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Biochemistry

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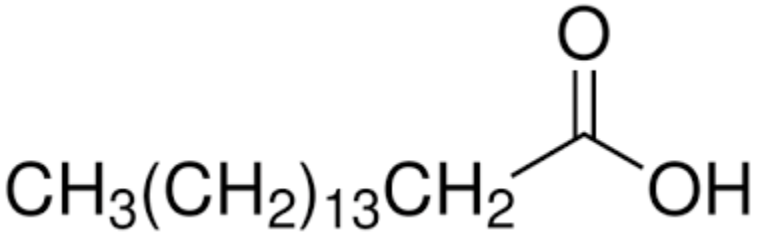
De Novo Synthesis of Fatty Acids

The process of fatty acid synthesis was studied by Feodor Lynen, who got Nobel prize in 1964. The pathway is referred to as Lynen's spiral. Important differences in synthesis and breakdown of fatty acids are given in Fatty acids are synthesized mainly by a de novo synthetic pathway operating in the cytoplasm. So, it is referred to as extramitochondrial or **cytoplasmic fatty acid synthase system**. The major fatty acid synthesized de novo is **palmitic acid,** the 16 C saturated fatty acid. The process occurs in liver, adipose tissue, kidney, brain, and mammary glands. Summary of de novo Synthesis The net reaction of de novo synthesis of fatty acid may be summarized as:



palmitic acid

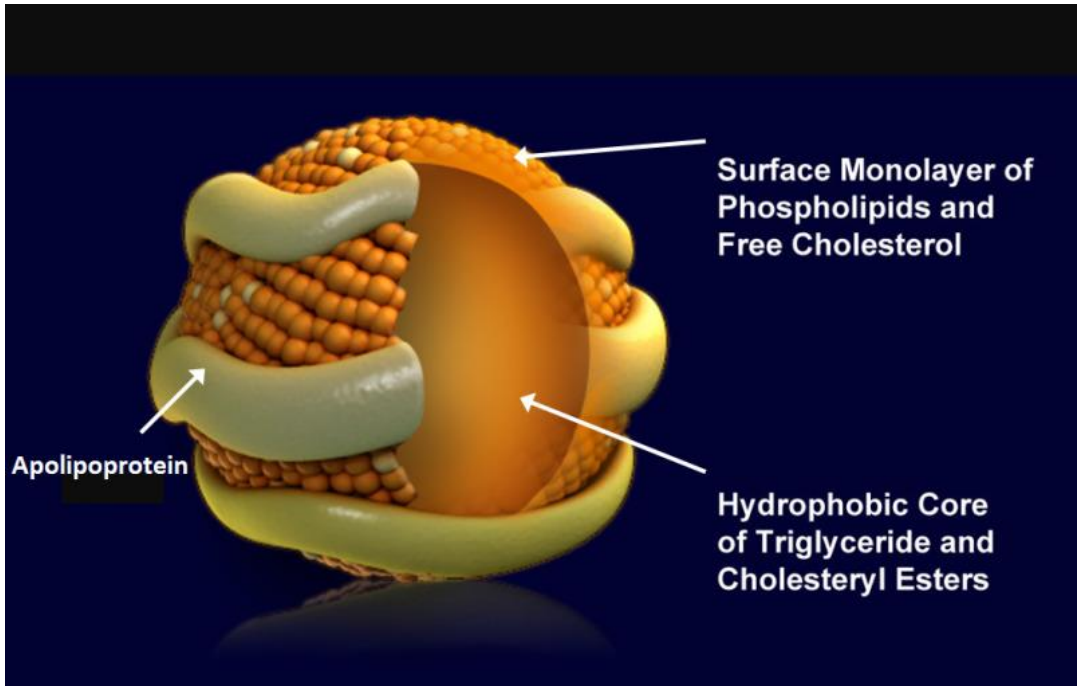
1Acetyl CoA +7Malonyl CoA +14NADPH +14H

→ 1Palmitate + 7CO 2 +14NADP + 8CoA+ 6H_2O

Fatty acid synthesis is not an exact reversal of beta-oxidation

Lipoproteins

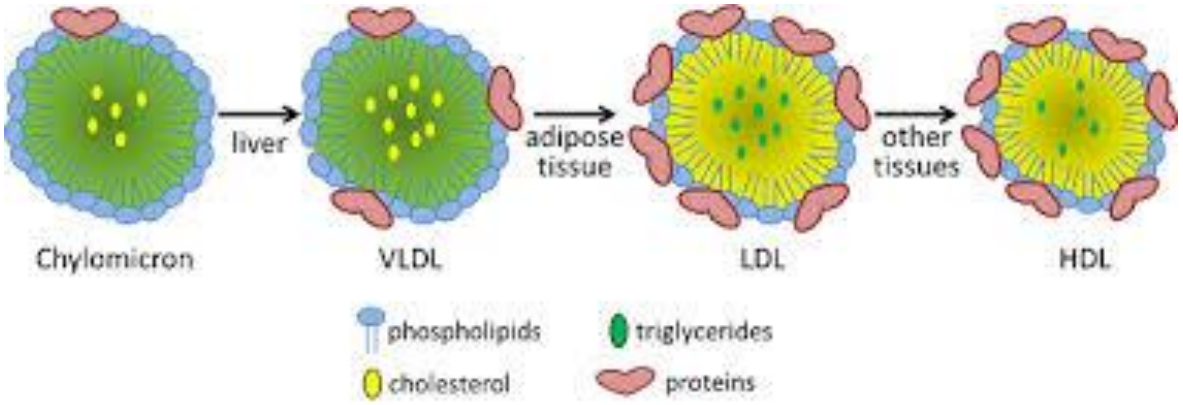
Lipoproteins are complex particles that have a central hydrophobic core of non-polar lipids, primarily cholesterol esters and triglycerides. This hydrophobic core is surrounded by a hydrophilic membrane consisting of phospholipids, free cholesterol, and apolipoproteins .Plasma lipoproteins are divided into seven classes based on **size**, **lipid composition**, and **apolipoproteins**



Classes of lipoprotiens

Plasma lipoproteins can be divided into seven classes based on size, lipid composition, and apolipoproteins

- chylomicrons,
- chylomicron remnants,
- Very Low-Density Lipoproteins (VLDL)
- VLDL remnants
- Intermediate-Density Lipoproteins (IDL)
- Low-Density Lipoproteins LDL
- High-Density Lipoproteins (HDL)
- Lipoprotein (a) (Lp (a))



1. chylomicrons

chylomicrons are the largest and least dense of all lipoproteins . they arise in the intestine and transport of **dietary triglycerides** and cholesterol to peripheral tissues and liver. The size of chylomicrons varies depending on the amount of fat ingested. A high fat meal leads to the formation of large chylomicron particles due to the increased amount of triglyceride being transported whereas in the fasting state the chylomicron particles are small carrying decreased quantities of triglyceride. The quantity of cholesterol carried by chylomicrons also can vary depending upon dietary intake

2. Chylomicron Remnants

The removal of triglyceride from chylomicrons by lipoprotein lipase in **peripheral tissues** results in smaller particles called chylomicron remnants. Compared to chylomicrons these particles are enriched in cholesterol and are **pro-atherogenic.**

3. Very low density lipoprotein (VLDL) These particles are produced by the liver and are **triglyceride rich** .When triglyceride production in the liver is increased, the secreted VLDL particles are large. However, VLDL particles are smaller than chylomicrons

4,5. intermediate density lipoprotein (IDL ,VLDL Remnants)

The removal of triglycerides from VLDL by muscle and adipose tissue results in the formation of IDL particles which are enriched in **cholesterol**. These IDL particles are **pro-atherogenic** .

6. Low density lipoprotin (LDL)

These particles are derived from VLDL and IDL particles and they are even further enriched in cholesterol. LDL carries the majority of the **cholesterol** that is in the circulation

7. High density liopoprotien (HDL)

These particles play an important role in reverse cholesterol transport from peripheral tissues to the liver, which is one potential mechanism by which HDL may be **anti-atherogenic.** In addition, HDL particles have **anti-oxidant**, **anti-inflammatory, anti-thrombotic**, and **anti-apoptotic** properties, which may also contribute to their ability to inhibit atherosclerosis. HDL particles are enriched in cholesterol and phospholipids

Types of cholesterol

HDL

GOOD CHOLESTEROL!
High Density Lipoprotein

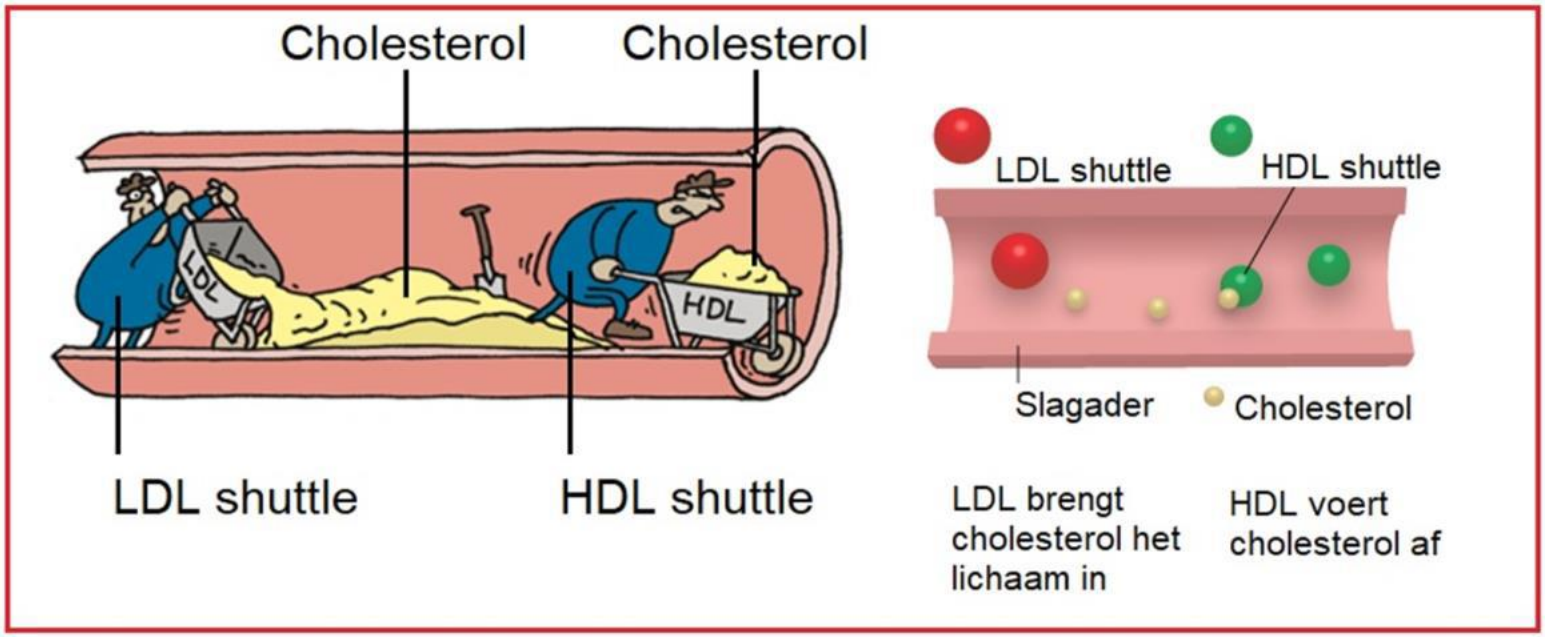
Good cholesterol (High Density Lipoprotein), carries excess cholesterol in your blood back to your liver where it's broken down and removed from your body. This means a high level of good HDL cholesterol can maintain your heart health.

LDL

BAD CHOLESTEROL!
Low Density Lipoprotein

Bad cholesterol (Low Density Lipoprotein) carries cholesterol to your cells. But when you have too much LDL it can build up in your artery walls, causing them to narrow. This reduces blood flow, which can be bad for your heart health.

Your total cholesterol level is made up of **both LDL and HDL cholesterol**. When you get your cholesterol checked make sure you find out both these levels.

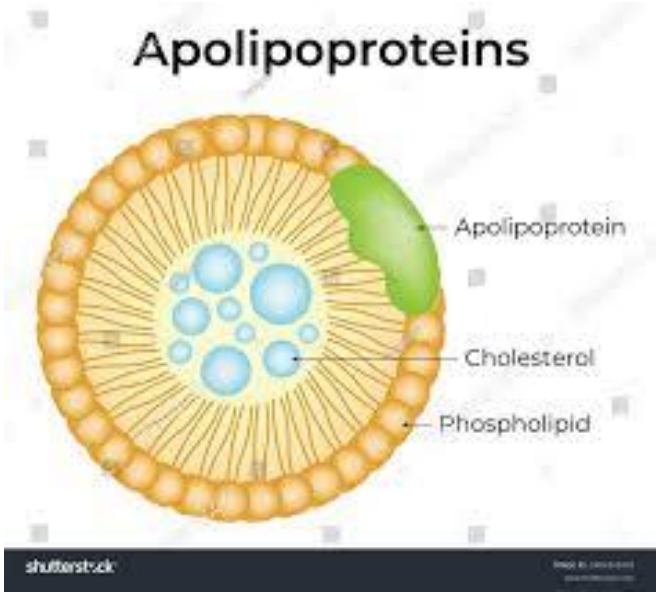

Cholesterol
Cholesterol
LDL
HDL
LDL shuttle
HDL shuttle
LDL shuttle
HDL shuttle
Slagader
Cholesterol
LDL brengt cholesterol het lichaam in
HDL voert cholesterol af

Apolipoproteins

Apolipoproteins have four major functions including

1) serving a structural role,
2) acting as ligands for lipoprotein receptors,
3) guiding the formation of lipoproteins, and
4) serving as activators or inhibitors of enzymes involved in the metabolism of lipoproteins .

Apolipoproteins thus play a crucial role in lipoprotein metabolism.



Type of Apolipoproteins

- **Apolipoprotein A-I**

Apo A-I is synthesized in the **liver and intestine** and is the major structural protein of **HDL** accounting for approximately 70% of HDL protein .High levels of Apo A-I are associated with a decreased risk of atherosclerosis.

- **Apolipoprotein A-II**

Apo A-II is synthesized in the **liver** and is the second most abundant protein on **HDL** accounting for approximately 20% of HDL protein. Apo A-II is a strong predictor of risk for CVD.

- **Apolipoprotein A-IV**

Apo A-IV is synthesized in the **intestine** during fat absorption. Apo A-IV is associated with chylomicrons and high-density lipoproteins, but is also found in the lipoprotein-free fraction. Its precise role in lipoprotein metabolism remains to be determined but studies have suggested a role for Apo A-IV in **regulating food intake**

- **Apolipoprotein A-V**

Apo A-V is synthesized in the **liver** and associates with **triglyceride** rich lipoproteins. It is an activator of LPL mediated lipolysis and thereby plays an important role in the metabolism of triglyceride rich lipoproteins

- **Apolipoprotein B-48**

Apo B-48 is synthesized in the **intestine** and is the major structural protein of chylomicrons and chylomicron remnants. There is a single molecule of apo B-48 per chylomicron particle.

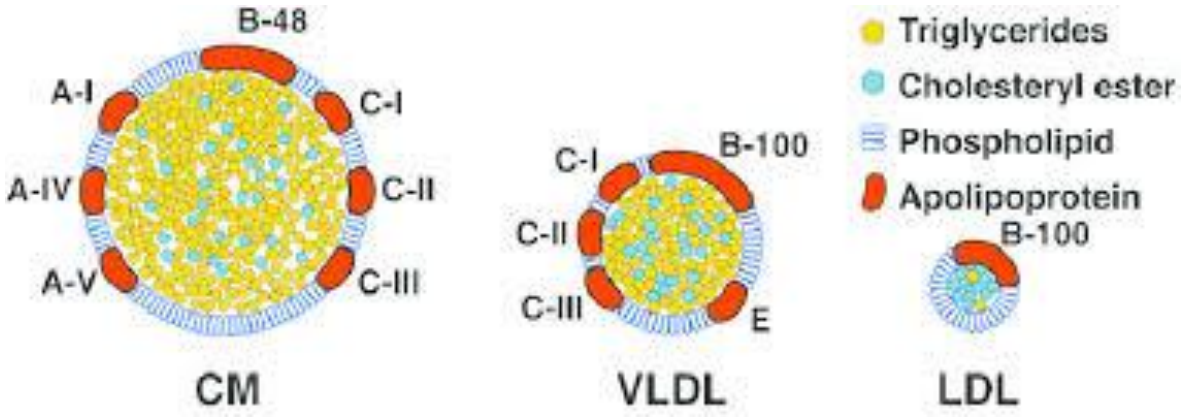
- **Apolipoprotein B-100**

Apo B-100 is synthesized in the **liver** and is the major structural component of VLDL, IDL, and LDL. There is a single molecule of Apo B-100 per VLDL, IDL, LDL and Lp(a) particle. High levels of Apo B-100 are associated with an increased risk of atherosclerosis. High levels of Apo B-100 are associated with an increased risk of atherosclerosis.

- **Apolipoprotein C**

The C apolipoproteins are synthesized primarily in the liver and freely exchange between lipoprotein particles and therefore are found in association with chylomicrons, VLDL, and HDL

- **Apo C-II** is a co-factor for lipoprotein lipase (LPL) and thus stimulates triglyceride hydrolysis and the clearance of triglyceride rich lipoproteins
- **Apo C-III** is an inhibitor of LPL. Additionally, Apo C-III inhibits the interaction of triglyceride rich lipoproteins with their receptor



Apolipoprotein E

Apolipoprotein E is synthesized in many tissues but the liver and intestine are the primary source of circulating Apo E. Apo E exchanges between lipoprotein particles and is associated with chylomicrons, chylomicron remnants, VLDL, IDL, and a subgroup of HDL particles.

❖ Apolipoprotein (a)

Apo (a) is synthesized in the liver. This protein is a homolog of plasminogen and its molecular weight varies from 300,000 to 800,000. It is attached to Apo B-100 via a disulfide bond. High levels of Apo (a) are associated with an increased risk of atherosclerosis. Apo (a) is an inhibitor of fibrinolysis and can also enhance the uptake of lipoproteins by macrophages, both of which could increase the risk of atherosclerosis

Thank You