

Biochemical Aspects of Digestion of Lipids

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Objectives

By the end of this lecture the Second Year 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 chylomicron
- Understand the clinical manifestations of diseases that involve defective lipid digestion and/or absorption (indigestion and malabsorption syndrome)

Overview

- Dietary lipid: 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 lipid 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

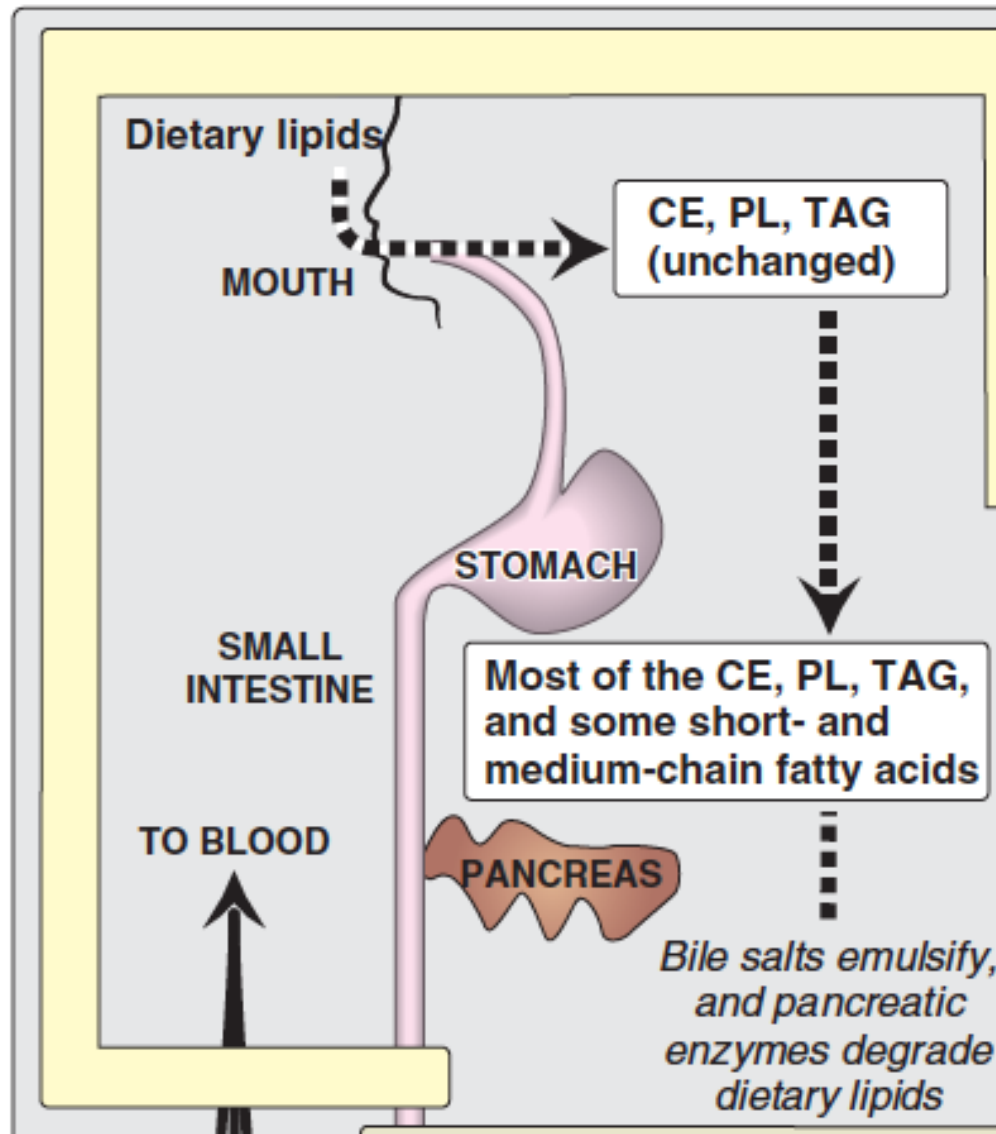
- Lingual lipase
- Gastric lipase

Small intestine

- Lipase / Co-lipase
- Cholesterol esterase
- Phospholipase A₂
- Lysophospholipase

Lipids digestion in the stomach

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



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

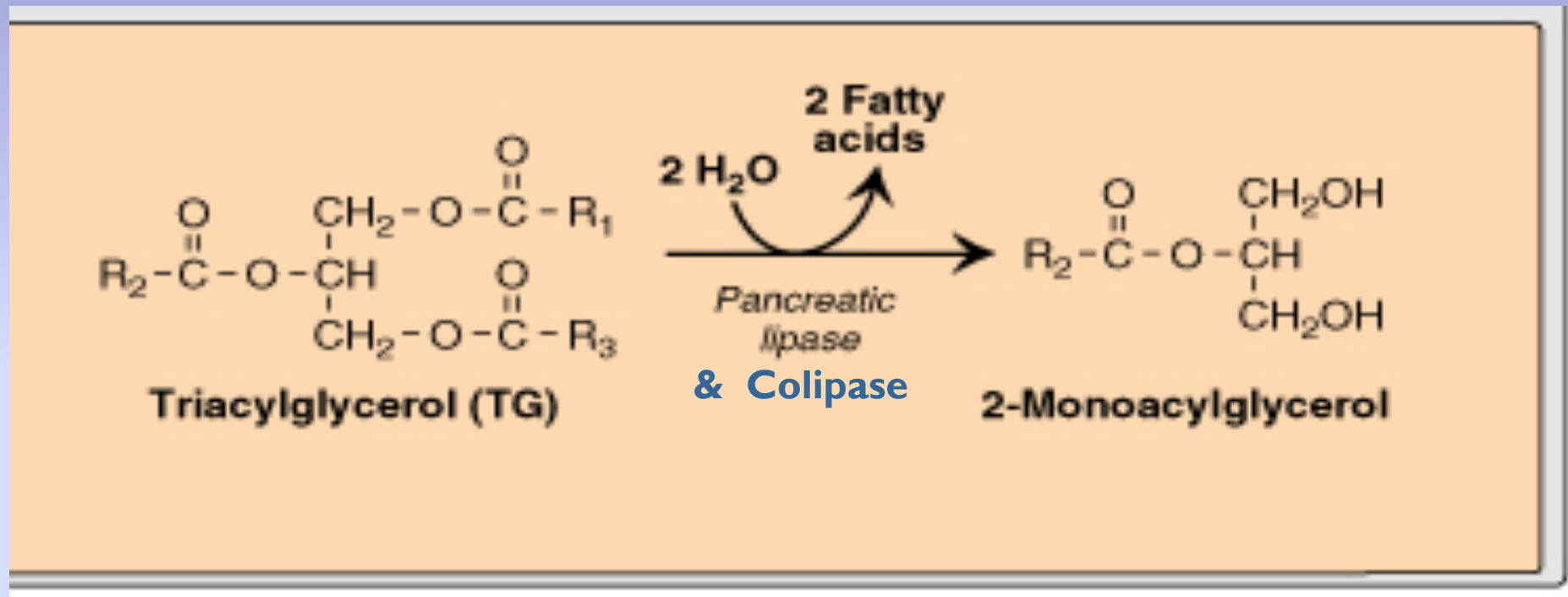
TAG degradation:

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

Cholesteryl ester degradation:

- Hydrolyzed by cholesterol esterase
- Produces cholesterol + FFAs

Digestion of TAG by Pancreatic Lipase

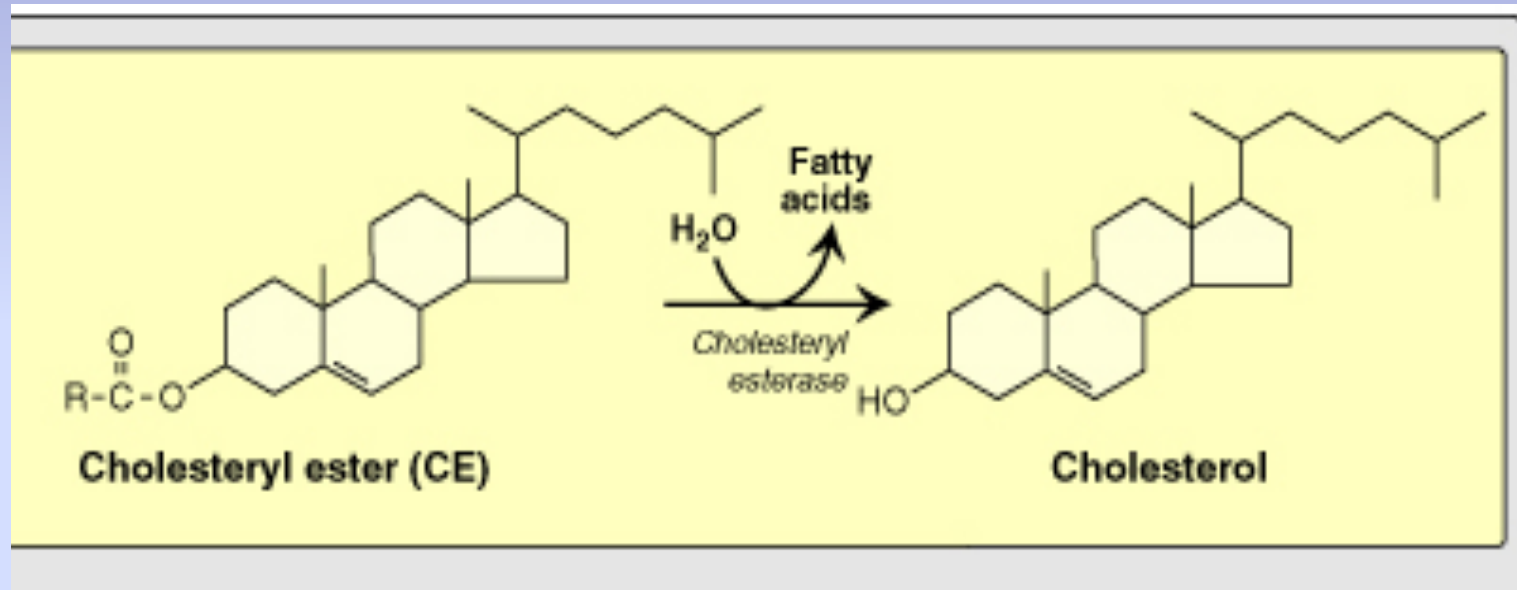


Pancreatic lipase :

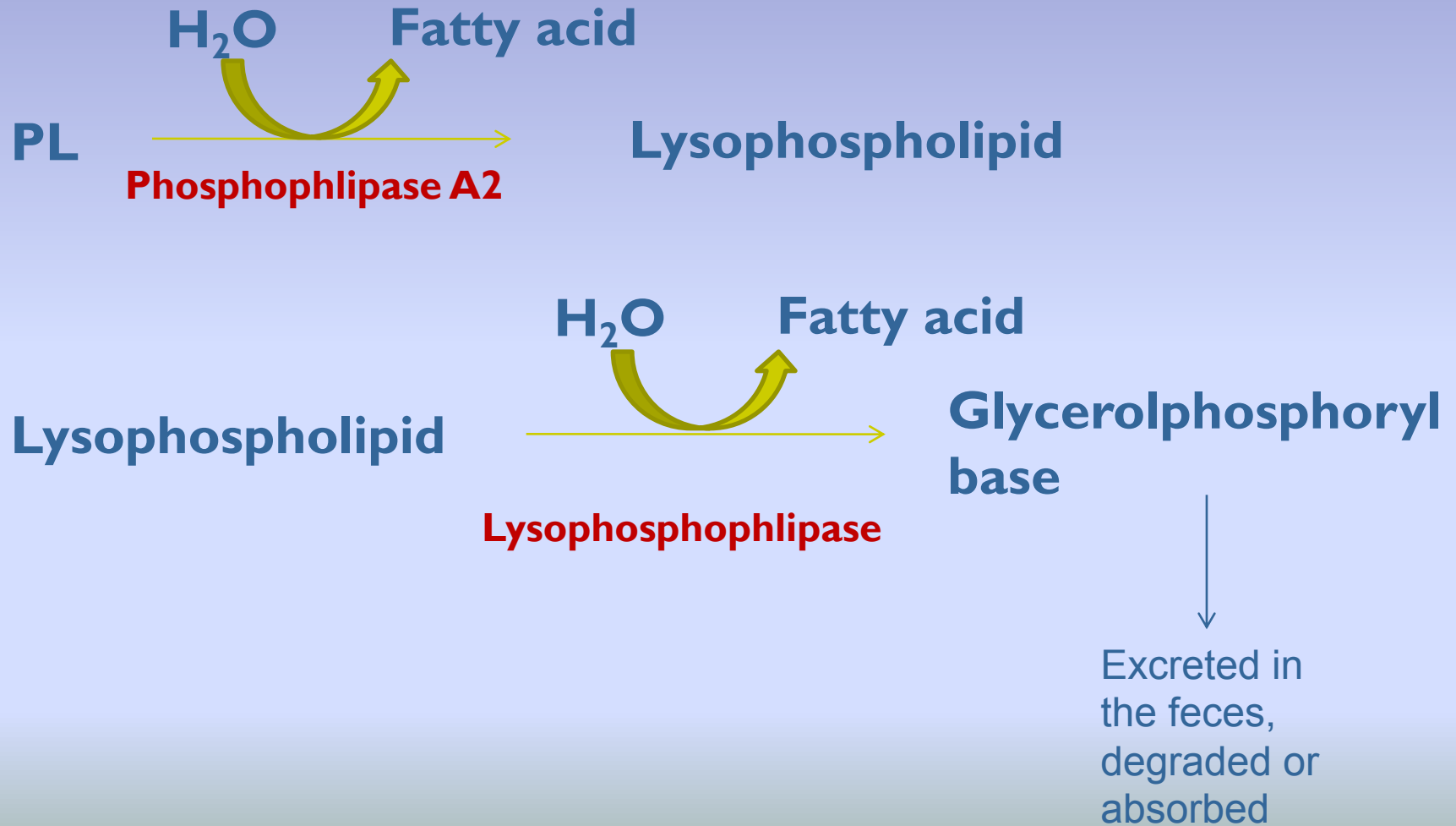
Found in high conc. in pancreatic secretion (2-3% of total proteins)

Inhibited by **Orlistat**, an antiobesity drug

Digestion of Cholesterol Ester by Cholesterol Esterase



Digestion of Phospholipids (PL) by Phospholipase A2 & Lysophospholipase



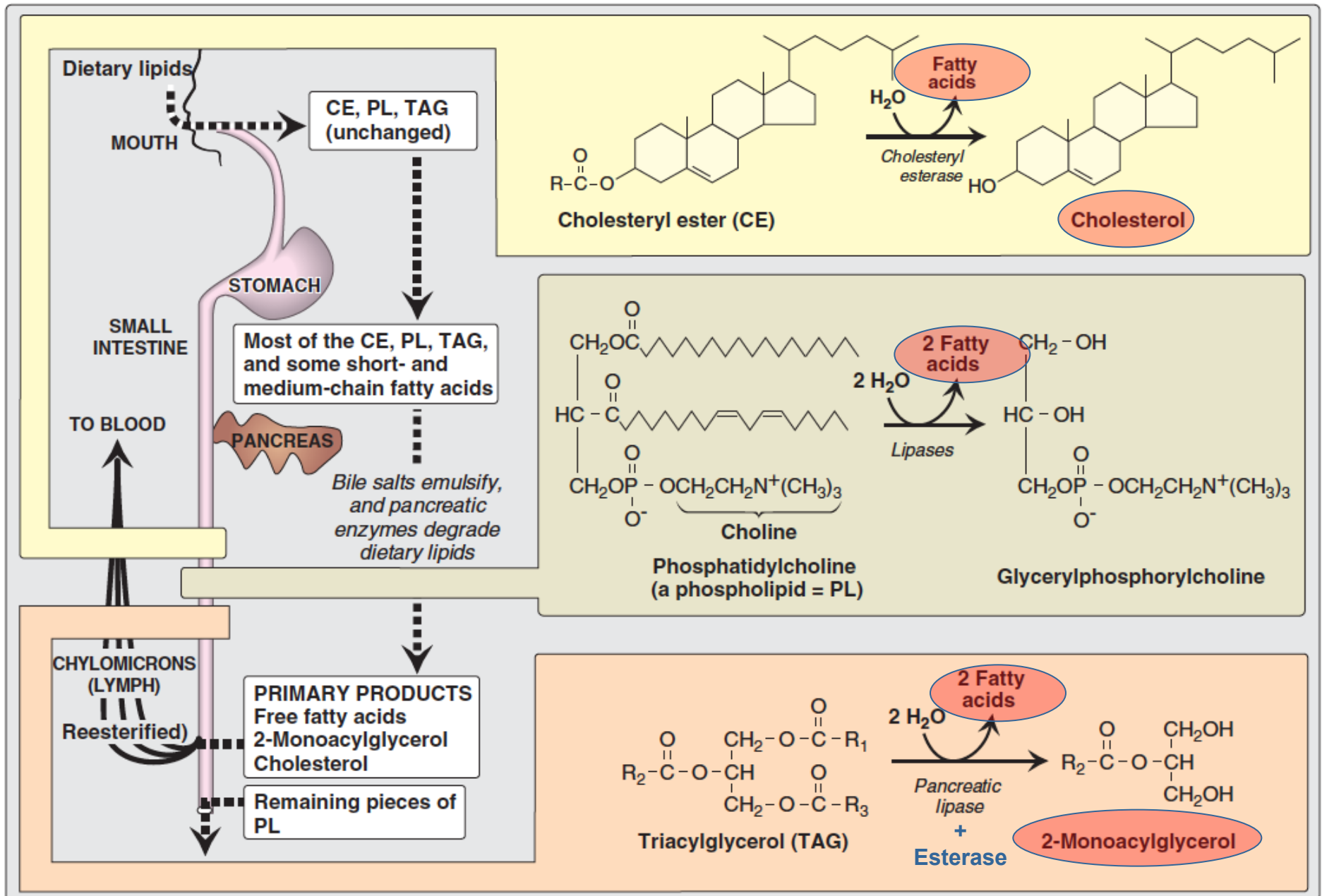


Figure 15.2
Overview of lipid digestion.

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 and liver to release bicarbonate
 - Neutralizes the pH of the contents before entering the small intestine

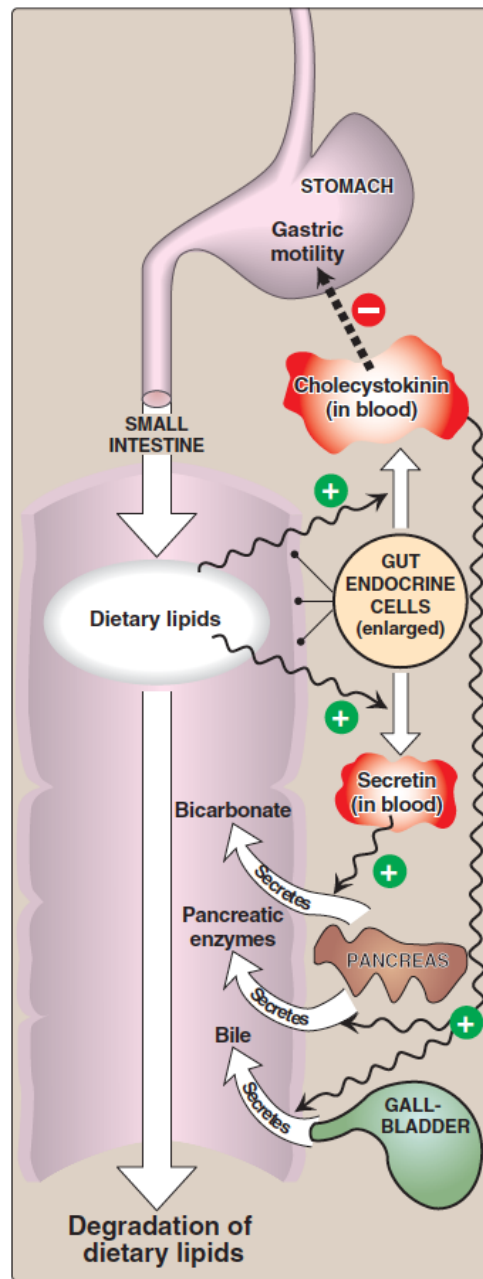
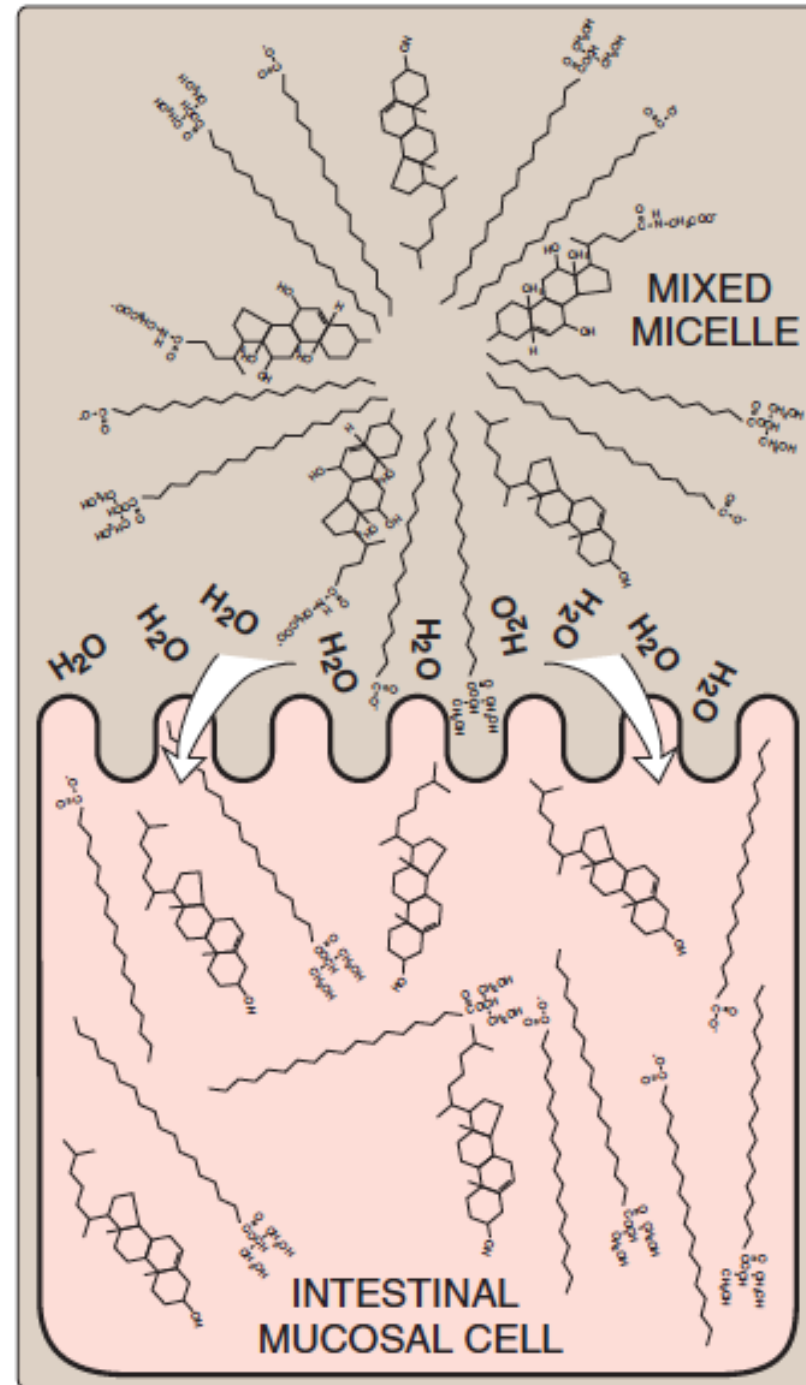


Figure 15.4
Hormonal control of lipid digestion in the small intestine.

Lipid absorption by enterocytes

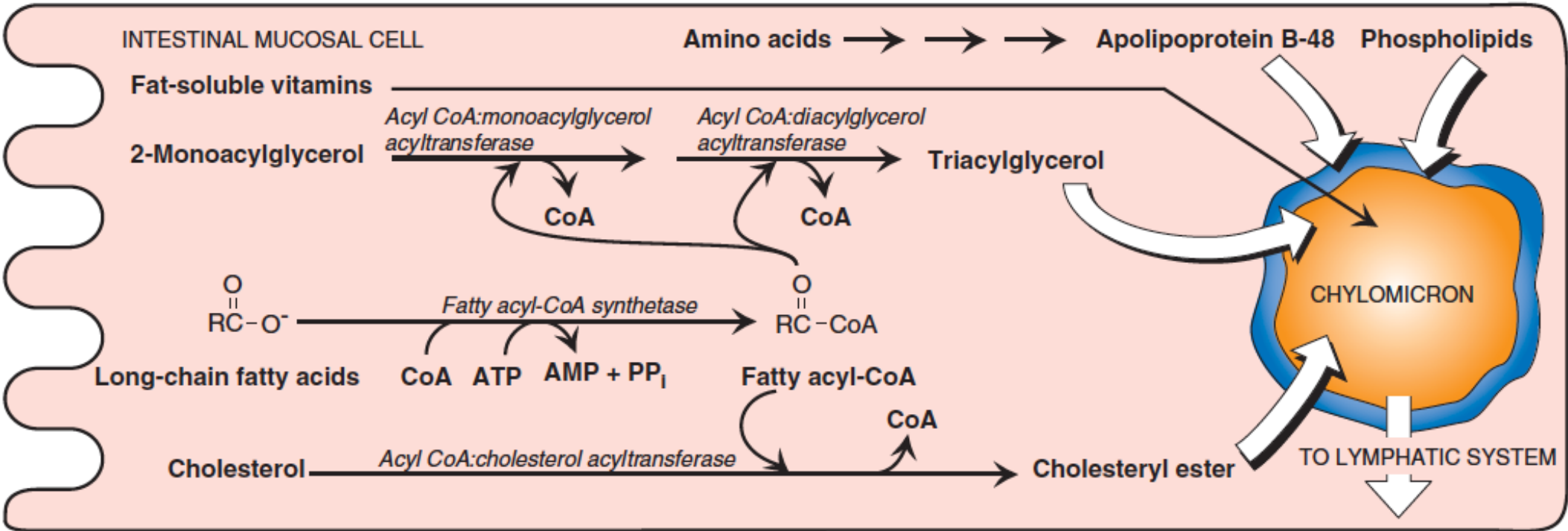
- Products of lipid digestion (FFAs, free cholesterol, 2-monoacylglycerol) combine with bile salts and fat-soluble vitamins
- They form mixed micelles (disk-shaped particles)
- Absorbed by brush border membrane of enterocytes
- Short and medium chain length fatty acids are absorbed directly

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 → activated to acyl CoA form
- 2-Monoacylglycerols → TAGs



INTESTINAL MUCOSAL CELL

Amino acids \rightarrow \rightarrow \rightarrow Apolipoprotein B-48 Phospholipids

Fat-soluble vitamins

2-Monoacylglycerol

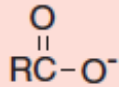
Acyl CoA:monoacylglycerol acyltransferase

Acyl CoA:diacylglycerol acyltransferase

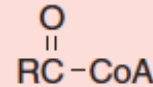
Triacylglycerol

CoA

CoA



Fatty acyl-CoA synthetase



Long-chain fatty acids

CoA

ATP

AMP + PP_i

Fatty acyl-CoA

CoA

Cholesterol

Acyl CoA:cholesterol acyltransferase

Cholesteryl ester

CHYLOMICRON

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

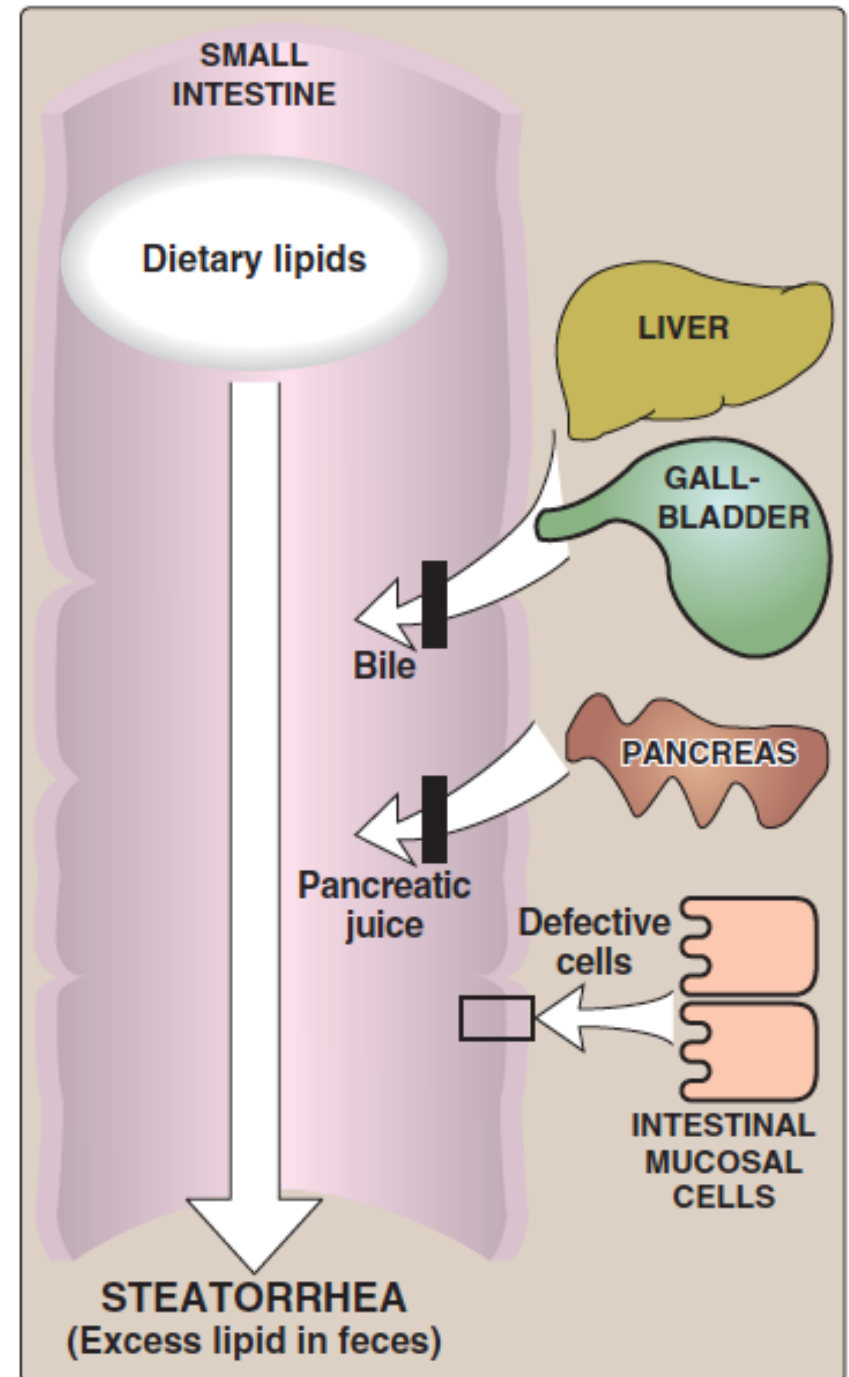
Secretion of chylomicrons by enterocytes

- By exocytosis into lymphatic vessels around villi of small intestine (lacteals) which enter into systemic circulation
- Serum becomes milky after a fatty meal

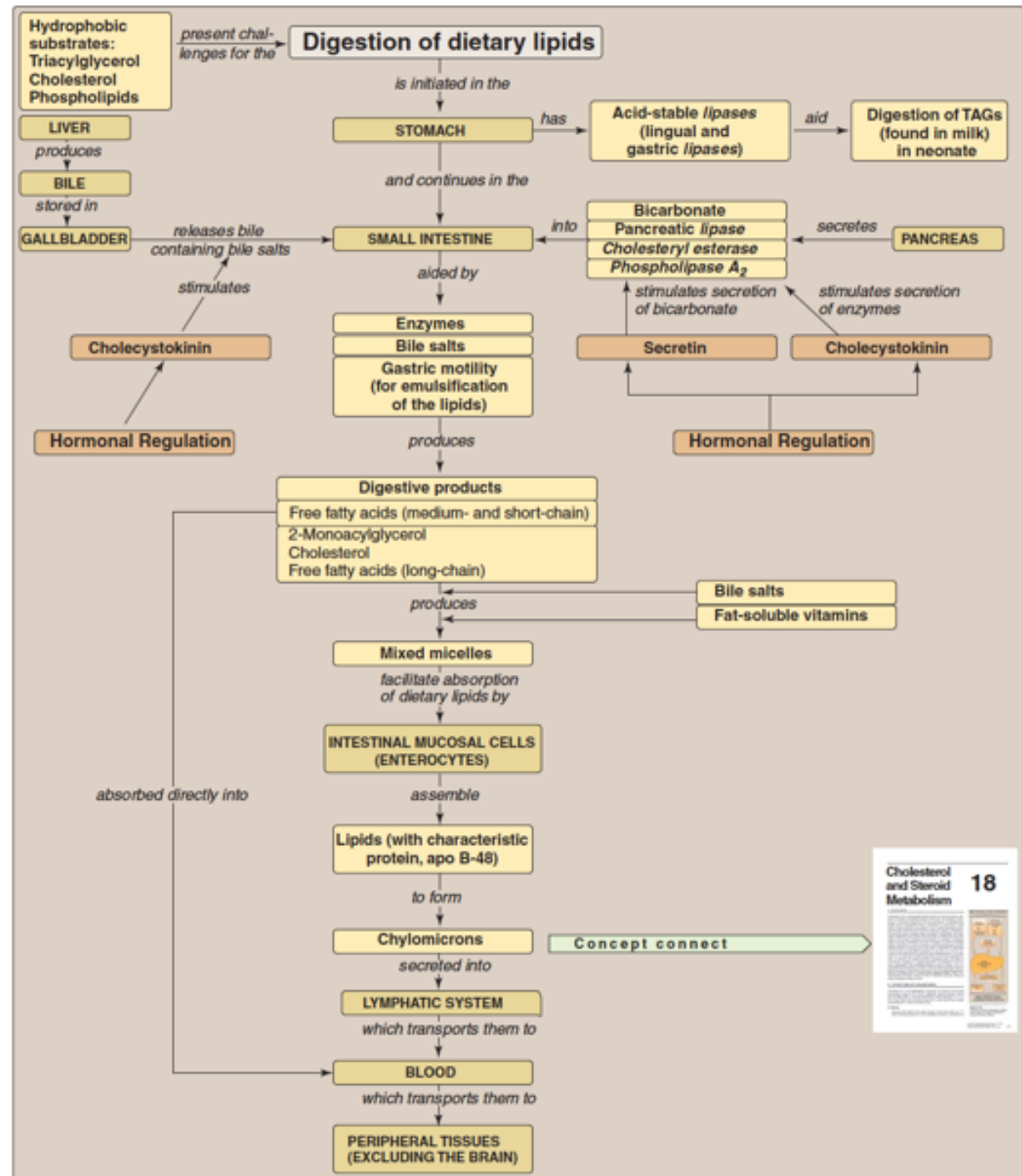


Lipid malabsorption

- 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