CHOLESTEROL
&
LIPOPROTEIN

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INTRODUCTION

- The word cholesterol is derived from Greek words,
- **Chole =bile**, **steros =solid**, **ol=alcohol.**
- It is widely distributed in the body.
- It is soluble in chloroform and other fat solvents.
- It is the most important animal steroid from which other steroid compounds are formed.

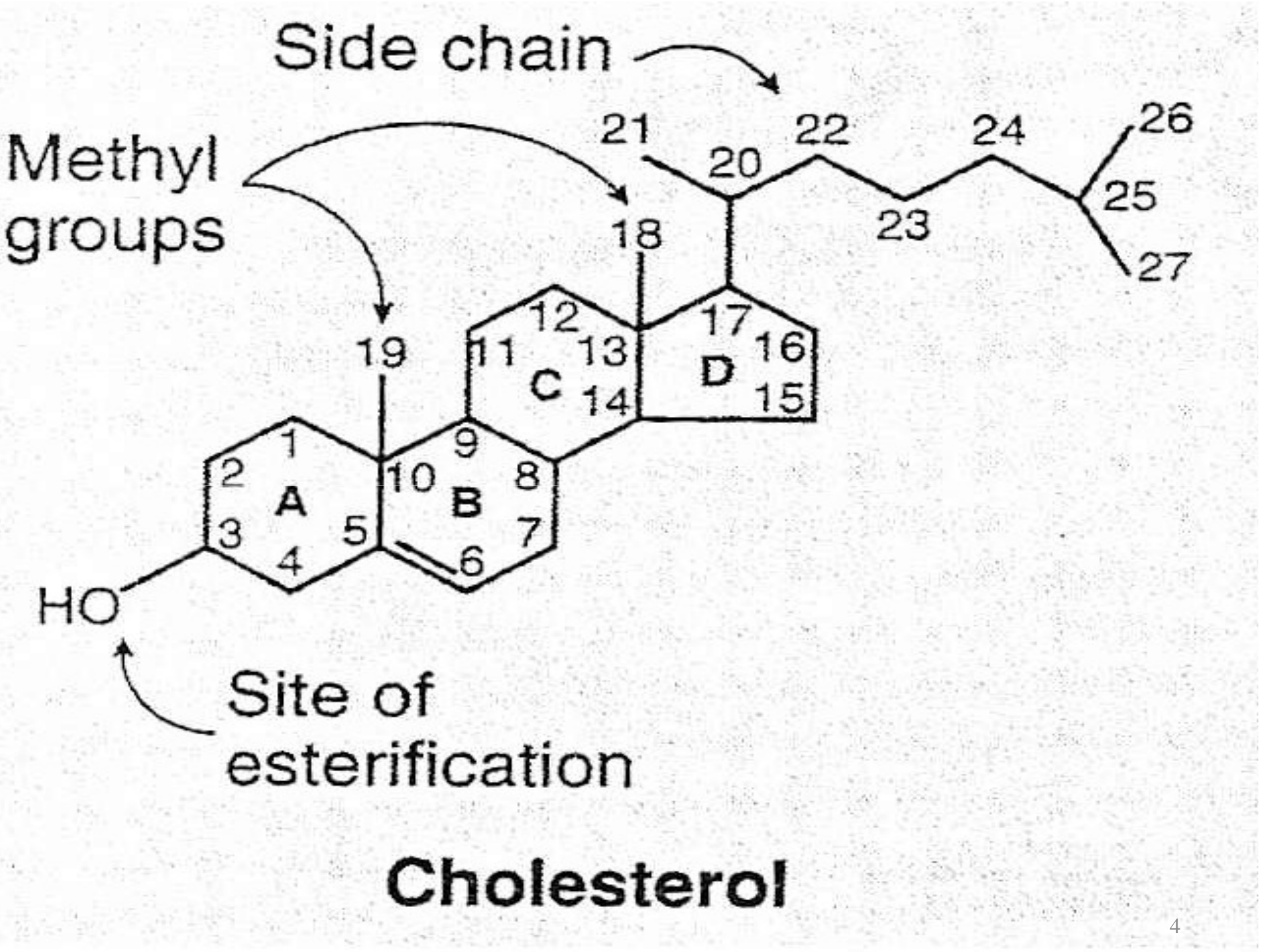
Significant of Cholesterol

1. **Cell membranes**: it is a component of cell membranes
2. **Nerve conduction**: it is a poor conductor of electricity, and helps to insulate nerve fibers.
3. **Bile acids and bile salts**:
4. **Steroid hormones**: Glucocorticoids, Androgens and Estrogens are synthesized from cholesterol.
5. **Vitamin D3**: it is synthesized from 7-dehydrocholesterol.
6. **Esterification**

- Cholesterol esterified to fatty acids = Cholesterol esters.

7. **Atherosclerosis**

- Increase level of abnormal cholesterol lead to CAD & CVD.


Side chain
Methyl groups
21
22
24
26
20
25
23
27
18
19
12
17
11
13
16
C
D
14
15
1
9
2
10
8
A
B
3
5
7
4
6
HO
Site of esterification
Cholesterol

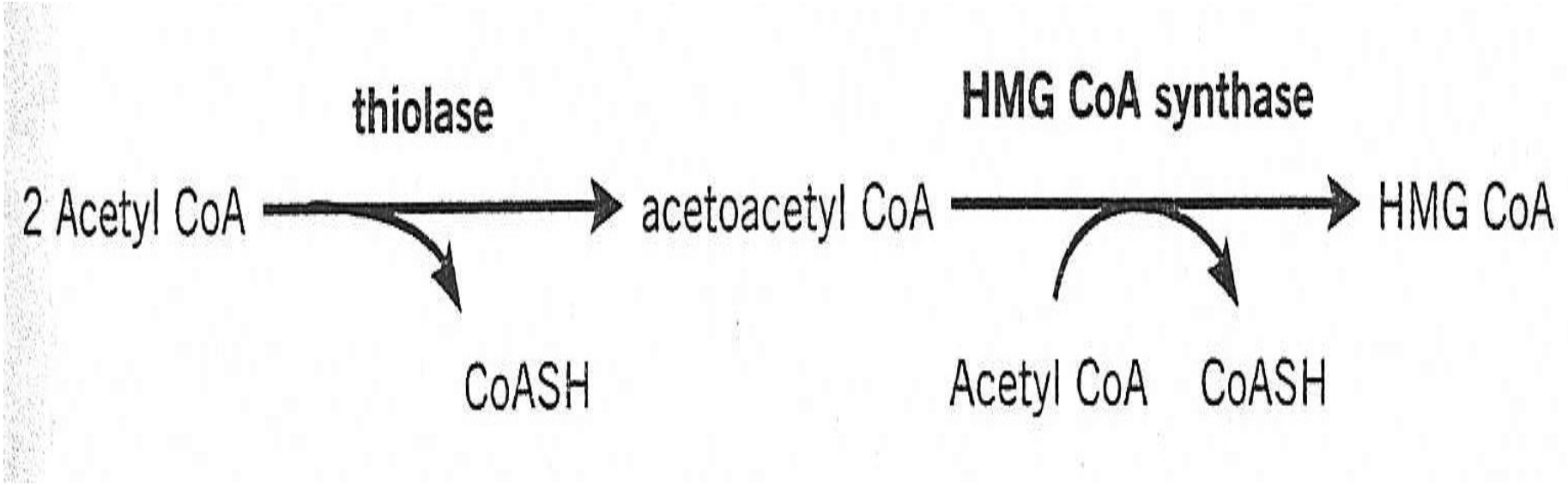
ABSORPTION OF CHOLESTEROL

- Absorption needs miceller formation.
- Inside the mucosal cell, cholesterol is re-esterified and incorporated into chylomicrons.
- The chylomicrons reach the blood stream through lymphatics.
- This dietary cholesterol reaches the liver through chylomicrons remnants.
- Plant sterols (sitosterol) decrease absorption of cholesterol.

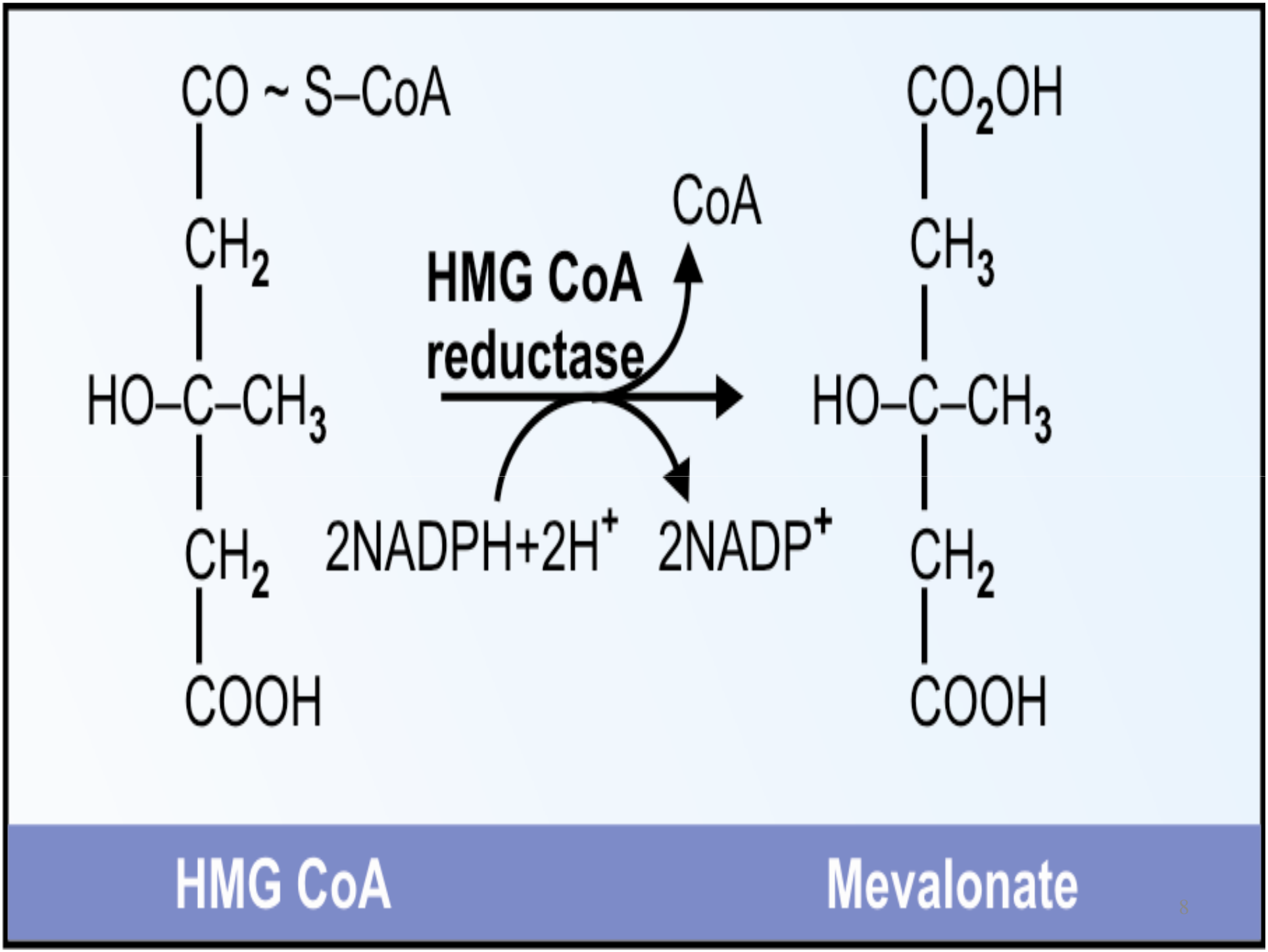
BIOSYNTHESIS OF CHOLESTEROL

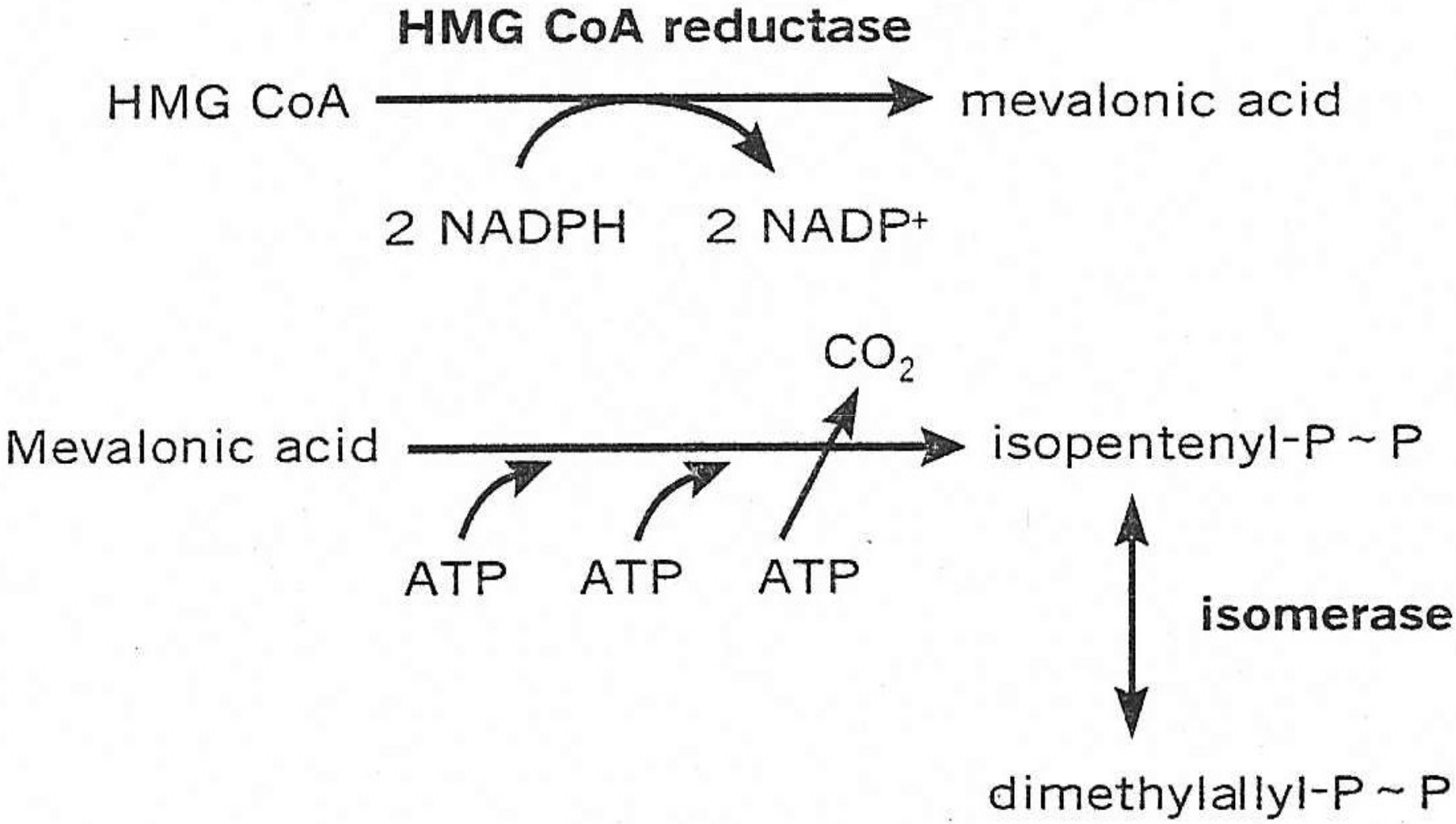
- Cholesterol is synthesised from Acetyl CoA.
- Partly Cytoplasm & Partly in Endoplasmic reticulum.
- Primary site: Liver (~1g/d)
- Secondary sites: Adrenal cortex, ovaries, testes
- All nucleated cells can synthesize cholesterol, including arterial walls.

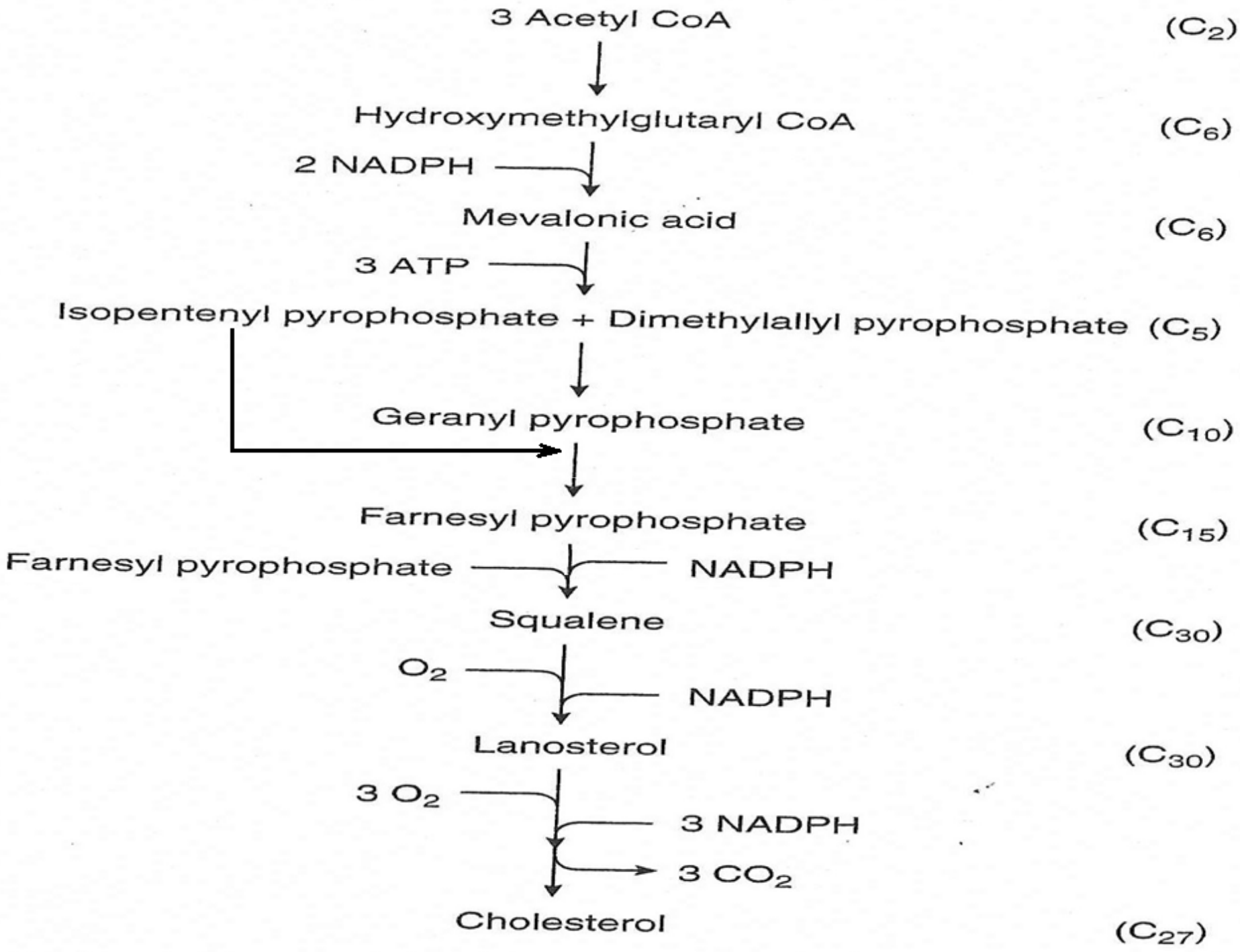
SYNTHESIS OF CHOLESTEROL



- **HMG CoA (3-hydroxy-3-methylglutaryl-CoA)** is present in both cytosol as well as mitochondria of liver.
- Mitochondrial pool = for ketone body synthesis
- Cytosolic pool = for cholesterol synthesis.


CO ~ S–CoA
CH2
HO–C–CH3
CH2
COOH
HMG CoA
reductase
CoA
2NADPH+2H+
2NADP+
CO2OH
CH3
HO–C–CH3
CH2
COOH
HMG CoA
Mevalonate


HMG CoA reductase
HMG CoA
mevalonic acid
2 NADPH
2 NADP+
CO2
Mevalonic acid
isopentenyl-P ~ P
ATP
ATP
ATP
isomerase
dimethylallyl-P ~ P


3 Acetyl CoA
(C2)
Hydroxymethylglutaryl CoA
(C6)
2 NADPH
Mevalonic acid
(C6)
3 ATP
Isopentenyl pyrophosphate + Dimethylallyl pyrophosphate
(C5)
Geranyl pyrophosphate
(C10)
Farnesyl pyrophosphate
(C15)
Farnesyl pyrophosphate
NADPH
Squalene
(C30)
O2
NADPH
Lanosterol
(C30)
3 O2
3 NADPH
3 CO2
Cholesterol
(C27)

Regulation of Cholesterol Synthesis

- Rate limiting enzyme is ***HMG CoA reductase***.

1. Regulation at transcription

- Long term regulation
- Regulation of transcription of the gene of HMG CoA reductase.
- Increase Cholesterol
    - Suppress transcription of the gene for HMG CoA reductase
    - Synthesis of cholesterol decrease.
- Low Cholesterol
    - Induce transcription of the gene for HMG CoA reductase
    - Synthesis of cholesterol increase.
- Patient taking "Statin" drug
    - Decrease cholesterol
    - Induce gene for HMG CoA reductase = Increase Enzyme Conc.

Regulation of Cholesterol Synthesis

2. Covalent modification of enzyme:

- Phosphorylatation of enzyme = Inactive enzyme.
- Dephosphorylation of enzyme = Active enzyme.

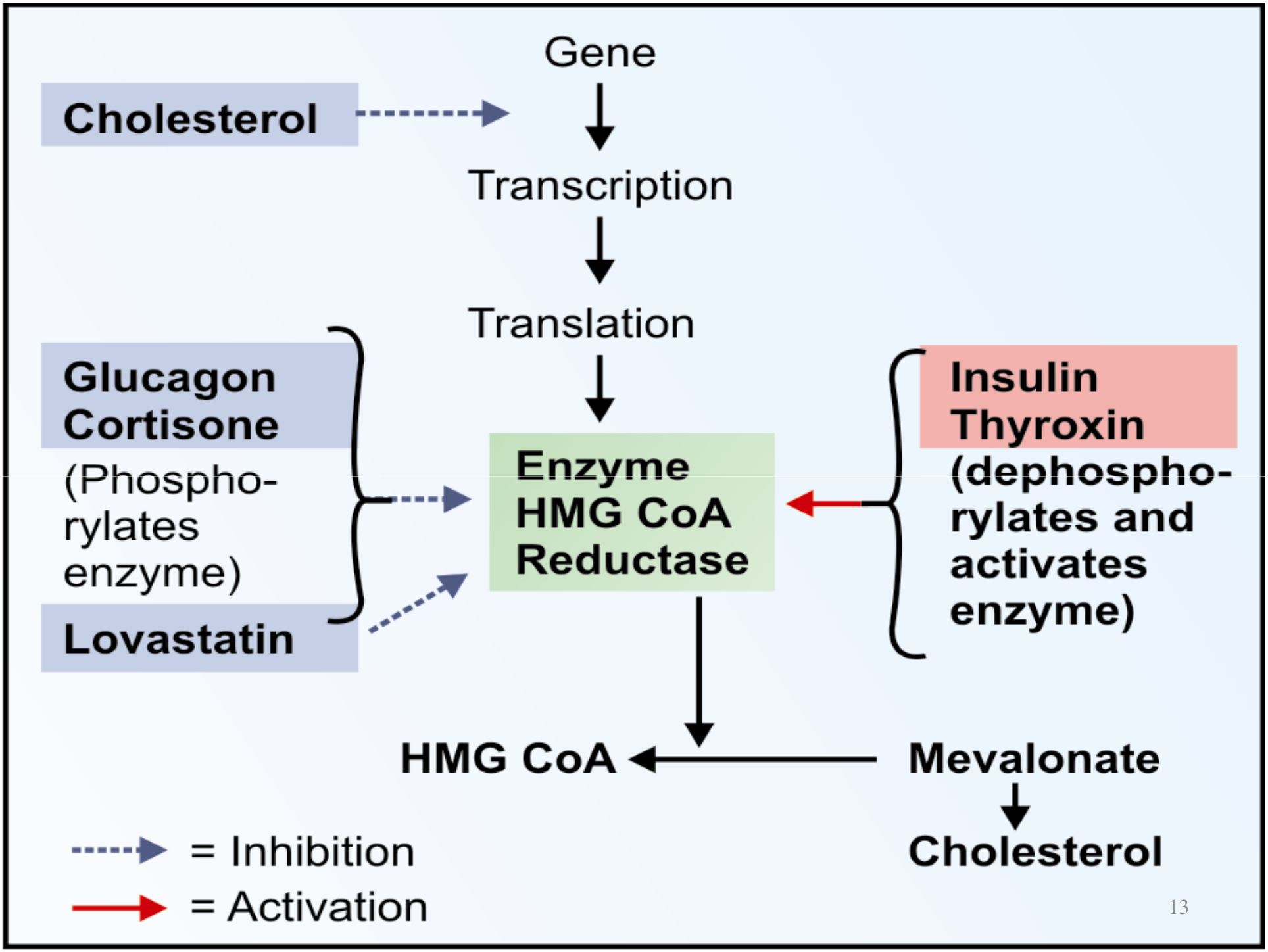
3. Insulin and thyroxine increase the activity .

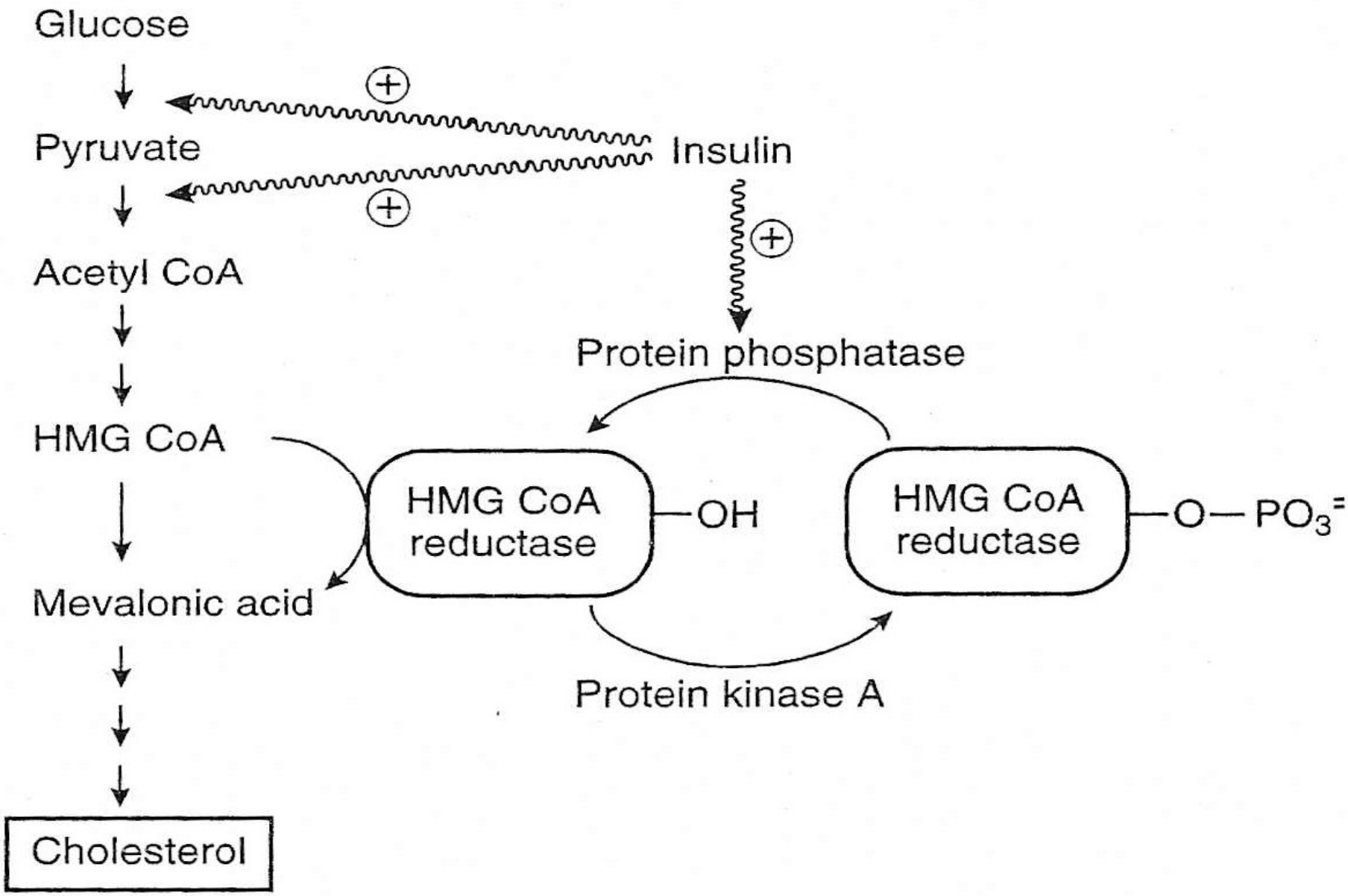
4. Cortisol and Glucagon decrease its activity.

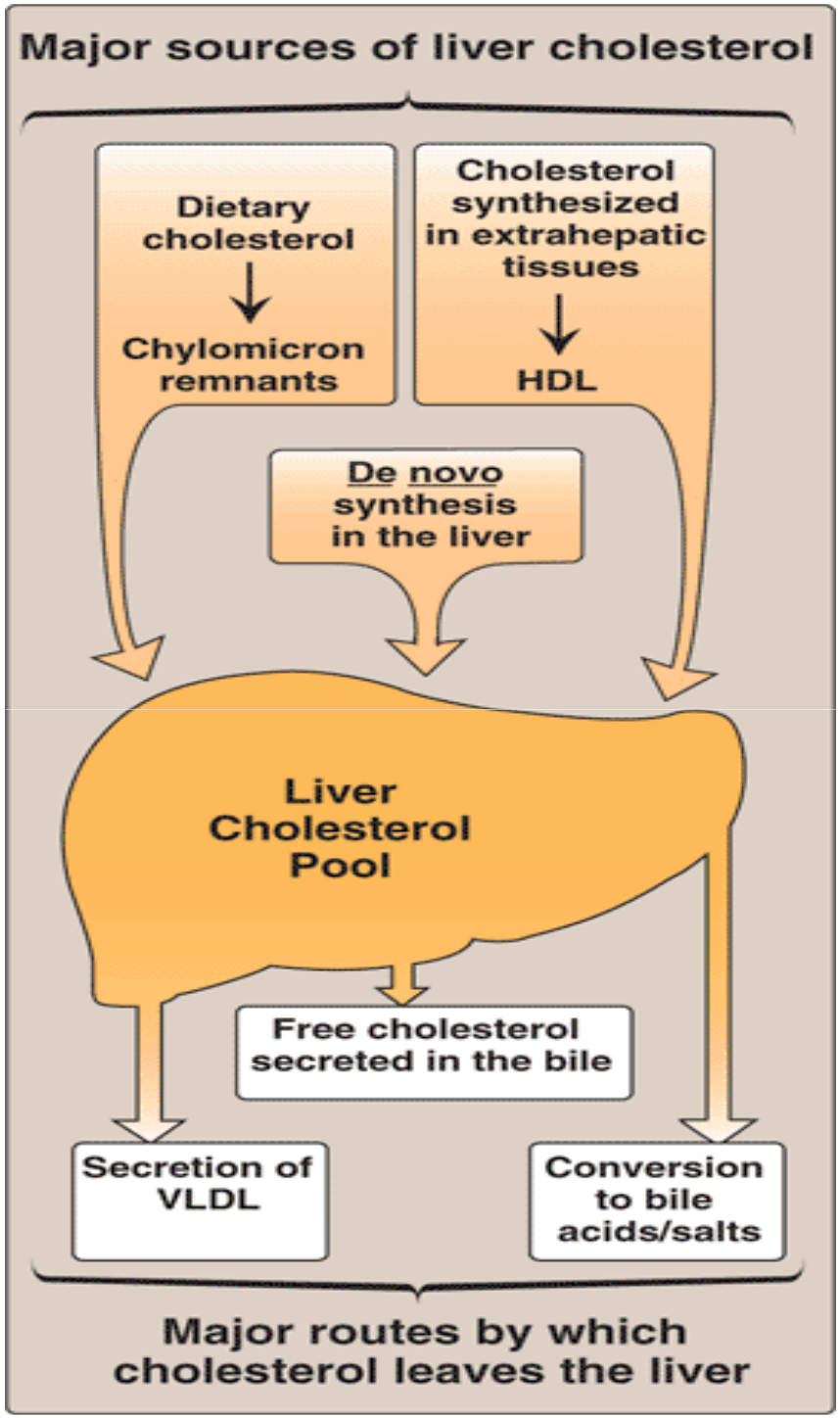
5.Drugs :

- ‘Statin’’ group of drugs are competitive inhibitors of HMG CoA reductase.

  e.g. Atorvastatin. Simvastatin


Gene
Cholesterol
Transcription
Translation
Glucagon
Cortisone
(Phospho-
rylates
enzyme)
Lovastatin
Enzyme
HMG CoA
Reductase
Insulin
Thyroxin
(dephospho-
rylates and
activates
enzyme)
HMG CoA
Mevalonate
Cholesterol
= Inhibition
= Activation

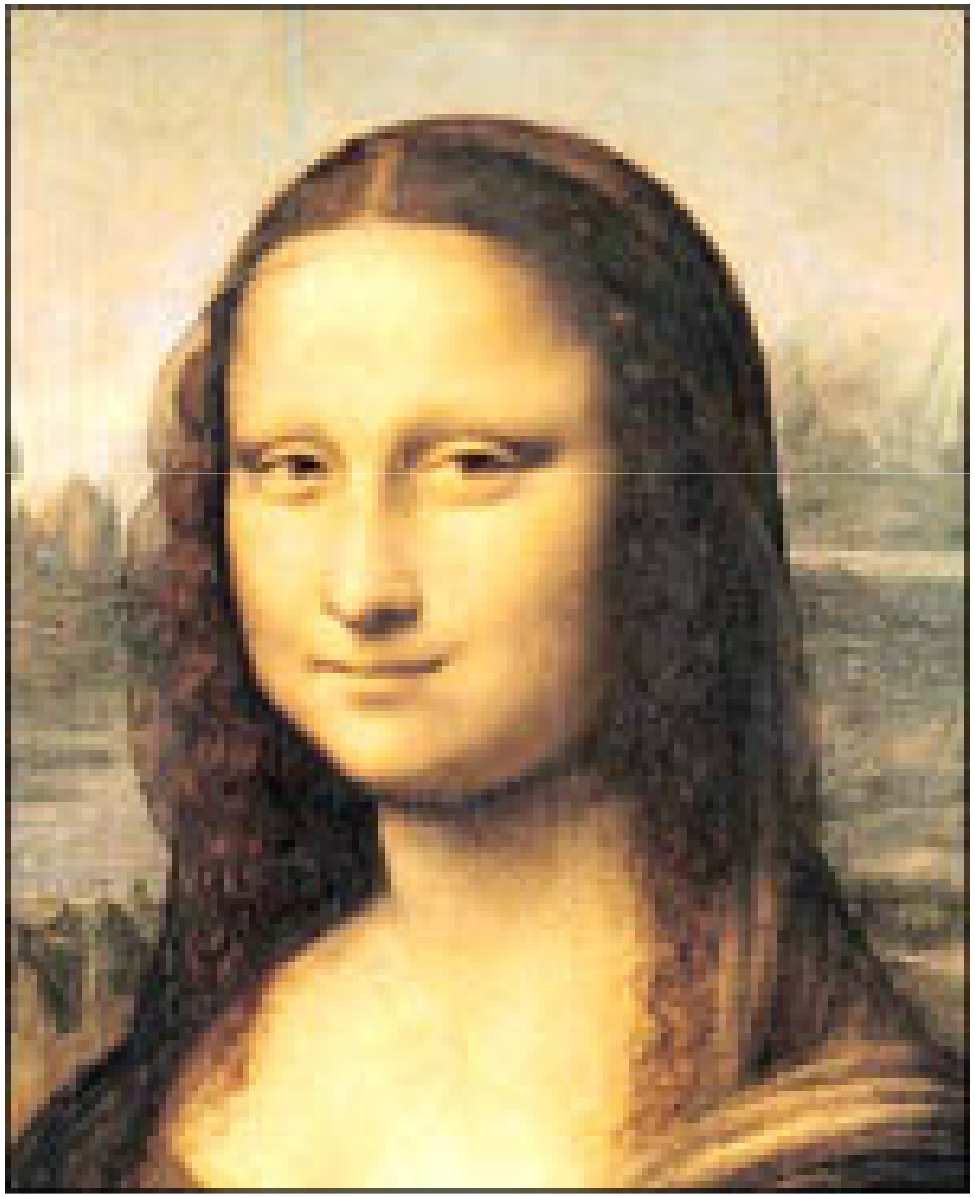

Glucose
Pyruvate
Acetyl CoA
HMG CoA
Mevalonic acid
Cholesterol
Insulin
Protein phosphatase
HMG CoA reductase
OH
HMG CoA reductase
O— PO3=
Protein kinase A


Major sources of liver cholesterol
Dietary cholesterol
Chylomicron remnants
Cholesterol synthesized in extrahepatic tissues
HDL
De novo synthesis in the liver
Liver Cholesterol Pool
Free cholesterol secreted in the bile
Secretion of VLDL
Conversion to bile acids/salts
Major routes by which cholesterol leaves the liver

EXCRETION OF CHOLESTEROL

- Average diet = 300 mg of cholesterol/day.
- Body synthesize = 700 mg of cholesterol/day.
- Total 1000mg
- About 500 mg of cholesterol = excreted through bile.
- 95% of this cholesterol is reabsorbed from intestines.
- Plant sterols = inhibit the reabsorption of cholesterol.

Was Mona Lisa suffering from hypercholesterolemia?



Plasma Lipid

Plasma Lipid

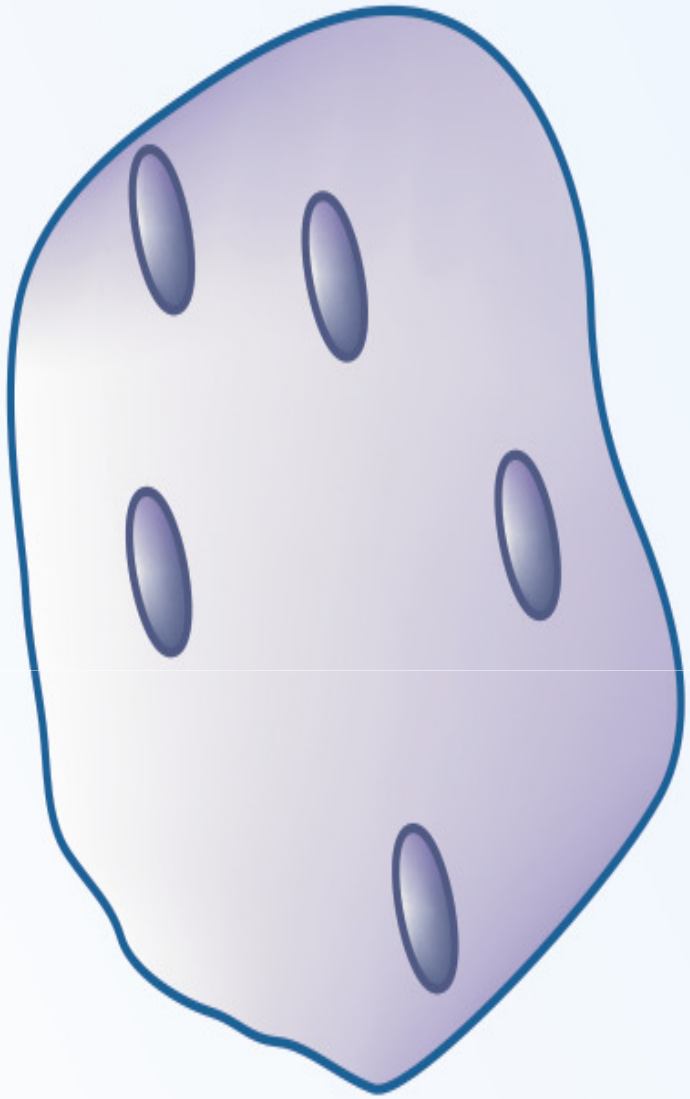
- Total plasma lipid is 400-600 mg/dl.
- One-third is cholesterol
- One-third is TGs
- One-third is phospholipid.
- **Lipoproteins (Lp) =** Lipid + Protein
- **Apolipoprotein =** The protein part of lipoprotein.

CLASSIFICATION OF LIPOPROTEINS

- Five major types:

1. Chylomicrons
2. VLDL or pre beta lipoproteins
3. IDL or broad beta lipoproteins
4. LDL or beta lipoproteins
5. HDL or alpha lipoproteins

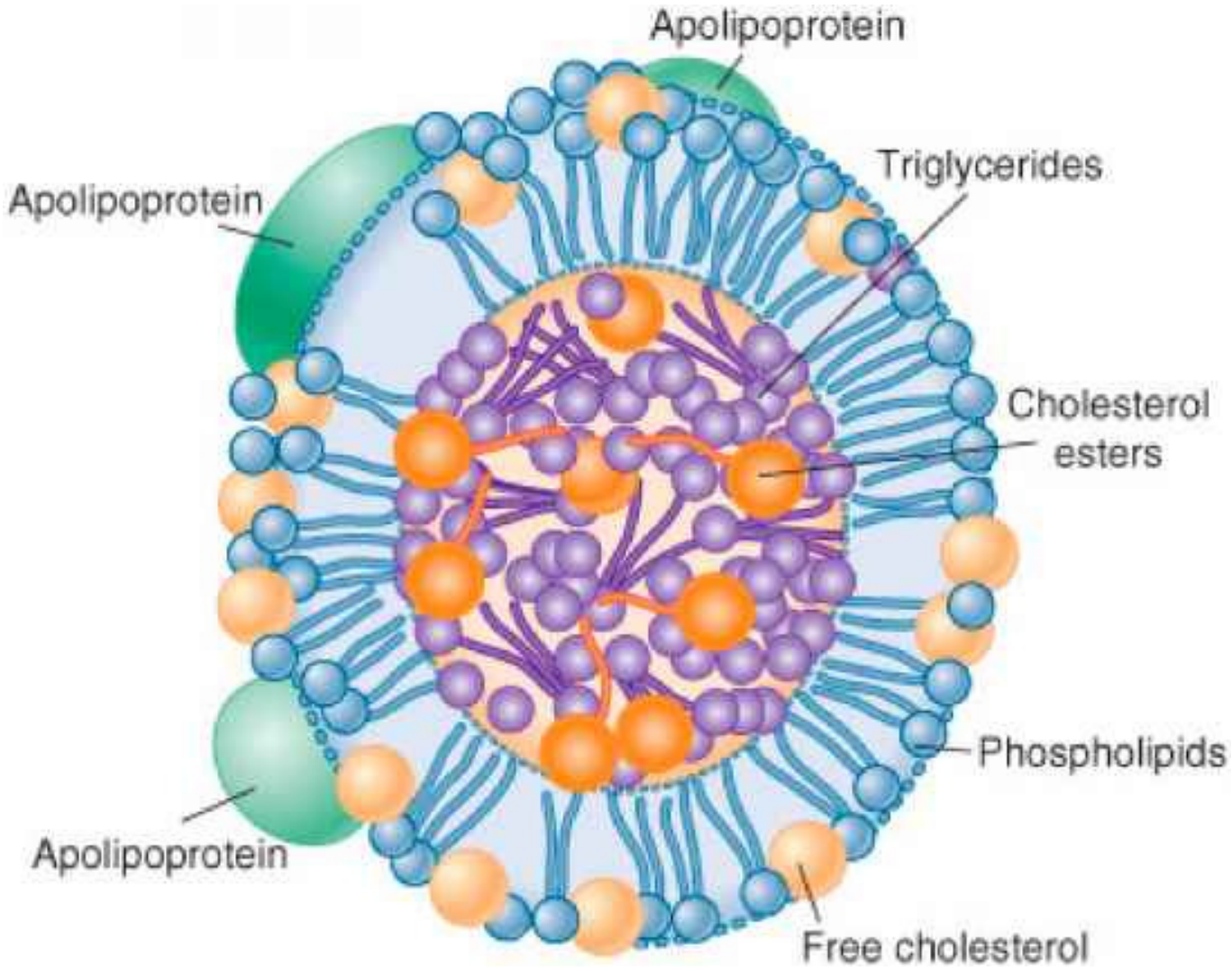
- Free fatty acids (FFA) or non-esterified fatty acids (NEFA) are complexed with albumin, not generally considered as lipoproteins.



Chylomicron

VLDL IDL LDL HDL

Lipoprotein



Lipoprotein

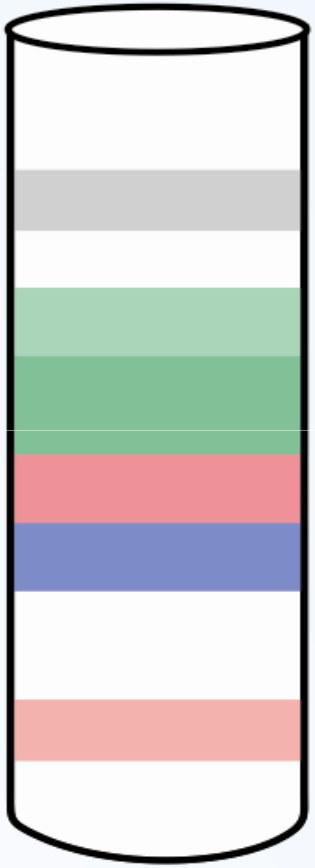
- Outer Part made up of
  - Polar part of proteins
  - Polar heads of phospholipids
  - Cholesterol.
- This inner core consists
  - Hydrophobic TAGs
  - Tails of phospholipids.
- The apoproteins increase the solubility of lipids.

Separation by ultracentrifugation

- Fat is less dense than water; so fat floats on water.
- Lipoproteins
  - High lipid content
  - Low density
  - Floats on centrifugation.
- Lipoproteins
  - High protein content
  - High density
  - Sediment easily

ULTRACENTRIFUGATION

LIPOPROTEINS
(density g/L)



Chylomicron

VLDL

IDL

LDL

HDL

FFA

ELECTROPHORESIS

LIPOPROTEINS
(mobility)

Chylomicron
(origin)

VLDL(beta)

IDL(broad β)

LDL(broad β)

HDL(alpha)

FFA=albumin

Positive

VLDL = very low density lipoproteins; IDL= intermediate density lipoproteins; LDL = low density lipoproteins; HDL= high density lipoproteins; FFA = free fatty acid

Lipoprotein Types & Composition

Lipoprotein	Source	Diameter (nm)	Density (g/mL)	Composition		Main Lipid Components	Apolipoproteins
				Protein (%)	Lipid (%)		
Chylomicrons	Intestine	90-1000	<0.95	1-2	98-99	Triacylglycerol	A-I, A-II, A-IV,[a] B-48, C-I, C-II, C-III, E
Chylomicron remnants	Chylomicrons	45-150	<1.006	6-8	92-94	Triacylglycerol, phospholipids, cholesterol	B-48, E
VLDL	Liver (intestine)	30-90	0.95-1.006	7-10	90-93	Triacylglycerol	B-100, C-I, C-II, C-III
IDL	VLDL	25-35	1.006-1.019	11	89	Triacylglycerol, cholesterol	B-100, E
LDL	VLDL	20-25	1.019-1.063	21	79	Cholesterol	B-100
HDL	Liver, intestine, VLDL, chylomicrons					Phospholipids, cholesterol	A-I, A-II, A-IV, C-I, C-II, C-III, D,[b] E
HDL_1		20-25	1.019-1.063	32	68		
HDL_2		10-20	1.063-1.125	33	67		
HDL_3		5-10	1.125-1.210	57	43		
Preβ-HDL[c]		<5	>1.210				A-I
Albumin/free fatty acids	Adipose tissue		>1.281	99	1	Free fatty acids	

Apo-lipoprotein Function

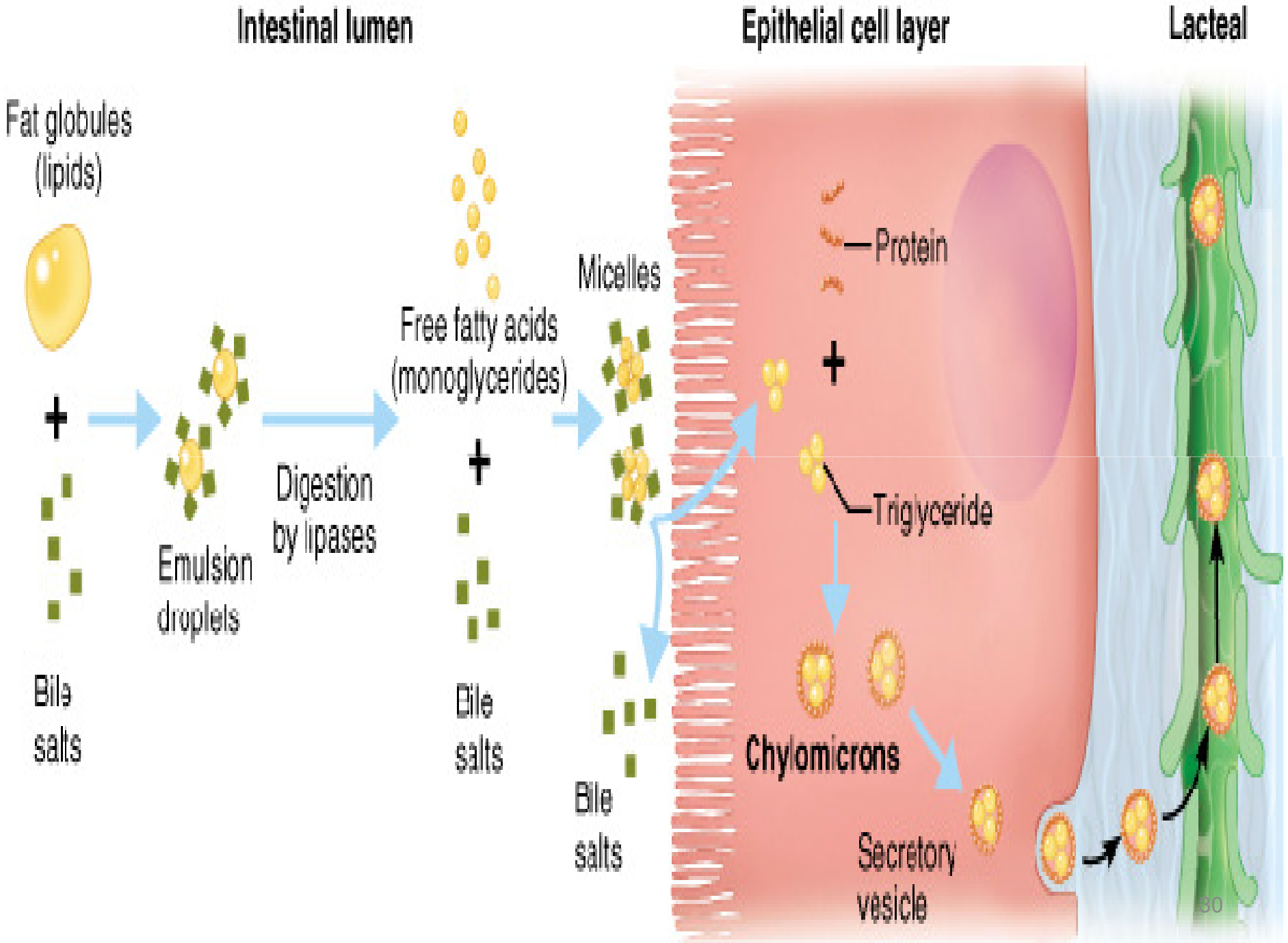
- Structural role
  - Apo B
- Enzyme cofactor
  - C-II for Lipoprotein Lipase
  - A-I for Lecthine Cholesterol Acyl Transferase (LCAT)
- Enzyme inhibitor
  - A-II and C-III for Lipoprotein lipase
  - C-I for Cholesterol ester transferase protein
- Act as ligand with receptor
  - A-I for HDL receptor
  - B-100 & E for LDL receptor
  - E for LDL receptor related protein (LRP)
- A-IV & D = No clear function
- Apo D is believed to be important factor in neurodegenerative disorders

Apoprotein	Component of	Function
Apo A-I	HDL-1	Activation of LCAT
Apo A-II	HDL-3	Inhibits LCAT, Stimulates hepatic lipase
Apo B-100	LDL, VLDL	Binds LDL receptor
Apo B-48	Chylomicrons	Major Structural component
Apo C-I	Chylomicrons, VLDL	Activation of LCAT
Apo C-II	Chylomicrons, VLDL	Activates extrahepatic Lipoprotein Lipase in vessels walls
Apo C-III	Chylomicrons, VLDL	Inhibit Lipoprotein Lipase
Apo E	IDL, VLDL, Chylomicrons	Ligand for hepatic uptake
Apo Lp (a)	Lp(a)	Attached to B-100, Impair fibrinolysis. Inhibit plasminogen

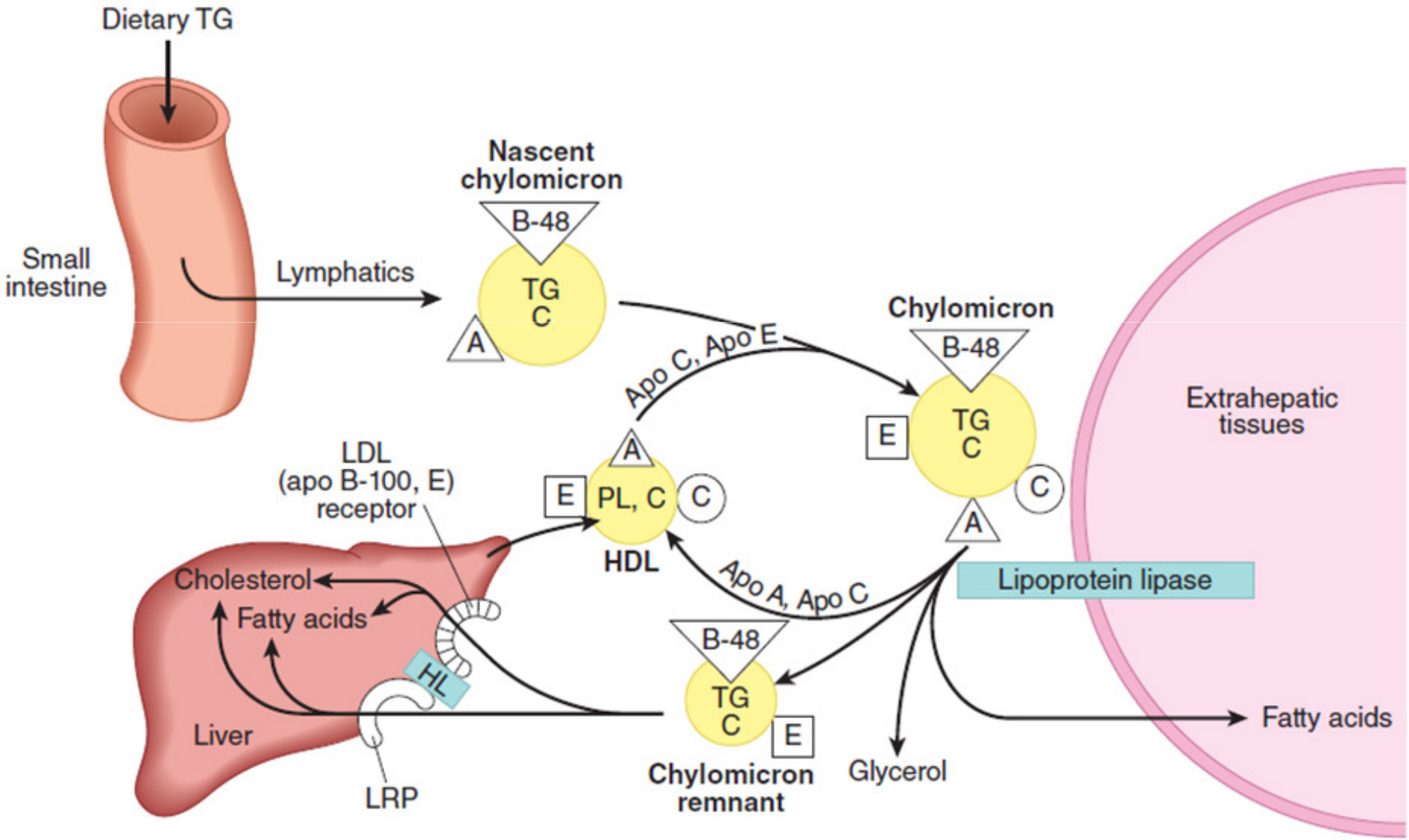
1. CHYLOMICRONS

Chylomicrons Synthesis :

- Formed in the intestinal mucosal cells
- Secreted into the lymphatic system.
- They are **rich in TGs**.
- In intestine mucosa phase
    - Contain only Apo A & Apo-B-48
- In the blood, when transported intestine to other tissue,
    - Added Apo C-II and Apo E
    - Through HDL.
- If the lipemic serum is kept overnight in the refrigerator, chylomicrons rise as a creamy layer to the top.


Intestinal lumen
Epithelial cell layer
Lacteal
Fat globules (lipids)
Bile salts
Emulsion droplets
Digestion by lipases
Free fatty acids (monoglycerides)
Bile salts
Micelles
Bile salts
Protein
Triglyceride
Chylomicrons
Secretory vesicle

Chylomicrons Metabolism



Chylomicrons Metabolism

- In Adipose tissue & Skeletal muscle
- Half life in blood is 1 hour.
- Endothelial layer of capillaries of adipose tissue, muscles and heart; but **Not in liver.**
    - Has lipoprotein lipase
    - Apo-C-II of chylomicron activates the LpL.
    - Hydrolyzes Triglyceride = FA + Glycerol.
    - Muscle or Adipose tissue take up Fatty acids.

Chylomicrons Metabolism

- Heparin
    - Release LpL from the tissues
    - Lipemia is cleared.
    - Post-heparin lipolytic activity.
- Deficiency of Apo C-II
    - Decreased LpL activity
    - Accumulation of chylomicrons & VLDL in blood.
- Insulin increases LpL activity.
    - Type -1 Diabetes Mellitus - Deficiency of Insulin
    - Decrease LpL activity
    - Accumulation of chylomicrons & VLDL in blood.

Chylomicrons Metabolism

- **Liver takes up "Chylomicrons remnants":**
  - TG content decreased
  - Chylomicrons shrink in size.
  - Containing **Apo-B48 and Apo-E**
  - Taken up by hepatic cells by receptor mediated endocytosis.
  - **Apo-E binds to the Hepatic receptors.**
- **Function:**
  - Transport form of dietary TGs from intestines to the adipose tissue for storage ; and to muscle or heart for their energy needs.

VLDL Synthesis

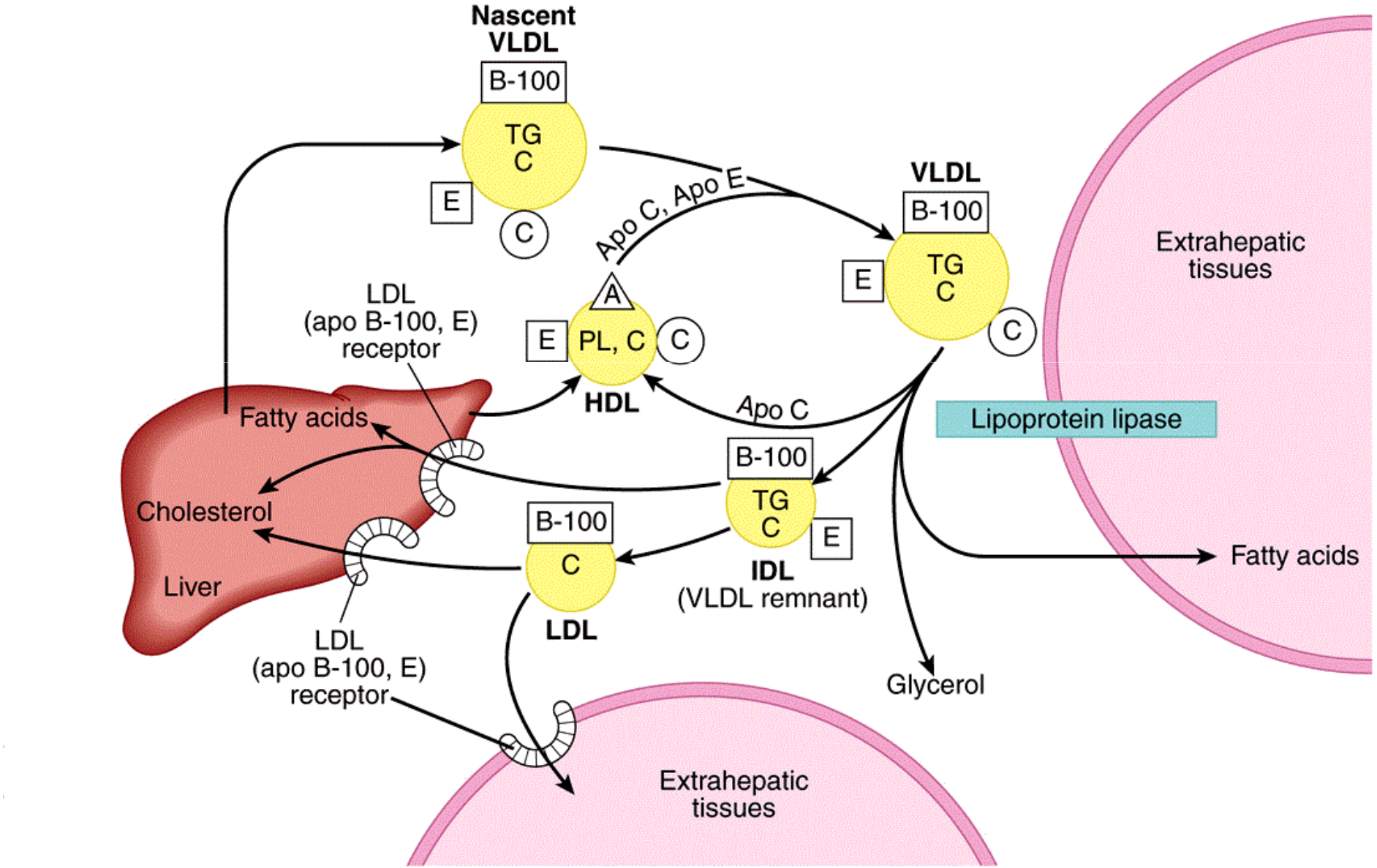
Nascent VLDL

- Synthesized **in liver** from Glycerol, Fatty acid & Cholesterol.
- **With Apo-B-100, C-I and E**.

VLDL

- Plasma HDL add apolipoprotein
- **Apo-C-II and Apo-E** added to Nascent VLDL

Very Low Density Proteins Metabolism



VLDL Metabolism

- Half-life of VLDL in serum =1-3 hrs.
- Reach the peripheral tissues
- Apo C-II activates Liporprotein Lipase (LpL)
- Liberated fatty acid is taken by Adipose tissue and Muscle.
- This remnant called IDL , contains
    - Less of Triglyceride
    - More of cholesterol.
- Major fraction of IDL further loses triglyceride and Converted to LDL.
- **Lipoprotein Cascade Pathway.**
    - Conversion of VLDL to IDL & to LDL
- IDL is taken up by the hepatic receptors.

VLDL Function

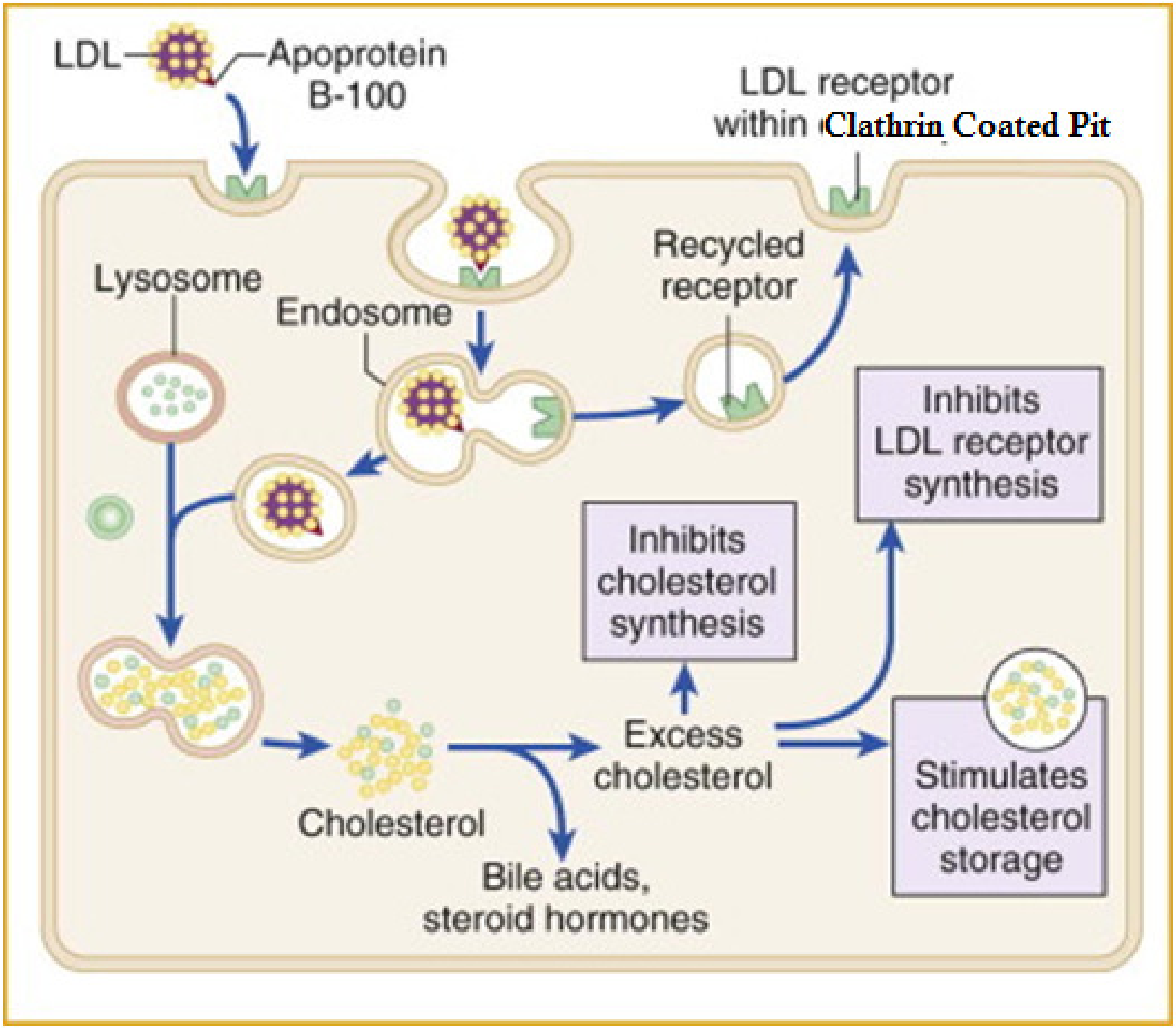
- VLDL carries **Triglycerides** (endogenous triglycerides) **from liver to peripheral tissues** for energy needs.

Low Density Lipoprotein

- Cholesterol rich lipoprotein
- Containing **only Apo-B-100.**
- Most of LDL particles are derived from VLDL.
- Half Life of LDL = 2 days

Low Density Lipoprotein Metabolism

- **LDL receptors**
  - Present on all cells
  - Most abundant in hepatic cells.
  - Located in specialized regions - **Clathrin Coated Pits.**
- **Apo-B-100 binds to the receptor**
- Receptor-LDL complex
- Internalized by Endocytosis.
- Vesicles fuse with lysosomes.
- Lysosomal enzymes
  - Degrade the apoproteins of the LDL
  - Hydrolyze the cholesterol esters to free cholesterol.
- Free receptors return to the membrane surface to bind new LDL.


LDL
Apoprotein B-100
LDL receptor within Clathrin Coated Pit
Recycled receptor
Lysosome
Endosome
Inhibits LDL receptor synthesis
Inhibits cholesterol synthesis
Excess cholesterol
Stimulates cholesterol storage
Cholesterol
Bile acids, steroid hormones

Low Density Lipoprotein Function

- LDL transports **cholesterol from liver to the peripheral tissues.**
- Positive correlation with cardiovascular diseases.
- About 75% of the plasma cholesterol is incorporated into the LDL particles.

LDL and Atherosclerosis

- **LDL Modification – Glycation.**
- **Oxidized LDL.**
- LDL infiltrates through arterial walls
- Taken up by macrophages = Scavenger cells.
- **“FOAM CELL”**
- Starting event of Atherosclerosis
- Coronary Artery Disease.
- **Bad Cholesterol** & **Lethally Dangerous Lipoprotein.**
- “Small dense LDL” (sdLDL) = Worst fraction of LDL, associated with coronary artery diseases.

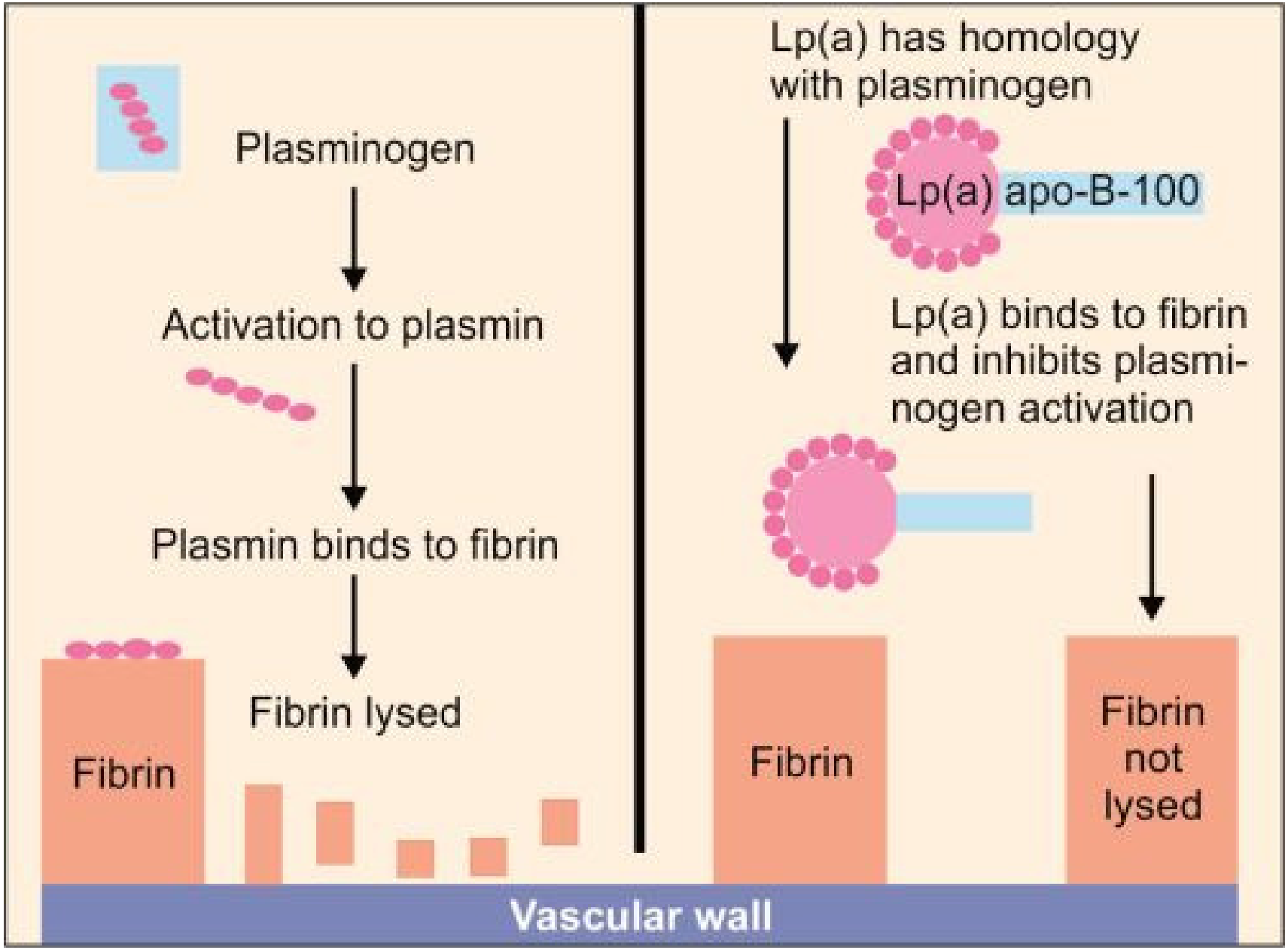
Apo Lipoprotein-A = Apo-A

- Constituent of HDL.
- **Anti Atherogenic.**

Lipoprotein (a) = Lp(a)

- Associated with LDL.
- **Highly Atherogenic**
- **Attached to apo-B-100** by a disulfide bond.
- Lp(a) has significant homology with plasminogen.
- So it interferes with plasminogen activation
- **Impairs fibrinolysis.**
- This leads to unopposed intravascular thrombosis and possible myocardial infarction.

Lp(a) and Plasminogen



High Density Lipoprotein Metabolism

- Transport cholesterol from peripheral tissue to liver.
- HDL = Apo A-I, Apo A-II, Apo-C , Apo-E
- **Major reservoir of Apo-C & Apo-E**

High Density Lipoprotein Metabolism

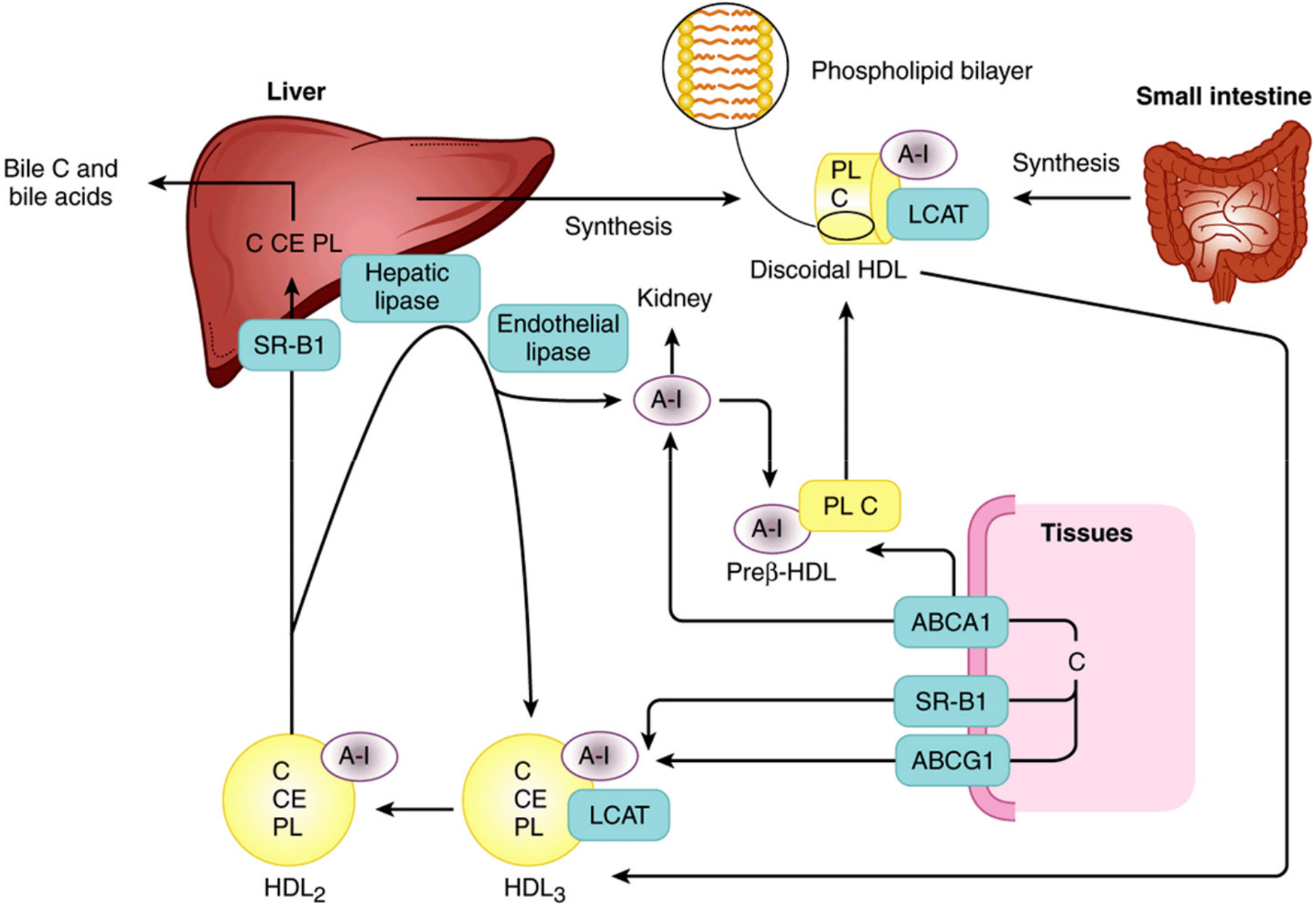
- Intestine cell synthesized Component of HDL
- Nascent HDL – Discoid in shape.
- Apo-A-I of HDL activates **LCAT** .
  - Lecithin - Component of phospholipid bilayer of HDL disc.
  - 2nd carbon of lecithin - one molecule of PUFA.
  - PUFA transferred to cholesterol to form cholesterol ester.
- Esterified cholesterol internalized to HDL disc.
  - **Cholesterol Efflux Regulatory Protein – ABC Protein**
  - **ATP Binding Cassette (ABC) Transporter-A1**
- Internalization continuous till HDL became spherical
- Filled with lots of cholesterol esters = **"Mature HDL"** spheres

High Density Lipoprotein Metabolism

- **"Mature HDL"** Spheres **(HDL-3)**
- Taken by liver cells
- Apo-A-I mediated receptor mechanism.
- Hepatic lipase hydrolyzes HDL .
  - Phospholipid
  - Cholesterol ester
  - Triglyceride
- These cholesterol Utilized for
  - Bile acid synthesis

High Density Lipoprotein Metabolism

- **"Mature HDL"** Spheres **(HDL-3)**
- Some remain circulation
- Cholesterol Ester Transferase Protein (CETP)
  - Transfer to Cholesterol ester from HDL to
    - VLDL
    - IDL
    - LDL
  - Transfer Triglyceride into HDL
  - So More cholesterol can be taken up from periphery
- **HDL-2** = Higher TG and Spherical Shape
- Hydrolysed by Hepatic Triglyceride Lipase

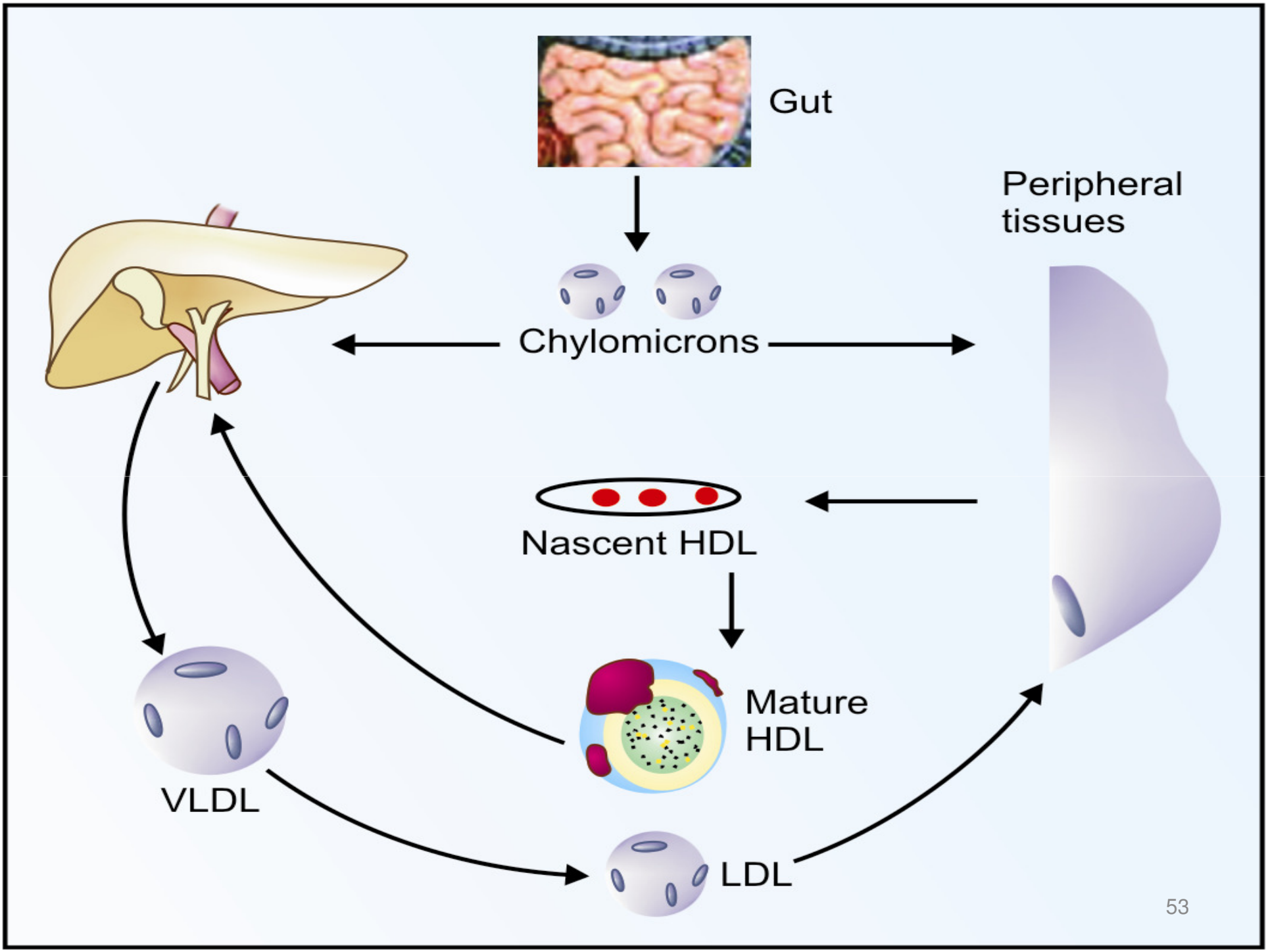

Liver
Bile C and bile acids
C CE PL
Hepatic lipase
SR-B1
Endothelial lipase
Synthesis
Phospholipid bilayer
Small intestine
Synthesis
PL C
A-I
LCAT
Discoidal HDL
Kidney
A-I
PL C
A-I
Preβ-HDL
Tissues
ABCA1
C
SR-B1
ABCG1
C CE PL
A-I
HDL2
C CE PL
A-I
LCAT
HDL3

High Density Lipoprotein Function

- Transport **cholesterol from peripheral tissue to liver.**
- Later excreted through bile.
- Called **Reverse cholesterol transport**
- Only excretory route of cholesterol is the bile.
- Excretion of cholesterol needs prior esterification with PUFA.
- **PUFA is anti-atherogenic**.

HDL Subfraction

- HDL-1
- **HDL-2 is Good – Anti-atherogenic**
    - HDL-2a
    - HDL-2b
- HDL-3
    - HDL-3a
    - HDL-3b
    - HDL-3c


Gut
Peripheral tissues
Chylomicrons
Nascent HDL
Mature HDL
VLDL
LDL

Free Fatty Acid

- Also known as N**on-Esterified Fatty Acids (NEFA).**
- It is complexed with **albumin** in plasma.
- Derived from lipolysis of TGs
- Transported
    - Heart
    - Skeletal muscle
    - Liver
    - Other soft tissues.
- Oxidized to supply energy
- Incorporated into tissue lipids by esterification.
- Half life of FFAs = only 1-2 minutes.

Plasma Lipid Profile

- Total - Cholesterol
- HDL - Cholesterol
- LDL - Cholesterol
- Triglycerides
- Apo-B level
- Apo-A-I level
- Lp(a) level
- Cholesterol / HDL Cholesterol Ratio
- LDL / HDL Cholesterol Ratio

Hypo-Lipoproteinemia

- **<u>Abeta Lipoproteinemia :</u>**
- Decrease All Apo-B containing lipoproteins
- Defect in **Microsomal Triglyceride Transfer Protein** .
- TG can not incorporated into VLDL and chylomicrons.
- LDL is absent.
- No Fat soluble vitamins absorption.
- Mental & Physical retardation.
- Blood TGs, cholesterol & phospholipids = Extremely low.
- Blindness may occur due to degenerative changes in retina.
- Erythrocytes have spiny projections **(Acanthocytes).**

Hypo-Lipoproteinemia

Hypo-Alphalipoproteinemia :

- Autosomal dominant condition
- HDL is decreased
- Increased risk of coronary artery diseases.

Tangier Disease

- Benign autosomal dominant condition.
- **ATP Binding Cassette Transporter-1 (ABC-1)** defective
- Defect in the efflux of cholesterol from cells to HDL
- Reduction of HDL levels
- Alpha band is absent in electrophoresis.
- Cholesterol esters are accumulated in tissues.
- **Manifestation**
    - Large orange yellow tonsils
    - Muscle atrophy
    - Recurrent peripheral neuropathies
    - Atherosclerosis.

Frederickson's classification of Hyper-lipoproteinemia

Type	Elevated Lipoprotein	Cholesterol	TG	Metabolic defect	Feature
Type -I	Chylomicron	N	Very High	Lipoprotein Lipase / Apo C-II deficiency	Xanthoma Hepatomegally
Type –IIA	LDL	High	N	LDL receptor defect Increase Apo B	Xanthoma Atherosclerosis
Type –IIB	LDL & VLDL	High	High	Increase Apo B	Corneal arcus
Type -III	Broad beta – VLDL & Chylomicron	High		Abnormal Apo-E / Increase Apo C-II	Palmar Xanthoma, Vascular disease
Type -IV	VLDL	N	High	Over production of VLDL, Increase Apo C-II	Associate with DM, Heart disease & Obesity
Type -V	VLDL Chylomicron	N	High	Secondary to other causes	IHD

Type I- Hyperchylomicronemia

- **Lipoprotein lipase deficiency**
- **Apo C-II deficiency**
- Manifestation in Young Age
- Severe Lipemic sample
- Lipemia retinalis
- Post Heparin Hepativ Lipolytic Absent

Type IIA- Primary Familial Hypercholesterolemia

- LDL receptor defect in Liver & Peripheral
  - Reduce number of LDL receptor deficiency
  - Defective binding of B-100 to LDL receptor.
    - Substitution of glutamine for arginine at 3500th AA in Apo B-100
    - **Familial Defect Apo B**
  - Receptor-LDL complex is not internalized
- Elevation of LDL
- Survival upto second decade of life
- Due to ischemic heart disease.

Type IIA- Secondary Familial Hypercholesterolemia

- Hypothyroidism
- Diabetes mellitus
- Nephrotic syndrome
- Cholestasis

Type IIB- Hypercholesterolemia

- Excessive production of Apo-B
- Elevation of both cholesterol and TGs
- LDL and VLDL are elevated.
- The abnormalities are manifested only by the third decade of life.

Type III- Hyperlipoproteinemia

- Rare
- Broad Beta Band observed in electrophoresis
- Increase LDL and IDL .
- Palmar Xanthomas and Vascular disease
- **Floating Beta disease**
- **Broad Beta disease**

Type IV- Familial Endogenous Type

- Over production of VLDL
- Over production of TGs by liver.
- Manifestation in 4^{th} decade
- Increase Apo C-II level

Type V- Hyperlipoproteinemia

- Increase VLDL and Chylomicron
- Secondary to other disease
  - Obesity
  - Excessive Alcoholic ingestion
  - Renal Failure
  - Pancreatitis
- Other causes of Hyperlipoproteinemia
  - Hepatic Lipase defect
  - LCAT defect
  - Lp(a) excess.
  - Wolman’s disease

Atherosclerosis

Pathogenesis of Atherosclerosis

- **Free Radical** convert LDL into **oxidized LDL**
- Oxidized LDL **deposited in the subintimal** regions of arteries.
- Accumulate into **Macrophages**
- Macrophages become overloaded with cholesterol
- "**Foam cells**"
- In Early stages - Reversible if LDL get decrease.
- **Atherosclerotic plaque** - Narrowing of Vessel.
- **Fibrous proliferation** - due to liberation of inflammatory mediator from macrophages & platelets.
- **Narrow lumen** = Turbulent = **Thrombosis**
- Ischemia of the tissue = **Infarction** = Death of tissue

Risk Factor for Atherosclerosis

Modifiable Risk Factor

- Increase high carbohydrate diet
- Increase high cholesterol containing diet
- Trans Fatty acid intake
- Western Pattern diet
  - Packed food
- Sedentary life style
- Obesity
- Addiction
  - Smoking – Alcohol

Risk Factor for Atherosclerosis

Modifiable Risk Factor

- Familiar history
- Polluted Air
- Radiation – Gamma radiation , X-ray , UV rays
- Chemical
- Drugs
- Medical Condition
  - Diabetes Mellitus
  - Hypertension
  - Chronic inflammatory disease
  - Dyslipidemia
  - Hyperhomocysteinemia

Risk Factor for Atherosclerosis

- Dyslipidemia
  - Increase Total cholesterol
    - Normal : < 199 mg %
    - Borderline : 200 – 239 mg%
    - Abnormal : > 240 mg%
  - Increase LDL cholesterol
    - Normal : < 130 mg %
    - Borderline : 130 – 160 mg%
    - Abnormal : > 160 mg%
  - Decrease HDL cholesterol
    - Good : > 60 mg %
    - Normal : 40 – 60 mg%
    - Abnormal : < 40 mg%

Risk Factor for Atherosclerosis

- Dyslipidemia
  - Total Cholesterol / HDL ratio
    - Risk > 3.5
  - LDL:HDL ratio
    - Risk > 2.5
  - Increase Triglyceride
  - Increase Lipoprotein-a
  - Ratio of Apo B:A-I
    - Normal = < 0.4 Very good
    - Risk = > 1.4

Risk Factor for Atherosclerosis

Non - Modifiable Risk factor

- Advance age
- Genetic abnomalities
- Chronic stress

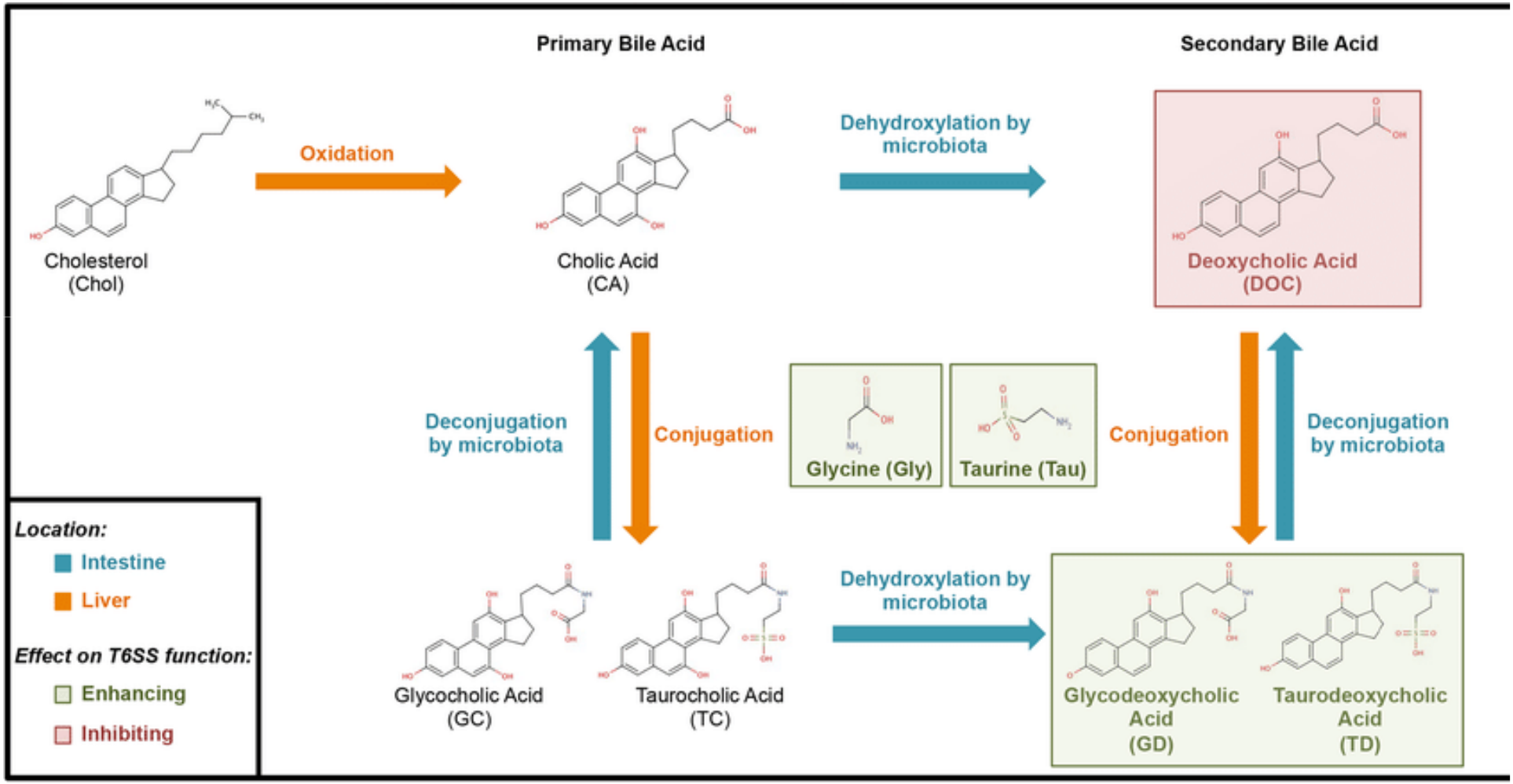
Prevention of Atherosclerosis

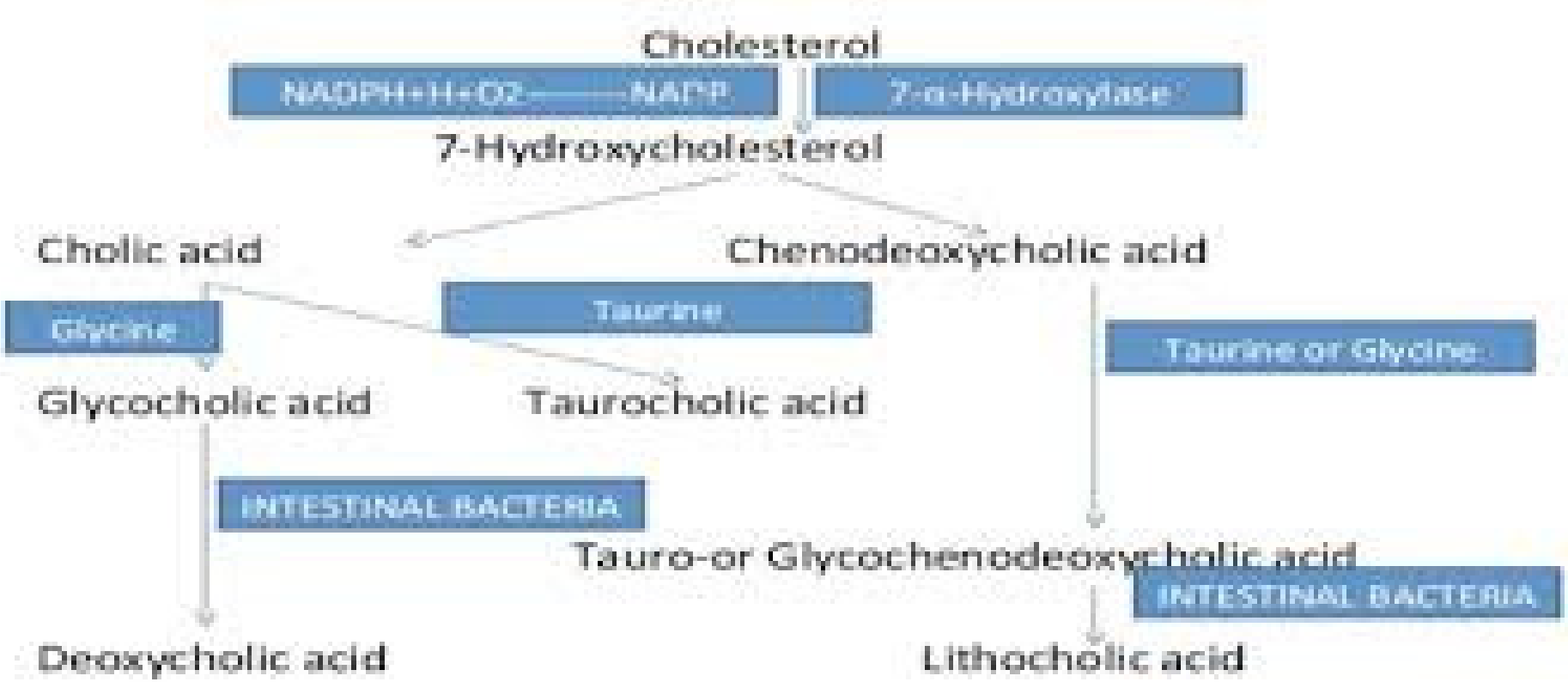
1. **Reduce Dietary cholesterol**
    - Eggs and meat contain high cholesterol so it should be avoided.
2. **Adequate intake of Vegetables oils and PUFA:**
    - Vegetable oils - Sunflower oil
    - Fish oils contain PUFA.
3. **High Fiber diet**
    - Green leafy vegetables – Salad – Fruits
    - Reduce reabsorption of bile salts
    - Decrease Choletserol
4. **Avoid High Carbohydrate diet with high glycemic index**
5. **Avoid Western Patten Diet – Pack food**
6. **Avoid cigarette smoking & Alcohol ingestion**

Prevention of Atherosclerosis

7. **Regular Exercise**
    - To reduce obesity
8. **Bile acid binding resins (cholestyramine)**
    - Decrease the reabsorption of bile acids.
9. **HMG CoA reductase inhibitors**
    - Statin drugs – Atorvastatin , Levostatin
10. **Nicotinic acid**
    - To reduce triglyceride and VLDL level
11. **Anti-Platelet**
    - Aspirin - To prevent thrombus formation
12. **Anti-oxidants**
    - Decrease oxidation of LDL
13. **Take regular medication for other medical disease – HT ,DM**

Bile Acid Synthesis




Cholesterol
NADPH+H+O2
NADP
7-α-Hydroxylase
7-Hydroxycholesterol
Cholic acid
Chenodeoxycholic acid
Taurine
Glycine
Taurine or Glycine
Glycocholic acid
Taurocholic acid
INTESTINAL BACTERIA
Tauro-or Glycochenodeoxycholic acid
INTESTINAL BACTERIA
Deoxycholic acid
Lithocholic acid

Thank You