

Cholesterol Metabolism

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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