Cholesterol Metabolism

Dr Abdul Lateef

Assistant Professor

Dept of Biochemistry

**CHOLESTEROL - INTRODUCTION:**

Exclusively found in animals – Animal sterol

Total body content – 2g/kg body weight.

Amphipathic in nature – hydrophilic and hydrophobic regions in structure.

Cholesterol is the precursor of all other steroids, such as sex hormones, bile acids, and vitamin D.

It occurs in foods of animal origin such as egg yolk, meat, liver, and brain.

**Cholesterol Structure**

Cyclopentanoperhydrophenanthrene structure consists of four fused rings

Cholesterol contains a hydroxyl group at C3, double bond between C5 & C6, eight-membered hydrocarbon chain at C17, & methyl groups at C10 & C13

**Cholesterol** **Synthesis**

Obtained through diet or synthesized in body.

Synthesized in many cells, but mostly in the liver and intestine

Acetyl coenzyme A (acetyl CoA) is the precursor to cholesterol synthesis

Synthesis occurs in cytosol and microsomes of cells.

**Cholesterol synthesis**

It can be divided into five steps:

Step 1. Acetyl-CoA forms HMG-CoA and mevalonate.

Step 2. Mevalonate forms active isoprenoid units.

Step 3. Six isoprenoid units form squalene.

Step 4. Squalene is converted to lanosterol.

Step 5. Lanosterol is converted to cholesterol.

**Acetyl-CoA is the source of all carbon atoms in cholesterol**

**The reducing equivalents are supplied by NADPH**

**ATP provides energy.**

Regulation of cholesterol synthesis

Cholesterol biosynthesis is controlled by the rate limiting enzyme HMG coA reductase.

***3 mechanisms***:

**Feed back control**. - ↑cholesterol ↓the transcription of gene responsible for HMG coA synthesis.

**Hormonal regulation** - ↑- Insulin and thyroxine

 ↓ - Glucagon and glucocorticoids

**Inhibition by drugs** – Statins are a group of drugs which competitively inhibit the synthesis of HMG coA reductase.

**Cholesterol Transport**

Chylomicrons , LDL & VLDL transport cholesterol to other cells through the bloodstream

Chylomicrons package cholesterol in intestine, while VLDL packages in liver

HDL – reverse cholesterol transport

Role of LCAT: Lecithin cholesterol acyl transferase

HDL and LCAT are responsible for the transport and elimination of cholesterol from the body.

LCAT is a plasma enzyme, synthesized by the liver.

The cholesterol esters forms an integral part of HDL. In this manner the cholesterol from the peripheral tissue is trapped in HDL, by the reaction catalysed by LCAT and then transported to liver for degradation and excretion. This mechanism is called as REVERSE CHOLESTEROL TRANSPORT.

Transport of cholesterol

Fates of Cholesterol

The steroid nucleus of the cholesterol cannot be metabolised in humans.

50% of cholesterol is converted to bile acids.

Other fates:

* Cell membranes
* Cholesterol Ester
* Biliary Cholesterol
* Vitamin D
* Synthesis of steroid hormones.

Cholesterol Esters

Acyl-CoA cholesterol acyl transferase (ACAT) is an Endoplasmic Reticulum membrane protein

ACAT transfers fatty acid of CoA to C3 hydroxyl group of cholesterol

Excess cholesterol is stored as cholesterol esters in cytosolic lipid droplets

Bile acids/Salts

Bile acids :

Primary bile acid : Cholic acid and Chenocholic acid

Secondary bile acids : Glycocholic acid, Taurocholic acid.

Bile salts: Sodium and potassium salts of bile acids.

Bile acids & salts are effective detergents

Synthesized in the liver

Stored & concentrated in the gallbladder

Discharged into gut and aides in absorption of intraluminal lipids, cholesterol, & fat soluble vitamins.

Synthesis of Bile acids/Salts

Fate of Bile Salts
Enterohepatic circulation of bile

Thank you