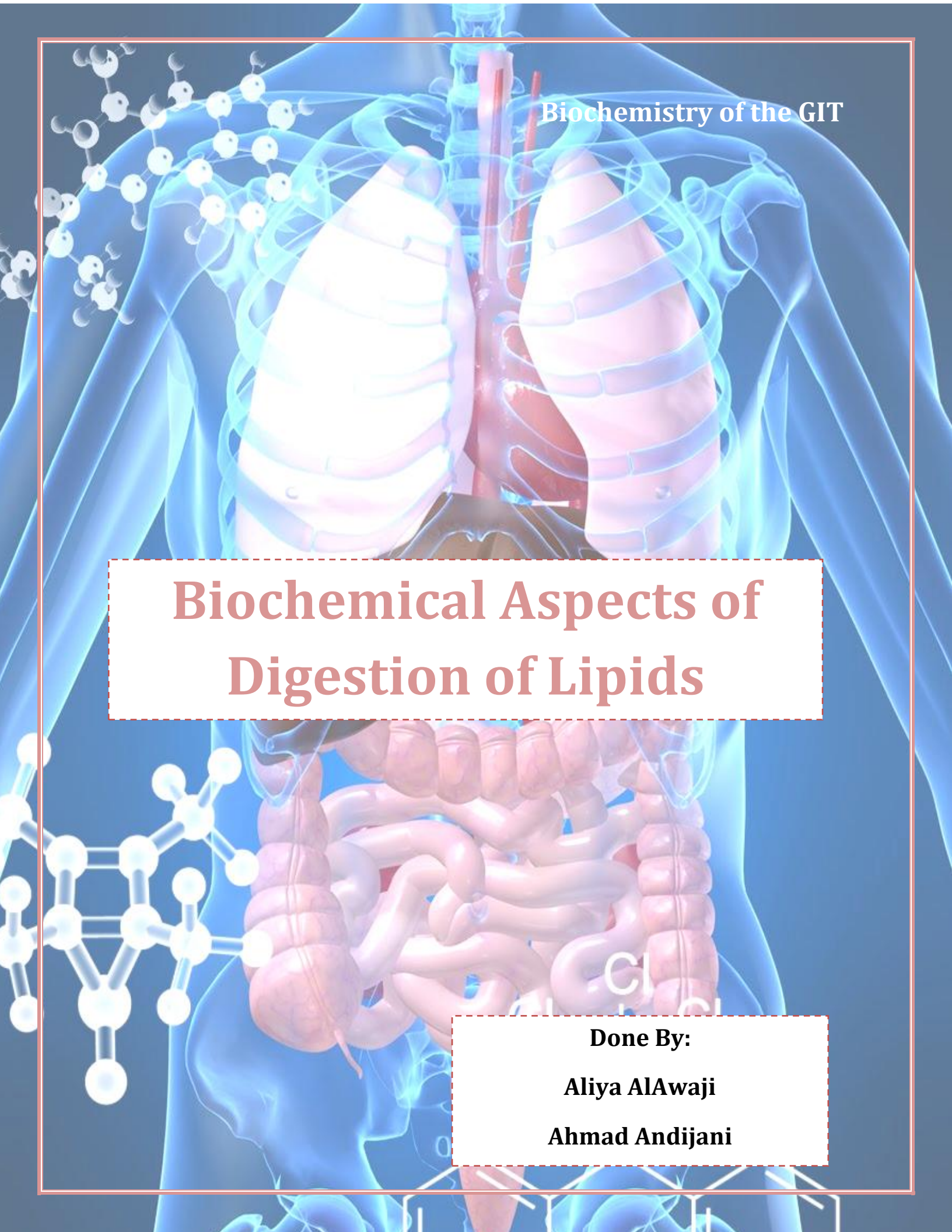

Biochemistry of the GIT

Biochemical Aspects of Digestion of Lipids

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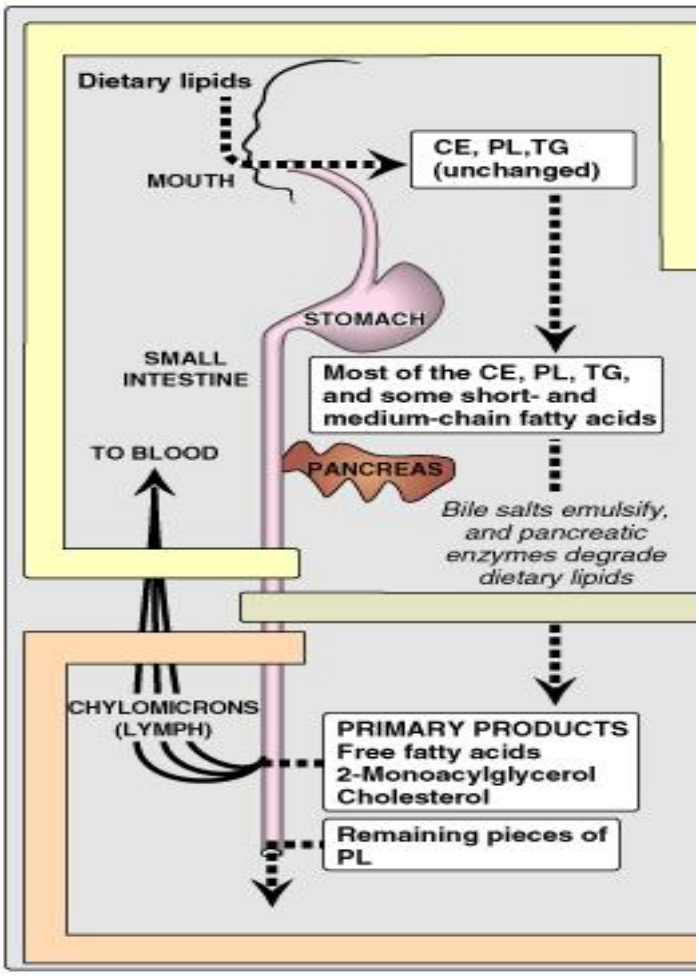
Dietary Lipids:

- Dietary lipids intake is **~81 g/day** (this average number is for the US population)
- Triacylglycerol is **~ (90%)**
- The remainder includes (**10%**):
  1. Cholesterol
  2. Cholesteryl ester (it's a cholesterol esterified with fatty acid)
  3. Phospholipids
  4. Glycolipids
  5. Free fatty acids



Lipid Digestion: Sites and Enzymes

Sites:

1. **The stomach**
2. **The small intestine**

Enzymes:

1. **Act in stomach:**

- **Mouth** (from the base of the tongue): Lingual lipase
- **Stomach** (from the gastric mucosa): Gastric lipase
- Both **lingual** and **gastric lipases** are acid stable; they have a **pH optimum** between 4 and 6.
- They act only on **short** and **medium** length fatty acids (<12 carbon fatty acid chains, e.g. milk).
- It is essential for **neonates** and **NOT** that important for adults unless they have **pancreatic insufficiency** (e.g. cystic fibrosis).

2. **Act in small intestine:**

- **Pancreatic enzymes**
  - **Lipase** and **co-lipase** → for **triacylglycerol**
  - **Cholesterol esterase**→ for **cholesteryl ester**.
    Gives product of Cholesterol and Fatty Acid from Cholesteryl Ester
  - **Phospholipase A2** → for **phospholipids**
  - **Lysophospholipase** → for **phospholipids**

- (Then we get primary products: **free fatty acids** + **2-monoacylglysrol** + **free cholesterol** + **reminisce of phospholipids,** which are usually **glycerol phospholipase**).
- (**Free fatty acids** + **2-monoacylglysrol** + **free cholesterol**) are taken up by the intestinal mucosa cells and make the **TGs** again from them and pack them as **chylomicrons** in which they get secreted in the **lymph**. That explains the ***milky appearance*** of the serum after a fat rich meal.

A. Digestion of lipids begins in the Stomach:

— **The effects of lingual and gastric lipases on TAG:**

- Little significance in adults. Because lipids are not yet emulsified. (unless they have pancreatic insufficiency).
- Important for digestion of milk fat in neonates and infants. 1)Milk is fluid doesn't need emulsification. 2)Triacylglecerol of milk contains short and medium chain.

B. Digestion of Lipids in Small Intestine:

- Digestion of lipids is preceded by **emulsification** using **bile salts** (braking down the fat droplet into smaller parts, hence increasing the surface area so they become more accessible to the enzymes present in the aqueous medium).
- Digestion in small intestine is hormonally controlled:

1. Cholecystokinin (CCK). Has another name called "Pancreozymin" due to it's function which release digestive enzymes. (not Bicarbonate nor water)
2. Secretin

These hormones control the secretion and the activity of the enzymes.

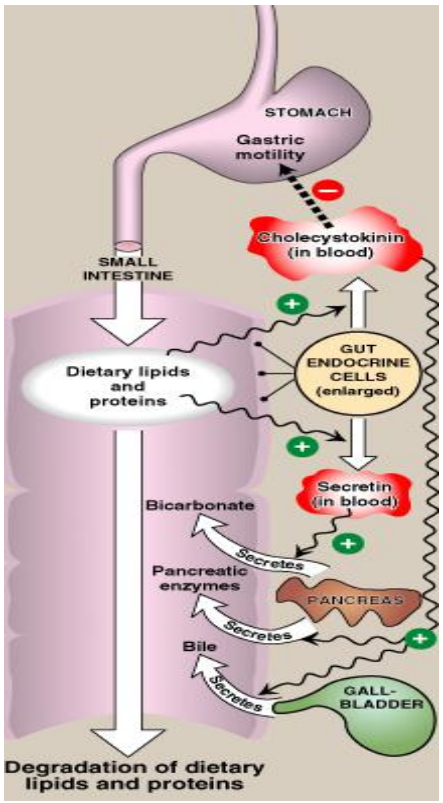
Emulsification of Dietary Lipids in duodenum:

- Emulsification increases the surface area of lipid droplets; therefore the digestive enzymes can effectively act.
- Mechanisms: These two mechanisms prevent from coalescing

1. **Mechanical mixing by peristalsis:** the rhythmic contractions and relaxations to mix the food with the bile salts.
2. **Detergent effect of bile salts:**
   - Bile salts interact with lipid particles and aqueous duodenal contents, stabilizing the particles as they become smaller, and preventing them from **coalescing**, which is (grouping of fat droplet together again).

Hormonal control of digestion in small intestine:

- The digestion in small intestine is **hormonally** controlled.
- Two small peptide hormones are released from cells of the **upper part of small intestine**:
  1. **Cholecystokinin** (**CCK**):
     - Secretion of pancreatic enzymes (excitatory).
     - Bile secretion (excitatory).
     - **Slow** release of gastric contents (inhibitory).
  2. **Secretin**: Secretin regulates PH.
     - Release of watery solution rich in **bicarbonate** by pancreas for **neutralization** of the acidic gastric content.



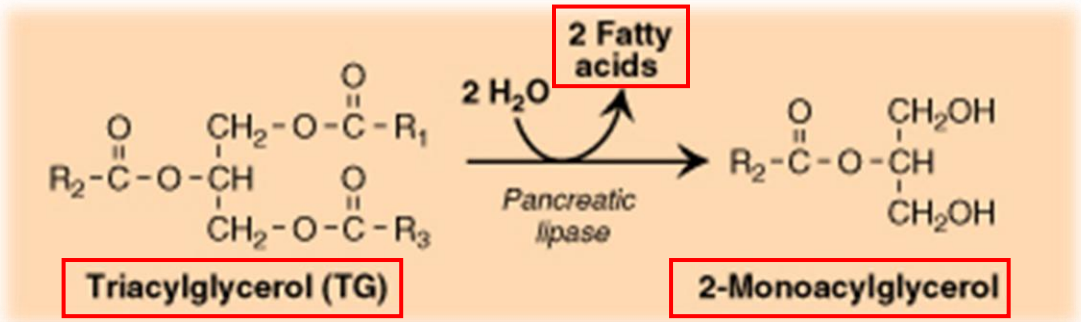
The gut hormones:

The gut hormone	Stimulus for secretion	Effects
1- Cholecystokinin (CCK)	The presence of partially digested proteins (& lipids) in the upper small intestine.	1. Stimulates the release of pancreatic digestive enzymes 2. Stimulates the contraction of the gall bladder & release of bile 3. Decreases gastric motility → slower release of gastric contents into the small intestine
2- Secretin	Low pH of the chyme entering the intestine.	- Stimulates the pancreas to release a watery solution rich in bicarbonate to neutralize the pH of the intestinal contents (to reach the optimum pH for digestive activity by pancreatic enzymes)

Pancreatic enzymes for Digestion of Lipids:

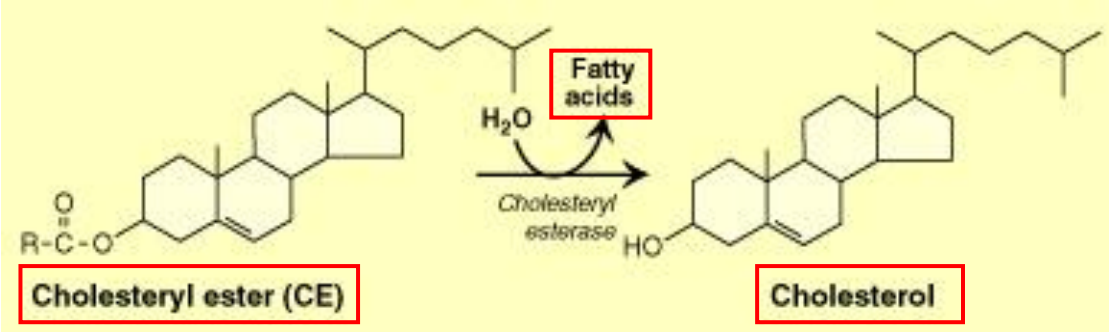
- **Pancreatic Lipase** and **co-lipase**
- **Cholesterol esterase**
- **Phospholipase A2**
- **Lysophospholipase**

Digestion of TAG by ***Pancreatic Lipase***:

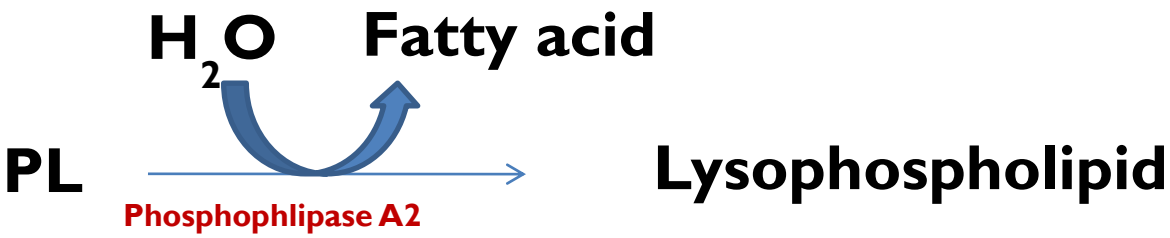


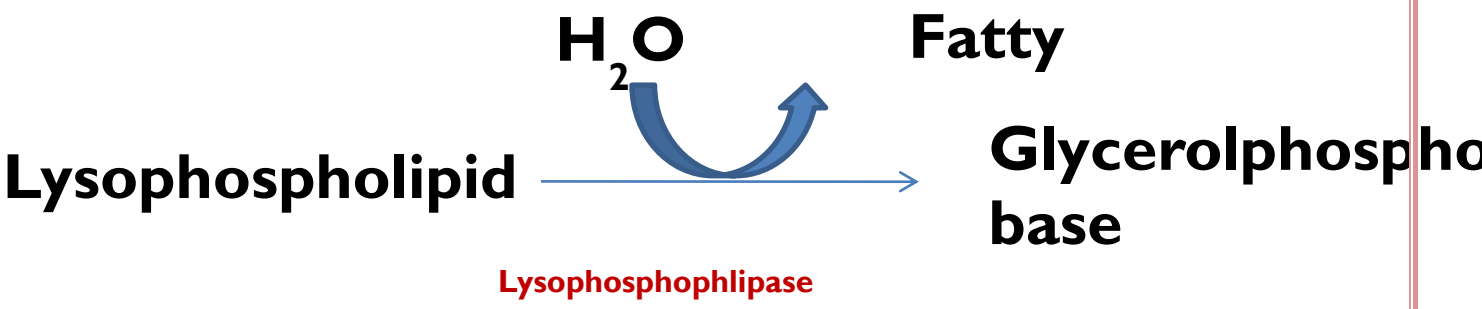
- **Pancreatic lipase**: Found in high conc. in pancreatic secretion (2-3% of total proteins)
- **Pancreatic lipase** requires **co-lipase** for its activity.
- Inhibited by ***Orlistat***, an antiobesity drug.

Digestion of Cholesteryl ester by *Cholesteryl Esterase*:



Digestion of Phospholipids (PL) by *Phospholipase A2 & Lysophospholipase:*

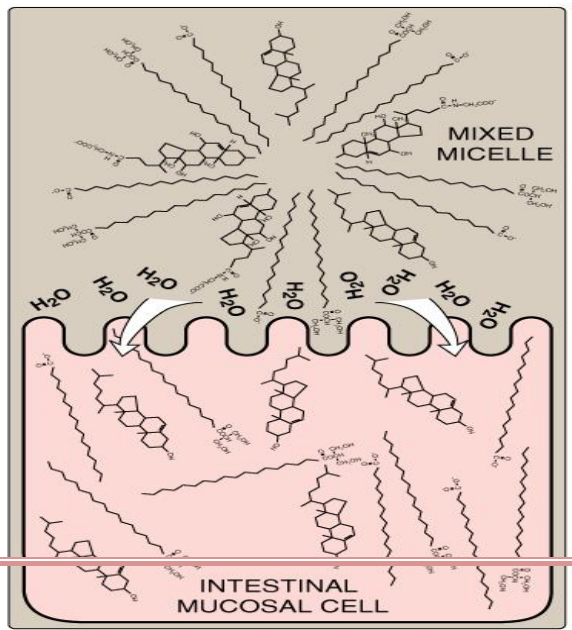




- ❖ **Lysophospholipid = phospholipid – 1 fatty acid**
- ❖ **Glycerolphosphoryl base = Lysophospholipid – 1 fatty acid**

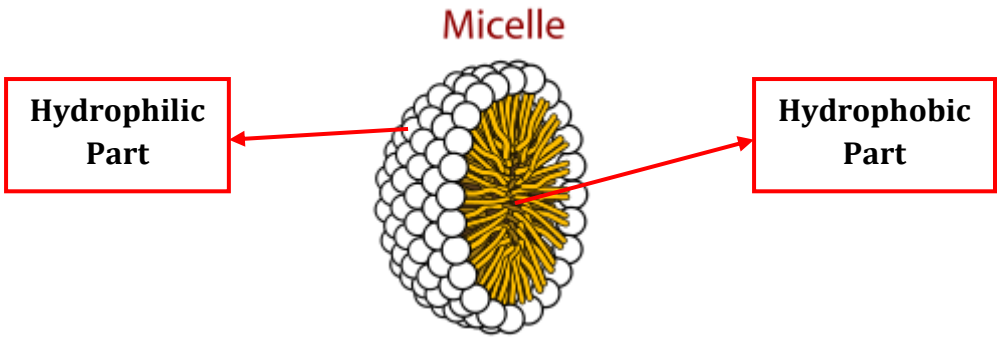
Main End products of lipid digestion:

- **2-Monoacylglycerol**
- **Cholesterol**
- **Free fatty acids**



Absorption of Lipids by Intestinal Mucosal Cells:

- **Mixed micelles**: Solubility is better than others, so they can pass.
  - **Disc-shaped clusters of amphipathic lipids (**lipids that contain both **hydrophilic** and **hydrophobic** ends**).**
  - **Arranged with their hydrophobic groups on the <u>inside</u> and their hydrophilic groups on the <u>outside</u>.**
- **Micelle includes end products of lipid digestion, bile salts and fat-soluble vitamins**
- **Short- and medium-chain fatty acids <u>DO NOT</u> require mixed micelle for absorption by intestinal cells.**



Resynthesis of Lipids by Intestinal Mucosal Cells:

1. Activation of **free long chain fatty acids** into → ***<u>fatty acyl CoA</u>*** **(**by the enzyme **acyl CoA synthetase)** → then it can interact with **(e.g. monoacylglycerol** → into **diacylglycerol** → into **triacylglycerol).**

2. **Synthesis of**

   - **TAG** from **monoacylglycerol**
   - **Cholesterol ester** from **cholesterol**
   - **Phospholipids** from **glycerolphosphoryl base**

3. **Short- and medium-chain fatty acids are <u>NOT</u> converted into their CoA derivatives. Instead, they are released into portal circulation, carried by serum albumin.**

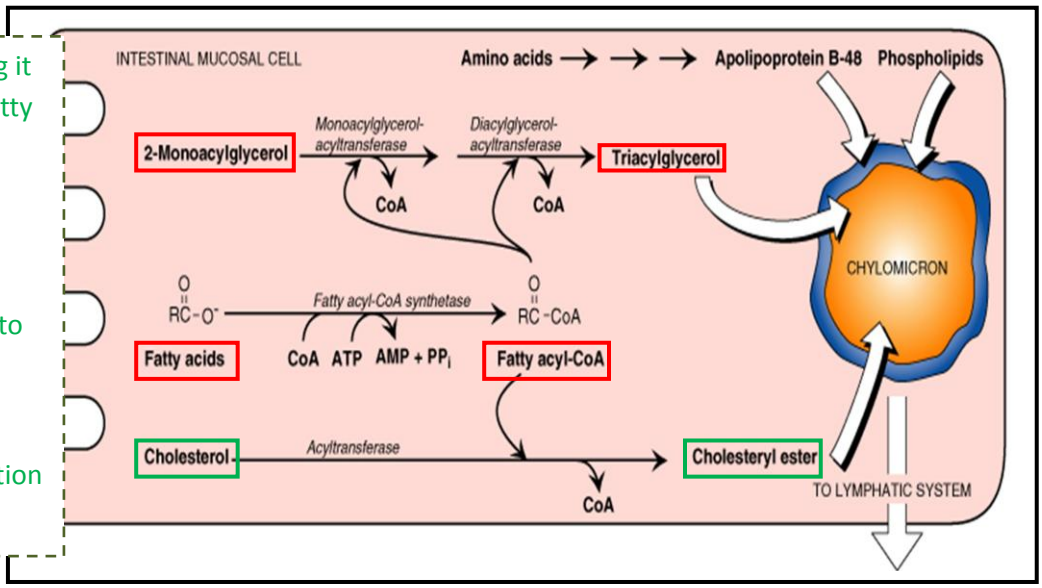
Resynthesis of Lipids and assembly of Chylomicrons by Intestinal Mucosal Cells:

Re-synthesis to be absorbed by making it more hydrophilic; by converting the fatty acid in the active form (acyl CoA)

CoA= Co-enzyme of bantothenic acid (Vitamin B complex)

Short & Medium chain= goes directly to portal vein structure.

Long chaing- undergo lipoprotein structure then to lymphathetic circulation then to the general circulation.



Assembly of Chylomicrons by *Intestinal Mucosal Cells*:

- **Assembly of chylomicrons:**
  - Newly synthesized **TAG** and **cholesteryl ester** are packaged as **lipid droplets** surrounded by thin layer of**:**
    1. **Apolipoprotein-48 (apo-48)**
    2. **Phospholipids**
    3. **Free cholesterol**
  - And the **core** consists of **TAGs** and **cholesteryl ester**.

Secretion of Chylomicrons by *Intestinal Mucosal Cells*:

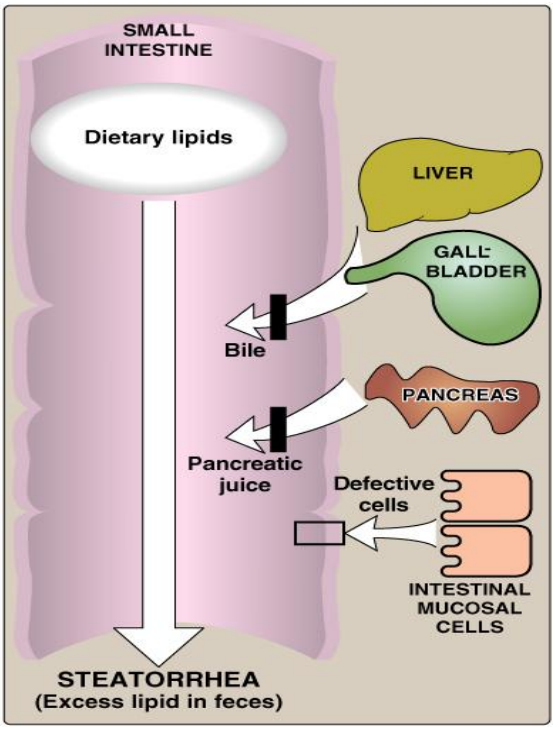
- **Secretion of chylomicrons:**
  - By **exocytosis** into **lymphatic vessels around villi** of small intestine **(lacteals)** then enter into **systemic circulation**
  - **Milky-appearance of serum after lipid-rich meal**

Abnormalities in Lipid Digestion/Absorption:

- **Liver and gall bladder diseases** causes defect in the bile salt**.**
- **Pancreatic insufficiency** causes defect in the pancreatic enzymes.
  - **e.g. chronic pancreatitis, cystic fibrosis, surgical removal of the pancreas**
- **Intestinal diseases:**
  - **e.g., Intestinal resection (**shortened bowl**) which lead to:**

→ **incomplete digestion & absorption of fat & protein → abnormal appearance of lipids (steatorrhea) & undigested protein in the feces (Malabsorption syndrome).**

Maldigestion/Malabsorption of Lipids:



Take home message:

- **Dietary lipids are relatively hydrophobic**
- **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 formation of mixed micelles**
- **Re-synthesis of TAGs, cholesteryl ester and PLs inside the intestinal mucosal cells**
- **Assembly and secretion of chylomicrons into lymphatic lacteals and then into systemic circulation**
- **Short- and medium-chain fatty acids:**
  1. **Do not require micelle for absorption**
  2. **Do not participate in re-synthesis of TAGs & PLs**
  3. **Released directly from intestinal cells into portal circulation**
- **Liver diseases, pancreatic insufficiency, or intestinal diseases → incomplete digestion and absorption of fat & protein → steatorrhea & appearance of undigested proteins in the feces (Malabsorpton syndrome)**