Biochemical Aspects of Digestion of Lipids

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GIT Block

Objectives

By the end of this lecture the Second Year Medicine students will be able to:

- Understand the process of digestion of dietary lipids including, the organs involved, the enzymes required, and the end products
- Study the synthesis, secretion and fate of chylomicrons
- Understand the clinical manifestations of diseases that involve defective lipid digestion and/or absorption (indigestion and malabsorption syndrome)

Overview

- Dietary lipids: organs and enzymes
- Lipid digestion in the stomach and intestine
- Lipid degradation by the pancreatic enzymes
- Pancreatic insufficiency
- Control of lipid digestion
- Lipid absorption, re-synthesis and secretion
- Lipid malabsorption
- Use of dietary lipids by the tissues

Dietary lipids

- Dietary lipids intake is ~81 g/day

  Triacylglycerol is >90%

  The remainder includes:
  - Cholesterol
  - Cholesterol ester
  - Phospholipids
  - Glycolipids
  - Free fatty acids

Dietary lipids: Organs and Enzymes

Stomach

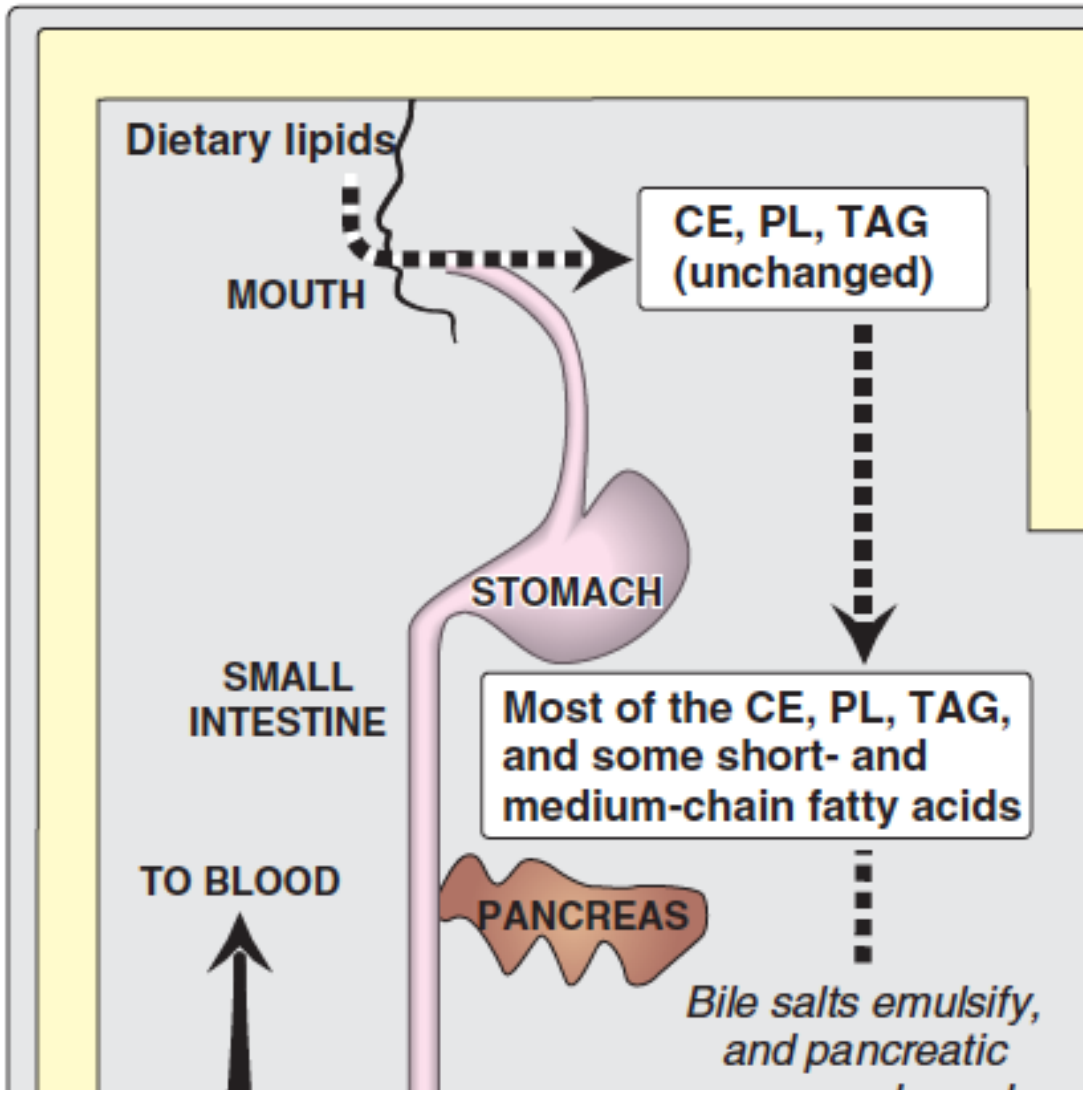
- Lingual lipase
- Gastric lipase

Small intestine

- Lipase / Co-lipase
- Cholesterol esterase
- Phospholipase A_2
- Lysophospholipase

Lipids digestion in the stomach

- Catalyzed by an acid-stable lipase (lingual lipase)
- Triacyglycerols (TAGs) are hydrolyzed by the lipases secreted by the:
  - Back of the tongue and gastric mucosa
- Acid lipases are important for lipid (milk fat) digestion in neonates and patients with pancreatic insufficiency


Dietary lipids
MOUTH
CE, PL, TAG
(unchanged)
STOMACH
SMALL
INTESTINE
Most of the CE, PL, TAG,
and some short- and
medium-chain fatty acids
TO BLOOD
PANCREAS
Bile salts emulsify,
and pancreatic

Lipid digestion in the small intestine

Emulsification:

- Occurs in the duodenum
- Increases surface area of lipid droplets
- To maximize the effect of digestive enzymes
- Two mechanisms:
    1. Detergent properties of bile salts in the bile
       Bile salts emulsify dietary lipid particles
    2. Mechanical mixing by peristalsis

Lipid degradation by pancreatic enzymes

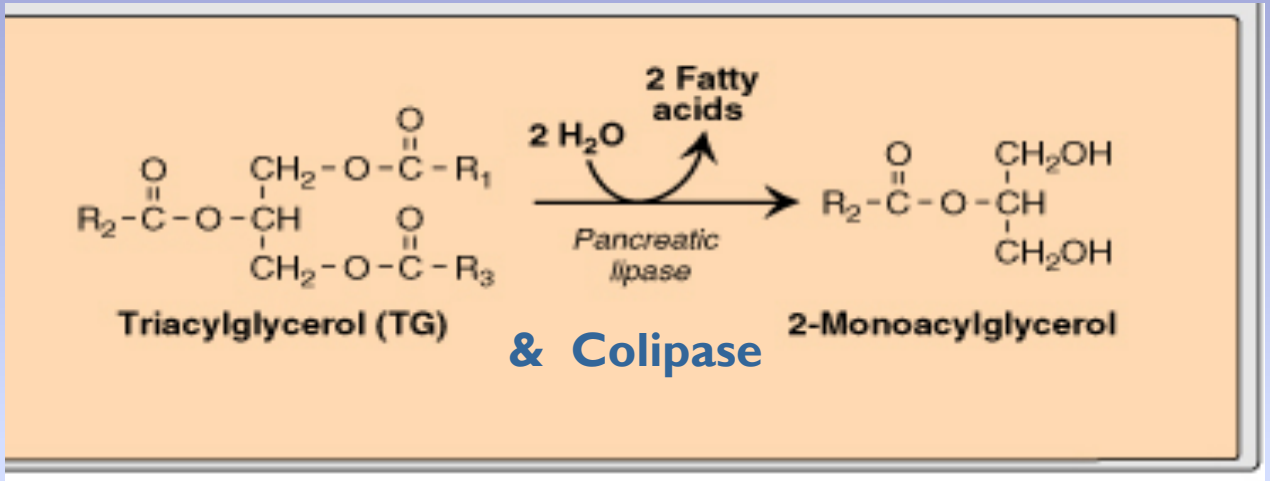
TAG degradation:

- Performed by pancreatic lipase, co-lipase
- Removes fatty acids at C1 and C3
- Leaving 2-monoacyglycerol and free fatty acids (FFAs)

Cholesteryl ester degradation:

- Hydrolyzed by cholesterol esterase
- Produces cholesterol + FFAs

Digestion of TAG by Pancreatic Lipase



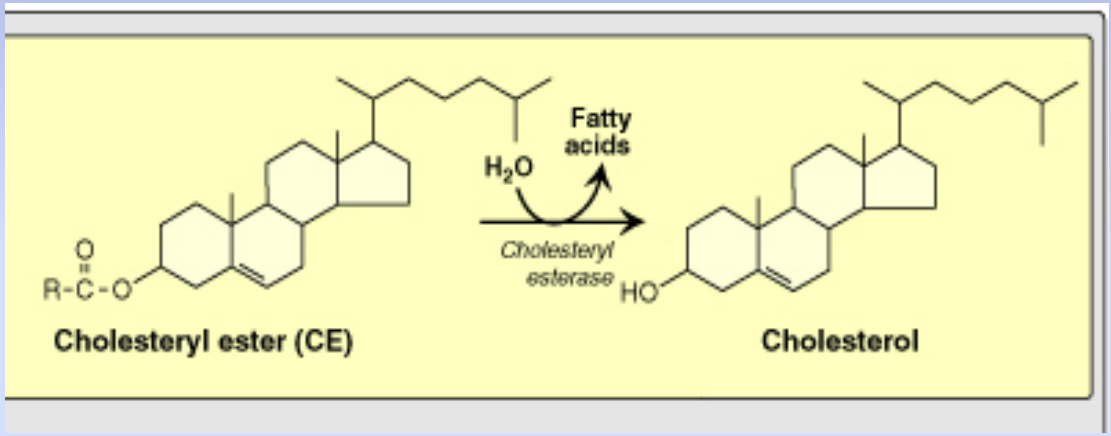
& Colipase

Pancreatic lipase :

Found in high conc. in pancreatic secretion (2-3% of total proteins)

Inhibited by Orlistat, an anti-obesity drug

Digestion of Cholesterol Ester by Cholesterol Esterase



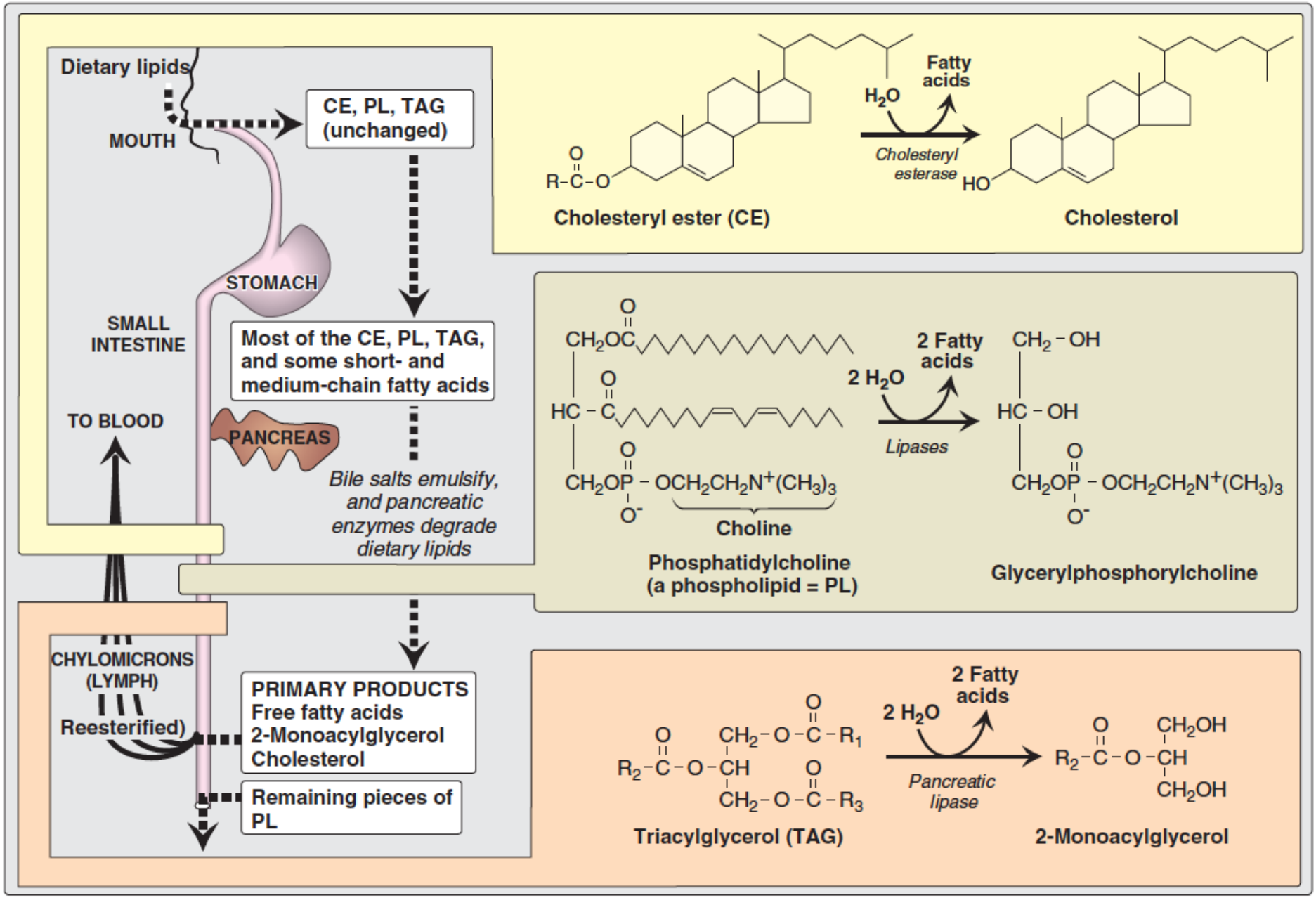
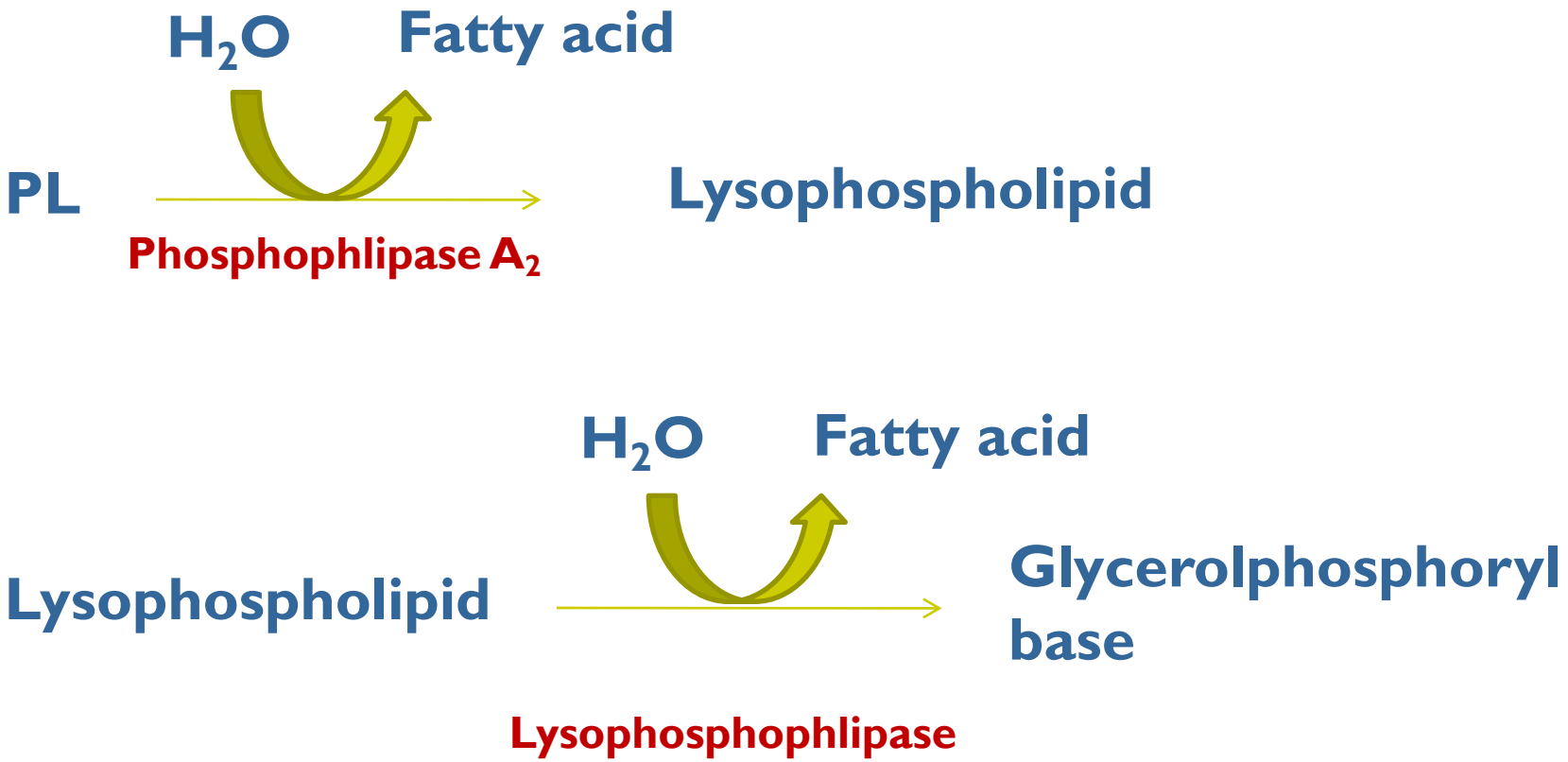


Figure 15.2
Overview of lipid digestion.

Phospholipid Degradation



Pancreatic insufficiency in cystic fibrosis (CF)

- CF is due to genetic mutations in CFTR (transmembrane conductance regulator protein)
- Functions as chloride channel on epithelium
- Defective CFTR causes:
  - Decreased secretion of chloride
  - Increased reabsorption of sodium and water
- Decreased hydration in pancreas thickens the pancreatic secretions
- Pancreatic enzymes are unable to reach the intestine
- Treatment: enzyme and fat-soluble vitamin supplementation

Control of lipid digestion

Controlled by hormones:

- Cholecystokinin (CKK)
  - Acts on gallbladder to release bile
  - Acts on pancreas to release enzymes
  - Decreases gastric motility (slow release of gastric contents)
- Secretin
  - Low pH stimulates its secretion
  - Acts on pancreas to release bicarbonate and liver to release bile
  - Neutralizes the pH of the contents before entering the small intestine

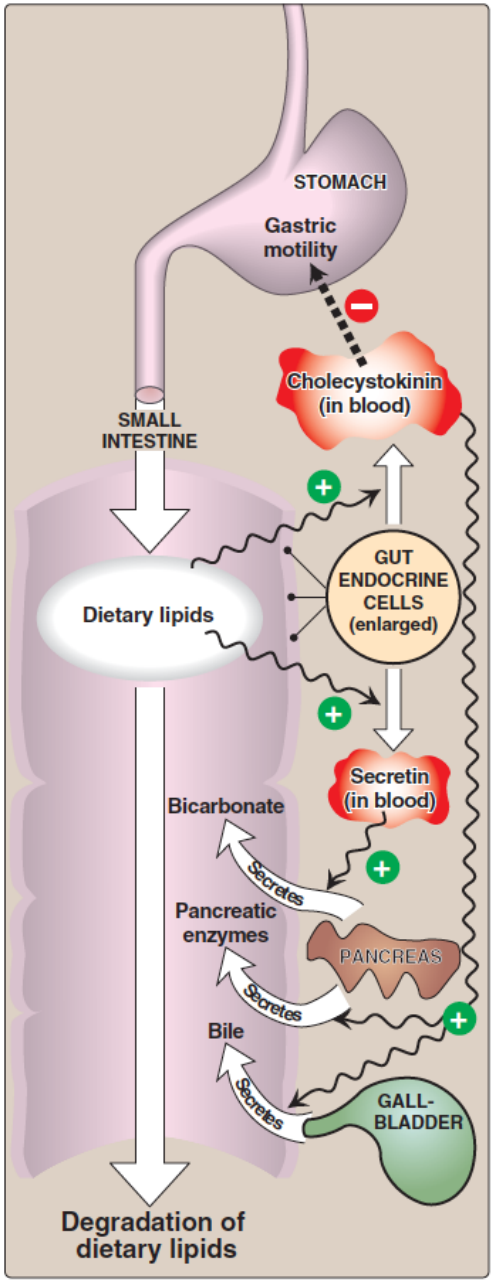


Figure 15.4
Hormonal control of lipid digestion in the small intestine.

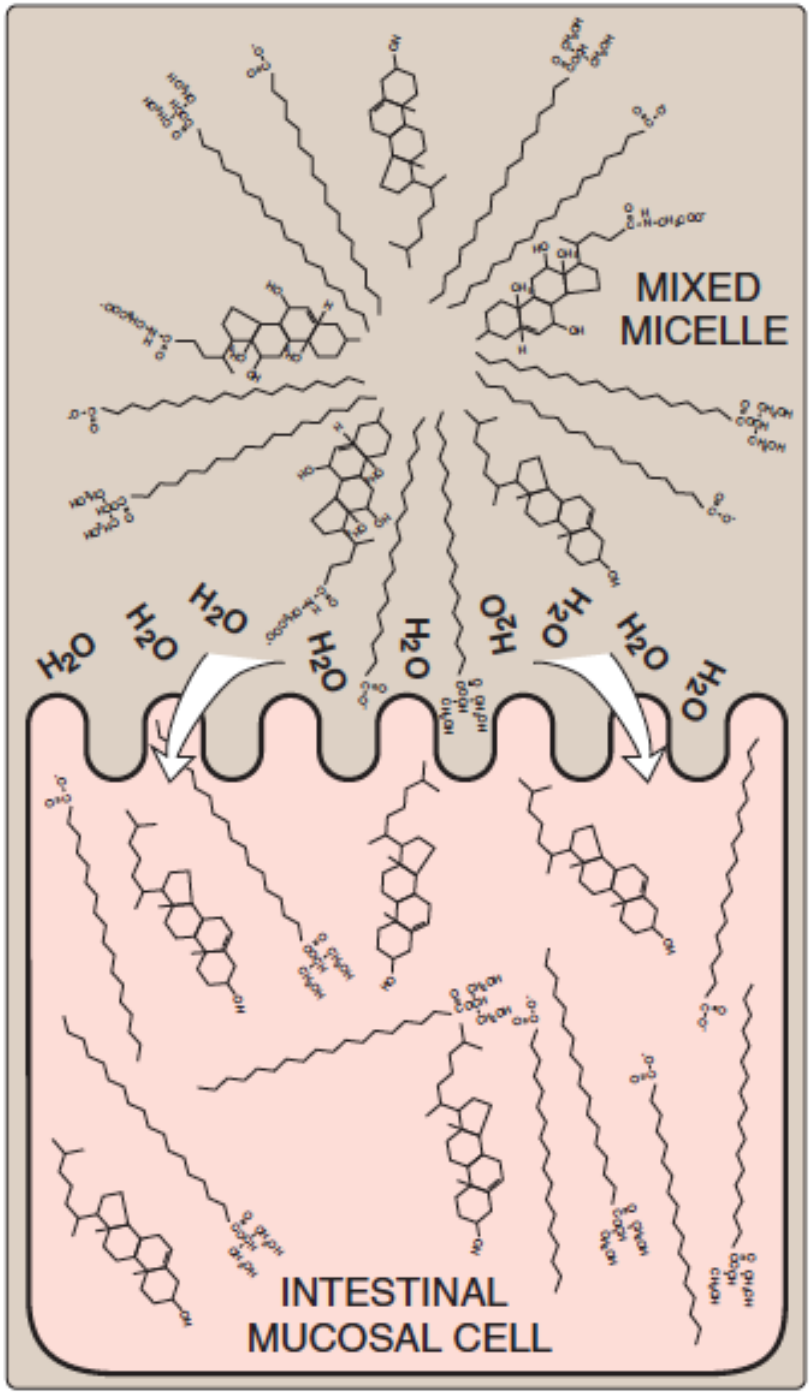
Lipid absorption by enterocytes

Products of lipid digestion

- FFAs, free cholesterol, 2-monoacylglycerol combined with bile salts and fat-soluble vitamins

- They form mixed micelles (disk-shaped particles)
- Absorbed by brushed border membrane of enterocytes
- Short and medium chain length fatty acids are absorbed directly

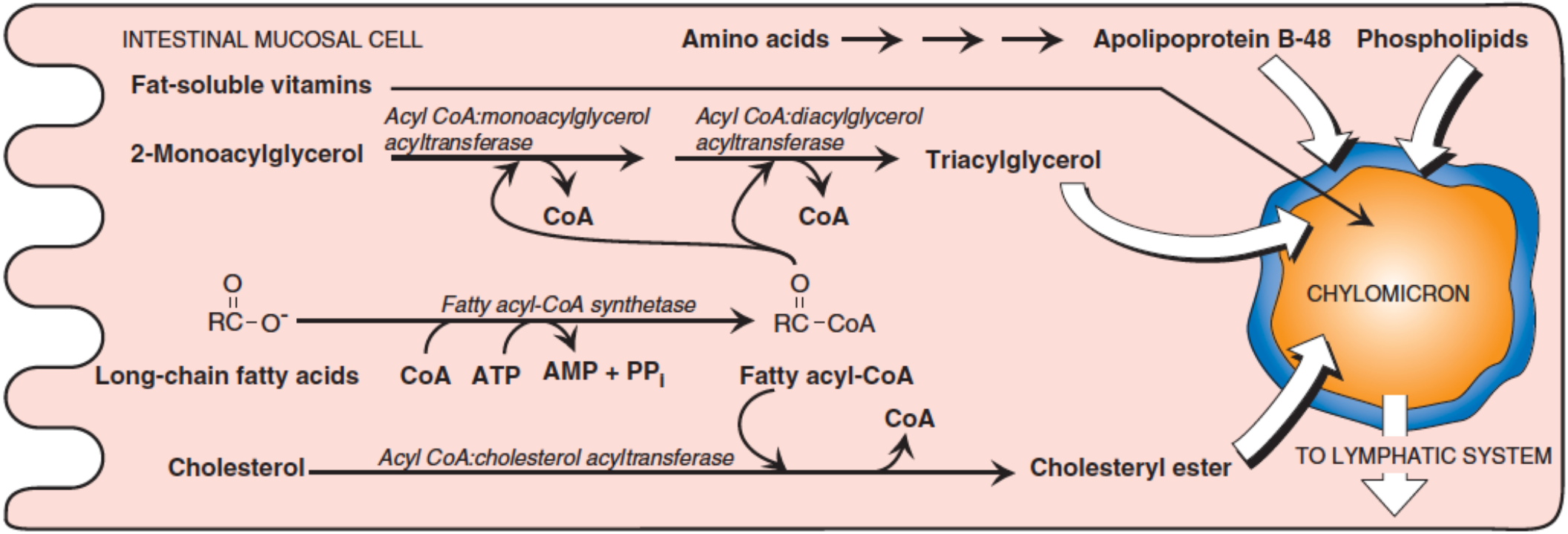
Mixed micelles are hydrophobic inside and hydrophilic outside



Resynthesis of TAG / Cholesteryl esters

- Digested lipids absorbed by enterocytes migrate to endoplasmic reticulum for complex lipid biosynthesis

- Fatty acids → Fatty acyl CoA
- 2-Monoacyglycerols → TAGs


INTESTINAL MUCOSAL CELL
Amino acids
Apolipoprotein B-48
Phospholipids
Fat-soluble vitamins
2-Monoacylglycerol
Acyl CoA:monoacylglycerol acyltransferase
Acyl CoA:diacylglycerol acyltransferase
Triacylglycerol
CoA
CoA
CHYLOMICRON
Fatty acyl-CoA synthetase
Long-chain fatty acids
CoA
ATP
AMP + PPi
Fatty acyl-CoA
CoA
Cholesterol
Acyl CoA:cholesterol acyltransferase
Cholesteryl ester
TO LYMPHATIC SYSTEM

Assembly of chylomicrons by enterocytes

- Newly synthesized TAG and cholesterol ester are packaged as lipid droplets surrounded by thin layer of:
  - Apolipoprotein B-48 (apo B-48)
  - Phospholipids
  - Free cholesterol

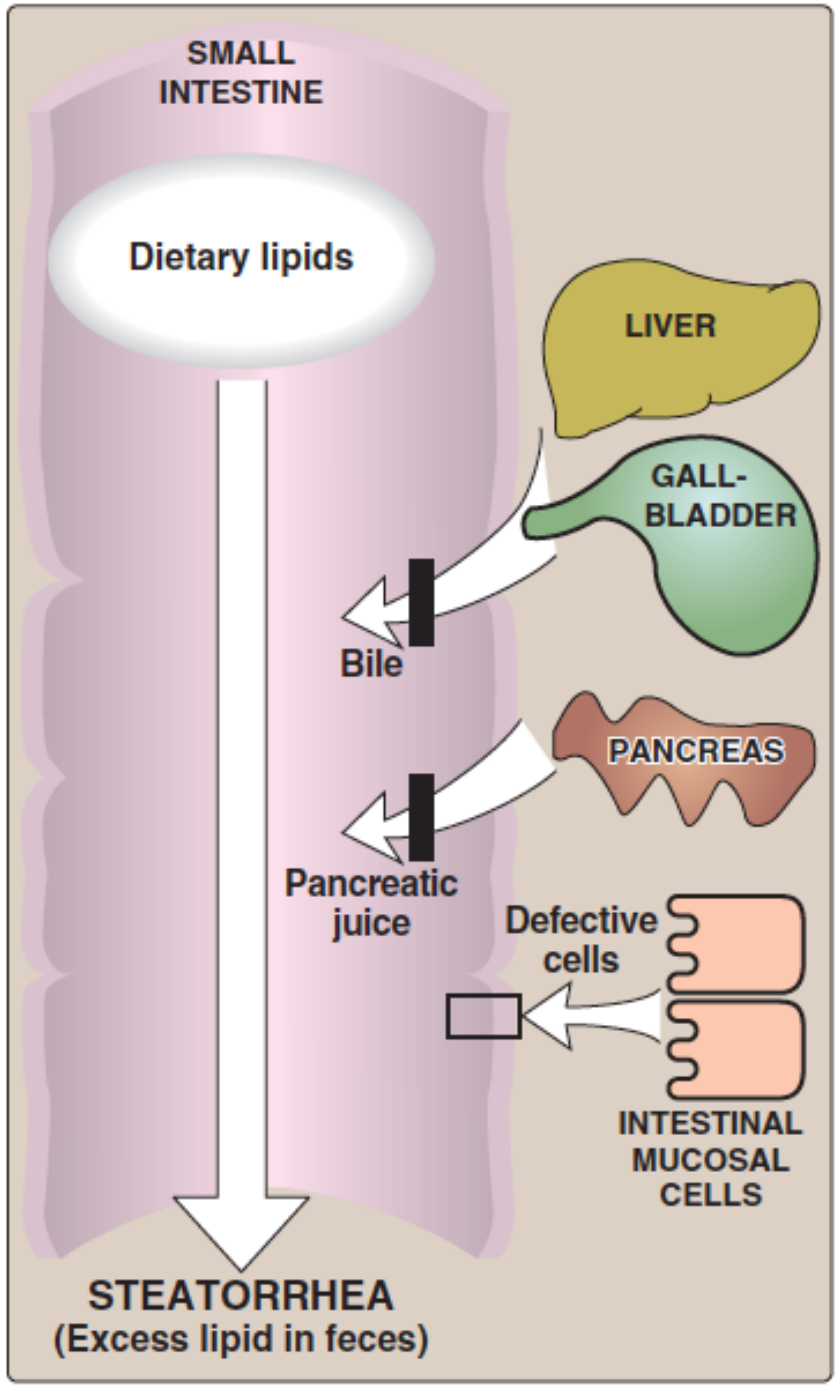
Secretion of chylomicrons by enterocytes

- By exocytosis into lymphatic vessels around villi of small intestine (lacteals) which enter into systemic circulation

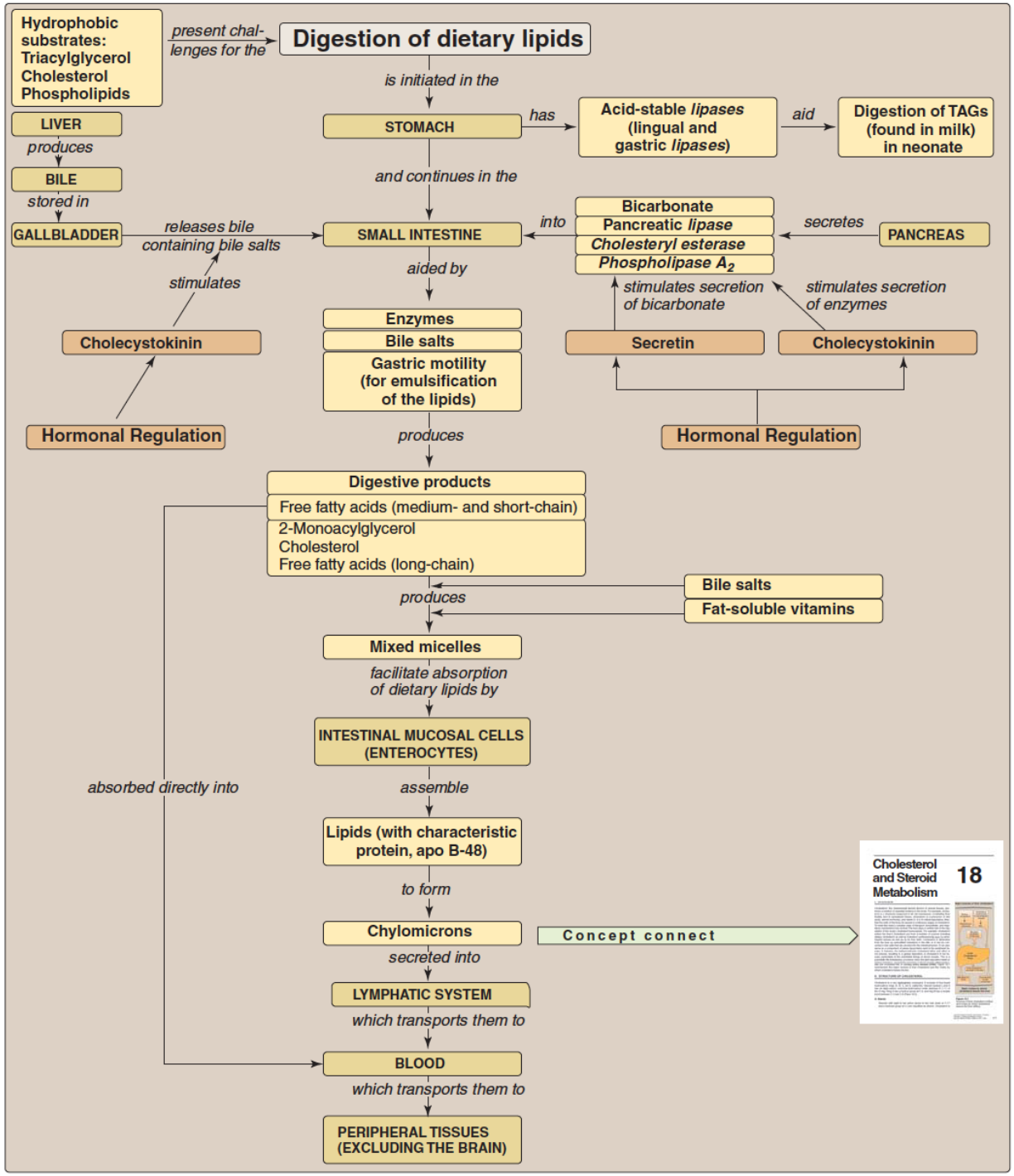
- Serum becomes milky after a fatty meal

Lipid malabsorption

- Increased excretion of lipids, fat-soluble vitamins and essential FAs in the feces
- Due to defects in lipid digestion or absorption
- Can be caused by CF or shortened bowel



Key concepts for digestion and absorption of dietary lipids



Take home message

- Lipid digestion begins in stomach
- Emulsification of lipids occurs in duodenum, helped by peristalsis and bile salts
- Intestinal digestion of lipids by pancreatic enzymes
- Lipid absorption by mixed micelles
- Re-synthesis of TAGs, cholesterol ester and PLs inside the intestinal mucosal cells
- Assembly and secretion of chylomicrons into lymphatic lacteals and then into systemic circulation

References

- Lippincott's Illustrated Reviews, Biochemistry, 5th edition, Denise R. Ferrier, Lippincott Williams & Wilkins, USA.
- Chapter 15: pages 173-180