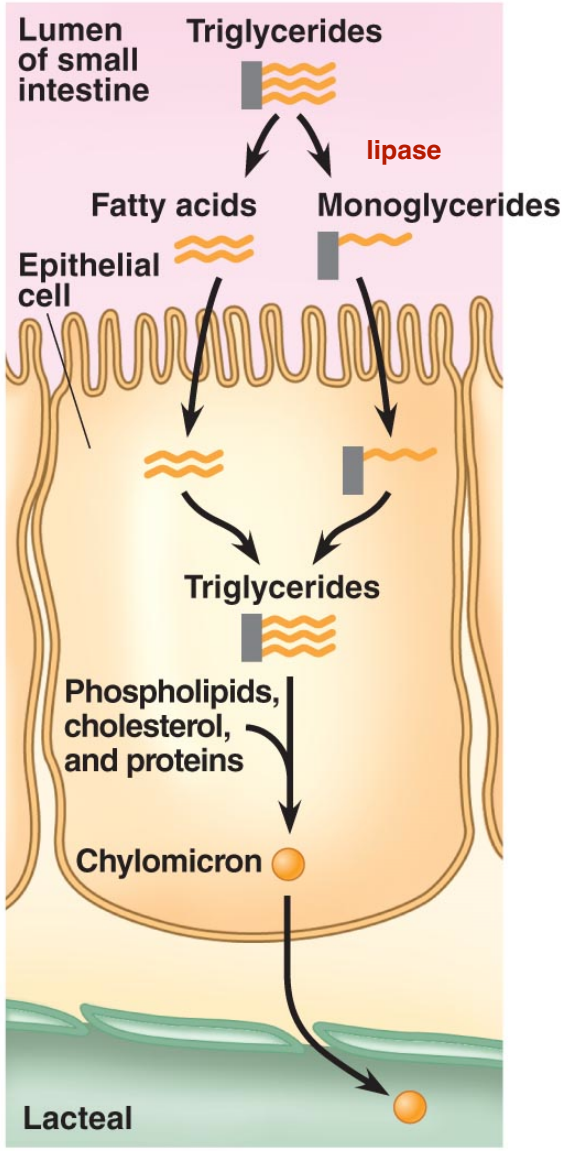


Figure 18.34

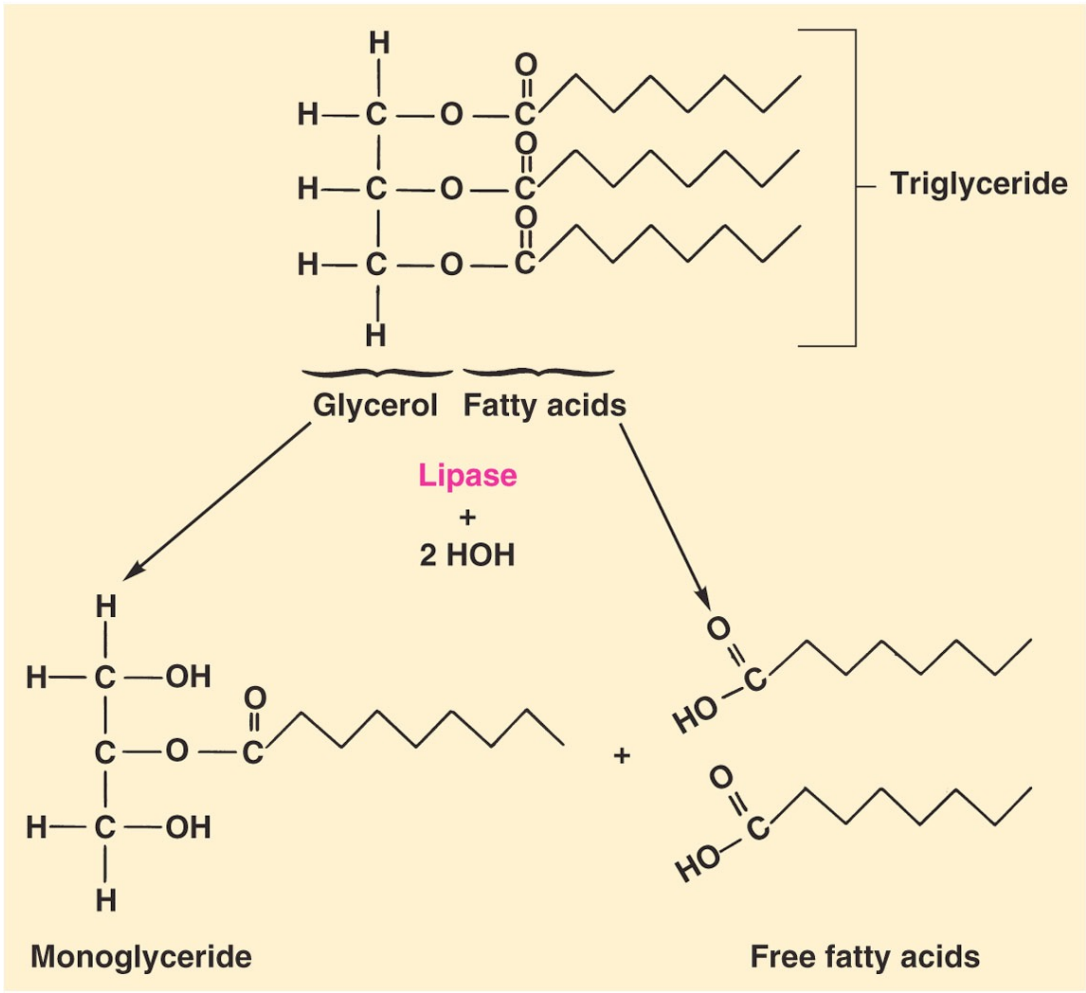
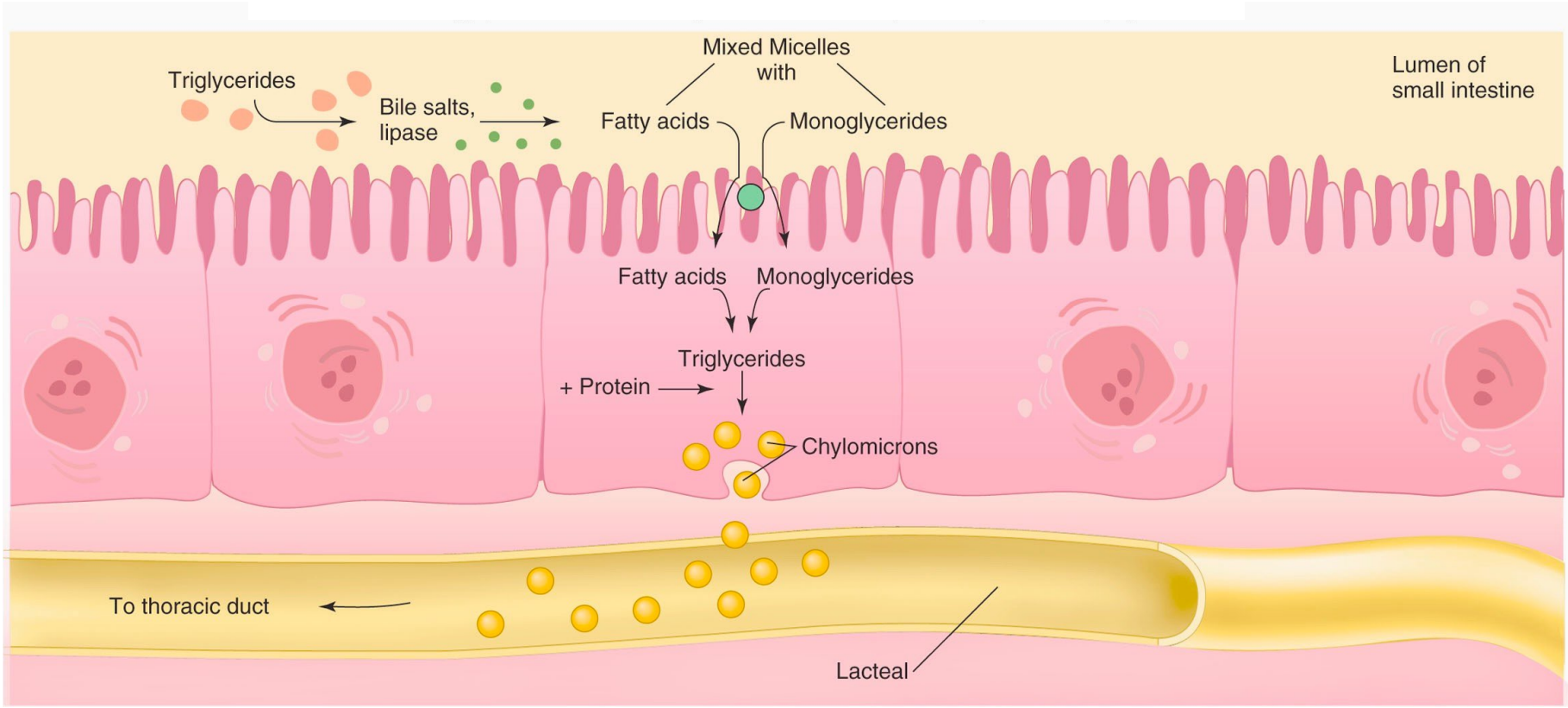

Triglyceride
Glycerol
Fatty acids
Lipase
+
2 HOH
Monoglyceride
Free fatty acids

Figure 18.36

Fat Absorption in Intestine -> lymph vessels



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bile salts
acid form of cholesterol that **emulsifies** fats to form **micelles**

Bile & Gallbladder Disorders

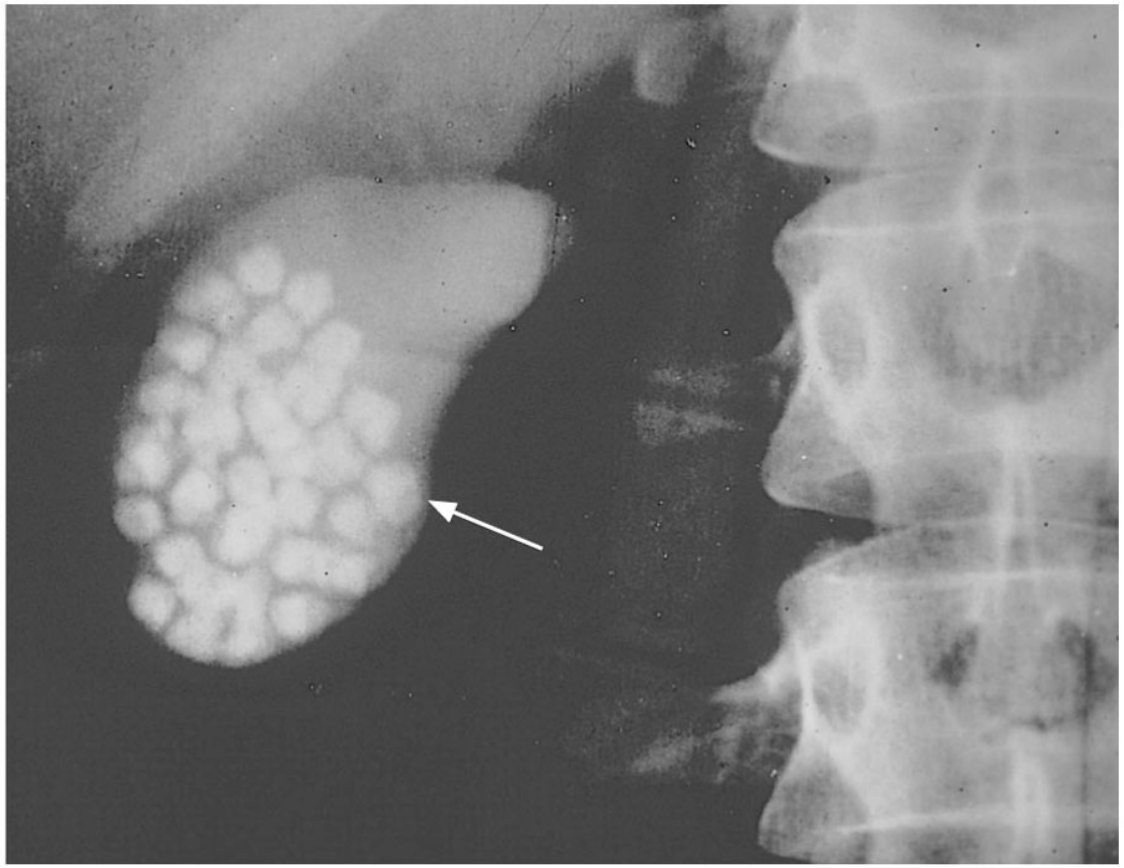
Cholecystitis
irritation of the gall bladder

Gall stones
solid cholesterol crystals formed by excess cholesterol secretion by liver and excess mucus by gall bladder. Cholecystectomy to remove gall bladder.

Jaundice
Yellow skin and tissue color caused by excess blood levels of bilirubin.
(low functioning liver; blockage of bile duct/gall bladder)

Neonatal Jaundice
Newborn liver lacks enzyme for conjugating bilirubin, so bilirubin accumulates in blood. Phototherapy with blue light converts bilirubin to more water-soluble form that can be eliminated by kidney.

Figure 18.26a



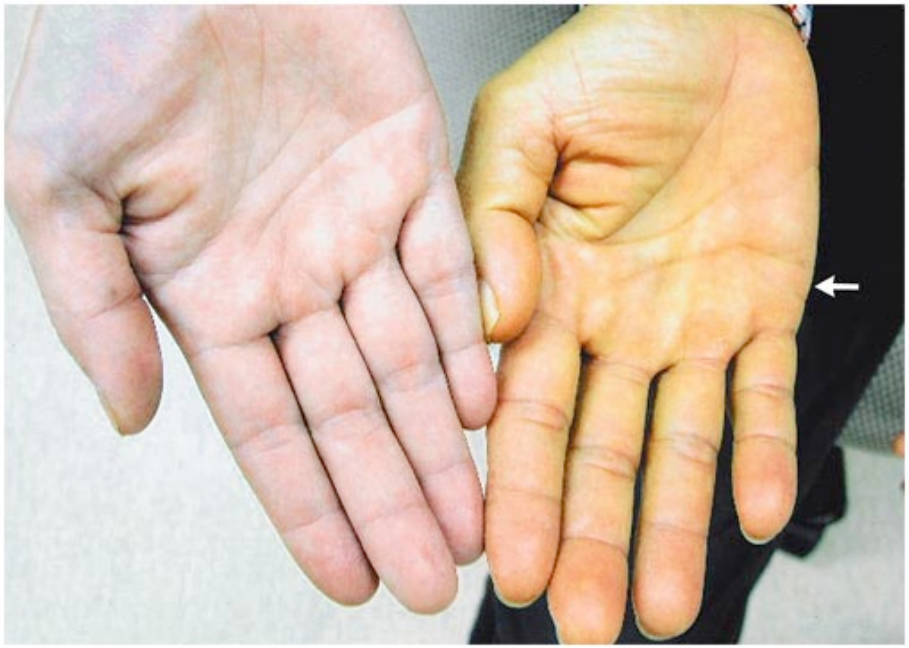
(a)

Figure 18.26b

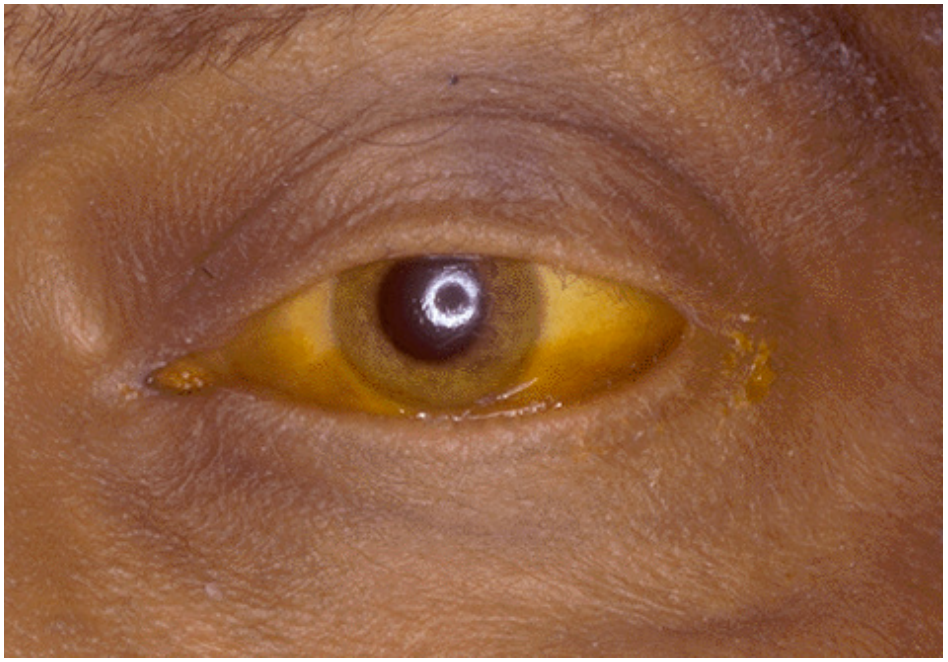
(b)

Jaundice

Excess bilirubin in blood looks yellow



http://pancreaticcanceraction.org/facts-figures/jaundice/



http://library.med.utah.edu/WebPath/CINJHTML/CINJ049.html

http://www.webmd.com/skin-problems-and-treatments/picture-of-jaundice

Neonatal Jaundice

Neonatal liver may lack enzymes to process bilirubin
Blue light phototherapy makes bilirubin more polar

Bile & Gallbladder Disorders

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irritation of the gall bladder

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