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Sheet Slides

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DOCTOR

فيصل الخطيب

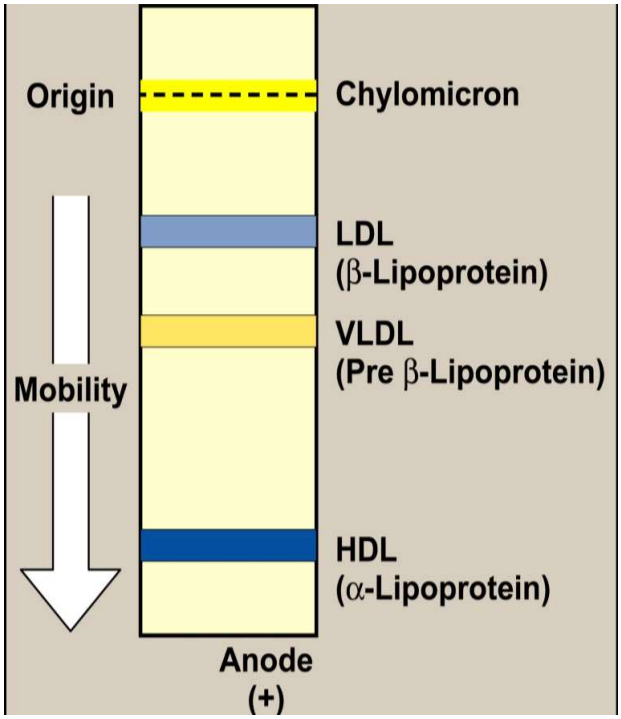
In the last lecture we briefly talked about lipoproteins, and we said that they have structural & regulatory roles, also we said that some of them are required to binding to cell surface receptors.

- **Apolipoproteins in different lipoprotein particles:**

lipoprotein	apo protein types	Lipoprotein role
Chylomicrons	Apo B, apo C, apo E.	Transport of dietary lipids from small intestines to different tissues
VLDL	Apo B, apo C, apo E	Transport of endogenous TAGs.
IDL	Apo B, apo E	
LDL	Apo B	Transport of cholesterol to different tissues
HDL	Apo A, apo C, apo E	Transport of cholesterol back to the liver for secretion

In addition to the role of each lipoprotein, from the above table you have to know that apo B is the only protein in the LDL and that it's not found in HDL, also you have to know that apo A is found only in the HDL particles.

- We know that plasma proteins can be separated **based on their charge to mass ratio** by applying them to electrical field, in this case we use a dye that reacts with proteins, but if we want to study lipoproteins **we will use a dye that reacts with lipoproteins**.
- Separation of lipoproteins by electrophoresis is common in medical labs (happens daily).
- Here, **chylomicron won't migrate** because of it has very small charge & large size.
- **The fastest is HDL** (aka a-lipoprotein because it migrates with a-proteins).
- VLDL called pre-B-lipoprotein because it is a bit faster than B-proteins.



➢ Digestion of dietary lipids:

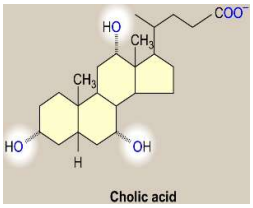
TAG + H_2O ⟶ 2FA + MAG (mono acyl glycerol).

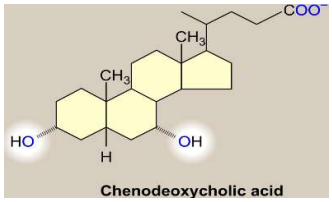
CE (cholesteryl esters) + H_2O ⟶ FA + cholesterol.

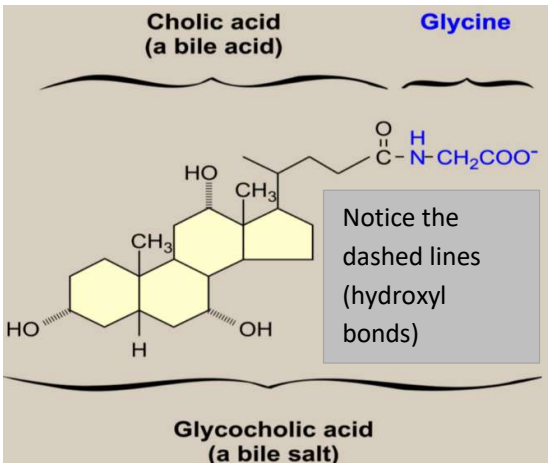
- TAG hydrolysis requires interaction with water, but we know that TAG couldn't interact with water, this question will take us to the next topic (bile acids).

➢ Bile acids:

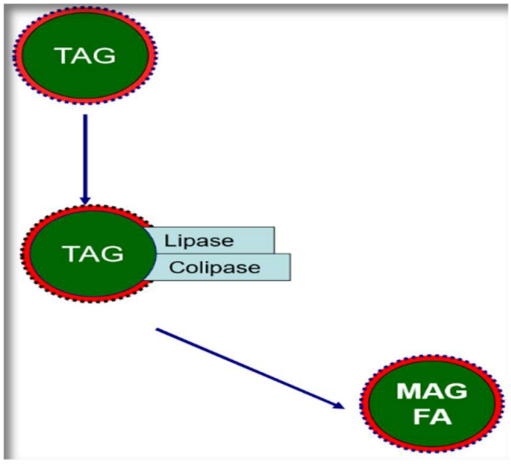
- Are steroid acids derived from cholesterol in the liver to act as **solubilizing agents**.
- Their structure is similar to the structure of cholesterol but they have **more hydroxyl groups** and their carboxyl group side chain contains **5 carbons rather than 8** in cholesterol.
- They are similar to phospholipids in their ability to form **micelles**.
- Examples include: (you only have to recognize that these structures are bile acids)
  1) **Cholic acid** (it isn't very strong acid).
  2) **Chenodeoxycholic acid**.
  3) **Glycocholic acid** (cholic acid conjugated with glycine = stronger acid = **bile salt**).
     - ✓ Bile acids & bile salts are used interchangeably.
     - ✓ Here we have very hydrophilic, ionic part that contain hydroxyl groups & non-polar part (the steroid nucleus).







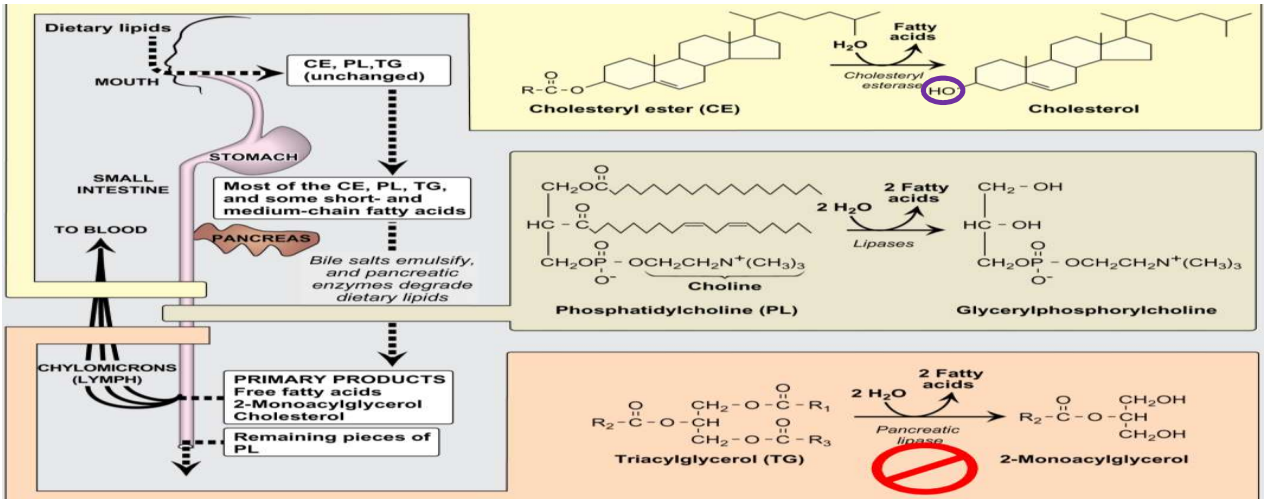
- They're excreted from the liver through the gallbladder, **they're stored in the gallbladder** until the person eats fat, then it will contract releasing the bile into small intestines.
- Bile acids & TAGs form micelles that have large surface area & small size, so this will facilitate mixing TAG with water.
- After forming TAG (core)-bile acids (surface) micelles, two enzymes (**lipase** that is secreted from pancreas & **colipase**) will degrade TAGs converting it to MAG & FA in the core of micelle.



➢ Digestion of TAG with short or medium FAs:

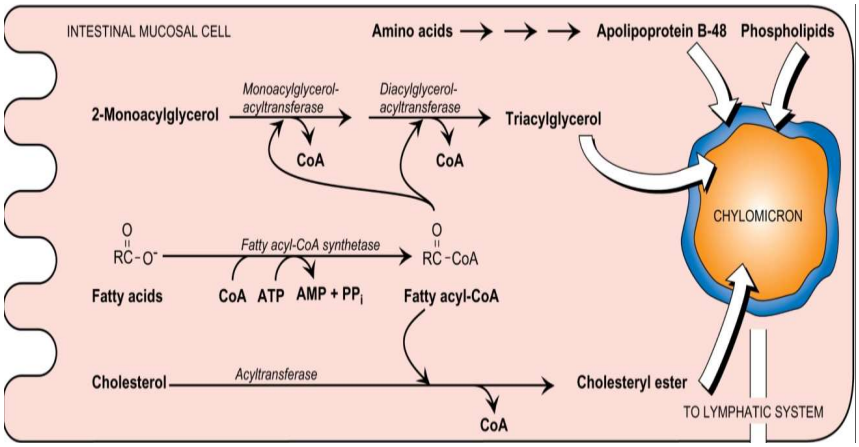
- Short & medium FAs are found in the dairy products.
- Their digestion begins in the stomach (lingual & gastric lipases), and doesn't require bile acids or pancreatic lipases (so they're significance in pancreatic insufficiency).
- They're acid stable.
- They're significance for neonatals (having short & medium FAs in milk makes the digestion of the fat in neonatals very rapid).

➢ **Digestion summary:**



- Cholesteryl esters can be hydrolyzed to cholesterol & FA.
- Phospholipids can be digested by **phospholipase** (pancreatic) (2 FAs are removed).
- TAG hydrolysis involves the cleavage of 2 FAs from C1 & C3 leaving acyl group on C2.
- The action of pancreatic lipase is the hydrolysis of 2 FAs.
- Pancreatic lipase is inhibited = no TAG hydrolysis will occur = there's no digestion = there's no absorption = the dietary fat will be excreted in feces = weight losing.
- There's a drug designed to treat obesity called **orlistat** does its work by inhibiting pancreatic lipase.
- There's no lipase secreted with saliva.
- The digestion products (FAs, MAGs, cholesterol, ……) form mixed micelles that will go through small intestines until they come to contact with intestinal mucosal cells that will absorb them simply by diffusion.

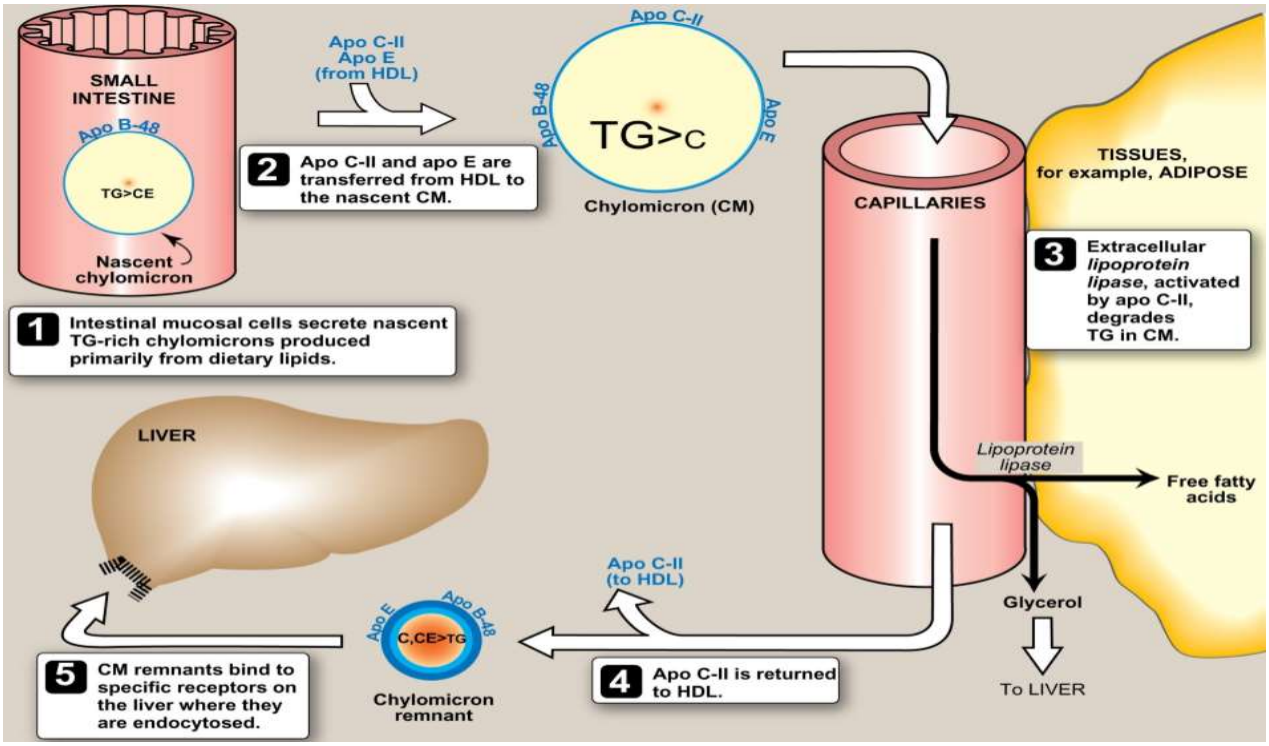
- After mixed micelles reach the small intestinal cells, TAG will be resynthesized from 2-MAG & from FAs. Also, cholesterol will be re-esterified to CE (cholesteryl esters), then TAG, CE, phospholipids, & apolipoprotein B-48 are used to produce **chylomicrons**.



- Then chylomicrons will be released into **lymph vessels** and migrate slowly until they reach **thoracic duct** that will release them into the **subclavian vein**.
- Why are chylomicrons released into lymph vessels instead of capillaries?
  To prevent the blockage of capillaries (narrow).

➢ **Transfer of TAG from chylomicrons & VLDL to different tissues:**

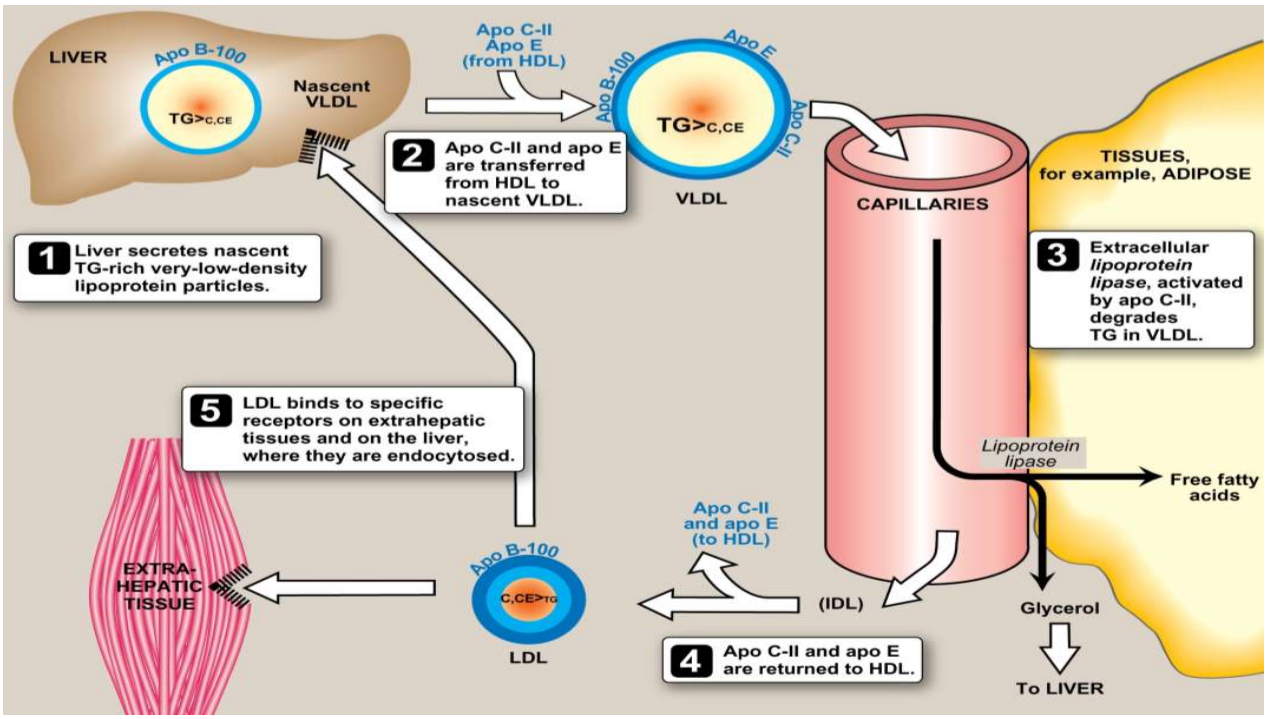
1) transfer of TAG from chylomicrons:



- **Nascent chylomicron**: newly synthesized chylomicron.
- **Lipoprotein lipase**: extracellular enzyme produced by endothelial cells & released the lumen of the capillary.
- **Apo C-2** is required to the activation of lipoprotein lipase that will convert TAG to FAs (diffuse into tissues) & glycerol (turn back to the liver).

- As a result of the hydrolysis of TAG, chylomicron will be smaller (**chylomicron remnant**).
- chylomicron remnant lacks apo C-2 that turns back to HDL.
- apo E is necessary for binding to cell surface receptors of the hepatocytes (this binding is followed by endocytosis).
- Muscles have higher affinity to get FAs than adipose tissue, why?
  Because there are different lipoprotein lipases in different tissues that differ in their affinity to chylomicrons, & muscle lipoprotein lipases have higher affinity than that in adipose tissue.

2) transfer of TAG from VLDL:



- This process is very similar to the previous one.
- **VLDL is synthesized in the liver**.
- TAG hydrolysis = lower TAG content = lower size = the remnants are mainly cholesterol &CE = the density will change as follow: VLDL ⟶ IDL ⟶ LDL.
- IDL can be taken by cells by endocytosis (50%) or continue to become LDL (50%).
- LDL contains only **apo B-100** that's important for binding to cell surface receptors of the liver & extra-hepatic tissues (in muscles).
- Notice that apo C-2 & apo E will turn back to HDL.

Good luck