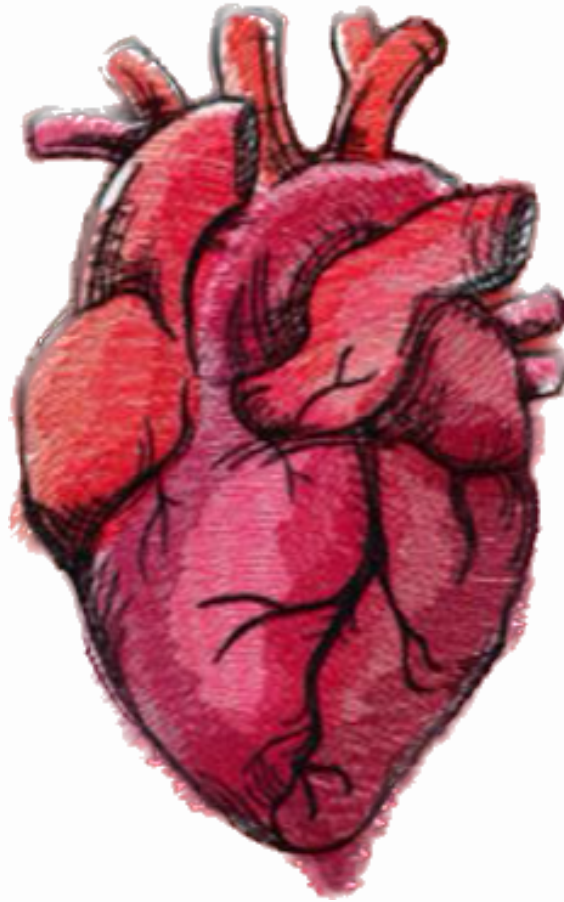




CARDIOVASCULAR SYSTEM



SUBJECT : Biochemistry

LEC NO. : 1 / plasma lipoprotein

DONE BY : Anas zakarneh

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بهاي المحاضرة راح نحكي عن اهم الlipid بجسمنا الموجوده بنسب معينة و مختلفة إذا صار فيها اختلال معين ممكن يسببلي أمراض خطيرة بالقلب و الأوعية الدموية

Plasma lipids

- In the fasting state (usually measured after 12 hours) :
 - The plasma total lipids ranges between 400-700 mg/dl
 - The plasma total cholesterol : 140-200 mg/dl
 - The plasma total phospholipids : 150-200 mg/dl
 - The plasma total triacylglycerols: 50-150 mg/dl
 - The plasma total free fatty acids (FFA): 10-20 mg/dl
 - Minute amounts of steroid hormones , fat-soluble vitamins, and carotenoids.

هسا احنا بس نيجي نعمل lipid profile measurement مهم جدا انو نكون في حالة صيام كامل ما لا يقل عن ١٢ ساعة تقريبا طب ليش؟

حتى نزيل تأثير الدهون اللي بحتويها الأكل يلي بناكله و بالتالي ما بتأثر على نتيجة التحليل

plasma lipids (cholesterol
(C) ,phospholipids (PL),triacylglycerol
(TAG) ,Free FA)

مهم نحفظ نسب السلايدات

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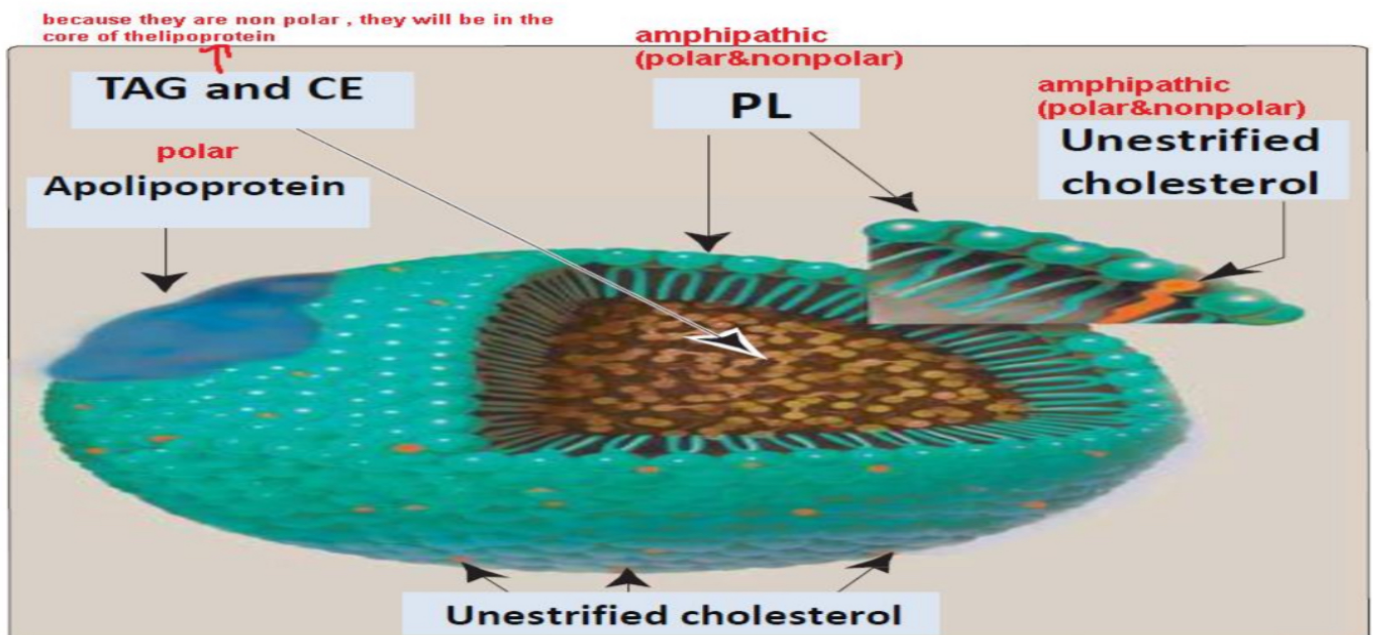
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- These lipids are found in plasma in the form of lipoprotein complex=plasma lipoproteins.
- The problem of transporting the hydrophobic lipids in an aqueous phase, the blood plasma, is solved by associating the insoluble (non polar) TAG and CE with the more soluble (amphipathic) PL,C, and proteins to form a **hydrophilic lipoprotein complex**.
- Each plasma lipoprotein particle contains:
 - 1- A non polar core composed of TAG and CE **Esterification causes nonpolarity**
 - 2- A single layer of polar lipids (PL and C) together with proteins called **apolipoproteins**

❖ **Amphipathic:** Like pl / cholesterol (oh group is polar) chemical compound possessing both hydrophilic (water-loving, polar) and lipophilic (fat-loving) properties.

هنا احنا بنعرف انو بتتواجد ال lipid بالبلازما بس بتكون على شكل lipoprotein (كره من الدهون محاطة ب proteins) هسا لأنها non-polar معناته ما بتقدر تمشي بالبلازما فبتحتاج إلى ناقل الها

Amphipathic molecule : يعني الو جزئين واحد يكون :
 Polar — (head of pl) يكون للخارج
 Non polar — (tail of pl) يكون متجه للداخل
 Apolipoprotein: the protein that covers the lipids
 Aqueous phase = blood plasma





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Lipoprotein have a non polar core contain (CE &TAGs) &polar lipid on the surface contain (PL &C) .

- **Apolipoproteins** are either peripheral (can be transferred) or integral (can not be transferred).
- They act as **activator for enzymes** (e.g. apo C II activator for lipoprotein lipase) and are **important for receptor mediated uptake** of plasma lipoproteins by certain tissues (e.g. receptors for apo E in liver cells for uptake of chylomicrons).

هسا يا سيدي العزيز عنا نوعين من الapolipoproteins طبعا الاثنين موجودين على الsurface الأول بقدر ينفصل و ينتقل لlipoproteins ثاني و هاض هو الperipheral اما النوع الثاني ما بقدر ينتقل لأنه integrated in the surface و هاض هو الintegral

_ function of apolipoprotein :

الوظيفة الأساسية لها هي نقل الدهون في البلازما بس في عنا كمان وظائف

% activator for lipoprotein lipase enzyme (mainly apo C II) .

ها الإنزيم مهم جداً في ال metabolism لأي نوع من الدهون ومن اسمه واضح أنه يكسر الدهون .

^important in the receptor mediated uptake , (apo E receptor on hepatocyte for uptake of chylomicrons) .

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Plasma lipoproteins: Tested by lipid profile test

Four major groups (fractions) of lipoproteins have been identified that are important physiologically and in clinical diagnosis. These are:

- 1- Chylomicrons (CM):** They are derived from intestinal absorption of triacylglycerols and other lipids.
- 2- Very low density lipoproteins (VLDL, or pre- β -lipoproteins):** They are derived from the liver for the export of triacylglycerols.
- 3- Low density lipoproteins (LDL or β -lipoprotein):** They are representing a final stage for catabolism of VLDL. High concentration of LDL cause coronary artery disease
- 4- High-density lipoproteins (HDL or α -lipoprotein):** They are involved in chylomicrons and VLDL metabolism as well as **cholesterol transport**.
- 5- Albumin + FFA (NEFA):** FFA was carried by albumin.

plasma lipoproteins fractions :

#CM :

منشأها من الدهون الممتصة من الغذاء يلي بناكله يوميا ولأنه الامتصاص بالأعضاء فبنحكي أنها derived from intestinal absorption , محتوها من البروتينات قليل تقريبا 2% وال 98% الباقيات هم دهون وبشكل رئيسي TAGs بس كمان الدهون الثانية موجودة .

VLDL:

واسمها الثاني pre beta lipoprotein رح نعرف ليش المحاضرة الجاي ان شاء الله منشأها الكبد وتساعد في نقل ال TAGs بالتالي لو صار عنا مشكلة وما تكونت ال VLDL ما رح يقدر الكبد يتخلص من ال TAGs ورح تتراكم فيه ويصير Fatty liver

#LDL or beta lipoprotein:

هاي اخر مرحلة (النهائية) من catabolism لل VLDL

#HDL or alpha - lipoprotein:

مهمة في عملية ال metabolism لل VLDL and CM

و مهمة في cholesterol transport

#Albumin + FFA(non estrified acid):

هسا عنا ال FFA بتكون non polar فلازم تتحمل على بروتين اللي هو ال albumin

يعني تقريبا 1٪ دهون

99٪ بروتين

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- Plasma lipoproteins are separated into different fractions by two methods:

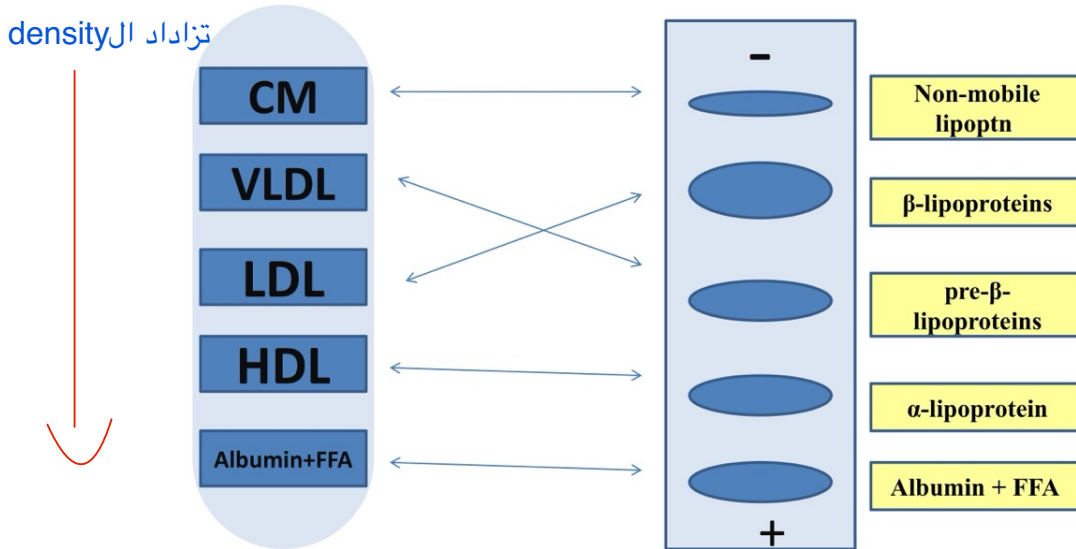
1- **Electrophoresis** (According to their mobility in electric field).

2- **Ultracentrifugation** : They are separated according to their **density**. The higher the protein content the higher the density of the particles. density = protein content

plasma lipoprotein separation methods:

^ electrophoresis : plasma lipoprotein will be separated based on their charge , size & shape .

^Ultracentrifugation : plasma lipoprotein will be separated based on their protein content (density)



هسا عنا هون باليسار في عنا ال tube اللي طلع من جهاز الطرد المركزي و موضح فيه ال lipoprotein حسب ال density ع اليمين عنا نتيجة جهاز الفصل الكهربائي القطب السالب فوق و الموجب تحت

لا تنسو انو شحنة البروتينات سالبة

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ركز معي هسا يا سيدي العزيز بدي اشركك الصفحتين الجايات 🙏

Chylomicron metabolism (cm)

هسا الcm مصدرها (intestinal mucosal cells) لأنها يتم امتصاصها من الغذاء اللي بناكله

و هي بتتكون تقريبا من 98% دهون و بشكل رئيسي الTAGs بس برضو بتحتوي على pl/ c/ CE

Pl: phospholipid // c: cholesterol // CE: cholesterol ester

و بتحتوي على 2% بروتينات

هسا في عنا شكلين للcm اللي همي nascent cm and mature cm

Nascent cm: in the beginning or early stage

يعني لساته موصاير عليها modification

Nascent cm : TAGs (mainly) +pl +c+CE+ApoA+Apo8-48

لا تخاف اللي فوق مش كود 🙏gta

هسا يا دمة هاي الnascent cm بتروح على systemic circulation عن طريق intestinal lymphatics و هي

بالطريق يا سيدي راح تشوف الHDL اللي حكينا عنها فوق بتلطف منه نوعين من apolipoprotein اللي همي Apo E and

Apo c

و هيك بصير عنا mature cm

Mature cm = nascent cm + Apo E + Apo C

طيب بتعرف يا حلو انو البروتينات اللي عملتلي maturation هي نفسها اللي راح تعمل degradation

شلون؟

بروح Apo c تحديدًا || Apo c بعمل activation لأنزيم اسمه lipoprotein lipase من اسمه راح يكسر الدهون و تحديدا

Hydrolysis of TAGs

فبكون الناتج أكيد glycerol + free fa

طيب وين يروحو هدول fa and glycerol

هسا الFA يا بتروح تتخزن بالadipose tissue او بنستهلكها حتى حتى ننتج طاقة في skeleta

Muscle

Most of the fatty acid (90%) are taken up by extrahepatic tissue , only 10 % remain in the

circulation bound to albumin & taken up by liver .

اما الglycerol حتى نستفيد منه لازم يتحول إلى phosphate glycerol يعني نضيفله فوسفات و احنا يا حلويين أخذنا انو

أضافه فوسفات محتاج kinase enzyme فمنطق يكون عنا إنزيم اسمه glycerol kinase موجود بالكبد بشكل رئيسي

فبتستفيد منه الكبد ب lipid synthesis / glycolysis / gluconeogenesis

هيك احنا بنكون تخلصنا من الTAG بنسبة كبيره اللي بضل عنا من الcm بنسميه cm remnant يعني بقايا

بكون حجمها اصغر و بتحتوي نسبه قليله من الTAG و نسبة اكبر من باقي الدهون طب من وين اجت النسبة الأكبر؟ في عنا بروتين

اسمه Cholesterol ester transport protein بعمل صفقة مبادلة بين الcm و الHDL بزوالHDL بالTAG و الcm

بالCE تمام لهون؟ خاوه تمام

هلا غير هيك محتوى البروتينات راح يتغير و السبب انو لما عملنا degradation للTAG بتفقد الcm الApo A و الApo c

للHDL اللي بالبالزما

maturation : Apo c & Apo E from HDL to CM

Degradation : Apo A & Apo C from CM to HDL

آخر اشي بصير بالبقايا

Apo E receptor mediated endocytosis by hepatocytes

و يصير لهم hydrolysis بالlysosome .

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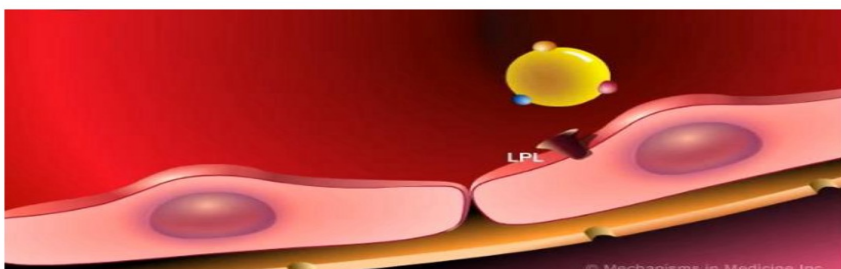
و الرب يبارك بالجميع



Chylomicron metabolism

- **Origin:** Chylomicrons are assembled in intestinal mucosal cells.
- **Structure & Function:** They are chiefly composed of the absorbed TAG to which are added smaller amounts of CE, C, PL, and proteins. Their function is to transport TAGs to various tissues and cholesterol to the liver.
- **Nascent chylomicron** principally contain 2 types of proteins, **apo A** and **apo B-48**.
- The nascent chylomicron transported to the plasma via lymphatics where it is rapidly modified (converted to mature chylomicron) by receiving **apo E** and **apo C** from **HDL**.
- **Degradation:**
 - Apo E present in CM is recognized by hepatic apo E receptor while apo C contains **apo C-II which is activator for lipoprotein lipase (LPL)**. This enzyme present extracellular anchored by heparan sulfate to the capillary walls of most tissue, but predominates in adipose tissues, cardiac and skeletal muscles.
 - Activated lipoprotein lipase can hydrolyze **triacylglycerol** present in CM to **glycerol & FFA**.
 - Fatty acids are stored by adipose tissues or used for energy by the muscle.

(most of the FFA ,about 90%, are taken up by the extrahepatic tissue where hydrolysis occur. The rest ,about 10%, remains in the circulation bound to albumin & is taken by the liver)





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- Glycerol is used by liver cells mainly, **due to high activity of glycerol kinase**, for example in lipid synthesis, glycolysis or gluconeogenesis.

(All glycerol resulting from hydrolysis of TAG remains in the circulation & is mostly taken up by the liver. It is not taken by other tissues due to the absence of glycerol kinase enzyme required for its utilization)

Fate of remnants:

- After triacylglycerol hydrolysis, the remaining part of CM is called **CM remnant** as it decreases in size (they have less percent of TAG and higher percent of C, CE, PL). Hydrolysis of TAG is associated with loss of apo A & apo C to plasma HDL, leaving a CM remnant.
- **Cholesterol ester transfer protein (CETP)** helps transfer of cholesteryl esters from HDL to chylomicron remnants in exchange with TAG. Thus, chylomicron remnants become **very rich in CE and poor in TAG**.
- The CM remnants are taken up by endocytosis by liver cells where their components are hydrolyzed by lysosomes
- The **uptake** is mediated by **specific remnant (Apo E) receptors** & is independent on the amount of C in the liver.

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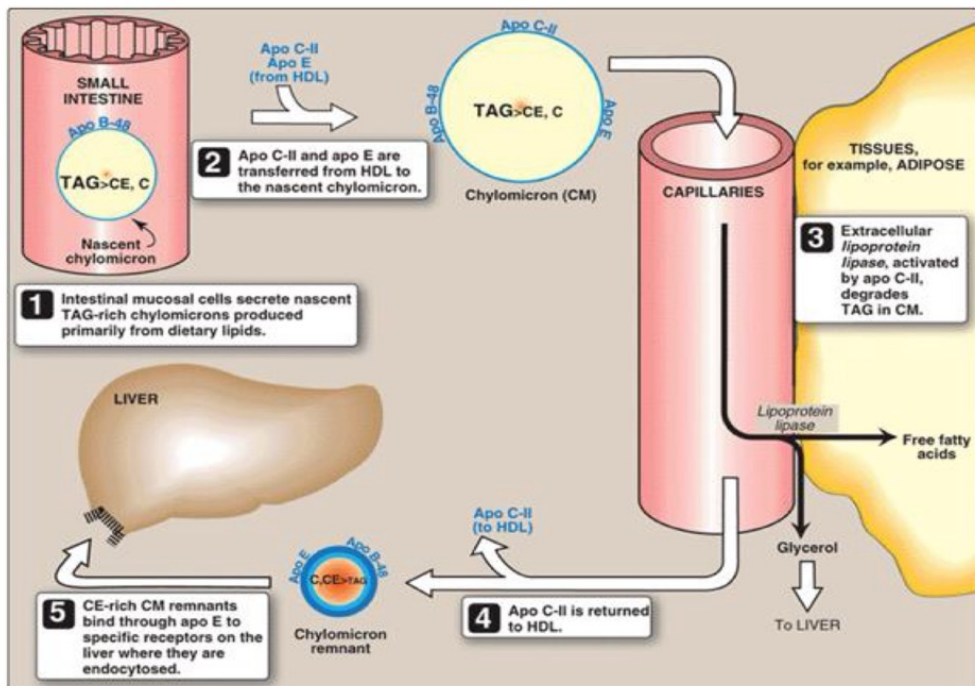
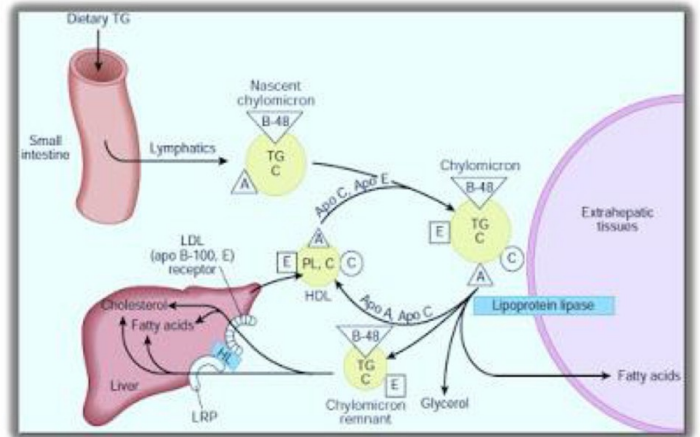
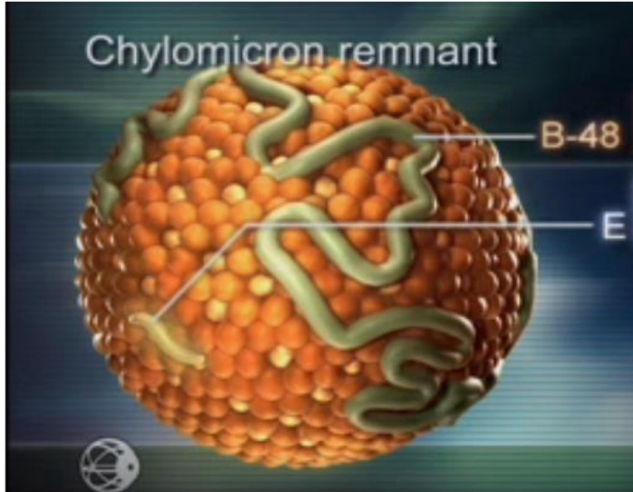


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Summary



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Quiz time

Q-1) A patient with a history of pancreatic dysfunction presents with elevated levels of chylomicron remnants in the plasma. Which cellular process is primarily responsible for the clearance of these remnants from the circulation?

- a) Receptor-mediated endocytosis by liver cells
- b) Hydrolysis by lipoprotein lipase (LPL)
- c) Transfer of cholesteryl esters by cholesterol ester transfer protein (CETP)
- d) Conversion into low density lipoproteins (LDL)

Q-2) What is the primary function of high-density lipoproteins (HDL) in plasma lipid metabolism?

- a) Transporting triacylglycerols to various tissues
- b) Facilitating the export of cholesterol from peripheral tissues to the liver
- c) Acting as precursors for the synthesis of chylomicrons
- d) Mediating the uptake of low density lipoproteins (LDL) by liver cells

Q-3) Which lipoprotein fraction is primarily responsible for the export of triacylglycerols synthesized in the liver?

- a) Chylomicrons (CM)
- b) Very low density lipoproteins (VLDL)
- c) Low density lipoproteins (LDL)
- d) High-density lipoproteins (HDL)

Answers

1) A

2) b

3) b

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