

Biochemical Aspects of Digestion of Lipids

Dr. Usman Ghani

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

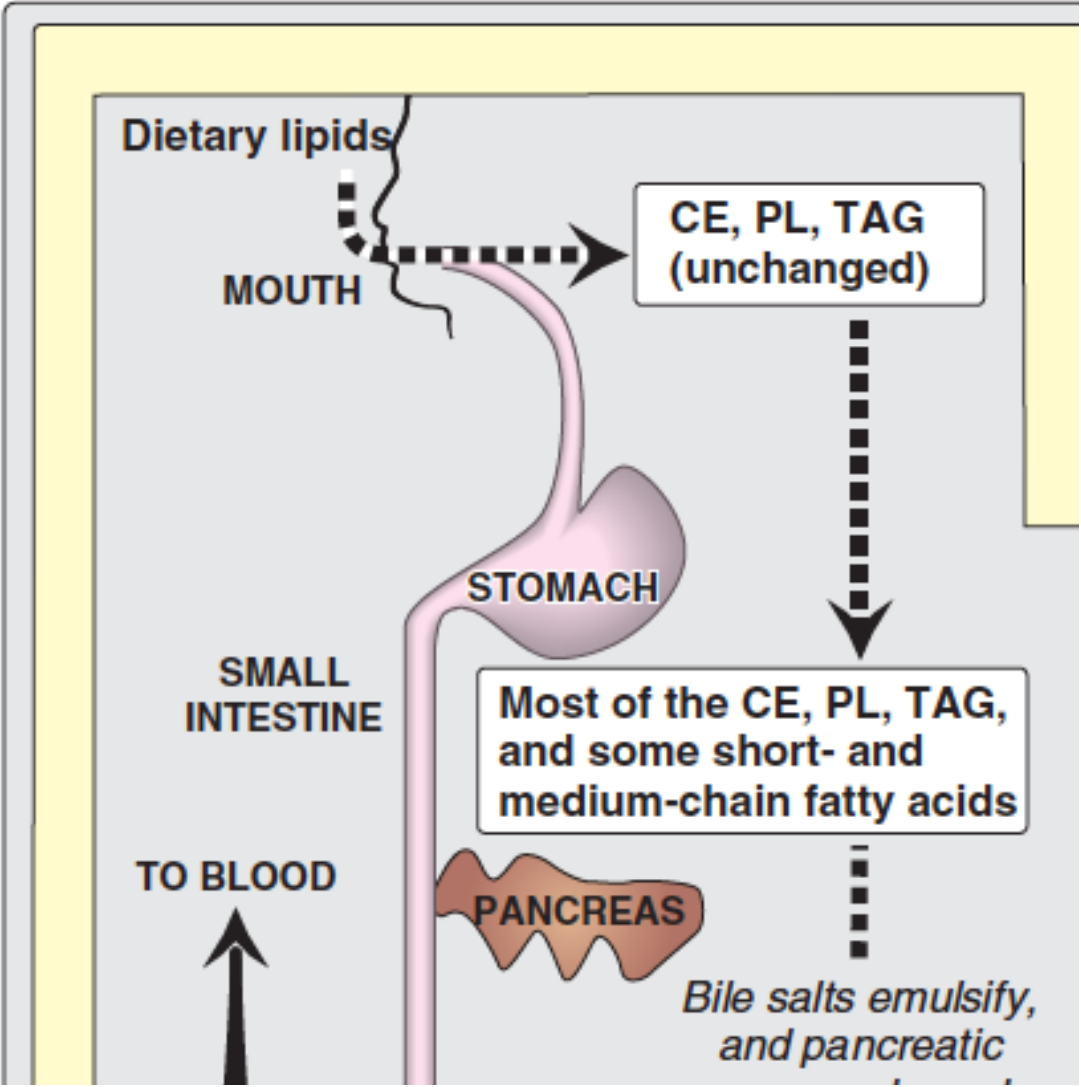
- Lingual lipase
- Gastric lipase

Small intestine

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

Lipids digestion in the stomach

- Catalyzed by an acid-stable lipase (lingual lipase)
- Triacylglycerols (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**



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

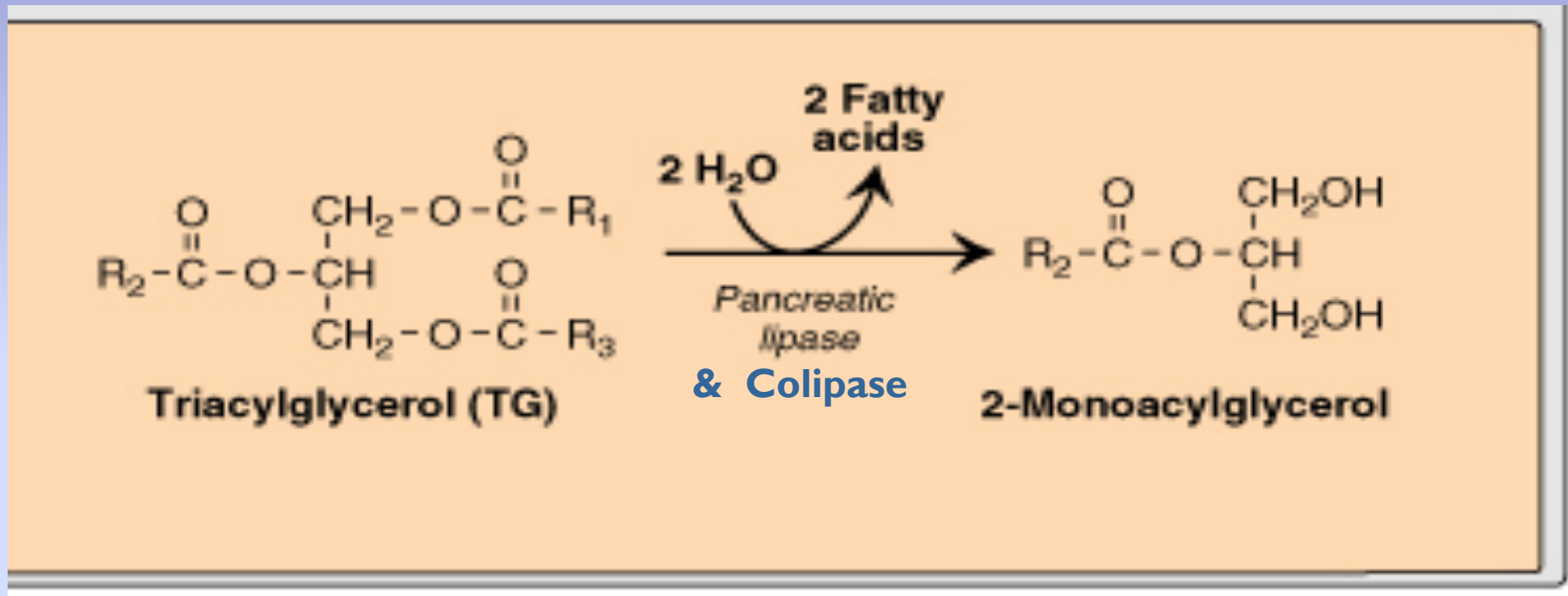
TAG degradation:

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

Cholesteryl ester degradation:

- Hydrolyzed by cholesterol esterase
- Produces cholesterol + FFAs

Digestion of TAG by Pancreatic Lipase

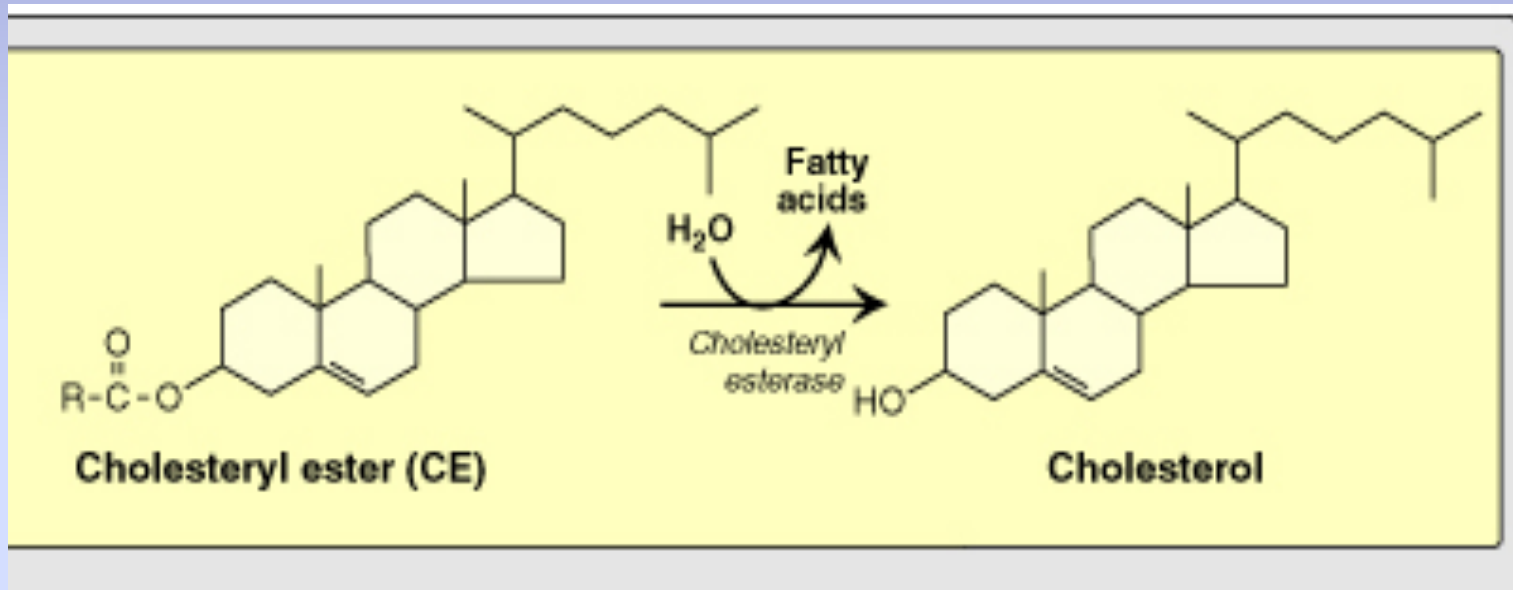


Pancreatic lipase :

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

Inhibited by **Orlistat**, an anti-obesity drug

Digestion of Cholesterol Ester by Cholesterol Esterase



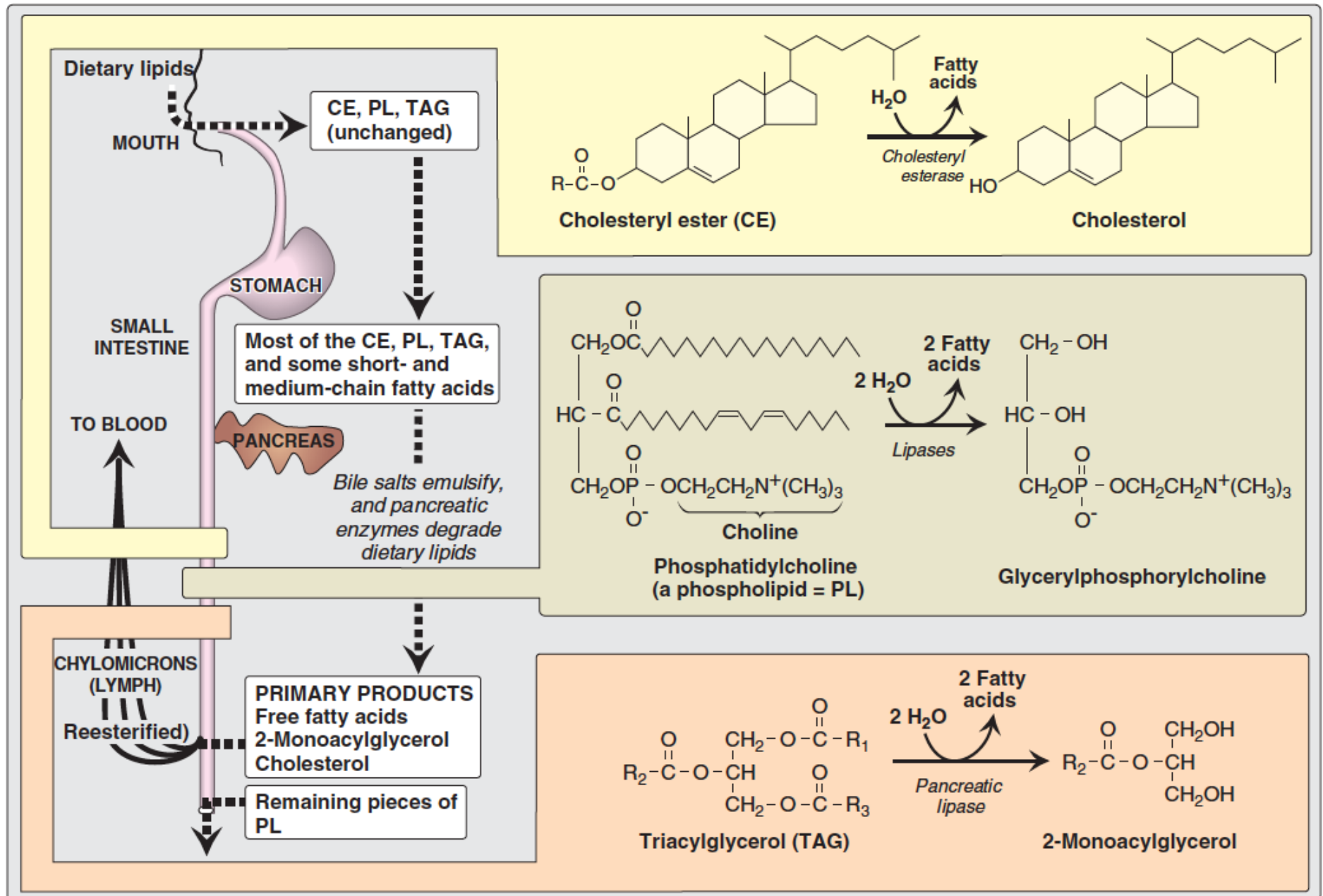
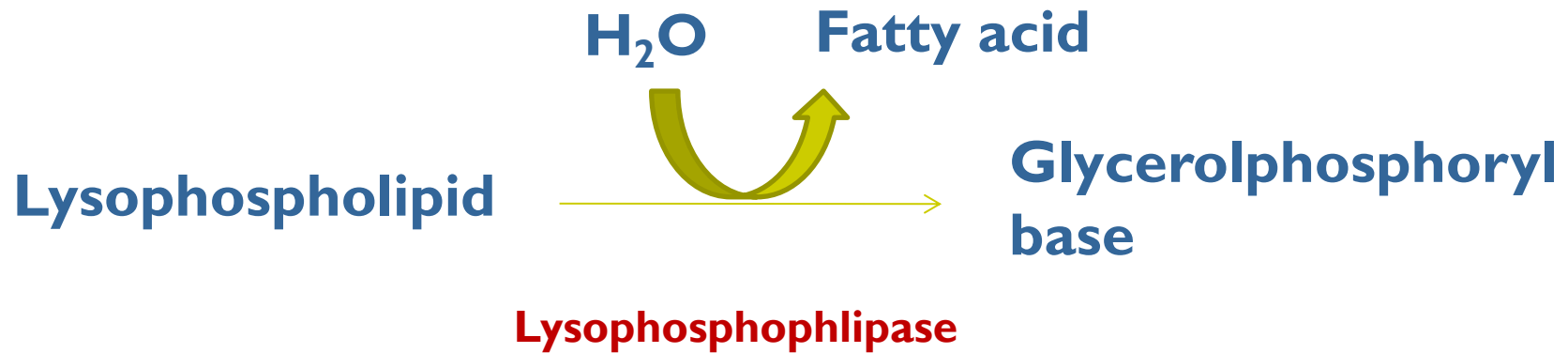
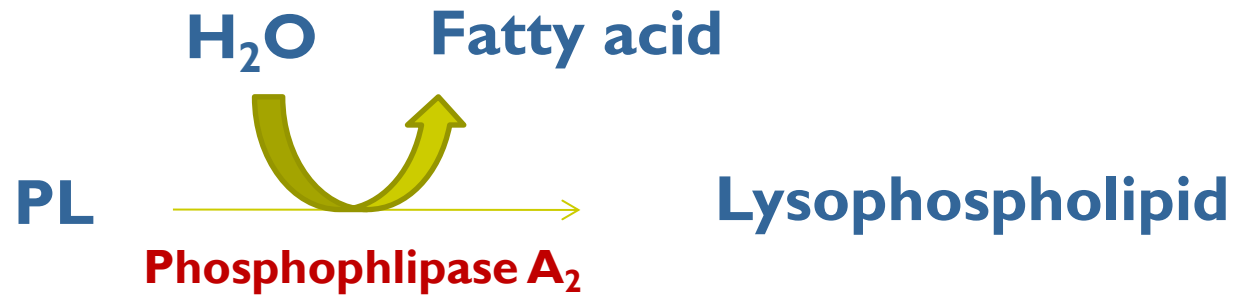


Figure 15.2
Overview of lipid digestion.

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

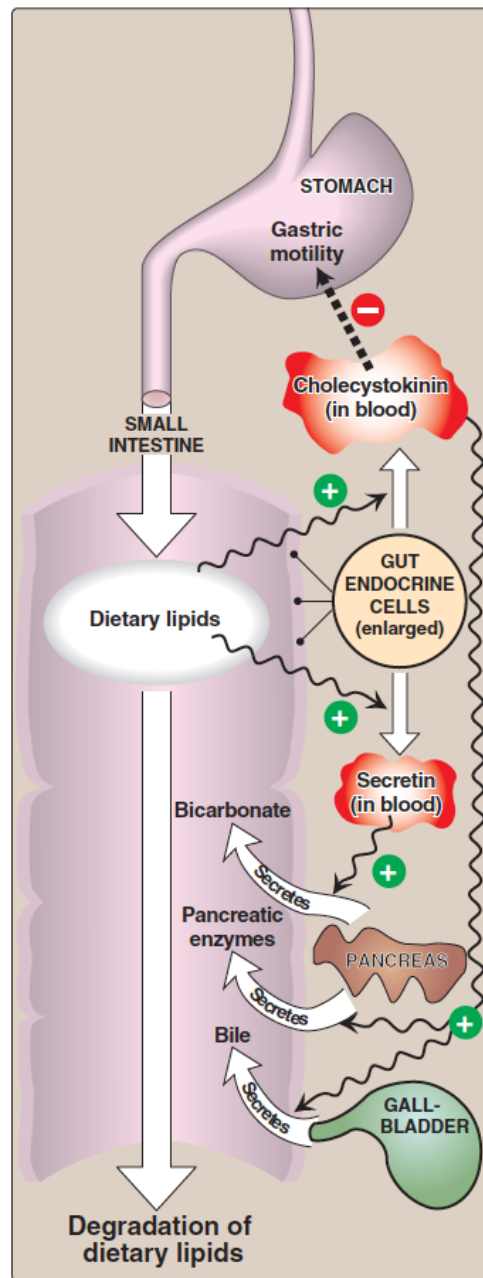


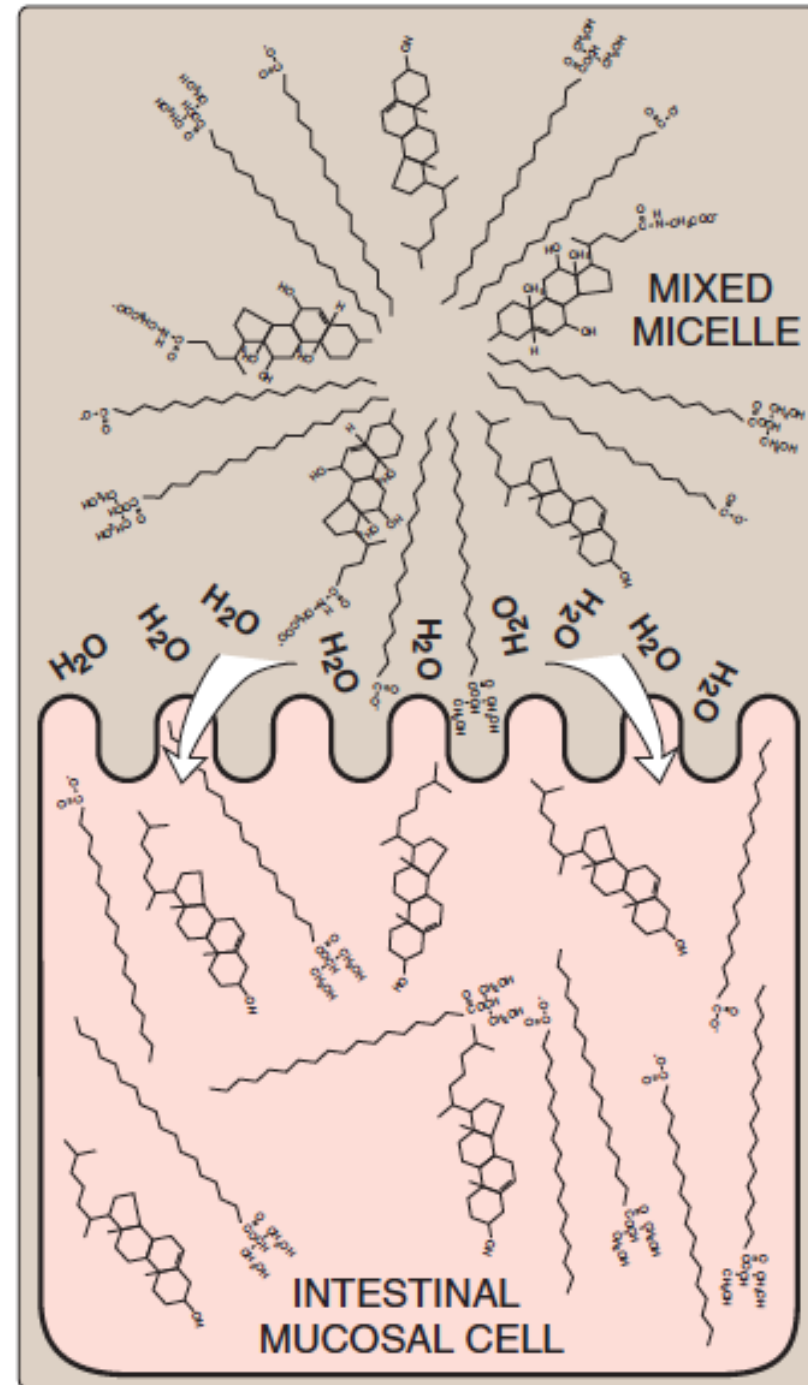
Figure 15.4
Hormonal control of lipid digestion in the small intestine.

Lipid absorption by enterocytes

Products of lipid digestion

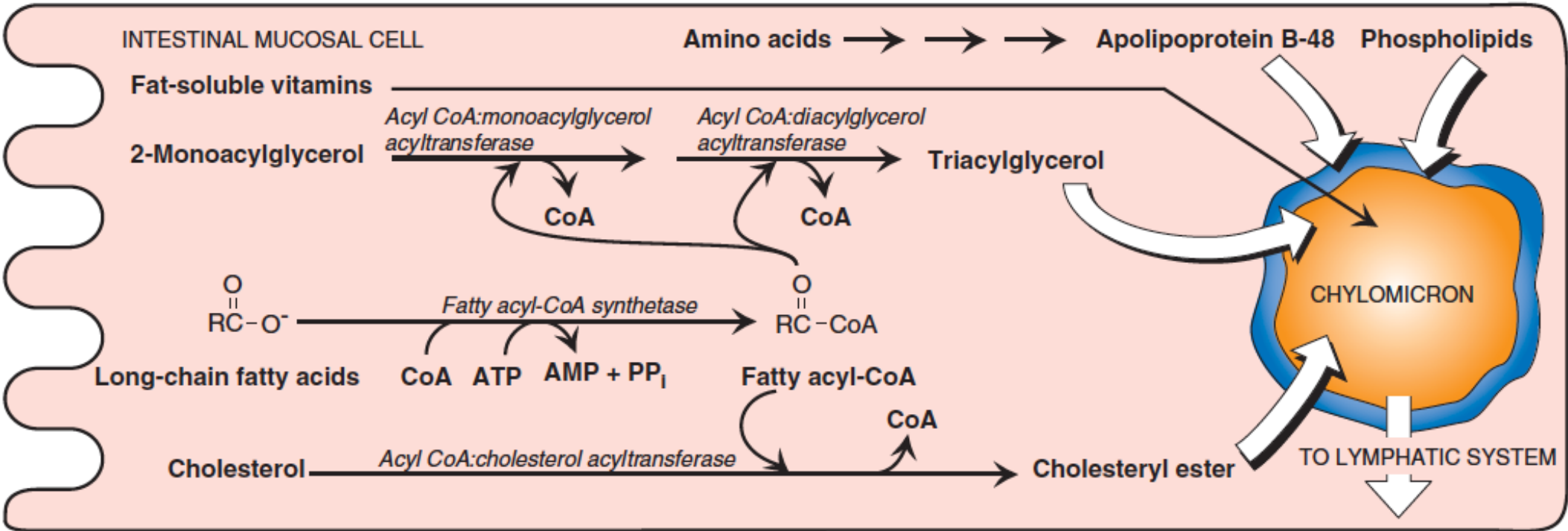
- FFAs, free cholesterol, 2-monoacylglycerol combined with bile salts and fat-soluble vitamins
- They form **mixed micelles** (disk-shaped particles)
- Absorbed by brushed border membrane of enterocytes
- Short and medium chain length fatty acids are absorbed directly

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-Monoacylglycerols → TAGs



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

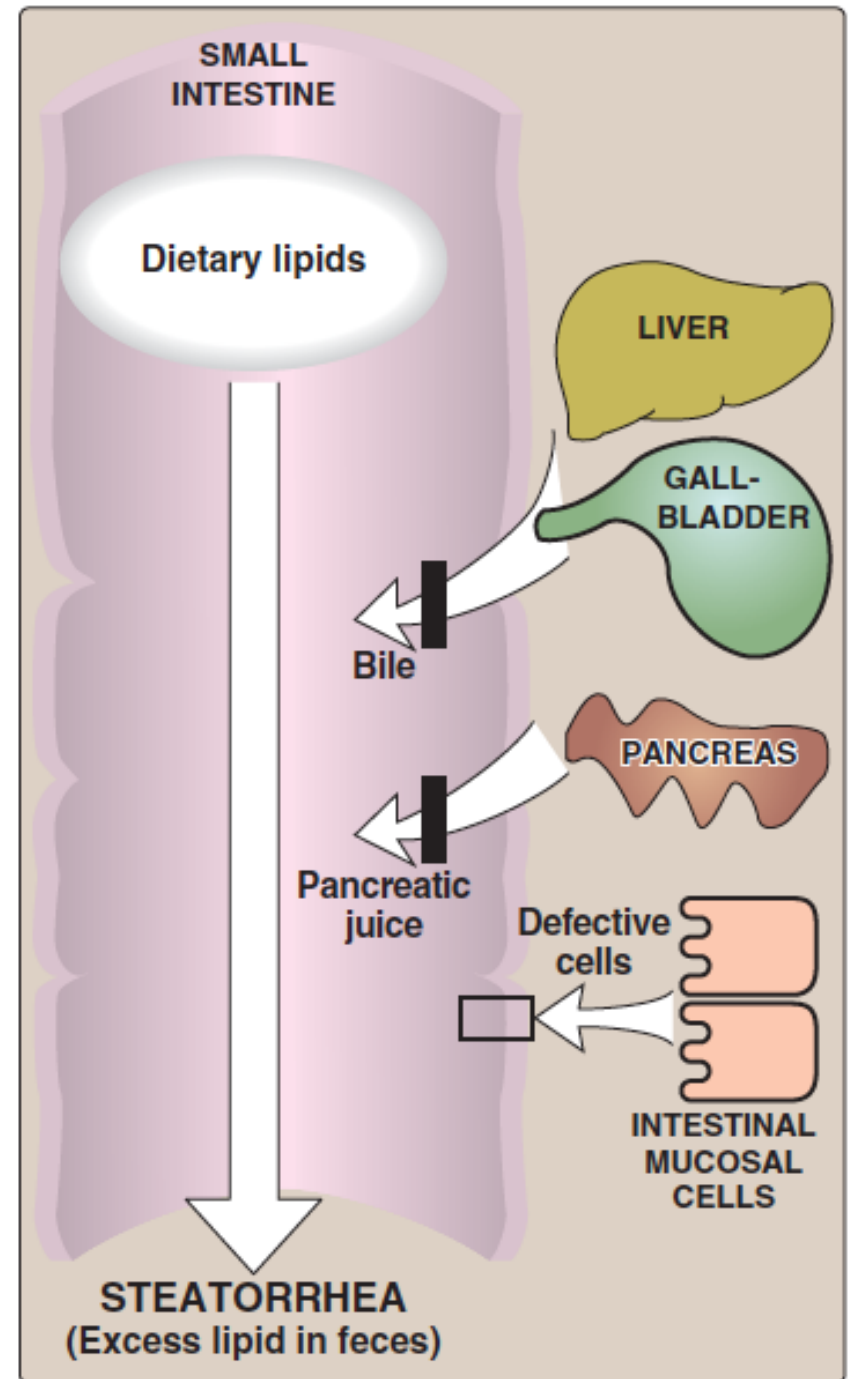
Secretion of chylomicrons by enterocytes

- 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



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