Lipid metabolism

Slide 1 — Lipid metabolism

العنوان هو **Lipid metabolism** يعني **أيض الدهون**.

الصورة فيها برغر، والهدف منها تذكيرك إن الدهون اللي نأكلها في الطعام، خصوصًا من الوجبات الدسمة، تدخل الجسم غالبًا على شكل:

Triglycerides / Triacylglycerols = ثلاثي الغليسريد أو ثلاثي الأسيل غليسيرول

وهذا هو النوع الرئيسي من الدهون الغذائية.

📌 **معلومة امتحانية:**
لما الدكتور يسألك: "Most dietary lipids are in which form?"
الجواب: **Triglycerides / Triacylglycerols**.

Lipid metabolism

- Lipids are water-insoluble organic molecules that can be extracted from tissues by nonpolar solvents
- Present as membrane associated, lipoproteins or droplets of triglycerides in adipose tissues
- They are the major source of energy
- Responsible for dissolving fat-soluble vitamins which have regulatory or coenzyme functions in the body
- Prostaglandins and steroid hormones play role in body's homeostasis

Lipid digestion

- An adult ingest 60-90 g of fat /day, 90% as triglycerides and the rest as cholesterol, phospholipids and free fatty acids.
- Digestion starts in stomach by lingual lipase and gastric lipase
- Triglycerides of short and medium chain length fatty acids (<12C) are the target of these enzymes.
- The enzymes are important in neonates to digest fat in milk and for people with cystic fibrosis (no pancreatic lipase)
- Emulsification of dietary lipid occurs in duodenum in presence of bile salts and perstalsis which will increase the surface area of digestion
- Bile salts are produced in liver and stored in gallbladder

Degradation by pancreatic enzymes

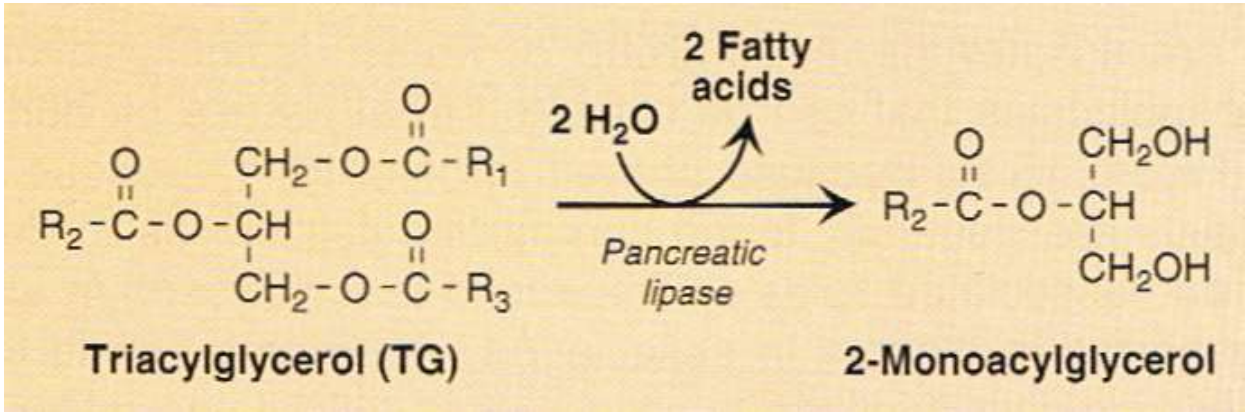
- **Triacylglycerol degradation:**
  - Degraded by pancreatic lipase to 2-monoacylglycerol and free fatty acids
  - Colipase (activated by trypsin) binds to the lipase in ratio 1:1 and anchors it to the lipid-aqueous interface

1:1 بنسبة pancreatic lipase كل جزيء colipase يرتبط بجزيء واحد من

سؤال امتحاني:
Function of colipase?
.Anchors pancreatic lipase to lipid-aqueous interface

  - Orlistat (antiobesity drug) inhibits gastric and pancreatic lipase and so decrease the absorption of fat

حواء مضاد للسمنة

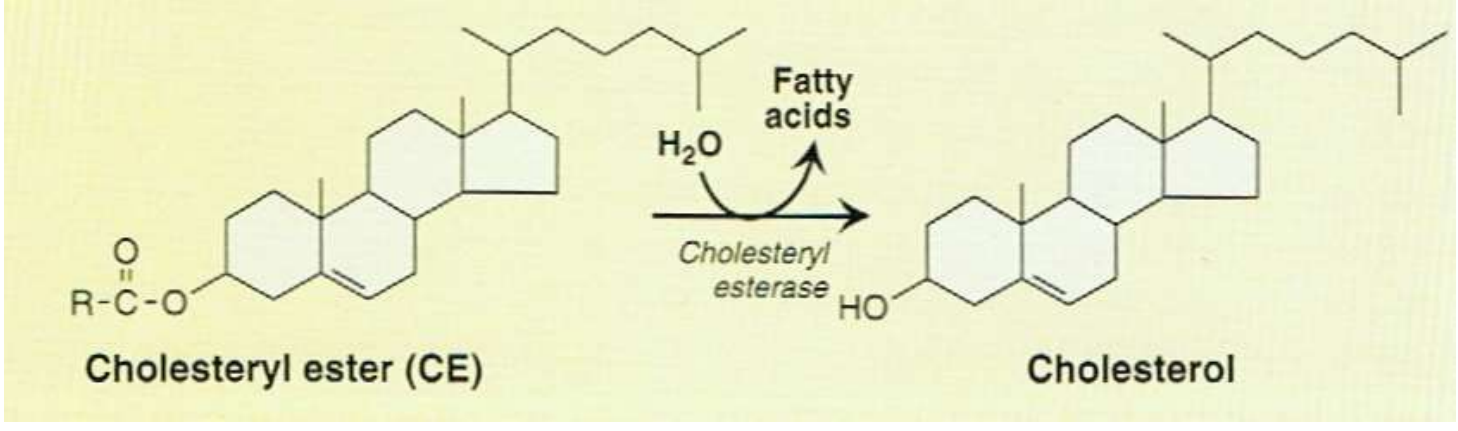


Degradation by pancreatic enzymes

- **Cholesteryl ester degradation:**
  - 10-15% of cholesterol is present in esterified form
  - It is hydrolyzed by pancreatic cholesterol esterase to cholesterol and free fatty acids
  - The activity of the enzyme is increased in the presence of bile salt

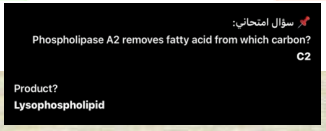
cholesterol esterase

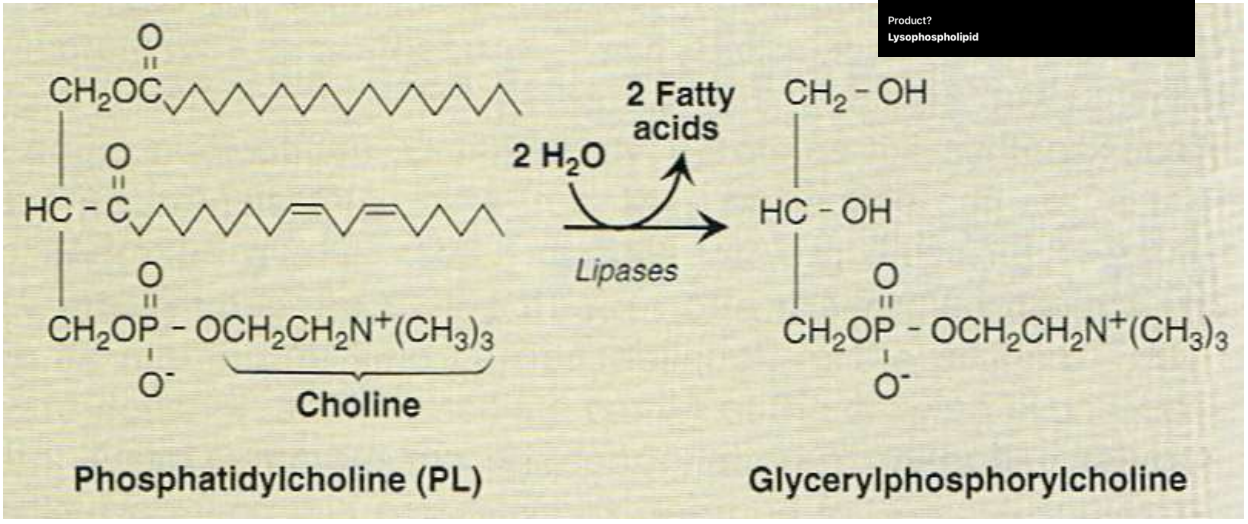
سؤال امتحاني:
Which enzyme digests cholesteryl esters?
Pancreatic cholesterol esterase
What increases its activity?
Bile salts



Degradation by pancreatic enzymes

- **Phospholipid degradation (like phosphotidylcholine):**
  - Degraded by **phospholipase A2** in presence of bile salts by removal of one fatty acid from C2 of PL to form lysophospholipid
  - Lysophospholipid is hydrolyzed by **lysophospholipase** leaving free fatty acid and glyceryl phosphoryl base that can excreted in feces, further degraded or absorbed

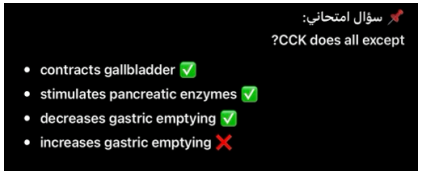




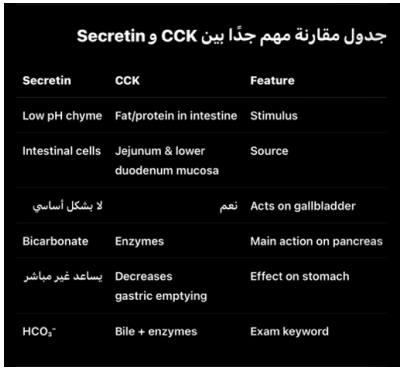
Control of lipid digestion

- It is hormonally controlled
  - cholecystokinin / CCK
  - secretin
  - Cholicystokinin (CCK) which is secreted from the mucosa of jejunum and lower duodenum and acts on:
    - Gallbladder to release bile
    - Pancreas to release pancreatic enzymes
    - Decrease gastric motility and so decrease gastric emptying

bile/gall gallbladder movement



- Secretin which is secreted by other intestinal cells in response to the lower pH of the chyme cause pancreas and liver to release bicarbonate which will neutralize the pH making it optimum for the pancreatic enzymes to work



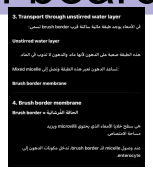
Absorption of lipids by intestinal mucosal cells

bile salts + Free Fatty acids, 2-monoacylglycerol, cholesterol, Lysophospholipids = نواتج الهضم مثل

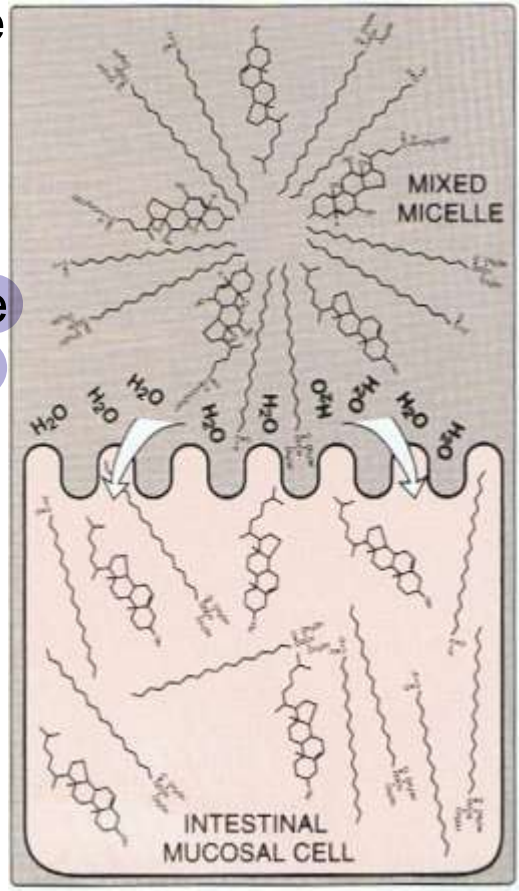
Mixed micelles

- The degradation products of lipids together with bile salts form mixed micelle (hydrophobic inside and hydrophilic outside)

- The hydrophilic surface facilitate the transport of the hydrophobic lipids through the unstirred water layer to the brush boarder membrane where they are absorbed.

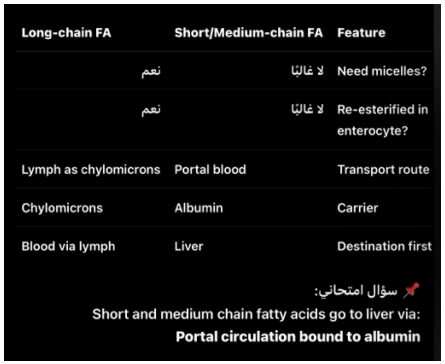


- Formation of mixed micelles is not required for the absorption of short and medium chain length fatty acids



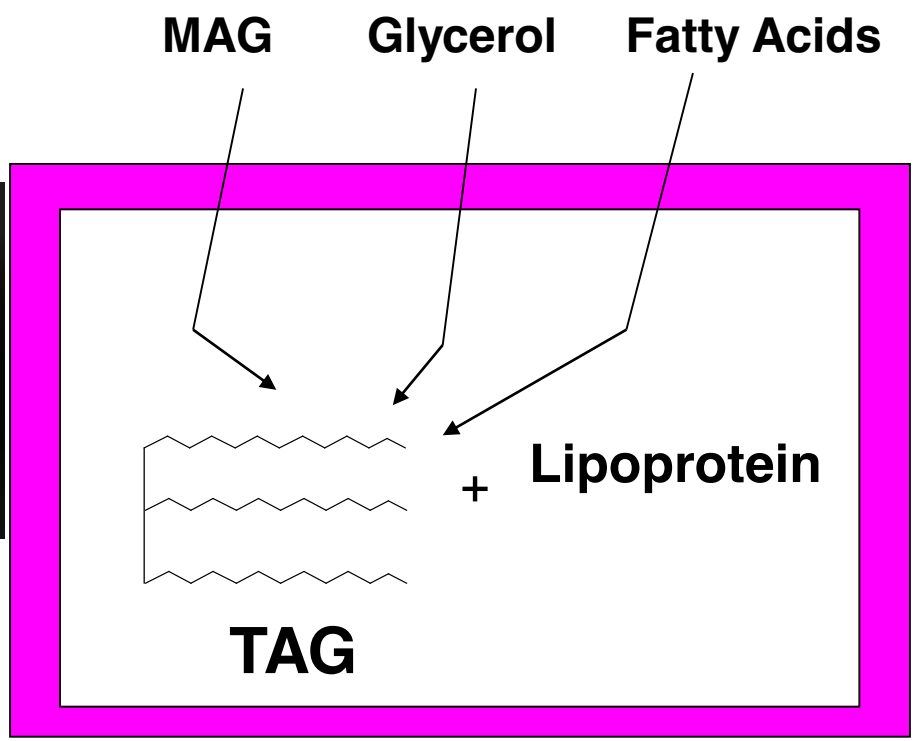
Absorption of lipids by intestinal mucosal cells

- In enterocytes triacylglycerol and cholesteryl esters are resynthesized
- Short and medium chain length fatty acids are not converted to their CoA derivatives but released into portal circulation and carried by serum albumin to the liver to be metabolized.



Long-chain FA	Short/Medium-chain FA	Feature
نعم	لا غالبًا	Need micelles?
نعم	لا غالبًا	Re-esterified in enterocyte?
Lymph as chylomicrons	Portal blood	Transport route
Chylomicrons	Albumin	Carrier
Blood via lymph	Liver	Destination first

📌 سؤال امتحاني:
Short and medium chain fatty acids go to liver via:
Portal circulation bound to albumin



4. Short and medium chain fatty acids are different

السلايد يقول:

Short and medium chain length fatty acids are not converted to their CoA derivatives

يعني لا يتم تحويلها إلى fatty acyl-CoA داخل enterocyte.

بل:

Released into portal circulation

يعني تروح مباشرة إلى:

Portal circulation = الدورة البابية

ثم تُنقل إلى الكبد بواسطة:

Serum albumin = ألبومين الدم

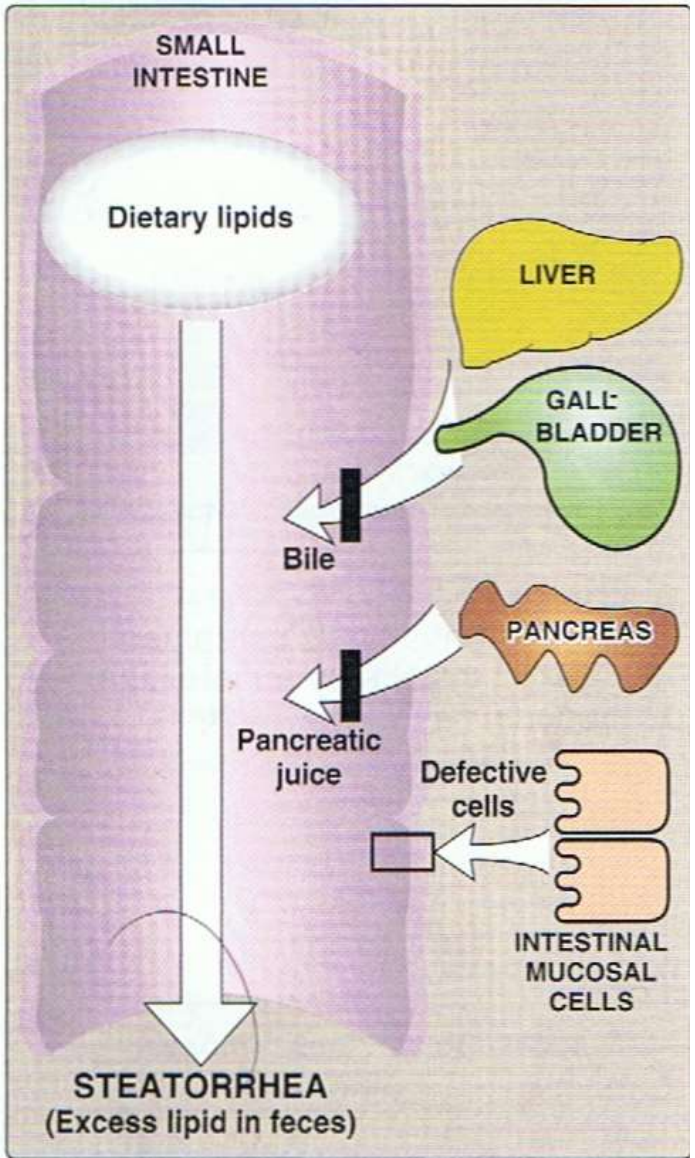
وجود دهون وأشوة في البراز

Lipid malabsorption (Steatorrhea)

أسبابها:

1. Cystic fibrosis
2. Shortened bowl

- Both causes decrease in absorption of lipids (including fat soluble vitamins and essential fatty acids) leading to increase in lipids in feces (Steatorrhea)



نقطة امتحانية شريرة

لو عندك مريض عنده steatorrhea، توقع نقص:

نقص	النتيجة
Vitamin A	مشاكل رؤية
Vitamin D	مشاكل عظام
Vitamin E	مشاكل عصبية/أكسدة
Vitamin K	نزيف بسبب نقص عوامل التخثر

Secretion of lipids from enterocytes

في الطبقة الخارجية:
- Phospholipids
- Unesterified cholesterol
- Apolipoprotein B-48

وفي الداخل:
- Triacylglycerol
- Cholesterol ester

لماذا هذا الترتيب؟
لأن chylomicron يتحرك في وسط مائي.
لازم يكون سطحه الخارجي مناسب للماء.

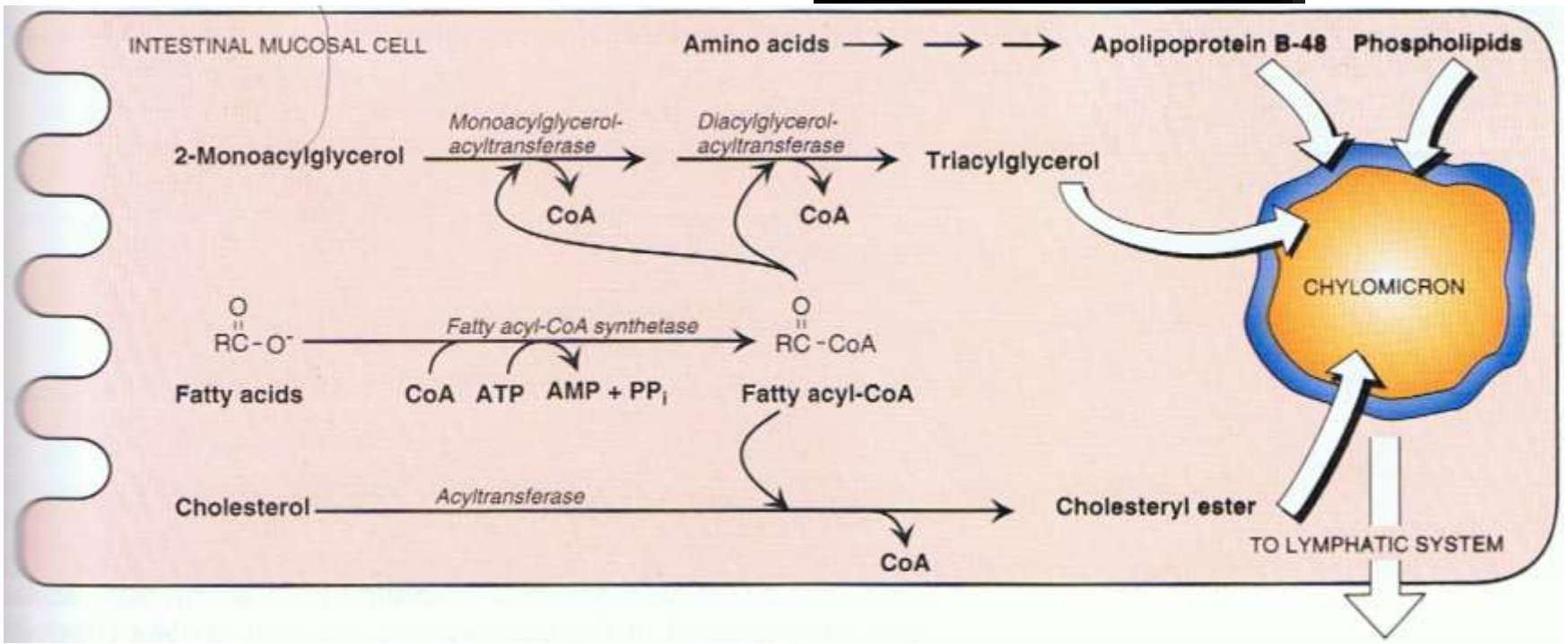
Outer layer
فيها:
- phospholipids: رأس محب للماء للخارج
- unesterified cholesterol: يساعد في الاستقرار
- Apo B-48: بروتين تركيبي مهم

Core
الداخل يحتوي الدهون الأكثر hydrophobic:
- TAG
- Cholesteryl esters

- Phospholipids, unesterified cholesterol, and (apolipoprotein B-48) are at the outer layer and triacylglycerol and cholesterol ester form chylomicrons. And this is released to the chyle (milky appearance)

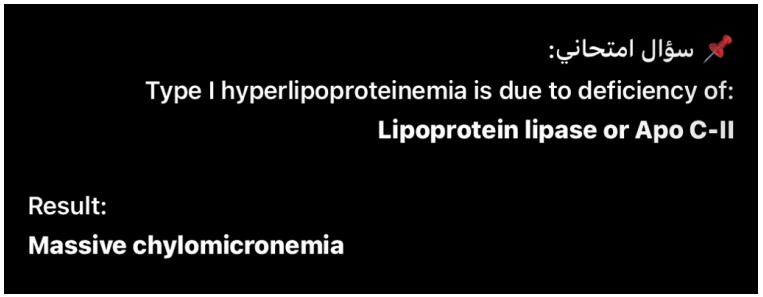
سؤال امتحاني:
Main apolipoprotein of chylomicrons synthesized in intestine:
Apo B-48

- This is released to blood



Use in tissue

- Triacylglycerol is broken down primarily in the capillaries of skeletal muscle, adipose tissues, heart, lung, kidney, and liver.
- Triacylglycerol in chylomicrons is degraded to free fatty acids and glycerol by lipoprotein lipase. This enzyme is synthesized primarily by adipocytes and muscle cells.
- Familial lipoprotein lipase deficiency (type I hyperlipoproteinemia) is a rare, autosomal recessive disorder that results from a deficiency of lipoprotein lipase or its coenzyme, apo C-II. The result is massive chylomicronemia.



Fate of free fatty acids

- The free fatty acids derived from the hydrolysis of triacylglycerol may directly enter adjacent muscle cells or adipocytes
- The free fatty acids may be transported in the blood in association with serum albumin until they are taken up by cells.
- Most cells can oxidize fatty acids to produce energy
- Adipocytes can also reesterify free fatty acids to produce triacylglycerol molecules, which are stored until the fatty acids are needed by the body.

Fate of glycerol

- Glycerol that is released from triacylglycerol used almost exclusively by the liver to produce glycerol 3-phosphate, which can enter either glycolysis or gluconeogenesis by oxidation to dihydroxyacetone phosphate