Lipid Digestion

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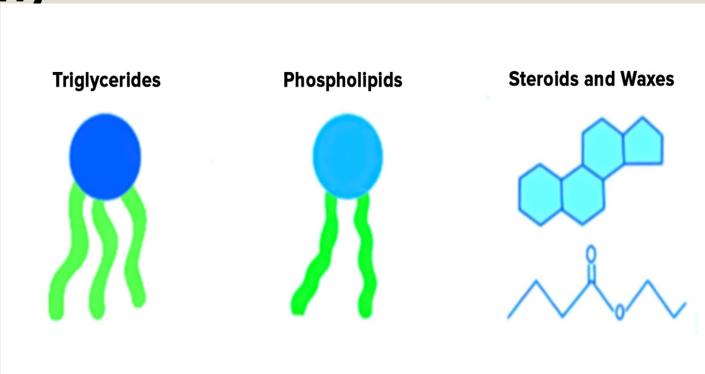
Aim

At the end of this lesson student should be able to define:

- **Different kinds of dietary lipids**
- **Dietary sources of lipids**
- **The different sites of lipids digestion in the human body**
- **Hormones and/or enzymes involved in lipids digestion**
- **Role of Bile salts in lipids digestion**
- **The clinical significance of lipids digestion and absorbance**

What is lipid….?

- **The term lipids includes a divers group of structurally distinct hydrophobic and amphipathic molecules.**
- **Substances in dietary foods and supplements**
- **Hydrophobic and soluble in ethanol (chloroform, alcohol & petroleum)**



Fat and waxes
(can be hydrolyzed by ester linkage)

Cholesterol and steroids
(can not be hydrolyzed)

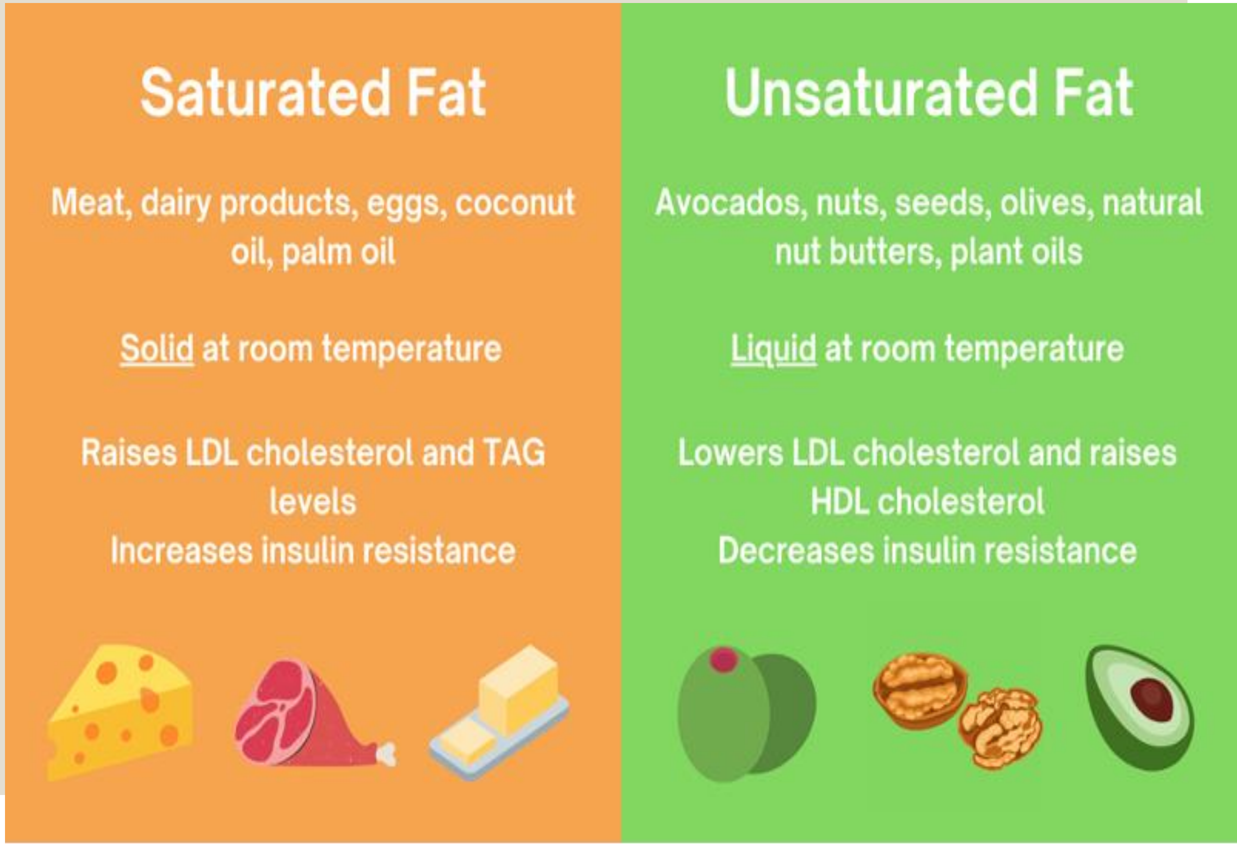
- **Fats & oils make up 95% of the nutritional lipids, the other 5% are steroids. Waxes are functional only**.

Different types of lipids

- **Saturated**
  - Animal oil and products like meat, milk, butter
  - Vegetable oil and products like coconut oil

- **Poly saturated**
  - Plan source oil like corn, cottonseed, sunflower oil and soybean oil

- **Monounsaturated**
  - Plant and animal product like olive oil, canola oil,
  - avocado and peanut oil



Dietary source of lipids

Triacylglycerols (TAGs) are the major fat in the human diet (90%). In addition to TAGs, free fatty acids, **phospholipids** , cholesterol and **cholesterol esters** are present in the foods we eat.

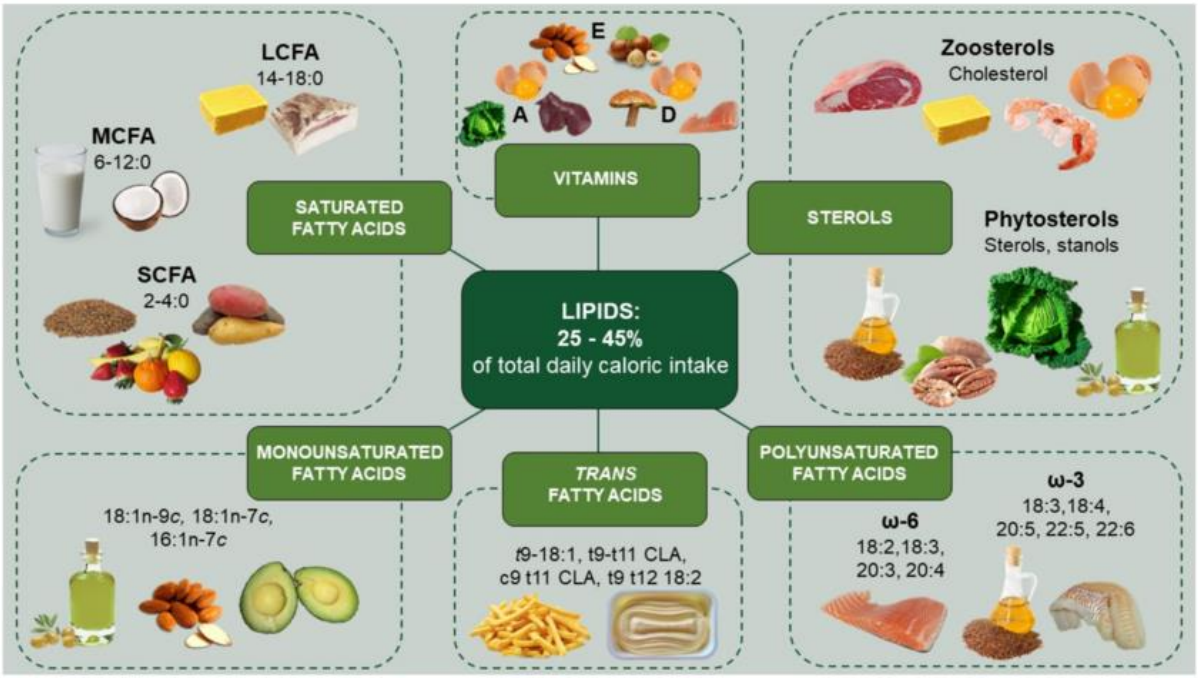
➢**Animal source:**

Diary products, meat (fish, pork, chicken,…),butter, egg

➢**Vegetable sources:**

Oil (sunflower, olive, ground nuts…)

Fat from vegetable sources (ex.Avocado….)



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Type of lipids in some oil

No cholesterol in products derived from plant sources!!

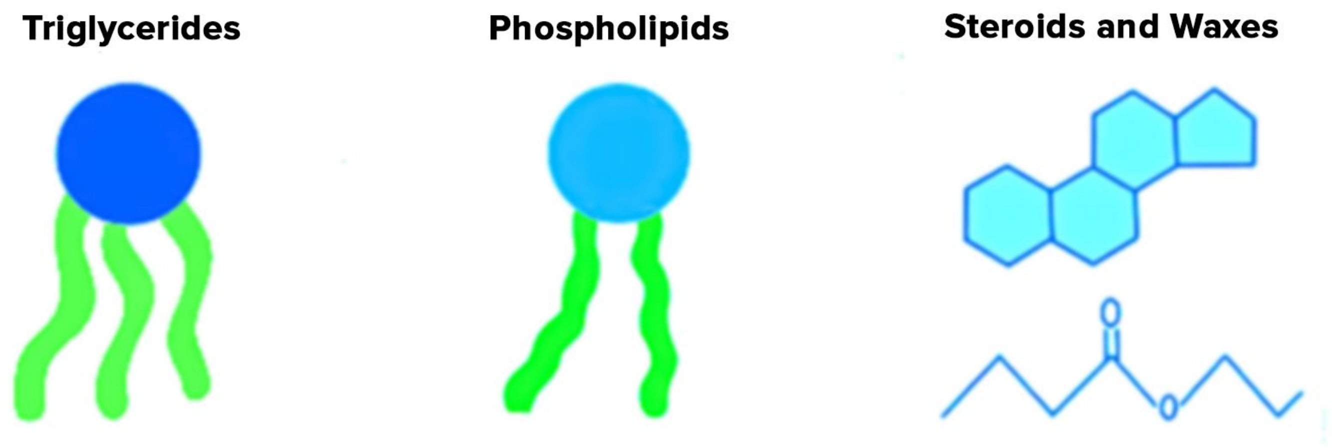
Biological property of Lipids:

➢ **Lipids can be synthesized in the body** using complex biosynthetic pathways or enter the body from exogenous sources (Dietary).

➢ **Functions:**
- Energy storage
- Used in cell membranes
- Involved in intracellular signalling
- Hormones synthesis
- Enzyme cofactors
- Maintenance of body temperature
- Fat soluble vitamin absorption …

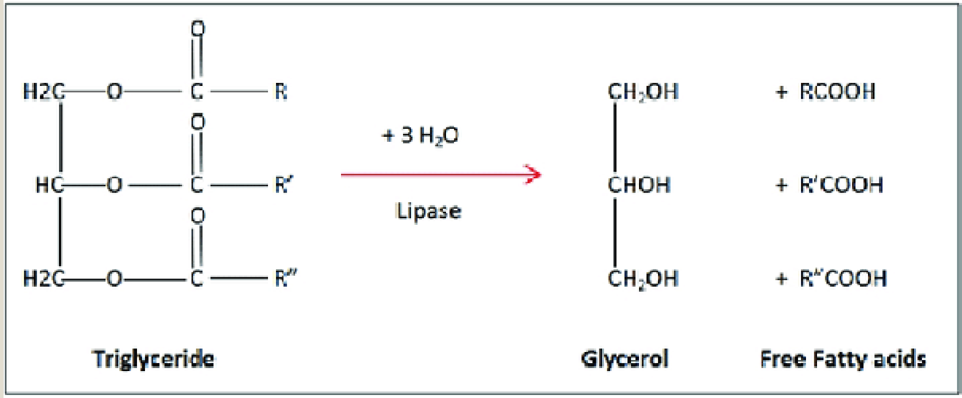
Most of the lipids found in the body fall into one of the below categories:

- Fatty acids
- Triacylglycerols
- Glycerophospholipids and sphingolipids
- Eicosanoids
- Cholesterol
- Bile salts
- Steroid hormones
- Fat-soluble vitamins

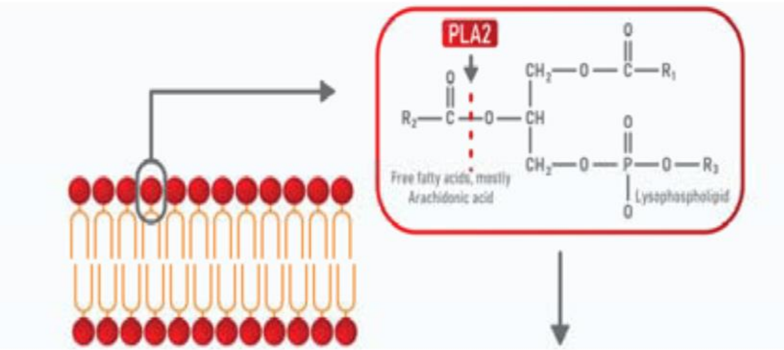


Digestion of Triacylglycerols and the Other Fats

- **Lingual lipase/ gastric lipase** (limited digestion)
- **Action of bile acid** : In the intestine, the **fats are emulsified** by bile salts.
- **Action of pancreatic lipase**: In the intestine **pancreatic lipase-** together with **colipase-** hydrolyses fatty acids of all chain lengths from position 1 and 3 of the glycerol moiety of the TAG, **producing free fatty acids and 2-monoacyl glycerol.**



- The pancreas also produces **esterases** that remove fatty acids from compounds such as cholesterol esters and
- **phospholipase A2 (PLA2)** that digests phospholipids to a free fatty acid and lysophospholipid.



Lingual lipase/ gastric lipase

- Hydrolysis of triacylglycerols is initiated by **lingual and gastric lipases**, which attack the sn-3 ester bond forming 1,2-diacylglycerols and free fatty acids, aiding emulsification.

- **Lingual lipase:**

Secreted by dorsal surface of tongue (parotid and sublingual salivary gland)

PH for their activation is low (pH 2.0 - 5) while the optimum pH is 4.0-4.5

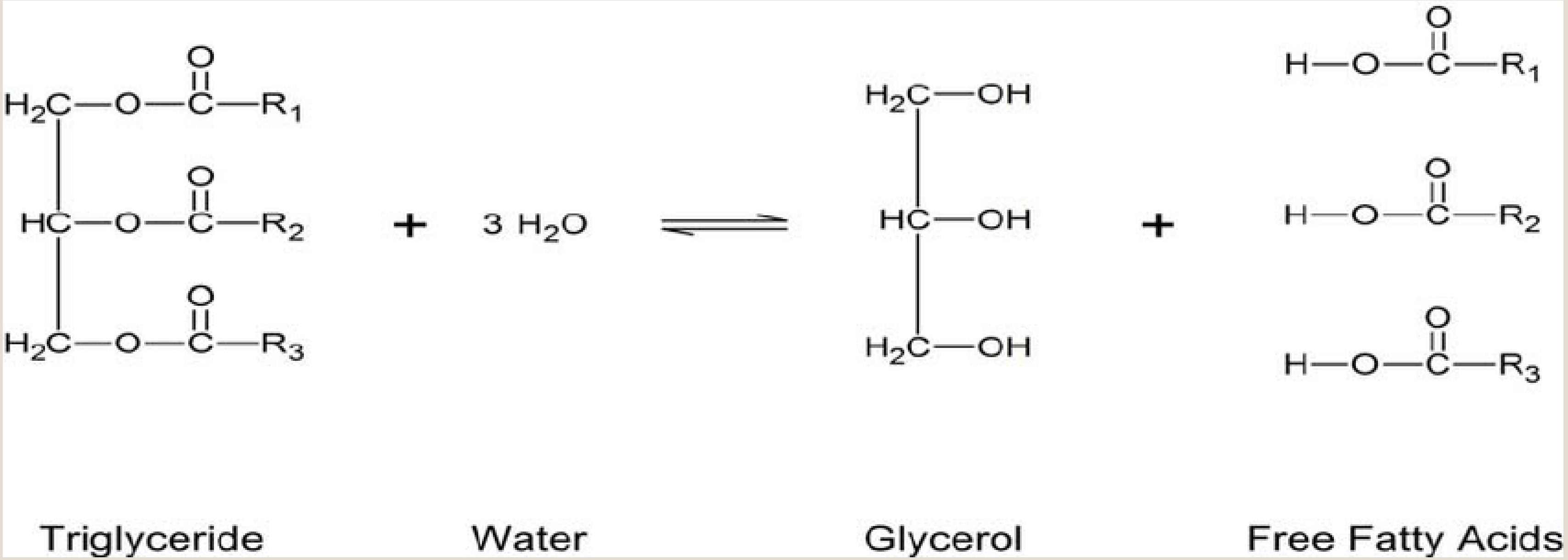
Act in Short chain TGS (SCT).

Milk fat contains short chain fatty acids which are esterified at -3 position, thus it is the best substrate for lingual lipase

Enzymatic action continues in stomach

Short chain fatty acids, released are absorbed directly from the stomach wall and enter the portal vein.

TGS are degraded by lipases in order to form FFA and glycerol



Lingual lipase/ gastric lipase

Enzymatic action continues in stomach

- **Gasteric enzyme:**

-Secreted in small quantities and:
- More effective at alkaline pH (average pH 7.8)
- Requires the presence of Ca^{++}
- Less effective in stomach due to acidic pH except when intestinal contents are regurgitated into the gastric lumen

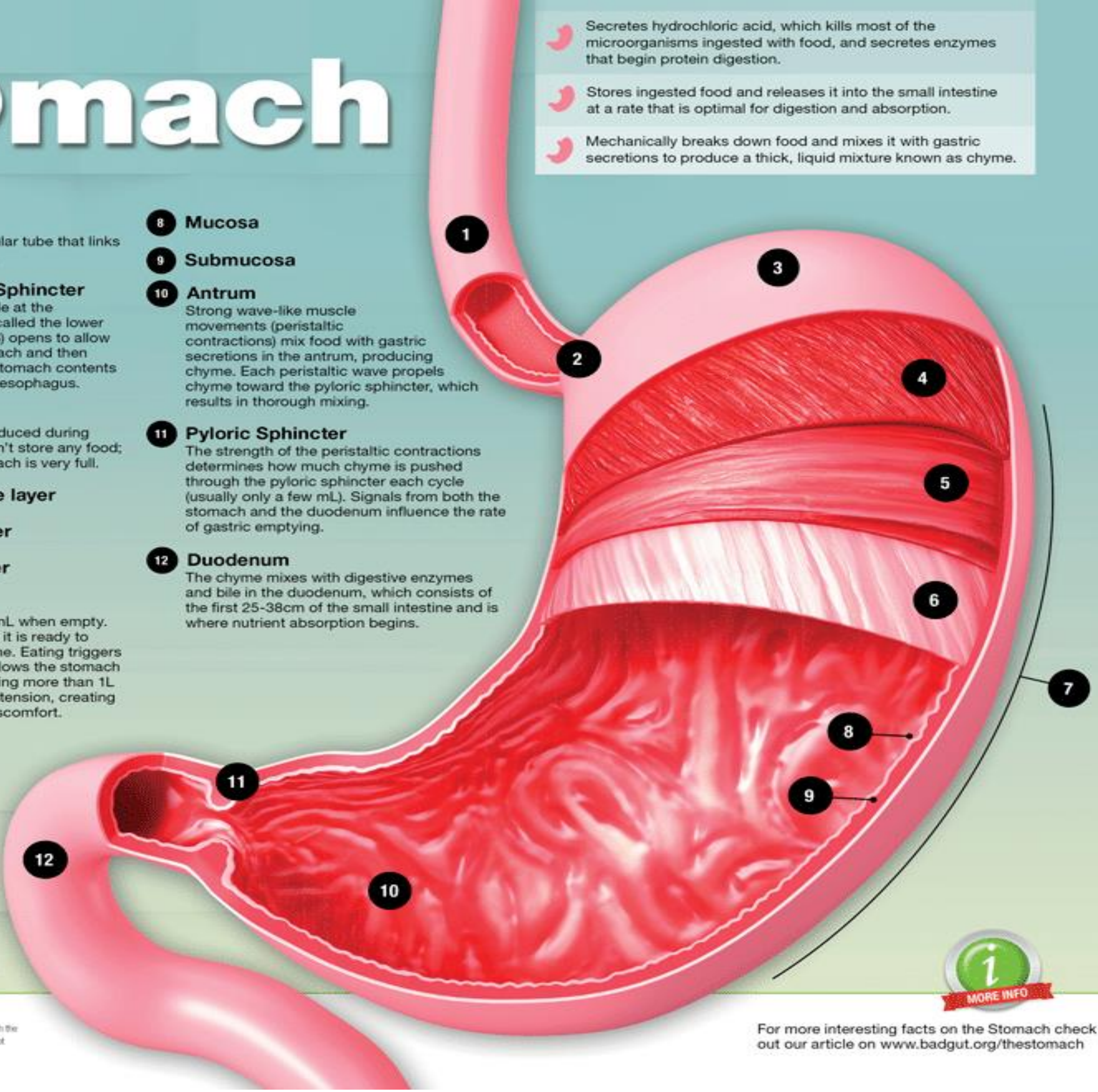
-**Not effective for long chain fatty acids, most effective for short and medium chain fatty acid**
- Milk, egg yolk, and fats containing short chain fatty acids are suitable substrates for its action

Short chain fatty acids are absorbed directly from the stomach wall and enter the portal vein.

Up to 30% digestion of triglycerides occurs in stomach.

THE Stomach

- Secretes hydrochloric acid, which kills most of the microorganisms ingested with food, and secretes enzymes that begin protein digestion.
- Stores ingested food and releases it into the small intestine at a rate that is optimal for digestion and absorption.
- Mechanically breaks down food and mixes it with gastric secretions to produce a thick, liquid mixture known as chyme.



1 Esophagus
The esophagus is a muscular tube that links the throat to the stomach.

2 Lower Esophageal Sphincter
A specialized ring of muscle at the bottom of the esophagus called the lower esophageal sphincter (LES) opens to allow food to pass into the stomach and then quickly closes to prevent stomach contents from flowing back into the esophagus.

3 Fundus
The fundus stores gas produced during digestion. It typically doesn't store any food; however, it can if the stomach is very full.

4 Longitudinal muscle layer

5 Circular muscle layer

6 Oblique muscle layer

7 Body
The body's volume is ~50mL when empty. Food is stored in here until it is ready to move into the small intestine. Eating triggers receptive relaxation that allows the stomach to expand to ~1L. Consuming more than 1L of food can cause over-distension, creating a feeling of fullness and discomfort.

8 Mucosa

9 Submucosa

10 Antrum
Strong wave-like muscle movements (peristaltic contractions) mix food with gastric secretions in the antrum, producing chyme. Each peristaltic wave propels chyme toward the pyloric sphincter, which results in thorough mixing.

11 Pyloric Sphincter
The strength of the peristaltic contractions determines how much chyme is pushed through the pyloric sphincter each cycle (usually only a few mL). Signals from both the stomach and the duodenum influence the rate of gastric emptying.

12 Duodenum
The chyme mixes with digestive enzymes and bile in the duodenum, which consists of the first 25-38cm of the small intestine and is where nutrient absorption begins.

Interesting Facts About the Stomach

Did you know? Just thinking about tasting, smelling, chewing, and swallowing food increases gastric secretions before you even eat anything!

Stomach acid is very acidic and contains enzymes that break down proteins, so at least every three days a new protective layer of mucus covering the stomach lining forms. Without it, the gastric juices would begin to macerate your stomach! Amazingly, the stomach secretes 2L of gastric juice every day.

A **peptic ulcer** is a sore in the lining of the stomach (gastric ulcer) or duodenum (duodenal ulcer). Most ulcers result from infection with bacteria called *Helicobacter pylori*, but another common cause is non-steroidal anti-inflammatory drugs such as ibuprofen and aspirin. Stress and spicy food do NOT cause ulcers.

Emotions can influence gastric motility. Depending on the person, sadness and fear tend to decrease motility whereas anger and aggression tend to increase it. Intense pain in any part of the body inhibits motility throughout the digestive tract.

Did you know? The stomach only absorbs certain medications (like aspirin) and small amounts of alcohol.

Vomiting is not a result of reverse peristalsis as you might expect. The force comes from the contraction of the respiratory muscles, (mainly the diaphragm) and the abdominal muscles. The brain signals to the stomach, esophagus, and associated sphincters to relax, allowing the gastric contents to travel upward and out.

In 1868, Adolf Kussmaul, of Germany, performed what historians believe to be the first esophago-gastroscopy on a professional sword-swallower. This insightful choice of patient allowed him to complete the procedure with an inflexible device on someone who was used to having uncomfortable objects in his upper GI tract!

For more interesting facts on the Stomach check out our article on www.badgut.org/thestomach

badgut.org
Gastrointestinal Society
Société gastro-intestinale

Canadian Society of Intestinal Research

Role of fat in gastric emptying

-Fats delay the rate of emptying in the stomach

- Action is brought about by secretion of enterogastrone

-**Enterogastrone inhibits gastric motility** and retards the discharge of bolus of food from the stomach

- Fats have a high satiety value.

- Any hormone secreted by the mucosa of the duodenum in the lower gastrointestinal tract in response to dietary lipids that inhibits the caudal (or "forward, analward") motion of the contents of chyme (e.x: secretin, Cholecystokinin and gastric inhibitory peptide).

*Chyme or chymus is the semi-fluid mass of partly digested food that is expelled by a person's or another animal's stomach, through the pyloric valve, into the duodenum

Why lingual and gastric lipases are important?

- Important for lipid digestion of infants since milk is the main source of energy in this period of time.

- It is important digestive enzymes in pancreatic insufficiency conditions such as **cystic fibrosis or other pancreatic disorders.**

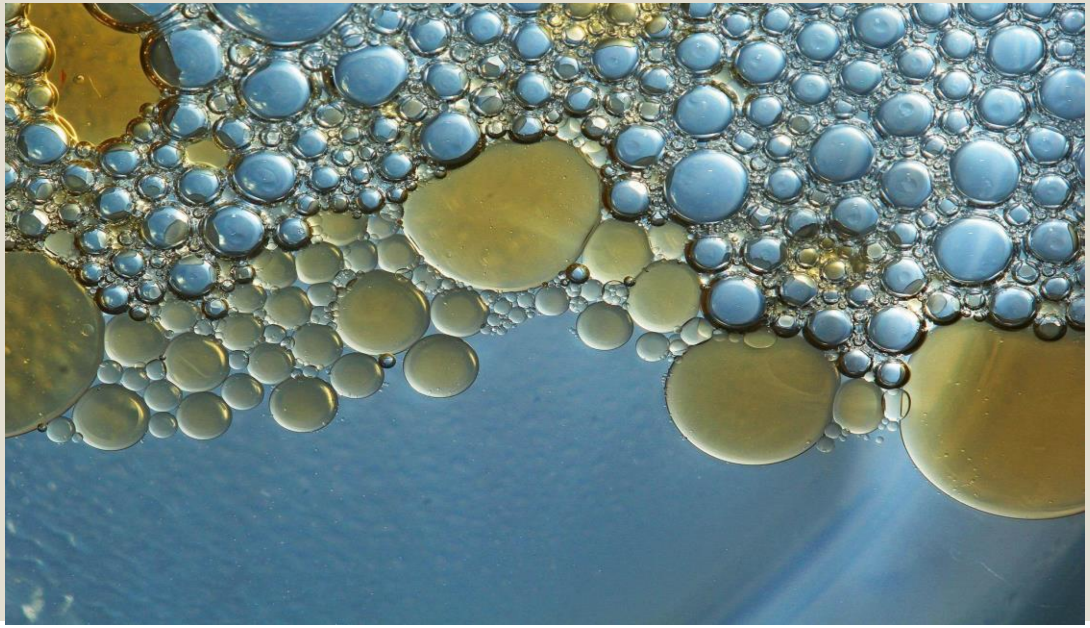
- **The enzyme secreted from lingual and gastric (lipases) system can degrade TGS with short and medium chain fatty acids in patients with pancreatic disorders despite a near or complete absence of pancreatic lipases.**

Emulsification

-Emulsification is pre-requisite for digestion of lipids .

Lipids are hydrophobic and therefore are poorly soluble in aqueous environments which presents inside the digestive tracks.

-While the lipases is water soluble and therefore can only work at the surface of lipids globules.



Emulsification

- **Take place in duodenum.**

- **Breaking up the fat globules into much smaller Emulsion droplets.**

Surface tension is reduced

Surface area of droplets is increased.

- This process is favored by **Emulsification agents** :

1. **Bile salts (Detergent action)**

2. Phospholipids

and

3.Peristalsis (mechanical mixing)

Digestion in small intestine

-Major site of fat digestion

-Effective digestion due to existence **of lipases and bile salt**

Bile salt act as an effective **Emulsifying agents for the fats**

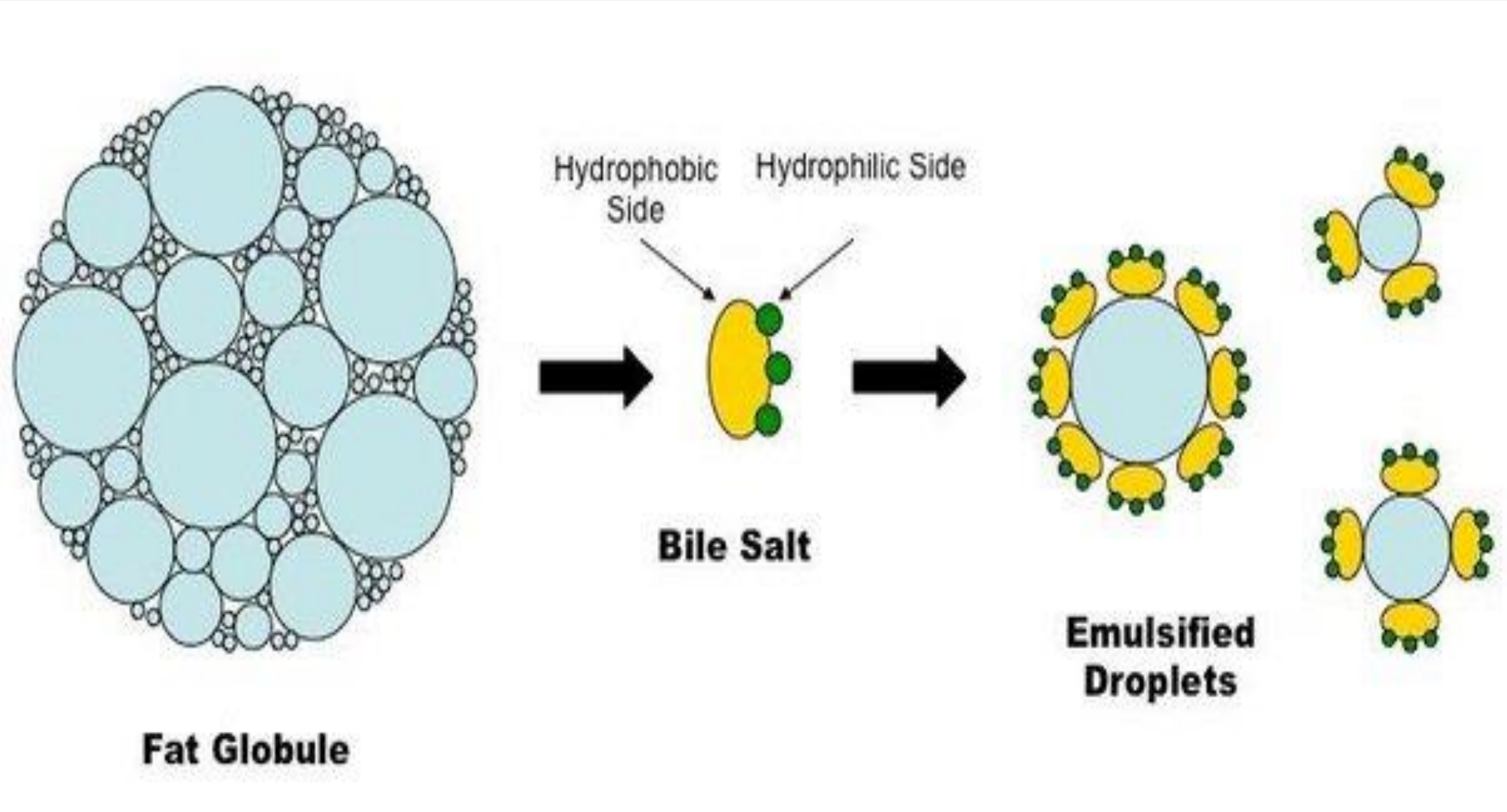
Bile Salt:

- The hydrophobic portions of bile salts intercalate into the large aggregated lipid, with the hydrophilic domains remaining at the surface.
- Helps in combination of lipase with two molecules of small proteins called colipases which in turn increases the lipases activity.
- Breakdown the large aggregates into smaller droplets.

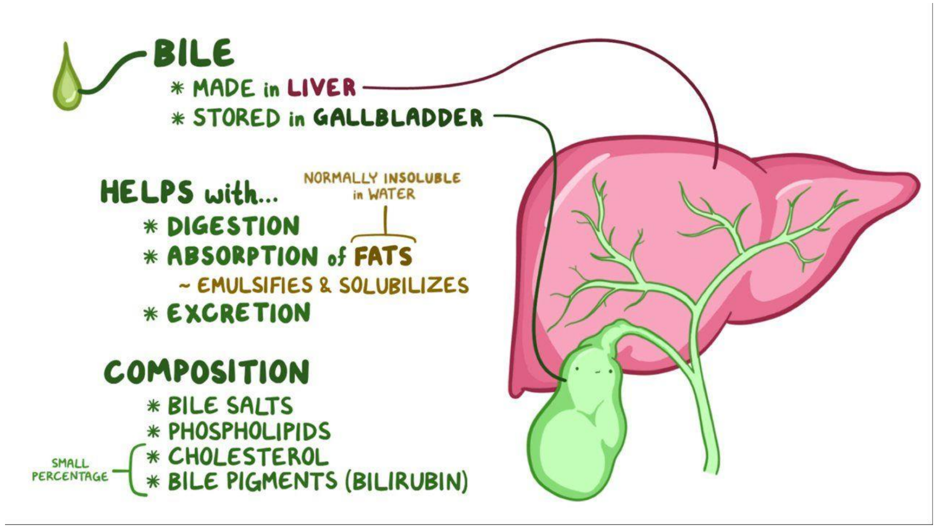
↓

Increase the surface area for action of lipase.

Emulsified Droplets



https://biologydictionary.net/bile-salts/



Bile salt

-Is derivatives of cholesterol.

- Bile salts are synthetized in the liver and are stored in the gall bladder.
- Secreted into small intestine.
- Act as detergents, are used to solubilize the triacylglycerols.
- The consist of sterol ring structure with a side chain to which a molecule of taurine or glycine is conjugated .
- Converting dietary fats into mixed micelles of bile salts and triacylglycerols.

Bile Juice

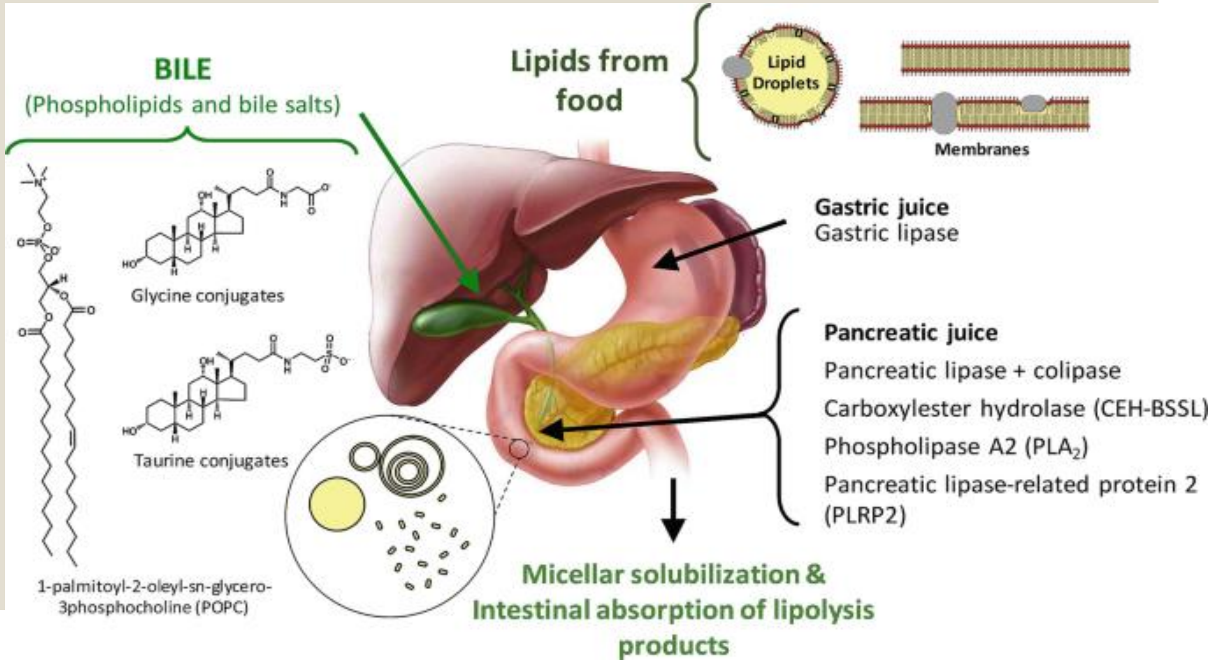
- Contains water, cholesterol, bile salts , proteins and bilirubin (waste product)
- Bile salts, which act as detergents, are used to solublize the triacylglycerols
- If bile contains too much cholesterol, it can harden into **gallstones.**
- **Gallstones's sizes can range from grain of sand up to a Pingpong ball!**
- If gallstone blocks the exit duct, then gallbladder may need to be removed

- Removal of gallstones by surgery is a common procedure
- In case of removal fat digestion becomes more difficult, but not impossible

Intestine’s Lipolytic enzymes

1. Pancreatic lipase with co-lipase.
2. Cholesterol esterase.
3. Phospholipase A2.

*The bile pH(7.7) Neutralise the acidic pH of the stomach – Provides optimum pH for the action of pancreatic enzymes .

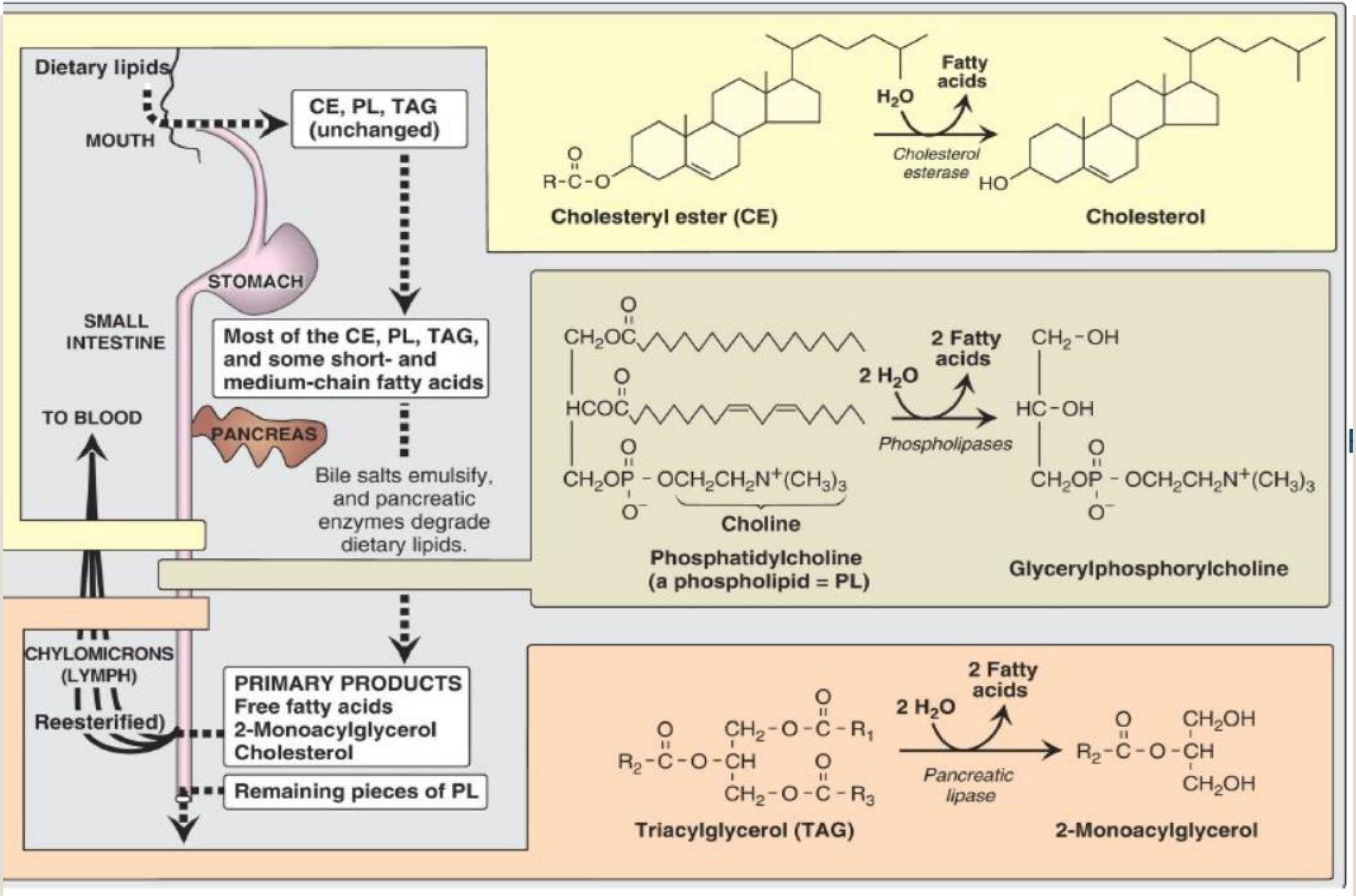


ISBN : 978-3-030-56908-2

Lipid degradation by pancreatic lipases

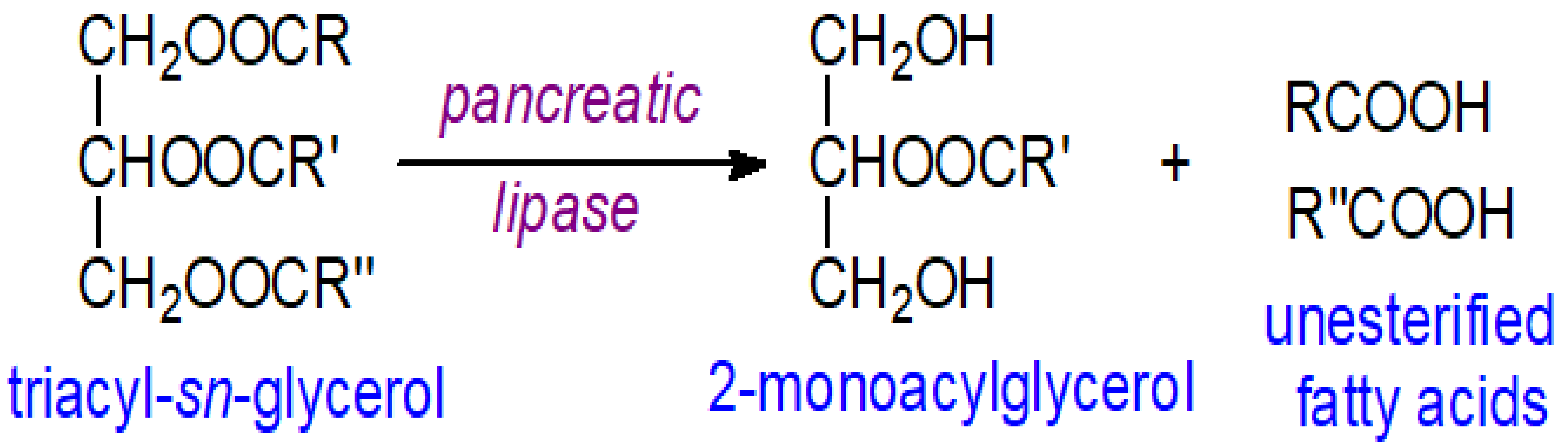
- **Content of pancreatic juice:**
  - Pancreatic lipases -> TGS
  - Phospholipase A2 -> Phospholipids
  - Cholesterol esterase -> Cholesterols

- **Pancreatic lipase**
  - **Hydrolyses of ester likage in the 1st and 3rd carbon atoms of FFA**
  - **It can not hydrolyze the ester linkages of position 2**
  - Digestion of TGS by removal of terminal FA to produce α,β diglycerids
  - Removal of other terminal FA by lipase to form β mono glyceride.



https://mail.almerja.com/reading.php?idm=158597

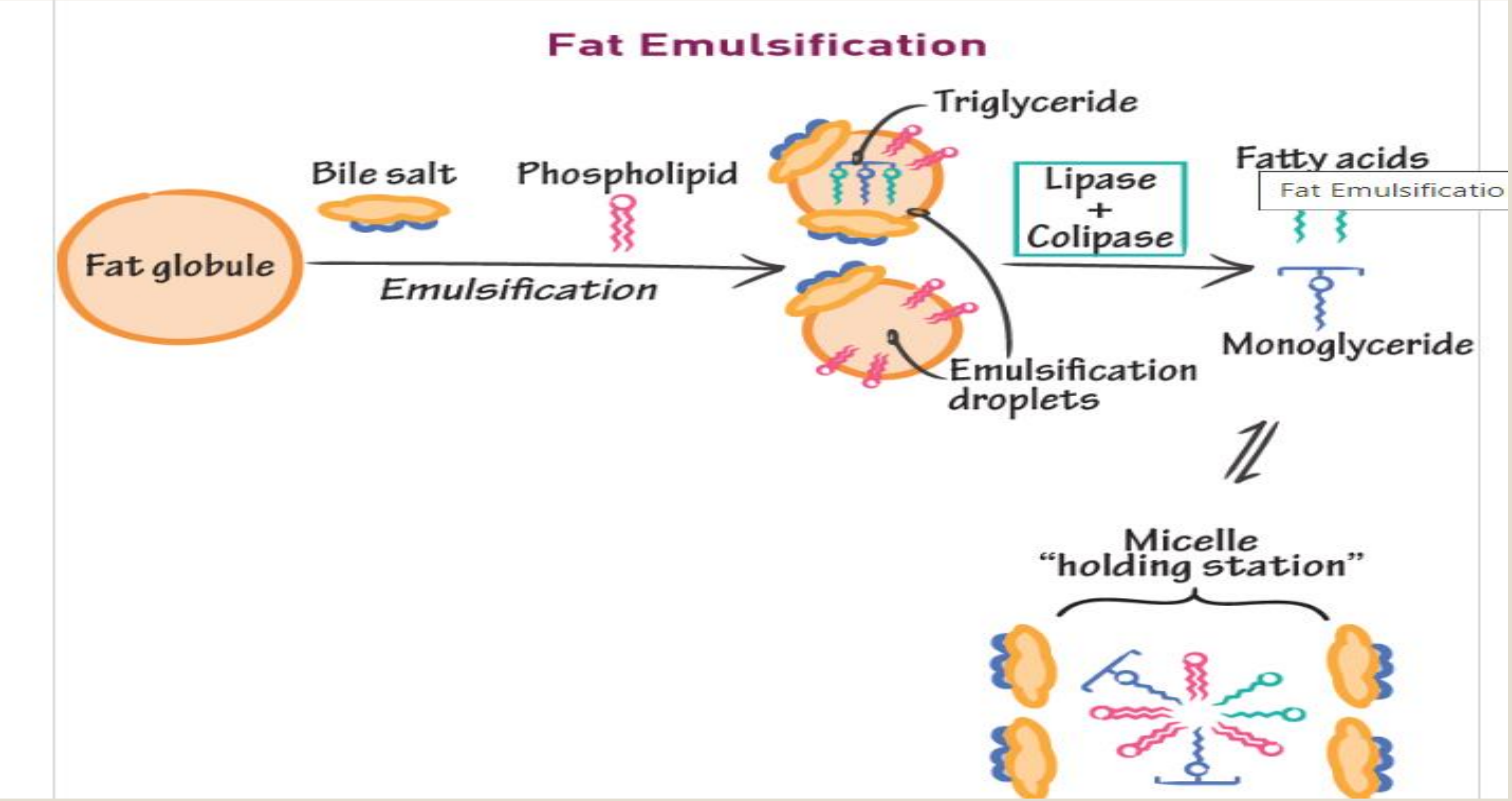
Hydrolysis of triacylglycerols with pancreatic lipase



Major end products :

- 2-MAG (78%)
- 1-MAG(6%)
- Glycerol and fatty acids (14%)

Finally dissolving the FA and MGS into micells to produce "mixed micelles"



https://ditki.com/course/biochemistry/glossary/physiological-process/fat-emulsification

Lipid absorbance

➢**Mixed micelle formation:**

• 2-monoglycerides, long chain fatty acids, cholesterol, phospholipids and lysophospholipids are incorporated into molecular aggregates to form mixed micelle.

• The micelles are spherical particles with a hydrophilic exterior and hydrophobic interior core .

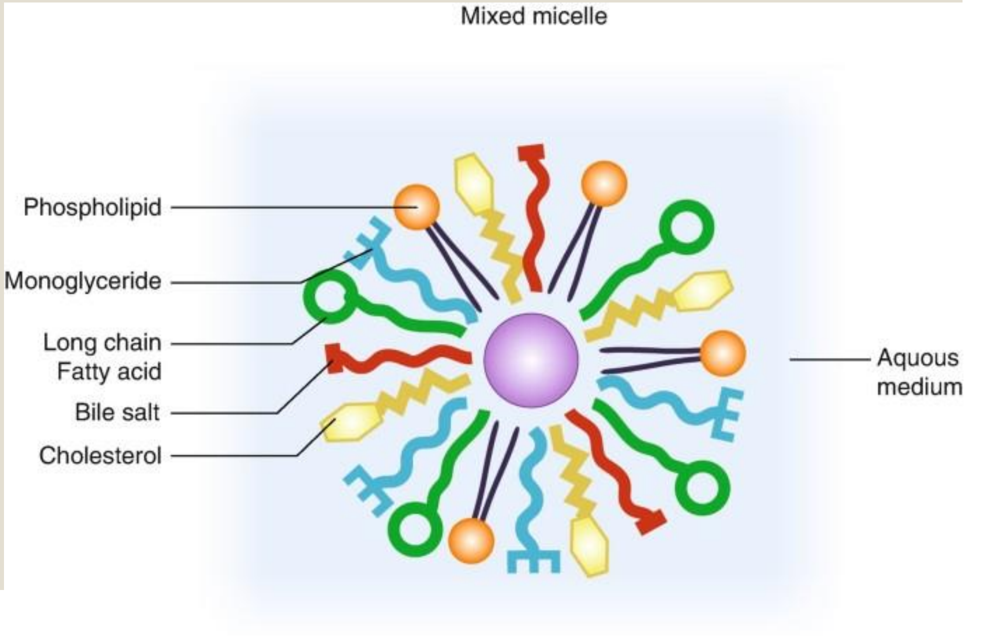
• Disc-shaped clusters of **amphipathic lipids.**

• Due to their detergent action , the bile salts help to form micellar aggregates.

-Micellar is essential for the absorption of fat soluble vitamins A, D and K.

-The micelles are aligned at the microvillous surface of the jejunal mucosa.

-Fatty acids, **2 -MAG and other digested products passively diffuse into the mucosal cell.**



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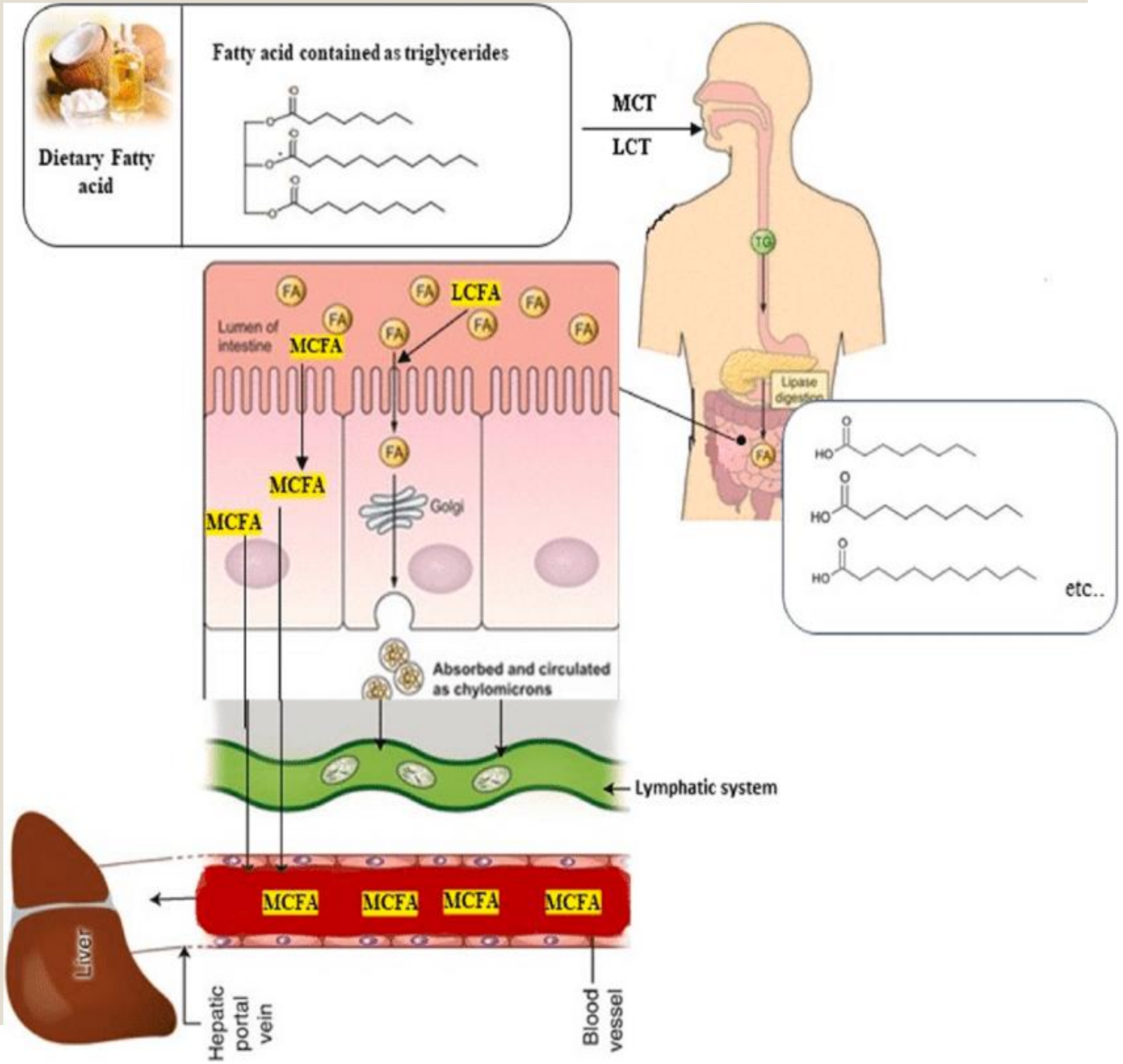
Lipid absorbance

- Glycerol, short chain and medium chain FA absorb directly from intestinal lumen to portal vein and then to liver.

- Long chain FA and free cholesterol and β acylglycerol with bile salts form mixed micelles.



DOI:10.1016/j.jff.2021.104724

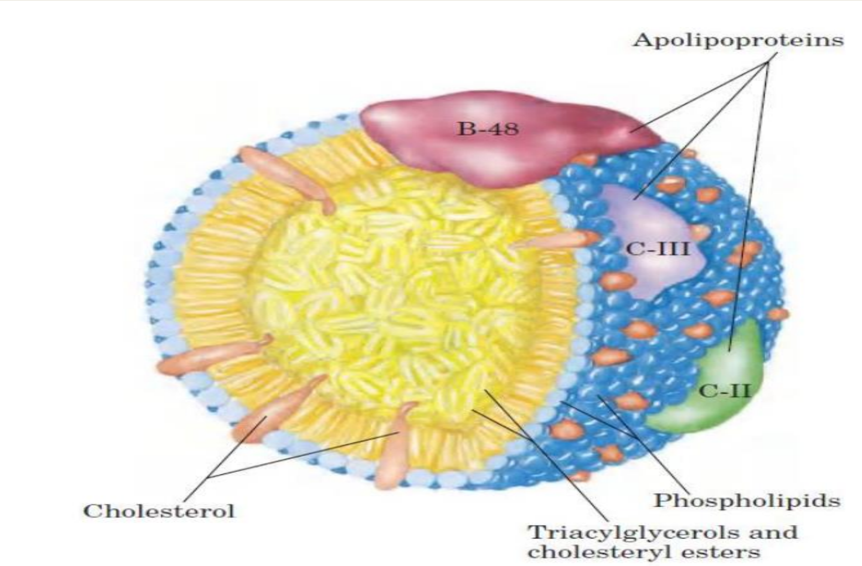
Chylomicrons

- Triacylglycerol – Cholesterol ester – Phospholipids – Apo protein B48 and apo together form a Chylomicrons .

- The chyle (milky fluid) from the intestinal mucosal cells loaded with Chylomicrons are transported through the lacteals into the thoracic duct and then emptied into lymph circulation.

- Serum may appear milky after a high fat meal due to the presence of **Chylomicrons** in circulation.

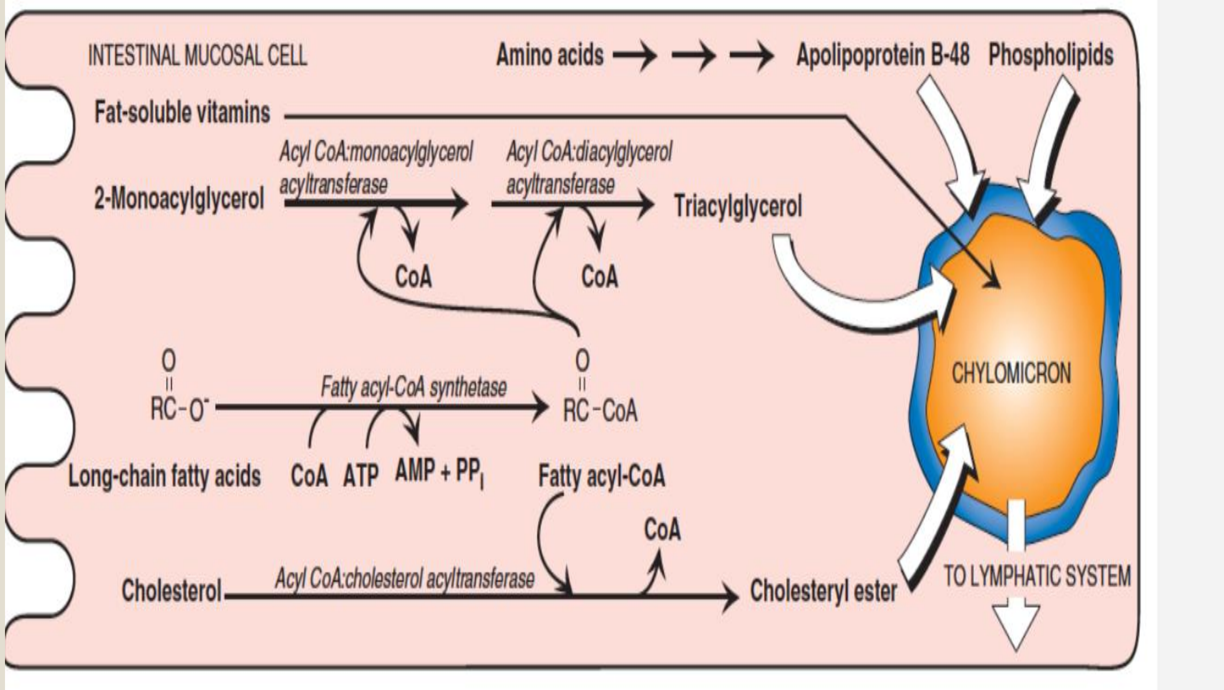
- Normally the lipemia clears within a few hours by the uptake of Chylomicrons by tissues.



Chylomicrons assembly is essential for TAG absorption and acquisition of fat-soluble vitamins

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

A. Apolipoprotein B-48 (apo B-48)
B. Phospholipids
C. Free cholesterol



-Microsomal triglyceride transfer protein (MTTP) enzyme is required for the assembly of chylomicron

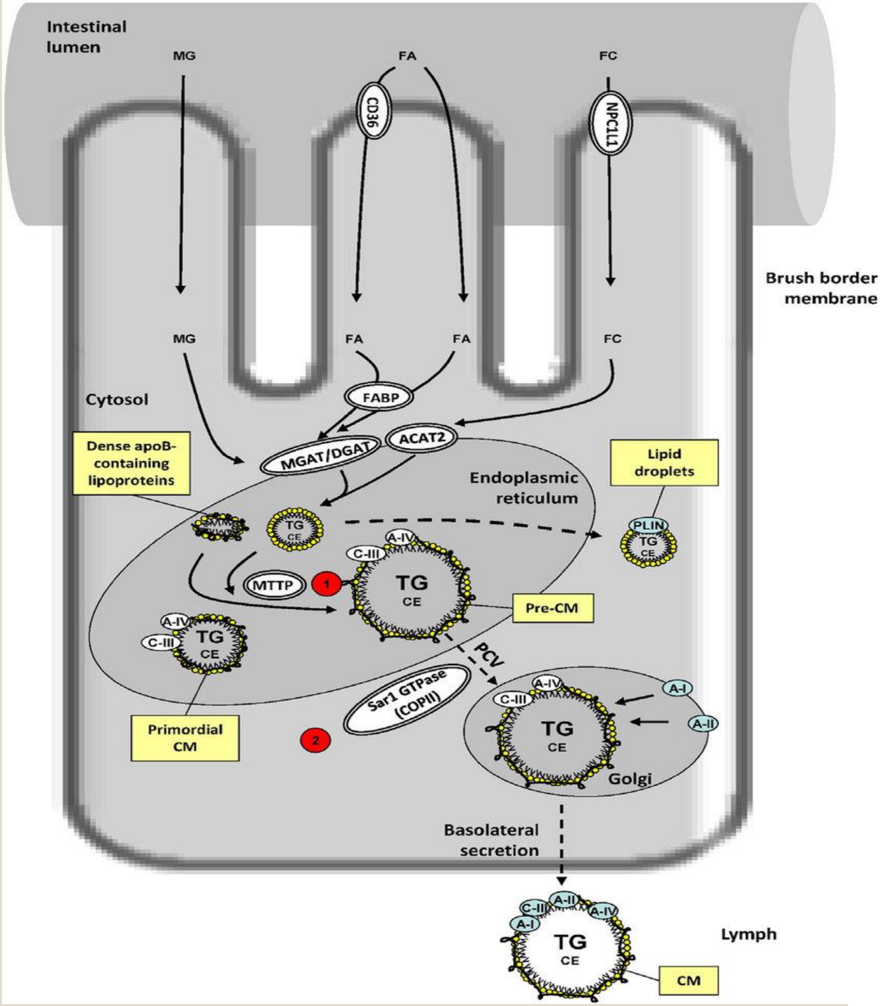
1.The long-chin length fatty acids are first converted into there activated form by fatty acyl-coenzyme A synthase.
2.Using the fatty acyl CoA derivatives the Monoacylglycerols are converted to TAGs by Monoacylglycerol acyltransferase and Diacylglycerol acyltransferase .
3. Lysophospholipids are reacylated to form phospholipids by acyltransferases.
4. Cholesterol is esterified with a fatty acid by acyltransferase to form cholesteryl ester.
5. Amino acids will give Apolipoprotein B-48

Chylomicrons assembly is essential for TAG absorption and acquisition of fat-soluble vitamins

-The re-esterified TAG in enterocytes is incorporated into CM, initially as precursor lipoproteins in the ER of the enterocyte .

-Pre-CM are transported from ER in prechylomicron <u>transport vesicles</u> (PCTV) for final lipidation in the <u>Golgi apparatus</u>.

-Mature CM are secreted across the <u>basolateral membranes</u> of the cells into the lymph.



1. Chylomicron will be secreted by Exocytosis from enterocytes.

2. Into the lymphatic vessels around villi of small intestine (lacteals)

3. Enter into systemic circulation.

4. Milky appearance of serum after lipid-rich meal.

Fate of Chylomicrons

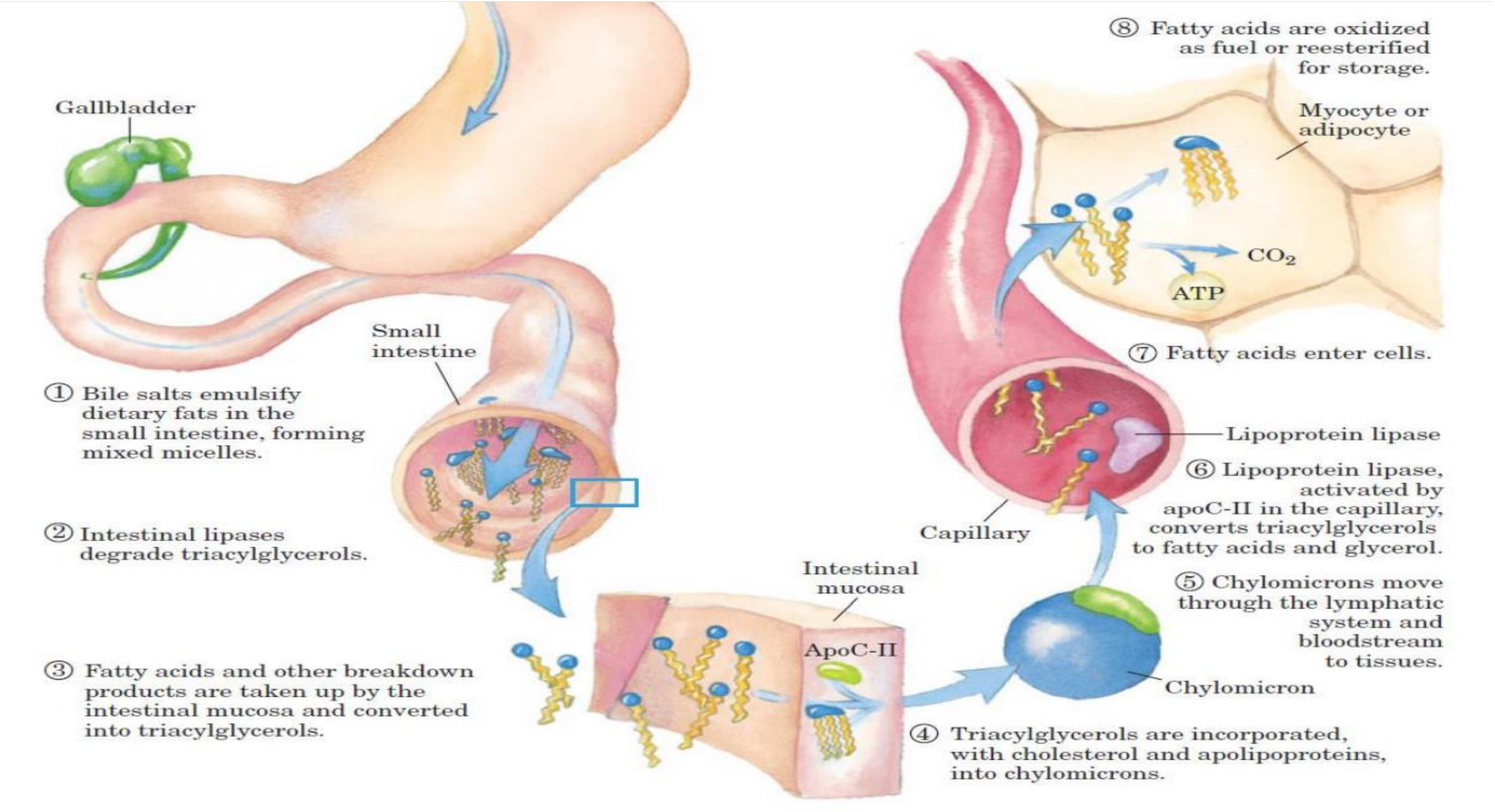
-The absorbed (exogenous) triglycerides are transported in blood as Chylomicrons.

1.They are taken up by adipose tissues and liver.

2. Liver synthesises endogenous triglycerides. These are transported as VLDL and are deposited in adipose tissue.

3. During starvation states, triglycerides in adipose tissue are hydrolysed to produce FFA .

4.In the blood, they are transported, complexed with albumin. These FFA are taken up by the cells and are then oxidized to get energy .


Gallbladder
Small intestine
① Bile salts emulsify dietary fats in the small intestine, forming mixed micelles.
② Intestinal lipases degrade triacylglycerols.
③ Fatty acids and other breakdown products are taken up by the intestinal mucosa and converted into triacylglycerols.
Intestinal mucosa
ApoC-II
④ Triacylglycerols are incorporated, with cholesterol and apolipoproteins, into chylomicrons.
Chylomicron
⑤ Chylomicrons move through the lymphatic system and bloodstream to tissues.
Capillary
Lipoprotein lipase
⑥ Lipoprotein lipase, activated by apoC-II in the capillary, converts triacylglycerols to fatty acids and glycerol.
⑦ Fatty acids enter cells.
Myocyte or adipocyte
CO_2
ATP
⑧ Fatty acids are oxidized as fuel or reesterified for storage.

Clinically significant

➢ **Lipid malabsorption:**

-Increased excretion of lipids, fat-soluble vitamins and essential FAs in the feces Due to: **defects in lipid digestion or absorption**

-Lipid malabsorption, resulting in increase lipid in the feces this condition known as **Steatorrhea (Fatty poops).**

- **Steatorrhea** can be caused by disturbances in lipid digestion and/or absorption such as: defect in the bile from the liver or gall bladder, pancreatic juices from pancreas or defective intestinal mucosal cells.

Clinically significant

-Chyluria:

- There is an abnormal connection between the urinary tract and lymphatic drainage system of the intestine. Urine appears milky due to lipid droplets.

-Chylothorax

-Can result from an abnormal connection between the pleural cavity and thoracic duct

Clinically significant

Defective absorption may be due to diseases:

1.Coeliac disease, Sprue, Crohn’s disease.

2. Surgical removal of intestine.

3. Obstruction of bile duct:

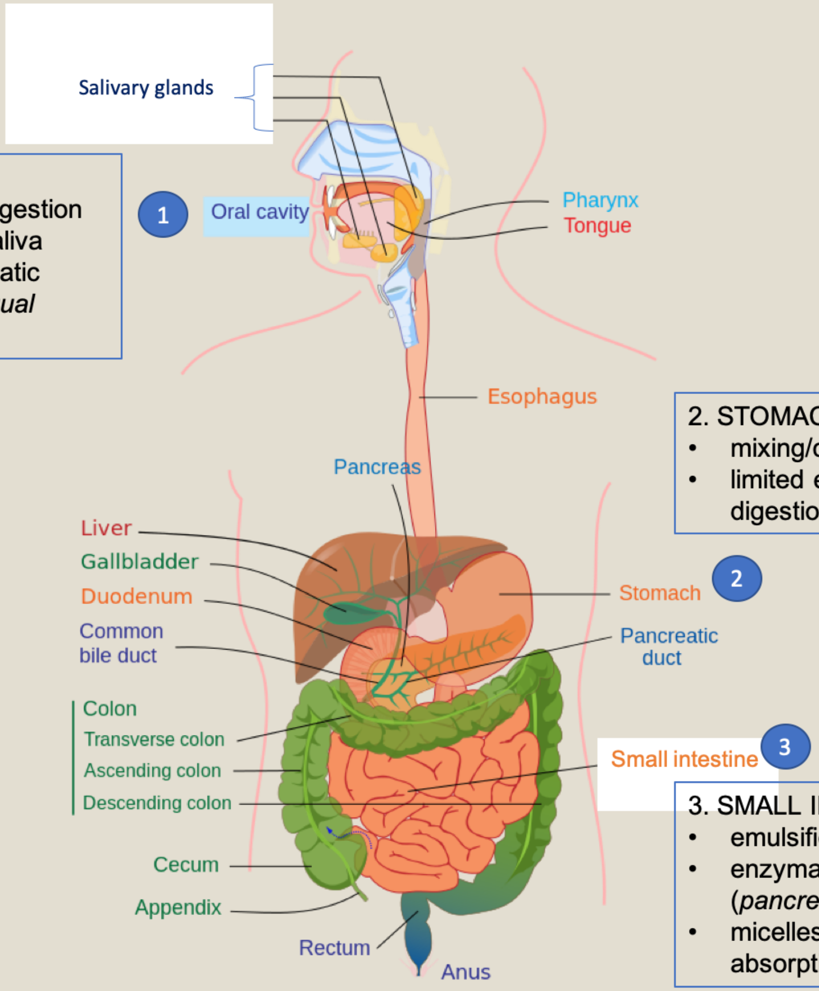
A.Gallstones

B. Tumours of head of pancreas

C. Enlarged lymph glands In such cases, triglycerides with short chain and medium chain fatty acids are digested and absorbed properly. because they do not required micellerisation for absorption.

Take home massage

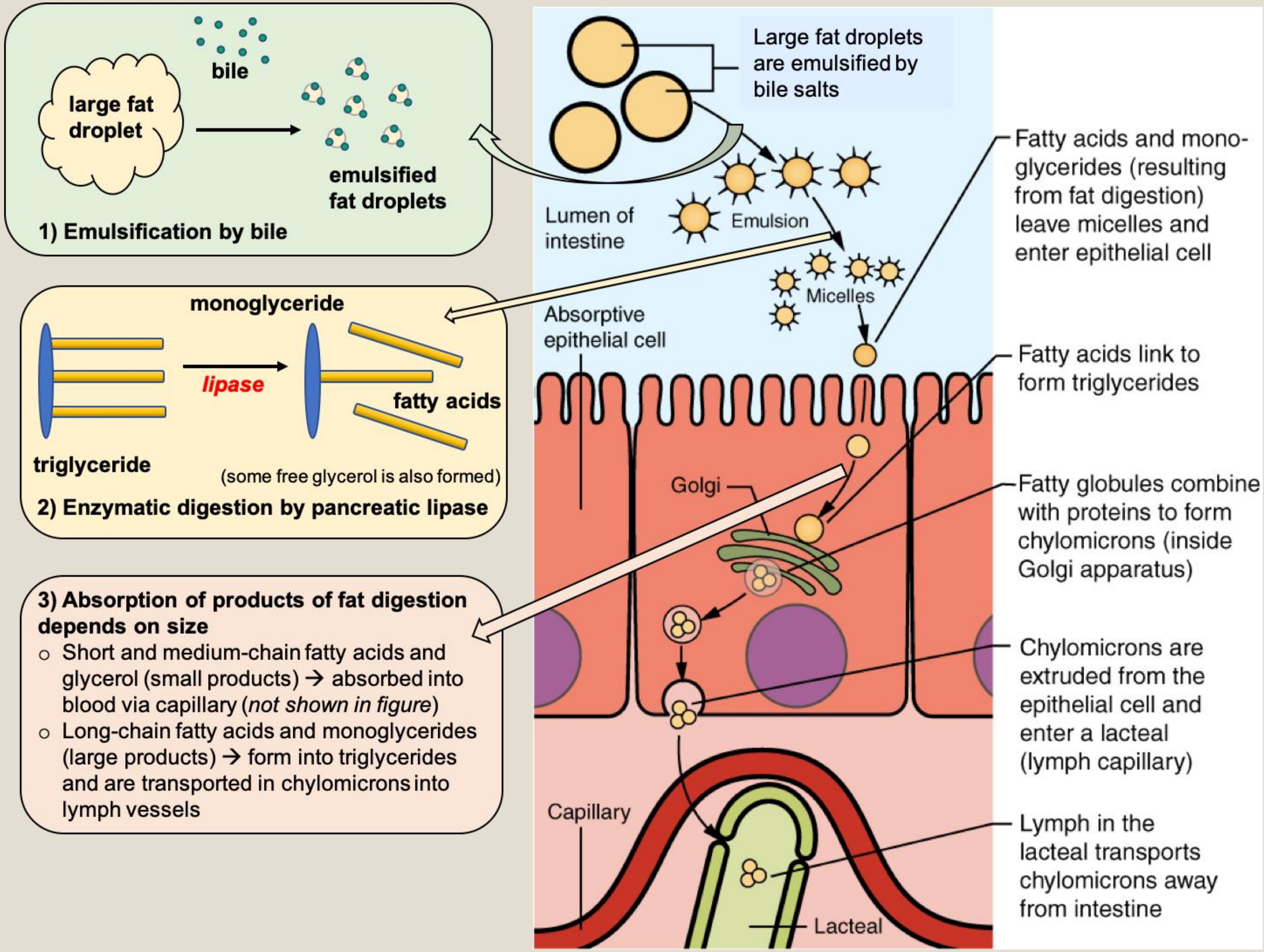
1. MOUTH
- mechanical digestion
- mixing with saliva
- limited enzymatic digestion (*lingual lipase*)



2. STOMACH
- mixing/churning
- limited enzymatic digestion (*gastric lipase*)

3. SMALL INTESTINE
- emulsification (bile)
- enzymatic digestion (*pancreatic lipases*)
- micelles help with absorption

Take home massage



3) Absorption of products of fat digestion depends on size

- Short and medium-chain fatty acids and glycerol (small products) → absorbed into blood via capillary (*not shown in figure*)
- Long-chain fatty acids and monoglycerides (large products) → form into triglycerides and are transported in chylomicrons into lymph vessels

https://openoregon.pressbooks.pub/nutritionscience/chapter/5d-digestion-absorption-lipids/

Learning objectives

- Describe Different kinds of dietary lipids
- Describe the process of lipids digestion in the human body
- Know the Hormones and/or enzymes involved in lipids digestion in different organ
- Describe the process of lipids absorbance
- The clinical significance of lipids digestion and absorbance

1.Steatorrhea is defined as:

A. Increased presence of Proteins in the feces

B. Increased presence of Lipids in the feces

C. Presence of Lipids in the urine

D. Presence of proteins and lipids in the feces

2.Where does most lipid digestion take place?

A. Stomach

B. pancreas

C. Duodenum

D. Mouth

3. What is the primary role of Bile Salts in Lipid Digestion?

A. Quicker transport of lipids to the stomach

B. Lipids Emulsification

C. Prevents digestion of lipids in the Stomach and mouth

D. Inhibits Secretin of other digestive enzyme

4.Mixed Micelles are disc shape particles with………….properties.

A. Hydrophilic

B. Hydrophobic

C. Amphipathic

D. Fat soluble

Please send the correct answer to nnasiri@med.uoa.gr by the 02.02.2024