




Biochemical aspects of digestion of lipids

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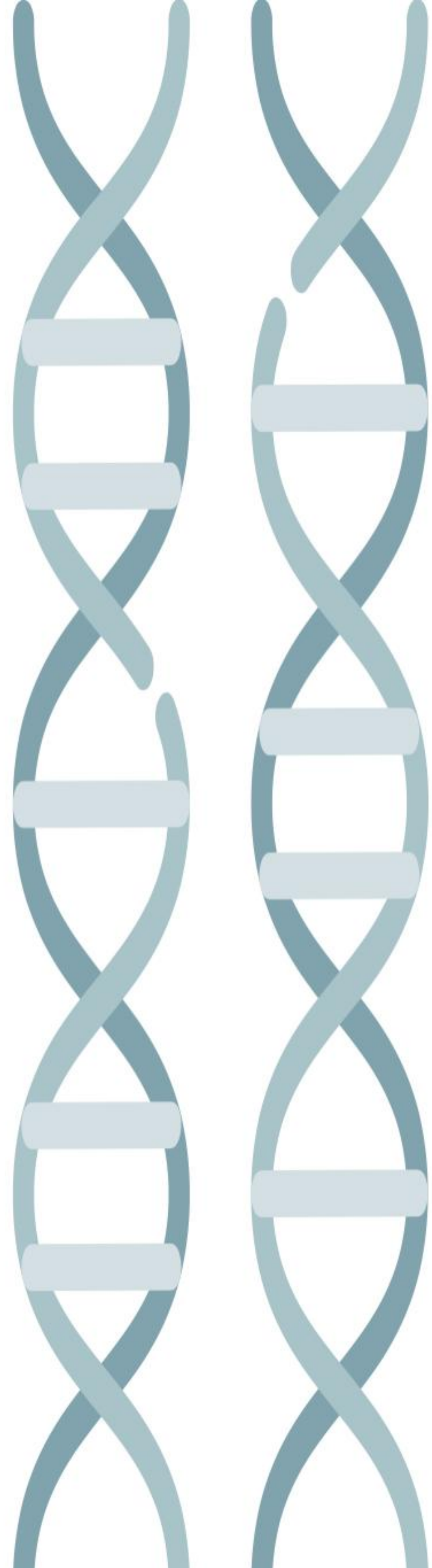
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Objectives

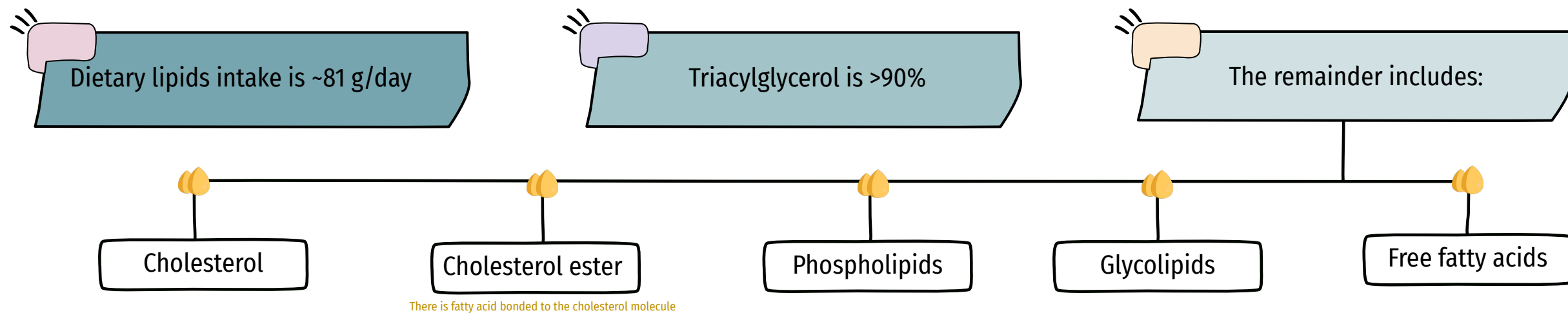
-  Understand the process of digestion of dietary lipids including, the organs involved, the enzymes required, and the end products.
-  Study the synthesis, secretion and fate of chylomicron
-  Understand the clinical manifestations of diseases that involve defective lipid digestion and/or absorption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

Overview

- Dietary lipid: organs and enzyme
- Lipid digestion in the stomach and intestine
- Lipid degradation by the pancreatic enzymes
- Dietary lipid: organs and enzymes
- Control of lipid digestion
- Lipid absorption, re-synthesis and secretion¹
- Lipid malabsorption
- Use of dietary lipid by the tissues



Dietary lipids



Organs and Enzymes

Stomach

- **Lingual lipase**
Called lingual because the source of the enzyme is under the tongue but it start digesting in the stomach.
 - **Gastric lipase**
- Both lingual lipase & gastric lipase are acting on **short** and **medium** fatty acid chain (less than 12 carbon).
-Chains with more than 12 carbons are considered long chains

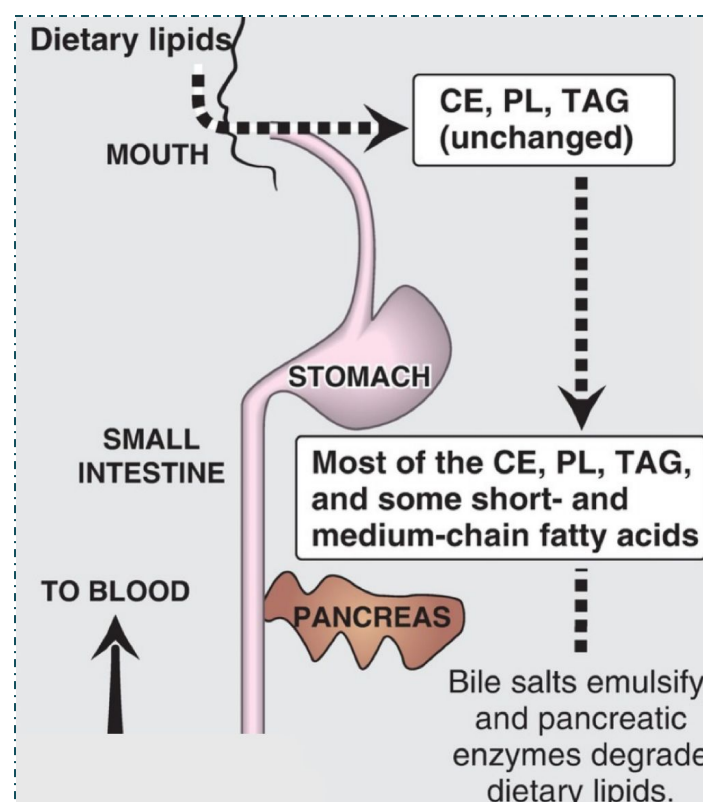
Small intestine

- **Pancreatic Lipase / colipase**
(colipase is not involved in the degradation, it's only helping the pancreatic lipase)
- **Cholesterol esterase**
- **Phospholipase A2**
(this enzyme will make one fatty acid and **lysophospholipid** which will be digested by **lysophospholipase**)
- **Lysophospholipase**

Lipid digestion

In the Stomach:

- Catalyzed by an **acid-stable¹ lipase** (lingual lipase)
- TAGs are hydrolyzed by the lipases secreted:
under the tongue and gastric mucosa.
- **Acid lipases are important for lipid (milk fat) digestion in:**
 - neonates Because neonates don't have a developed GI system.
 - patients with pancreatic insufficiency pancreatic secretions are not reaching the small intestine



In Small intestine:

Emulsification²:

- Occurs in the duodenum
- Increases surface area of lipid droplets
- To maximize the effect of digestive enzymes
- **Two mechanisms³:**
 1. Detergent properties of bile salts in the bile (bile salts emulsify dietary lipid particles)
 2. Mechanical mixing by peristalsis

1: Acid stable means that the enzyme doesn't get denatured in an acidic environment like the stomach

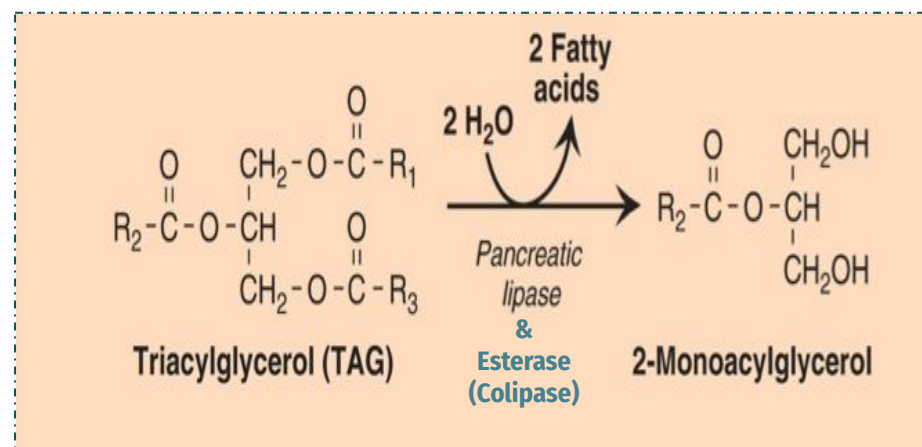
2: Emulsification: breaks down big lipid droplets into smaller ones which increases the surface area

3: Let's imagine the enzyme and fat like the water (enzym) and oil (fat). We need a spoon to mix them (mechanical mixing) and also we need a detergent مثل الصابون (bile salts) because Bile salt and phospholipids are amphipathic which means they have two ends, hydrophilic and hydrophobic that will make lipids (hydrophobic) available for the enzyme (hydrophilic)

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)**

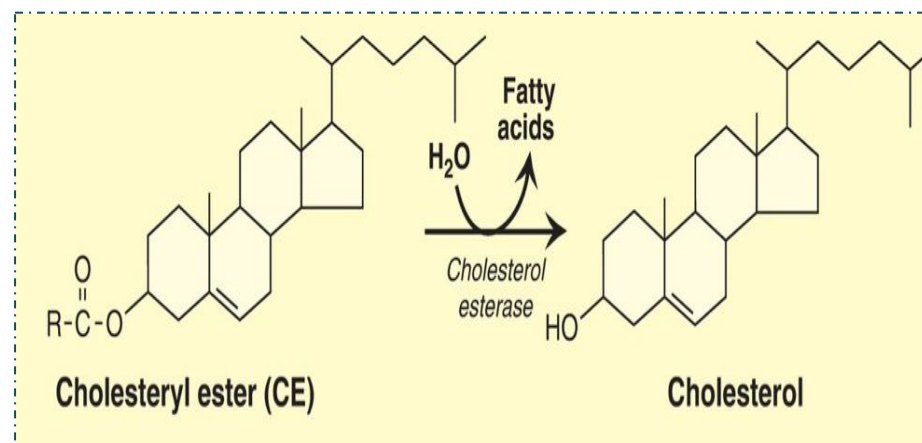


Pancreatic lipase:

- Found in high conc. in pancreatic secretion (2-3% of total proteins)
- It is inhibited by **Orlistat**, an antiobesity drug

Cholesteryl ester degradation

- Hydrolyzed by cholesterol esterase
- Produces **cholesterol** + **FFAs**



Digestion of phospholipids by phospholipase A2 & lysophospholipase

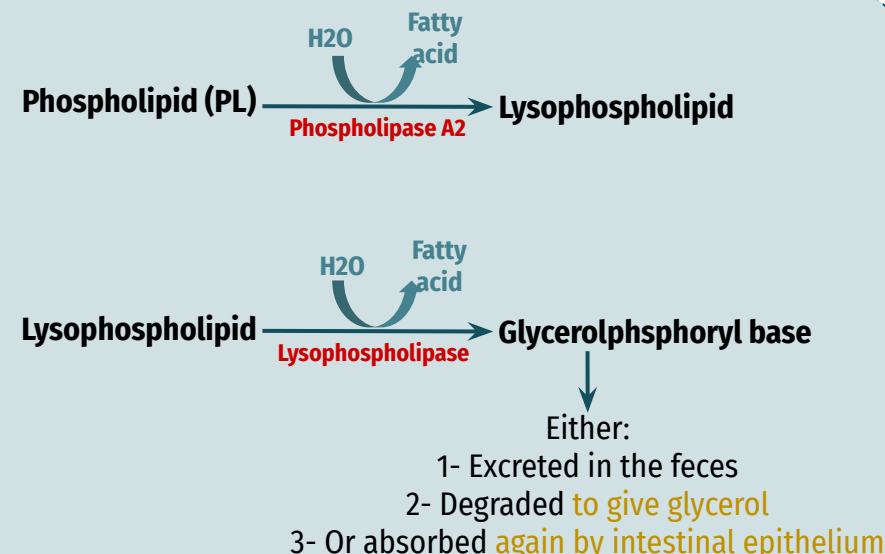
Two enzymes are responsible for digestion of phospholipids:

- 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

#437 Team

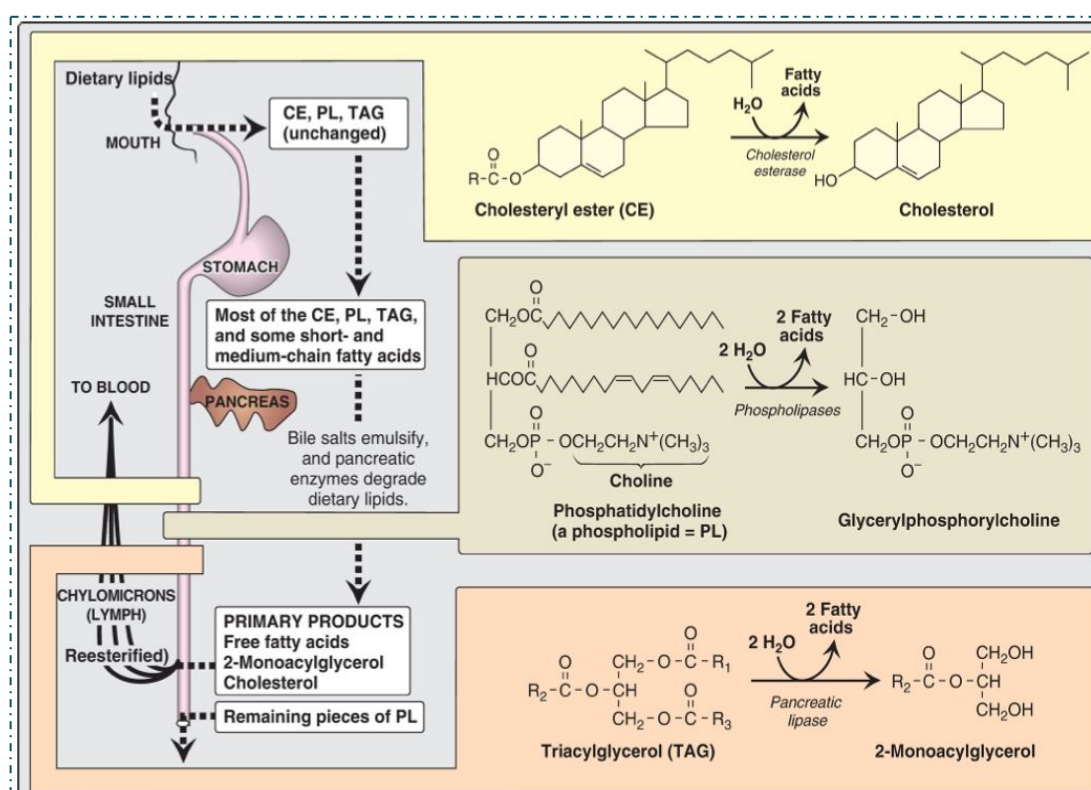


[Click here for original picture](#)

Doctor Note:

Not all phospholipids are degraded into Glycerophosphoryl base, a lot of PL they are just converted into Lysophospholipids and this Lysophospholipids are absorbed by intestinal epithelial cells.

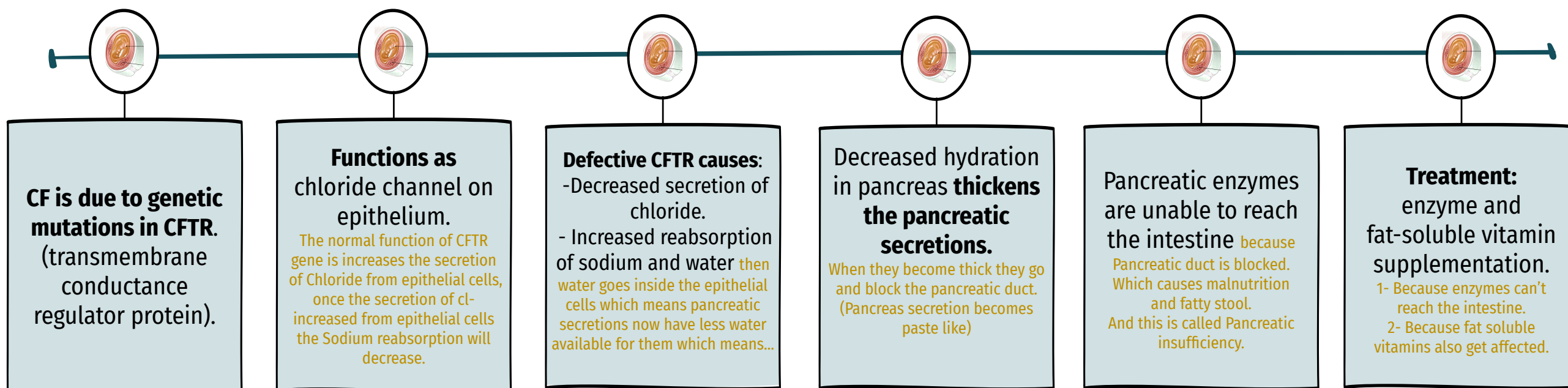
Overview of lipid digestion



After Ingestion of dietary lipids: #437 Team

- 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)



Control of lipid digestion

Controlled by hormones:

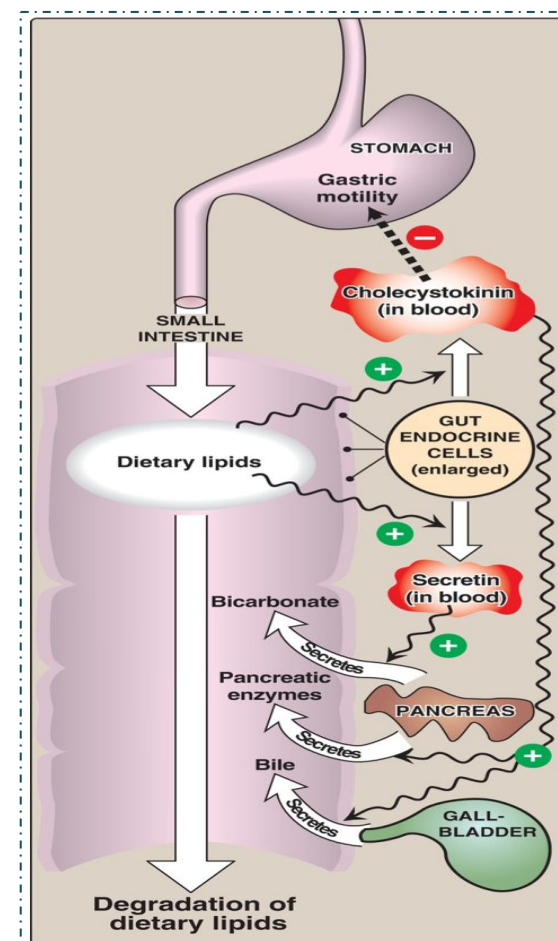
The source of hormones is intestinal mucosa

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. Because intestinal enzymes don't work at acidic pH

Cholecystokinin (CCK)

- Acts on **gallbladder** to release bile. (CCK increase the contraction of gallbladder and this lead to release of bile).
- Acts on **pancreas** to release **pancreatic enzymes**.
- Acts on **stomach** that will decrease gastric motility (slow release of gastric contents and this make sense because if you already have digestive food in your small intestine you don't want to overwhelm the intestine so release of gastric contents from stomach to intestine is slowed down). To insure maximum digestion in small intestines.
- Also it has another action on stomach It sends a signal to brain that the stomach is full, will discuss this later on.



Lipid absorption by enterocytes

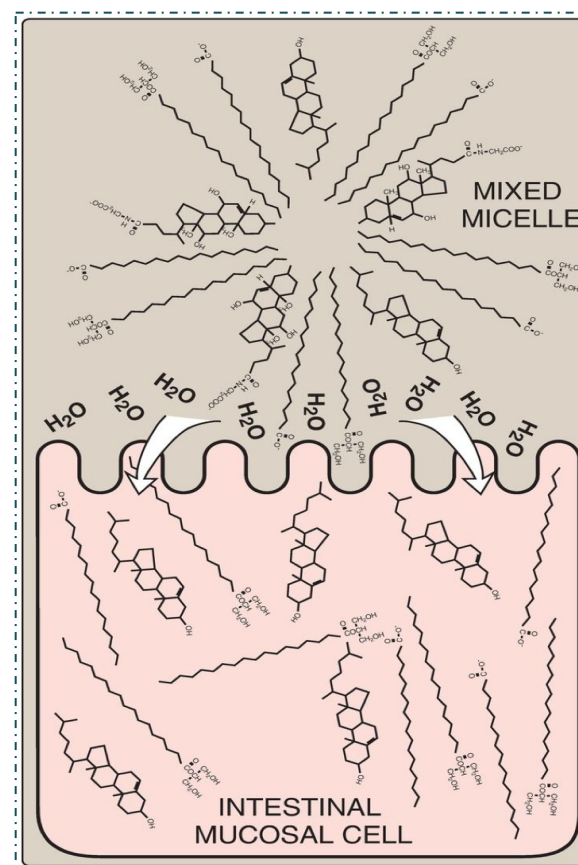
Products of lipid digestion (FFAs, free cholesterol, 2-monoacylglycerol.) combine with bile salts and fat-soluble vitamins.

To be able to be absorbed by the enterocytes they can't just enter to enterocytes they have to be packaged and we call their package as Mixed micelles...

They form mixed micelles (disk-shaped particles). It's composed of lipid it's composed of lipid digestion + fat soluble vitamin, and will get stabilized by bile salts and phospholipids

Absorbed by brush border membrane of enterocytes. Because the cell membrane is amphipathic with the hydrophilic side out too

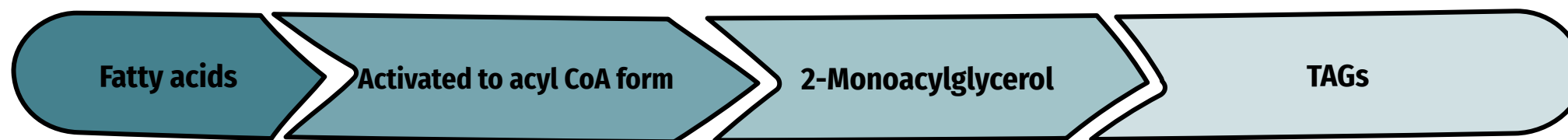
Short and medium chain length fatty acids are absorbed by enterocytes directly to the portal circulation, when they go to the circulation they are fatty acid so they can't be traveling as such, they are carried by protein called Albumin.



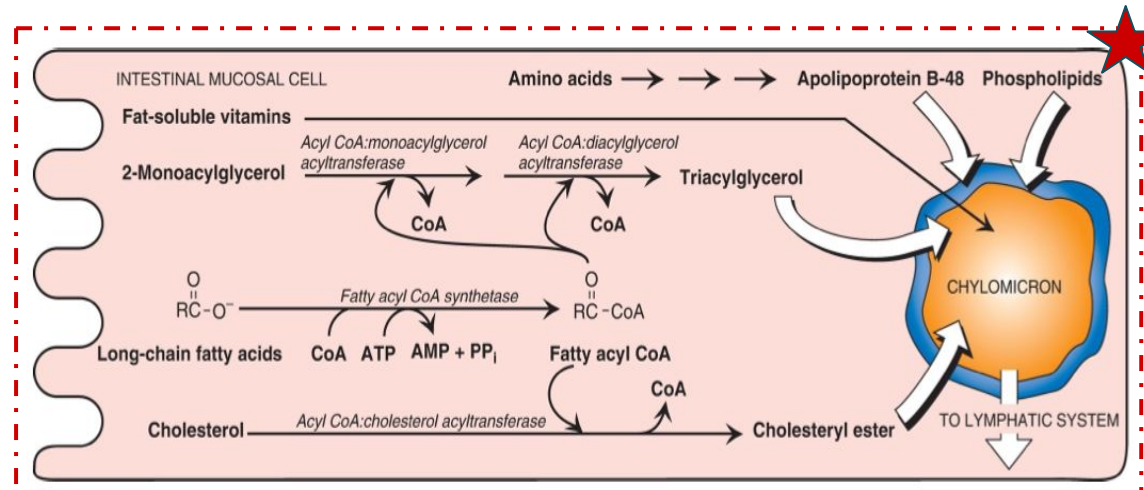
Mixed micelles are hydrophobic inside and hydrophilic outside. (amphipathic)

Resynthesis of TAG / Cholesteryl esters

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

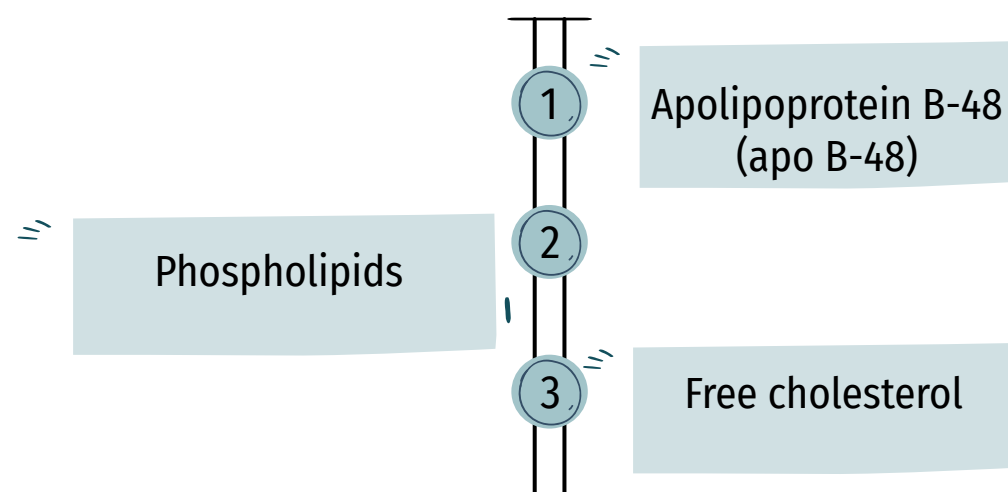


Female Dr: Remember Enzymes name.



Assembly of chylomicrons by enterocytes

Newly synthesized TAG and cholesterol ester are packaged as lipid droplets surrounded by thin layer of:

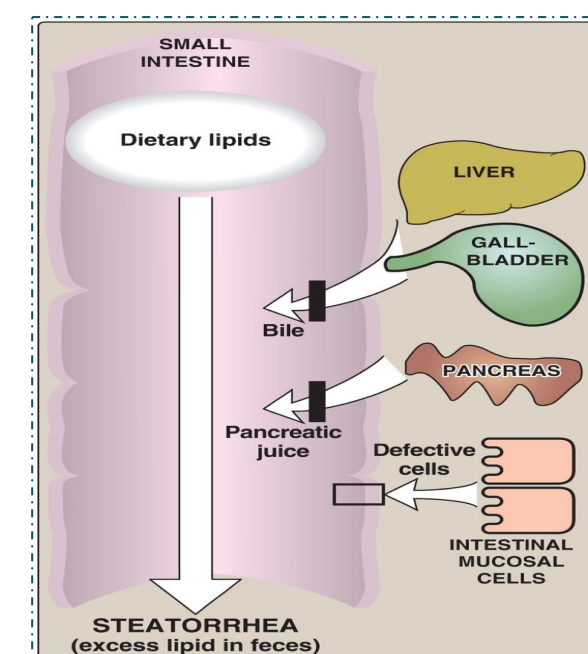
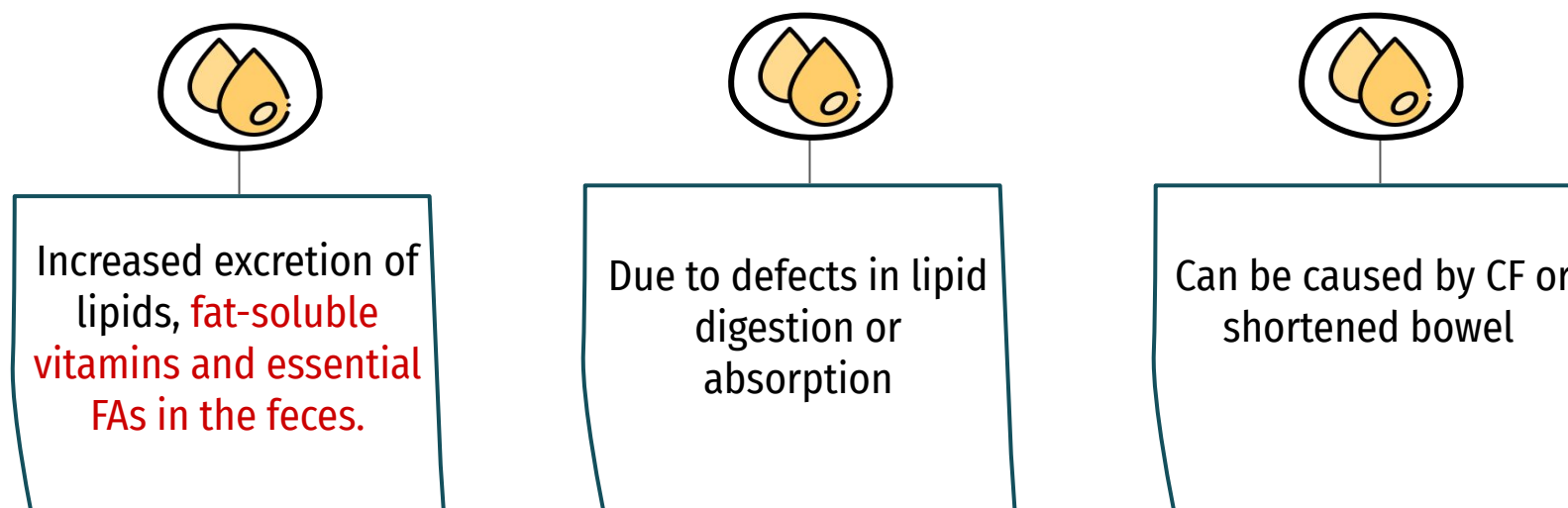


Secretion of chylomicrons by enterocytes

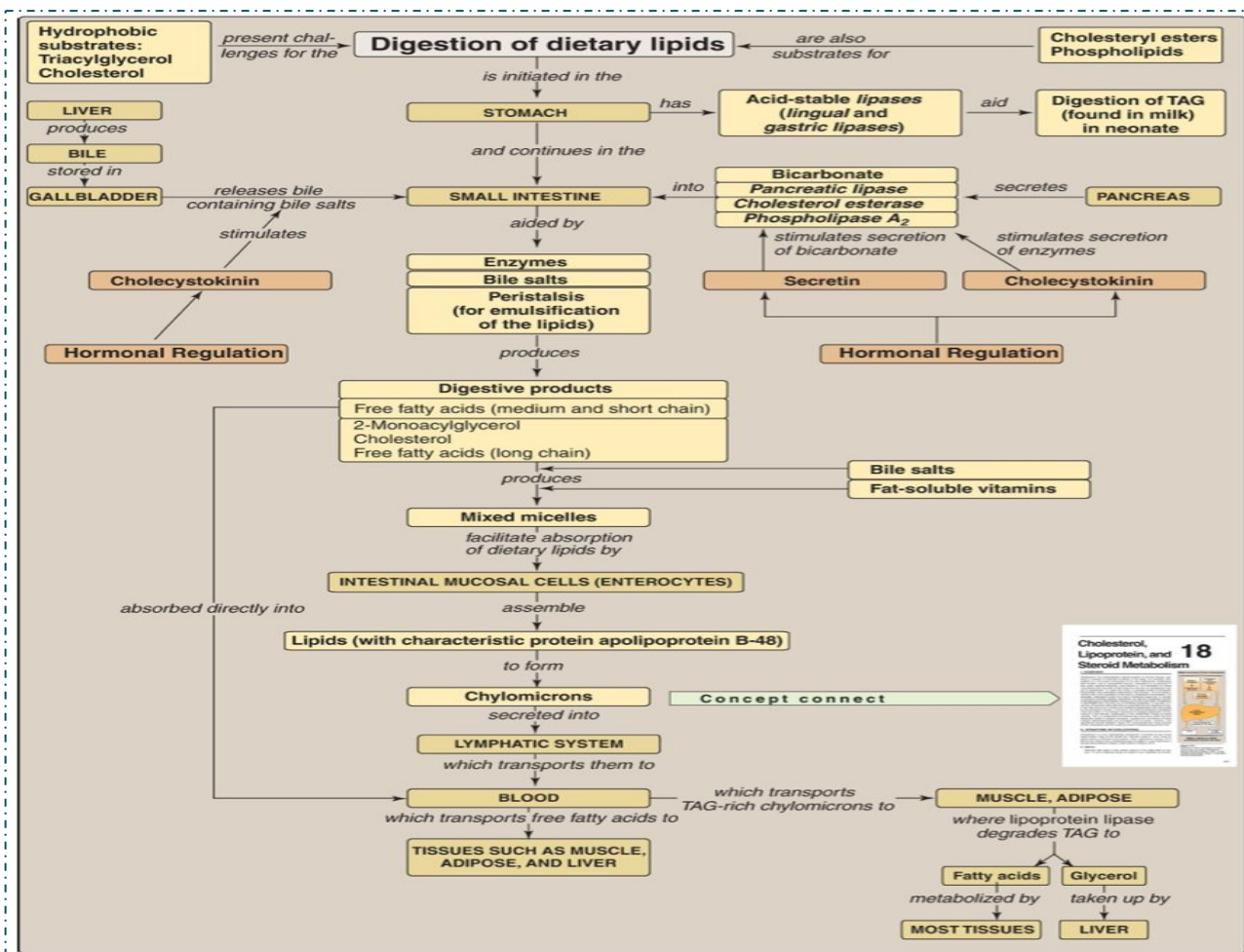
- By exocytosis into lymphatic vessels around villi of small intestine (lacteals) which enter into systemic circulation (**Chyle**) Once chyme reaches the intestine its called chyle , and chyle contains some undigested lipids , those lipids are gonna stimulate the release of CCK hormone. #Team 438
- Serum becomes milky after a fatty meal.¹



Lipid malabsorption

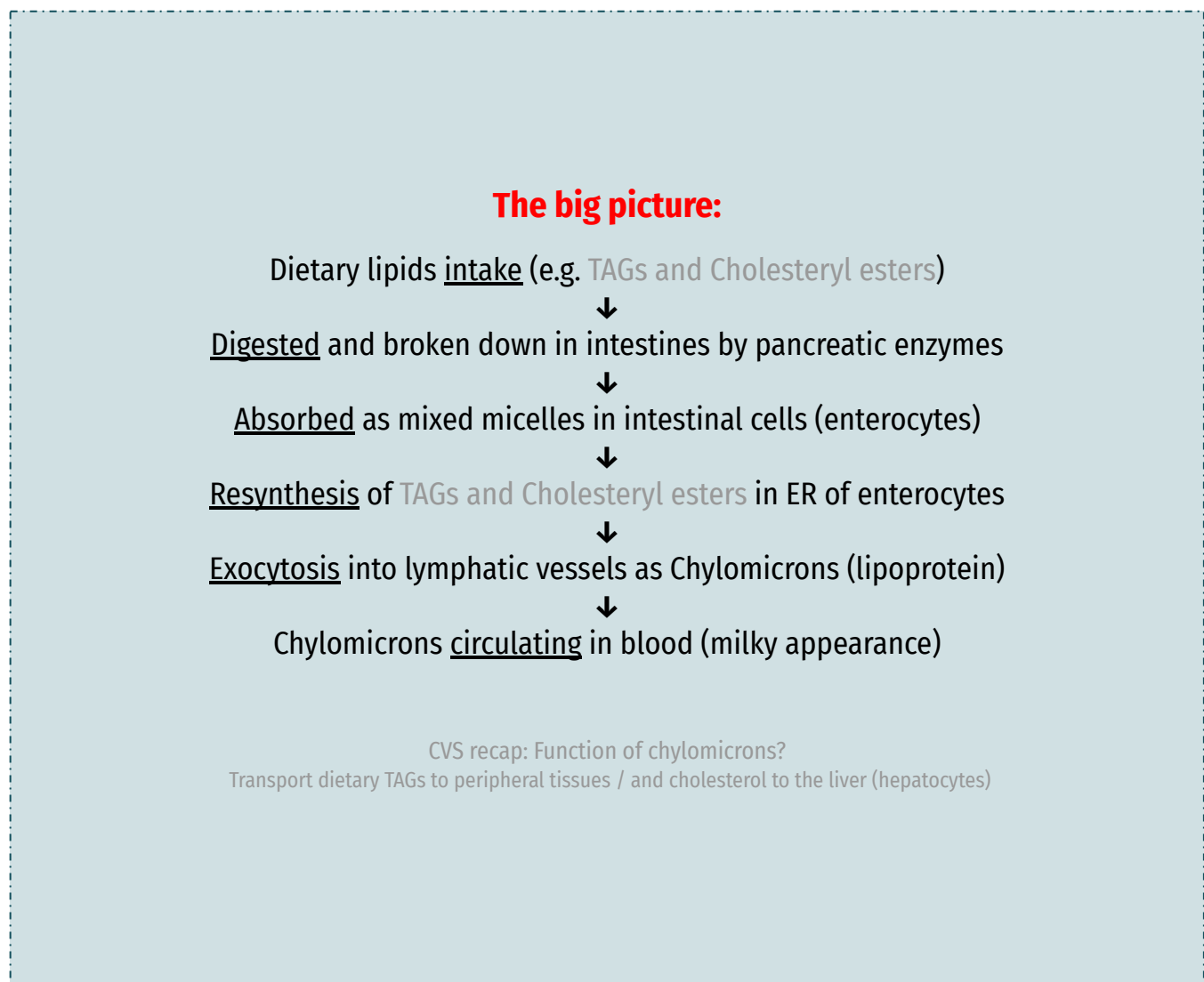


¹: In hyperchylomicronemia the patient can't clear his serum after a meal so they will have cloudy serum for a long period after a meal



Key concepts for digestion and absorption of dietary lipids.

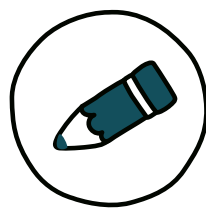
Special Thanks for Duaa



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.





Summary

Lipid Digestion

Examples of dietary lipids	<ul style="list-style-type: none">• Triacylglycerol• Cholesterol• Cholesterol ester• Phospholipids• Glycolipids• Free fatty acids
organs involved in lipid digestion	In the stomach and small intestine
enzymes required in lipid digestion	<ul style="list-style-type: none">• In stomach :<ol style="list-style-type: none">1)Lingual lipase2)Gastric lipase• In small intestines :<ol style="list-style-type: none">1)Lipase/Colipase2)Cholesterol esterase3)Phospholipase A24)Lysophospholipase
Cystic fibrosis	CF is due to genetic mutations in CFTR. (transmembrane conductance regulator protein) Functions as chloride channel on epithelium.
Defective CFTR causes	<ul style="list-style-type: none">• Decreased secretion of chloride.• Increased reabsorption of sodium and water.
treatment of cystic fibrosis	enzyme and fat-soluble vitamin supplementation.
Hormones controlling lipid digestion	<ul style="list-style-type: none">• Secretin acts on : pancreas and liver to release bicarbonate. effect : Neutralizes the pH of the contents before entering the small intestine.• Cholecystinin (CCK) acts on : pancreas to release enzymes. effect : Decreases gastric motility (slow release of gastric contents).

[Click here for other summary from amazing Duaa](#)

 **MCQs**

1- cholesterol + FFAs are the product of degradation of

A- cholesteryl ester

B-phospholipids

C-TAGs

D-Glycolipids

2- The major dietary lipid is :

A-Cholesterol

B-Cholesterol ester

C- Phospholipids

D-Triacylglycerol

3-Which of the following is inhibited by Orlistat?

A-pancreatic lipase

B- lingual lipase

C-phospholipase A2

D-lysophospholipase

4-Which of the following secretion is decreased in Defective CFTR?

A-sodium

B- potassium

C-water

D-chloride

5- Which of the following hormones can low PH stimulate its secretion ?

A- Cholecystokinin (CKK)

B-serotonin

C-secretin

D-both A&C

6-Short and medium chain length fatty acids are absorbed?

A-undirectly

B- directly

C-none

D-Both A&B

Answers key

1-A

2- D

3- A

4- D

5- C

6- B

SAQs

1- what are the enzymes used in lipid digestion in the small intestines?

- Lipase / CO-lipase
- Cholesterol esterase
- Phospholipase A
- Lysophospholipase

2- what are the products of lipid digestion?

FFAs, free cholesterol, 2-monoacylglycerol.

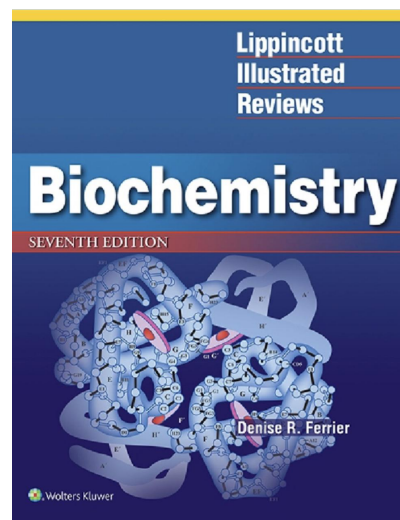
3- list the hormones that control lipids digestion?

1. Cholecystokinin (CKK)
2. Secretin

4- what is the enzyme responsible for degradation of TAGs? How can it be inhibited?

- A. Pancreatic lipase
- B. Orlistat

Resources Click on the book to download the resource





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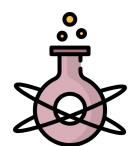
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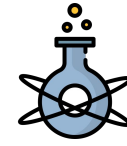
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