



"اللَّهُمَّ لَا سَهْلَ إِلَّا مَا جَعَلْتَهُ سَهْلًا، وَأَنْتَ تَجْعَلُ الْحَزْنَ إِذَا شِئْتَ سَهْلًا"

Biochemical Aspects of Digestion of Lipids

Biochemistry Team 437

Color index:
Doctors slides
Doctor's notes
Extra information
Highlights

GNT block

Objectives:

- 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:

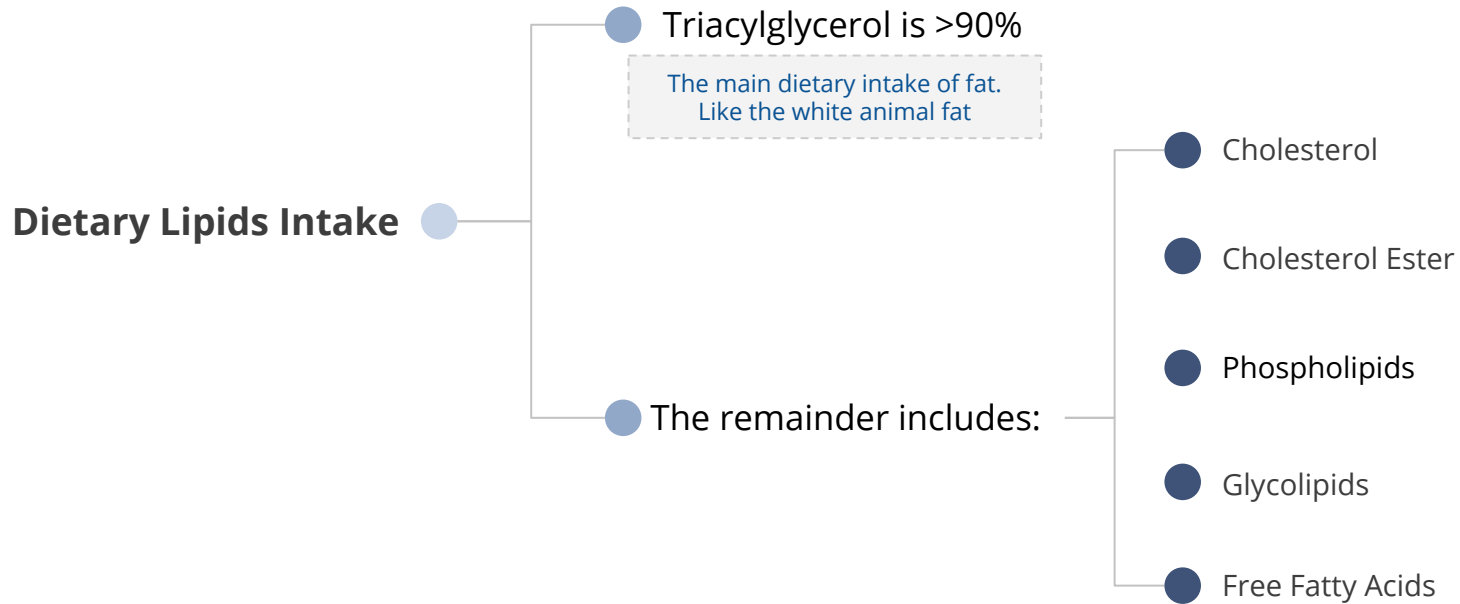
- Dietary lipid: organs and enzymes
- Lipid digestion in the stomach and intestine
- Lipid degradation by the pancreatic enzymes
- Pancreatic insufficiency
- Control of lipid digestion
- Lipid absorption, re-synthesis and secretion
- Lipid malabsorption
- Use of dietary lipid by the tissues



5:55 animation

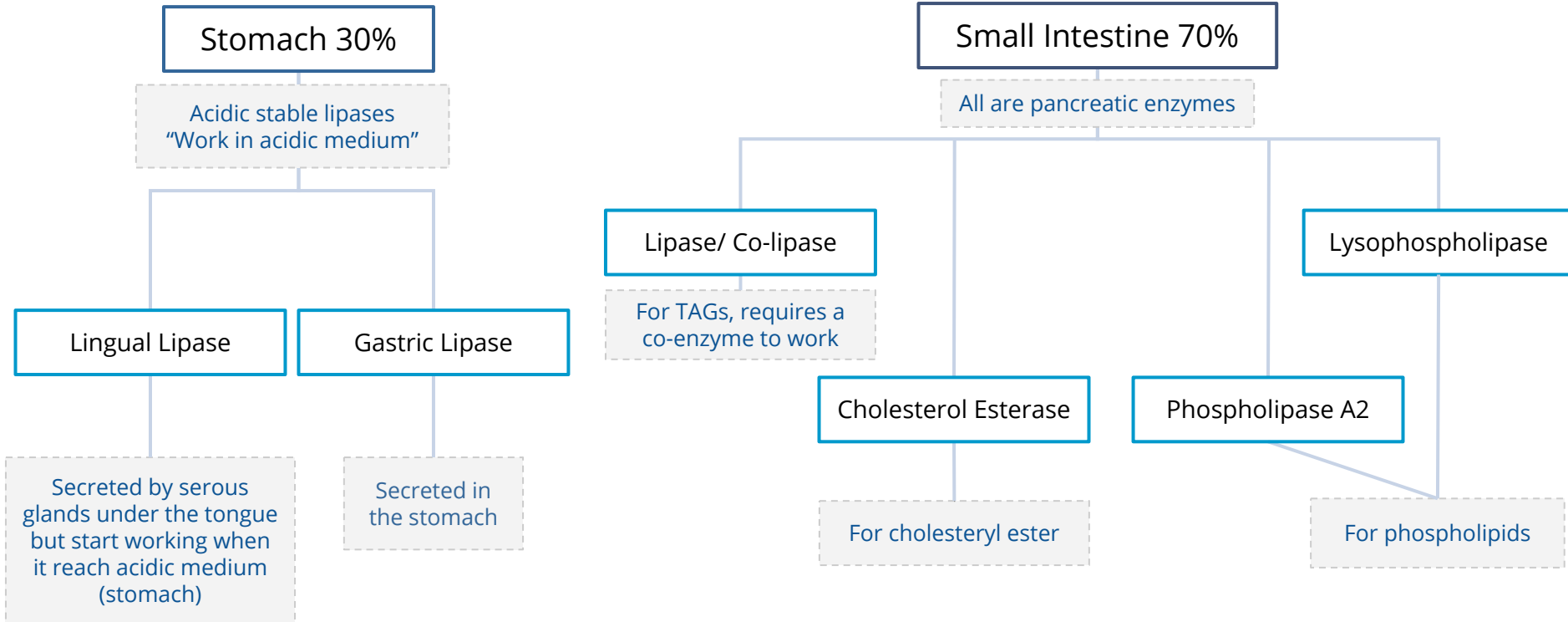
Dietary Lipids

- Dietary lipid intake is ~ 81 g/day



Digestion of Dietary Lipids: Organs & Enzymes

Digestion of lipids does not happen in the mouth, it starts in the stomach and finishes in the small intestine



Lipids Digestion In the Stomach

- Catalyzed by an **acid-stable** lipase (lingual lipase)
- Act Mainly on Triacylglycerols (TAGs)¹ 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**

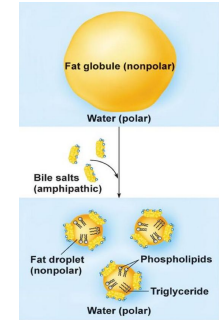
1. Not all , only short & medium Fatty acids " that have 12 or less carbons"
 - Most of dietary fatty acids are long chain fatty acids, so the contribution of these enzymes is minimal
2. Because it's a simple fat with short and medium chain fatty acids.

The main function of lipases is to remove fatty acids

Lipids Digestion In the Small Intestine

Emulsification:

- Occurs in the duodenum
- Increases surface area of lipid droplets
- To maximize the effect of digestive enzymes **by increasing exposed surface area**



Two mechanisms¹:

1. Detergent properties of **bile** salts, in the bile salts emulsify² dietary lipid particles

2. Mechanical mixing by peristalsis

1- Enzyme > hydrophilic. Lipids > hydrophobic .. so, how do they come in contact with each other?

By two mechanisms:

- When peristaltic movement mixes the fat and the fluid together, the fat particles break up and become smaller.
- The bile also separates and keeps the small particles of lipid separated by its detergent physical properties, Which allows the enzymes to work with more surface area.

2- **Emulsification** is a process that forms a liquid, known as an emulsion, containing very small droplets of fat or oil suspended in a fluid

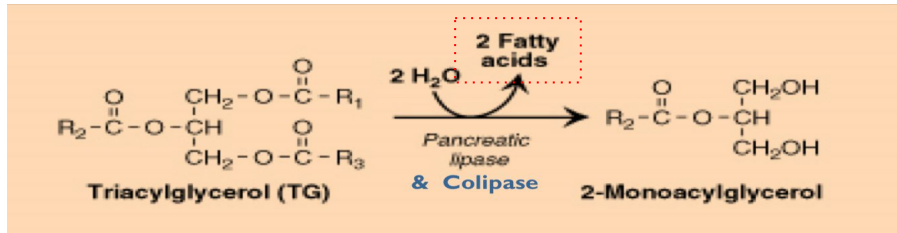
Lipids Degeneration by Pancreatic Enzymes

TAG Degeneration

Performed by pancreatic lipase, colipase

Removes fatty acids at C1 and C3, so **c2 FA remains**

Leaving **2-monoacylglycerol** & two free fatty acids (FFAs)

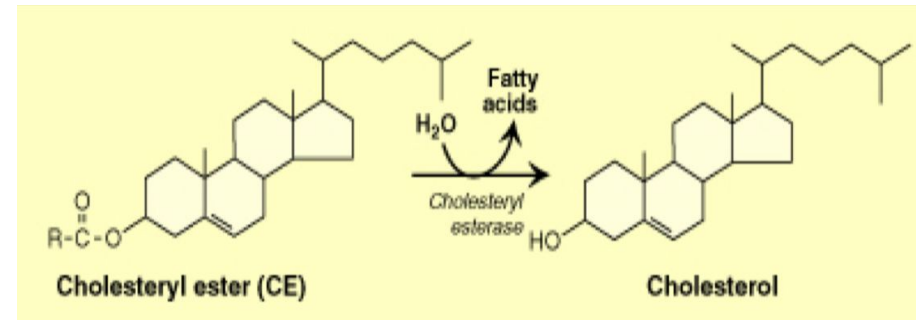


Pancreatic lipase is found in high conc. in pancreatic secretion (2-3% of total proteins) "Highly concentrated, highly efficient" Inhibited by **Orlistat**, an anti obesity drug.
 "Inhibition of pancreatic enzymes → indigestion of lipids → lipids are secreted and not absorbed"

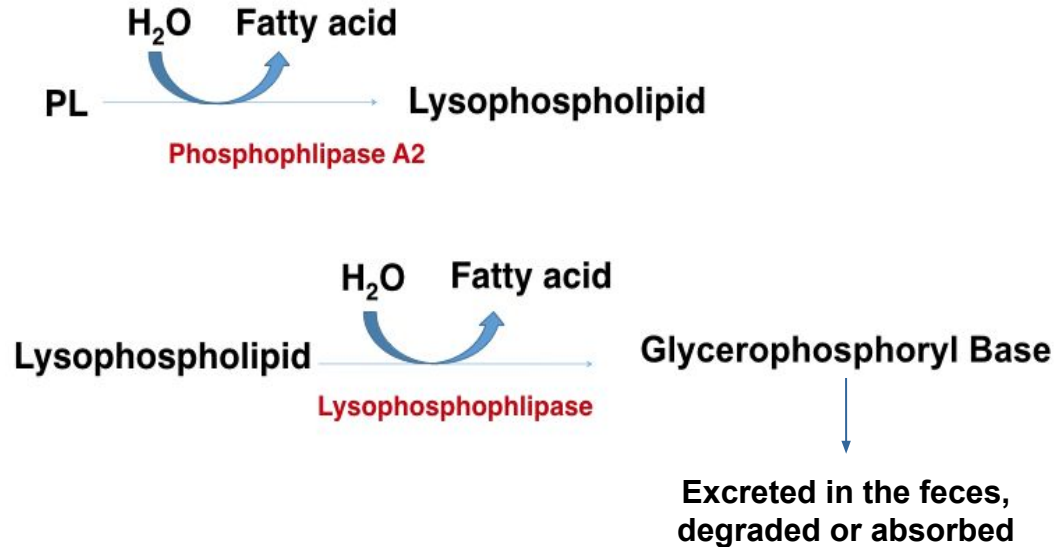
Cholesteryl Ester Degradation

Hydrolyzed by cholesterol esterase

Produces cholesterol + FFAs



Digestion of Phospholipids (PL) by Phospholipase A2 & Lysophospholipase



Two enzymes are responsible for digestion of phospholipids,

- Phospholipase A2
- Lysophospholipase

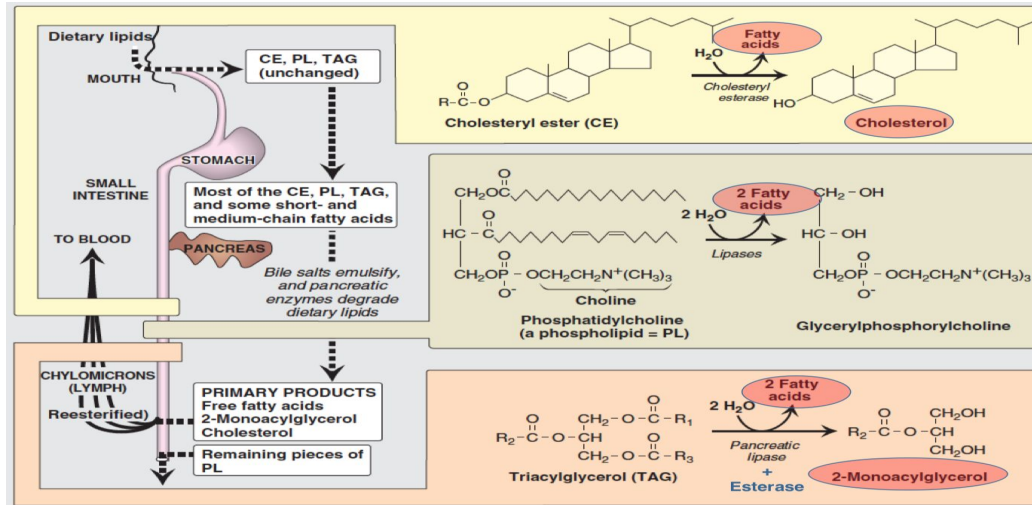
How do they work?

- Phospholipase A2 removes one fatty acid from the phospholipid and we get lysophospholipid
- Lysophospholipase acts on lysophospholipids to give us glycerophosphoryl base which can be excreted

Example of phospholipid digestion:

- Phosphatidylcholine → Lysophosphatidylcholine → choline

Overview of Lipid Digestion



After Ingestion of dietary lipids:

- In the mouth → Unchanged.
- In the stomach: some of the short, medium chain fatty acids are removed by lingual and gastric lipases, the remaining are the same
- The undigested long chain fatty acids reach the small intestine, Bile salts are released from the gallbladder to emulsify the lipids, then the pancreatic enzymes work on them.
- Pancreas also secretes bicarbonate to neutralize the chyme, because **the pancreatic enzymes cannot work in an acidic media.**
- End product [primary products]: free fatty acids, 2-monoacylglycerol, cholesterol.
- The end product molecules are taken into the enterocytes by mixed micelles "discussed in another slide", then they will be synthesized to complexes again: to TAG, which is carried by chylomicrons.
- **Chylomicrons carry dietary TAGs in the blood.**
- The presence of lipids in the GIT stimulates the secretion of and for the glands to secrete them.

Pancreatic Insufficiency In Cystic Fibrosis (CF)

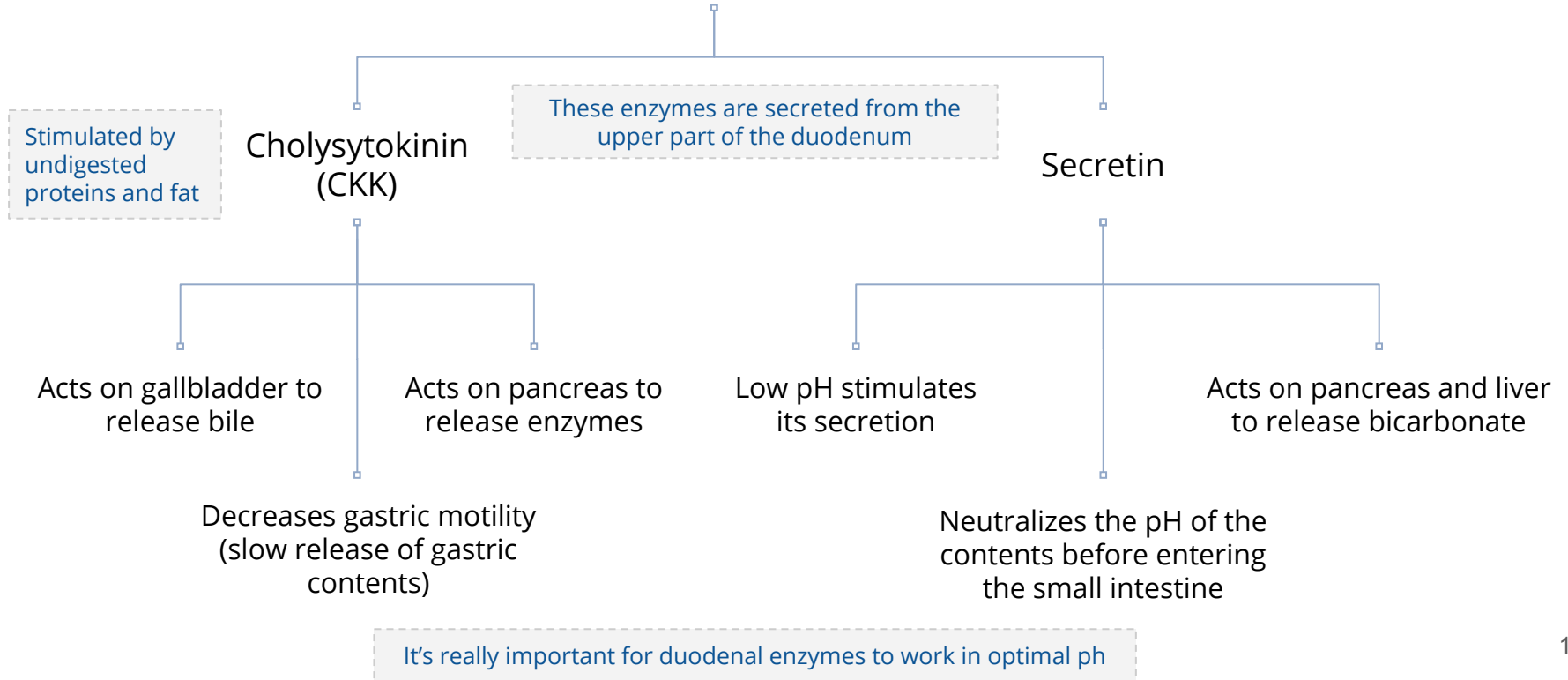


- CF is due to genetic mutations in CFTR ¹ (transmembrane conductance regulator protein)
- Functions as chloride channel on epithelium
- Defective CFTR causes:
 - Decreased secretion of chloride (stays in the cell, bringing water with it)
 - Increased reabsorption of sodium and water (which thicken the mucus)
- Decreased hydration in pancreas thickens the pancreatic secretions ²
- Pancreatic enzymes are unable to reach the intestine
- Treatment: enzyme and fat-soluble vitamin supplementation

1. Mutation of chloride channel
2. Because it is too thick, it can't reach the duodenum

Control of Lipids Digestion

Controlled by hormones:



Lipid Absorption by Enterocytes

- Products of lipid digestion (FFAs, free cholesterol, 2-monoacylglycerol) combine with bile salts and **carries** 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**

*Carriers of lipids from the lumen of the intestine to the enterocytes

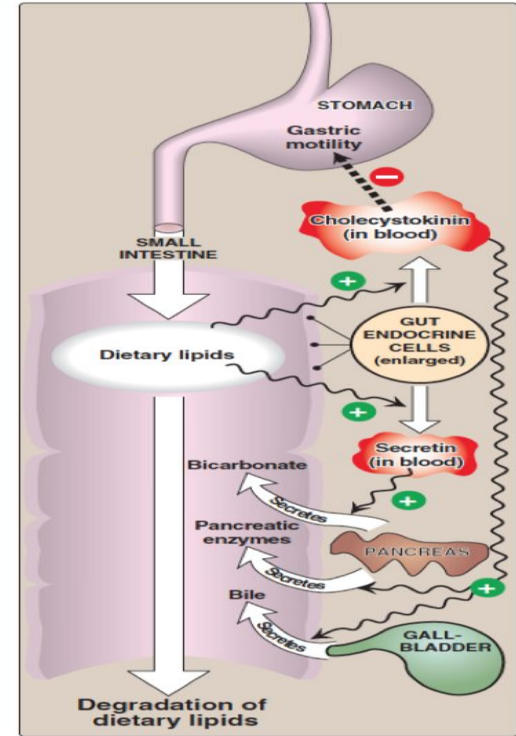


Figure 15.4
Hormonal control of lipid digestion in the small intestine.

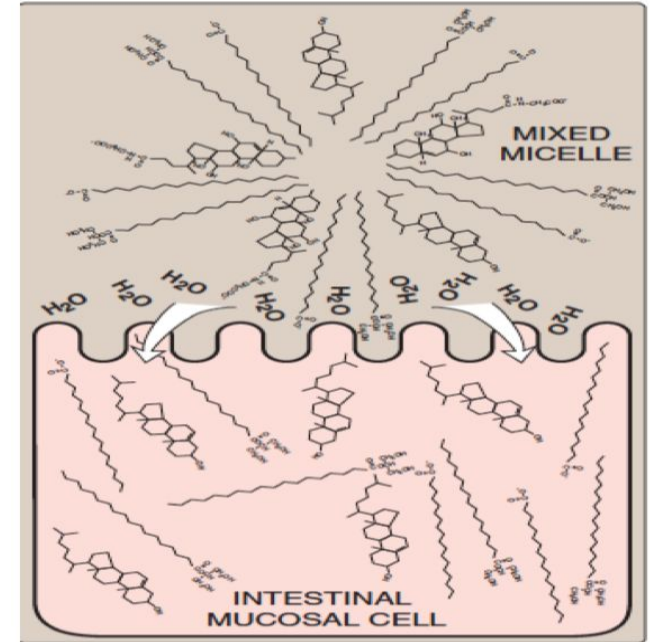
Resynthesis of TAG/ Cholesteryl Esters

- Digested lipids absorbed by enterocytes migrate to **endoplasmic reticulum** for complex lipid biosynthesis.
- Fatty acids* → activated to **acyl CoA** form
- 2-Monoacylglycerols → **TAGs**
- Cholesterol → cholesteryl ester

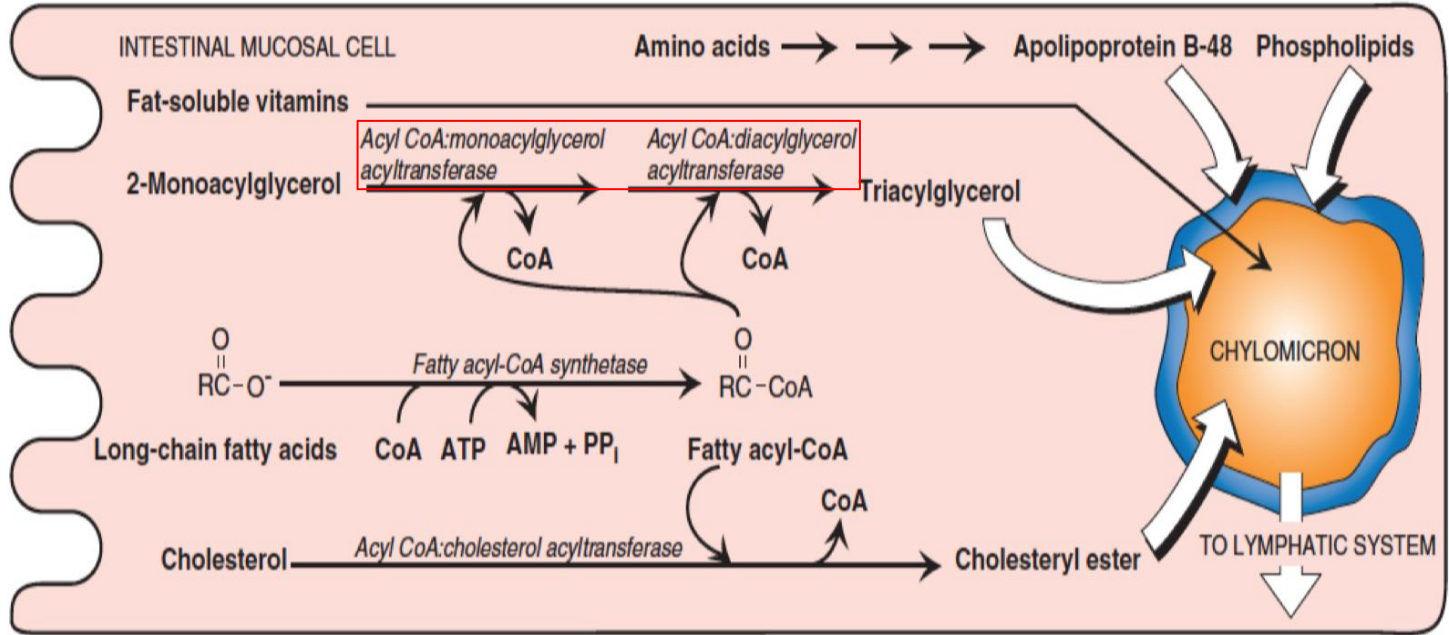
The body store fat in form of TAG, so it resynthesis immediately after it's absorbed.

*to make the complexes again, the body:

- First activates the fatty acids by turning them to acyl CoA
- Adding acyl coA to digested lipids to make them into complexes with the help of the enzyme **acyltransferase**
- Explained in details next slide



Mixed micelles are hydrophobic inside and hydrophilic outside



- Long fatty acid chains are converted to fatty acyl CoA by fatty acyl CoA synthase
- Fatty acyl CoA + cholesterol by the enzyme acyl CoA:cholesterol acyltransferase gives cholestrol esters
- 2-monoacylglycerol + Fatty acyl CoA by the enzyme Acyl CoA: monoacylglycerol gives → diacylglycerol → triacylglycerol (TAG)

The main enzyme is acyltransferase, all of the others are derivatives depending on the substrates

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

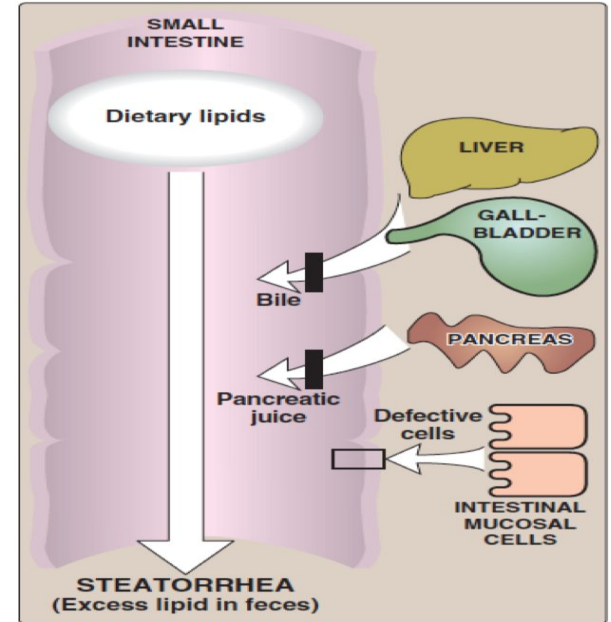


Presence of chylomicron in the plasma of a person after a fat rich meal

Lipid Malabsorption

- Increased **excretion of lipids**, fat-soluble vitamins and essential FAs in the feces
- Due to defects in lipid digestion or absorption*
 - Gallbladder defect, liver problem, pancreas problem which affects secretion of pancreatic enzymes
 - Problem in the enterocytes of the intestine leading to malabsorption
- Can be caused by CF or shortened bowel

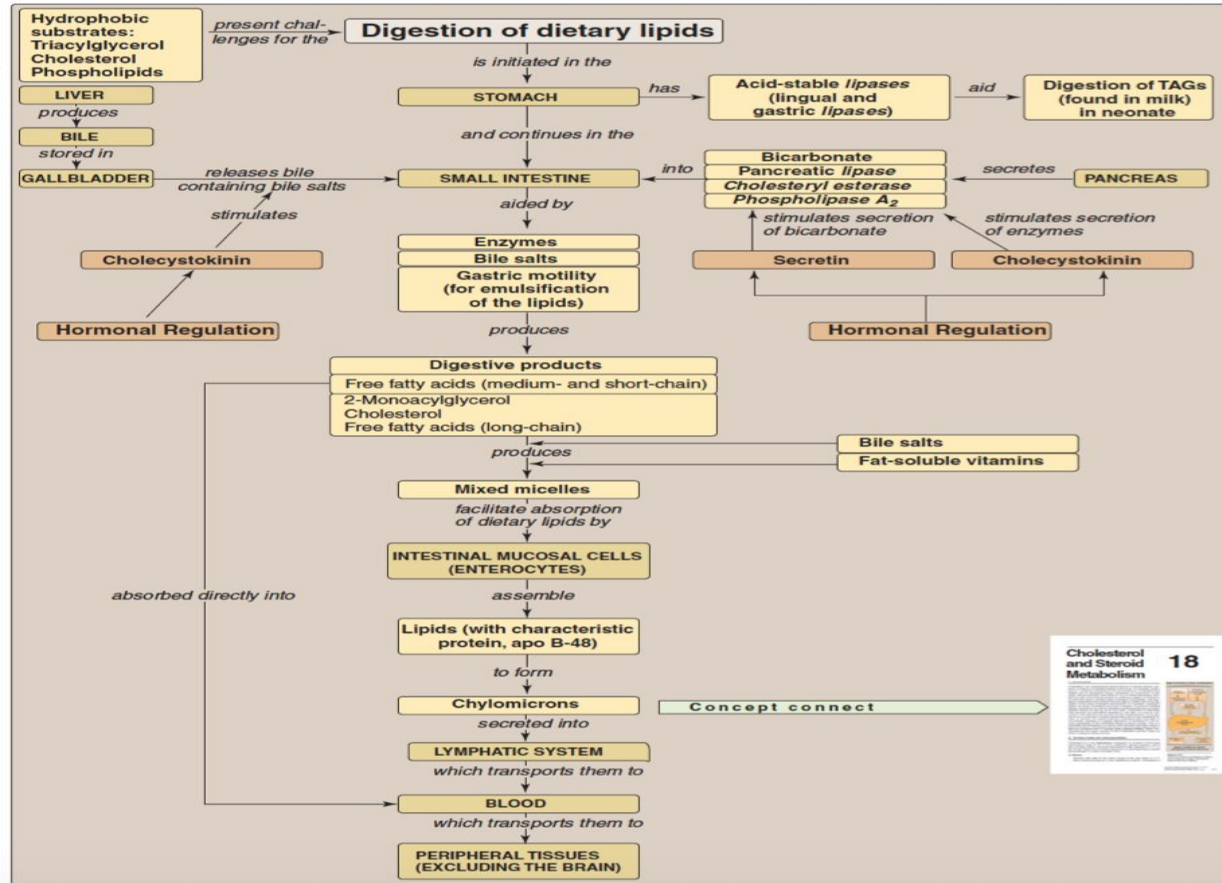
*Which leads to deficiency in fat soluble vitamin + essential fatty acid



Key Concepts for Digestion and Absorption of Dietary Lipids



Lippincott's Summary



Take Home Messages

- 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

Lipids digestion in the stomach	Lipid digestion in the small intestine	Lipid degradation by pancreatic enzymes	Pancreatic insufficiency in cystic fibrosis (CF)	Control of lipid digestion
<p>Catalyzed by an acid-stable lipase (lingual lipase)</p> <ul style="list-style-type: none"> • 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 	<p>Emulsification:</p> <ul style="list-style-type: none"> • Occurs in the duodenum • Increases surface area of lipid droplets • To maximize the effect of digestive enzymes ✓ Two mechanisms: <ol style="list-style-type: none"> 1- Detergent properties of bile salts in the bile Bile salts emulsify dietary lipid particles 2- Mechanical mixing by peristalsis 	<ul style="list-style-type: none"> ✓ 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: <ul style="list-style-type: none"> • Hydrolyzed by cholesterol esterase • Produces cholesterol + FFAs 	<p>CF is due to genetic mutations in CFTR (transmembrane conductance regulator protein)</p> <ul style="list-style-type: none"> ✓ 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 	<p>Controlled by hormones:</p> <ul style="list-style-type: none"> ❖ Cholecystikinin (CKK) <ul style="list-style-type: none"> • Acts on gallbladder to release bile • Acts on pancreas to release enzymes • Decreases gastric motility (slow release of gastric contents) ❖ Secretin <ul style="list-style-type: none"> • Low pH stimulates its secretion • Acts on pancreas and liver to release bicarbonate • Neutralizes the pH of the contents before entering the small intestine

Lipid absorption by enterocytes	Resynthesis of TAG / Cholesteryl esters	Assembly of chylomicrons by enterocytes	Secretion of chylomicrons by enterocytes	Lipid malabsorption
<ul style="list-style-type: none"> ❖ 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 	<ul style="list-style-type: none"> ❖ Digested lipids absorbed by enterocytes migrate to endoplasmic reticulum for complex lipid biosynthesis • Fatty acids → activated to acyl CoA form • 2-Monoacylglycerols → TAGs 	<ul style="list-style-type: none"> ❖ 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 	<ul style="list-style-type: none"> ❖ By exocytosis into lymphatic vessels around villi of small intestine (lacteals) which enter into systemic circulation • Serum becomes milky after a fatty meal 	<ul style="list-style-type: none"> ❖ 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

MCQs:

1- Lipid digestion mainly occur in:

- A. Stomach
- B. Small intestine
- C. Large intestine
- D. Pancreas

2- The major dietary lipid is:

- A. Free fatty acids
- B. Triacylglycerol
- C. Glycolipids
- D. Cholesterol Ester

3- Which of the following is a primary Apolipoprotein contributed in the synthesis of chylomicrons?

- A. APOE
- B. APO B100
- C. APO B48
- D. APOC

4- Mixed Micelles are classified as ()?

- A. Hydrophilic
- B. Hydrophobic
- C. Amphipathic
- D. Fat soluble

5- What is the function of Orlistat?

- A. Inhibit the pancreatic lipase
- B. Activate the pancreatic lipase
- C. Anti obesity drug
- D. Both A&C

6- Where does the emulsification occurs:

- A. Large Intestine
- B. Stomach
- C. Duodenum
- D. Pancreas

Girls team

- العنود المنصور
- ليلي الصَّبَاغ
- ريناد الغريبي

Boys team

- رهام الحلبي
- عبدالحكيم العنيق

Team leaders



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