Biological significance of cholesterol

BY
A.CAROLINE GRACE

INTRODUCTION

- **Cholesterol is found exclusively in animals, hence it is often called as animal sterol.**

- **Cholesterol is amphipathic in nature, since it possesses both hydrophilic and hydrophobic regions in the structure.**

- **Dietary sources of cholesterol is meat, egg and milk products.**

- **Cholesterol was first isolated from the gallstone in 1784.**

INTRODUCTION

Cholesterol

Cholesterol is the major sterol in animal tissues.
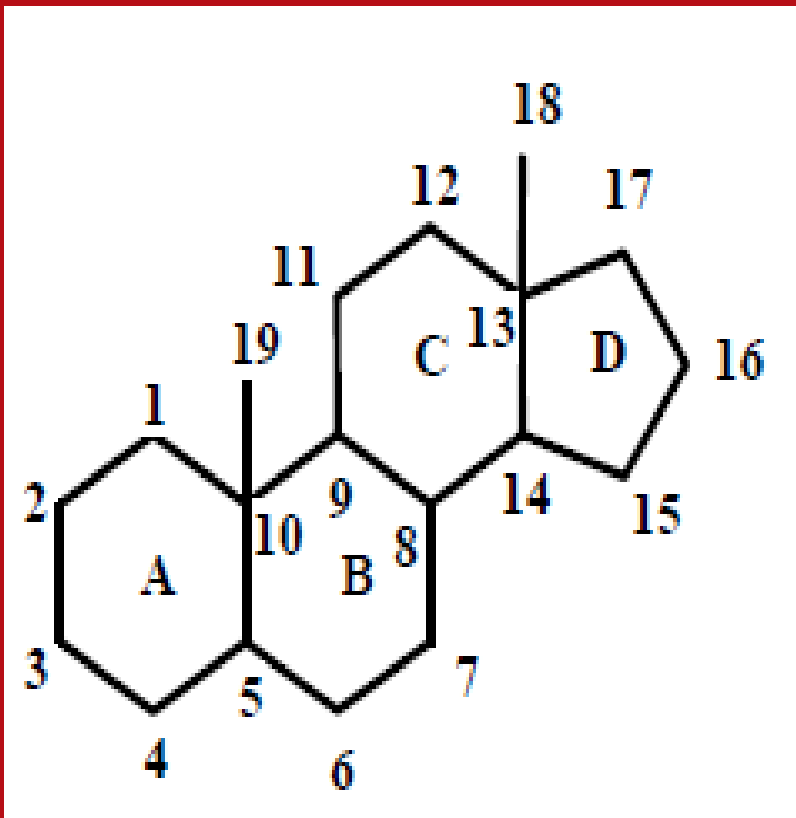
No vegetable oil contains any cholesterol.

Only a little portion of the body cholesterol is derived from diet.

The bulk of it is synthesized in the body.

STRUCTURE- CYCLOPENTANO PERHYDRO PHENANTHRENE RING

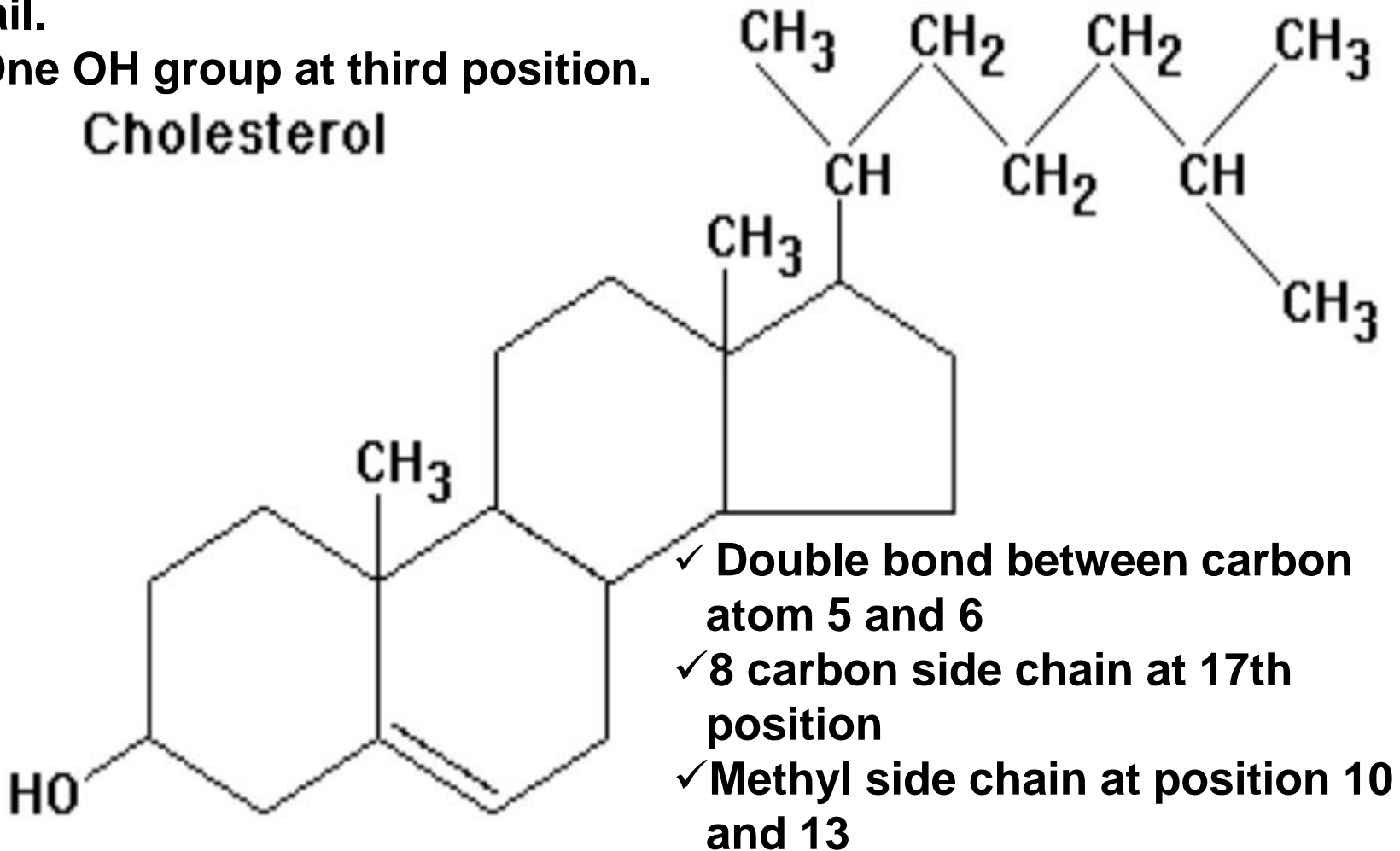✓ **Cholesterol contains a basic ring structure- cyclopentano perhydro phenanthrene ring**

✓ **The numbering of the ring system is given**

INTRODUCTION

✓ **Cholesterol contains 27 carbon atoms arranged into four fused rings (cyclopentano perhydro phenanthrene) and a hydrocarbon tail.**

✓**One OH group at third position.**

Cholesterol

CH_3 CH_2 CH_2 CH_3

CH CH_2 CH

CH_3 CH_3

CH_3

CH_3

HO

✓ **Double bond between carbon atom 5 and 6**

✓**8 carbon side chain at 17th position**

✓**Methyl side chain at position 10 and 13**

BIOLOGICAL SIGNIFICANCE

Cholesterol is essential to life, as it performs a number of important functions

1. It is a *structural component* of cell membrane.

2. Cholesterol is the precursor for the *synthesis of all other steroids* in the body. These include steroid hormones, vitamin D and bile acids.

3. It is an essential ingredient in the structure of *lipoproteins* in which form the lipids in the body are transported.

4. Fatty acids are transported to liver as cholesteryl esters for oxidation.

BIOSYNTHESIS OF CHOLESTEROL

➡ About 1 gm of cholesterol is synthesized per day in adults.

➡ Almost all tissues of the body participate in the cholesterol synthesis.

➡ The largest contribution is made by......

  ➢ LIVER (50%),

  ➢ INTESTINE (15%),

  ➢ SKIN,

  ➢ ADRENAL CORTEX,

  ➢ REPRODUCTIVE TISSUES.

BIOSYNTHESIS OF CHOLESTEROL

➡ The enzymes involved in the synthesis are found in the **CYTOSOL** and **MICROSOMAL** fractions of the cells.

➡ **Acetyl CoA** provides the carbon atoms in the cholesterol.

➡ The reducing equivalents are supplied by **NADPH** while **ATP** provides energy.

For production of 1 mole of cholesterol

✓ 18 moles of Acetyl CoA

✓ 36 moles of ATP

✓ 16 moles of NADPH

are required.

Steps of the Cholesterol Synthesis

Formation of HMG CoA

Formation of Mevalonate (6C)

Production of Isoprenoid units (5C)

Synthesis of Squalene

Conversion of .....

Squalene to Cholesterol (27C)

BIOSYNTHESIS OF CHOLESTEROL

Acetyl-coA

↓

HMG-CoA   **1**

↓

Mevalonate   **2**

↓

Isopentenyl pyro phosphate   **3**

↓

Squalene

↓   **4**

Lanosterol

↓   **5**

Cholesterol

BIOSYNTHESIS OF CHOLESTEROL

1. Synthesis of β-hydroxy β-methylglutaryl CoA (HMG CoA) : Two moles of acetyl CoA condense to form acetoacetyl CoA. Another molecule of acetyl CoA is then added to produce HMG CoA.

The cytosomal enzyme is involved in cholesterol synthesis whereas the mitochondrial HMG CoA synthase

2. Formation of mevalonate : *HMG CoA reductase* is the *rate limiting enzyme* in cholesterol biosynthesis. This enzyme is present in endoplasmic reticulum and catalyses the reduction of HMG CoA to mevalonate. The reducing equivalents are supplied by NADPH.

BIOSYNTHESIS OF CHOLESTEROL

Acetyl CoA ✚ Acetyl CoA

Thiolase → CoA-SH

Acetoacetyl CoA

— Acetyl CoA

HMG-CoA Synthase → CoA-SH

3-Hydroxy-3-Methyl Glutaryl-CoA (HMG-CoA)
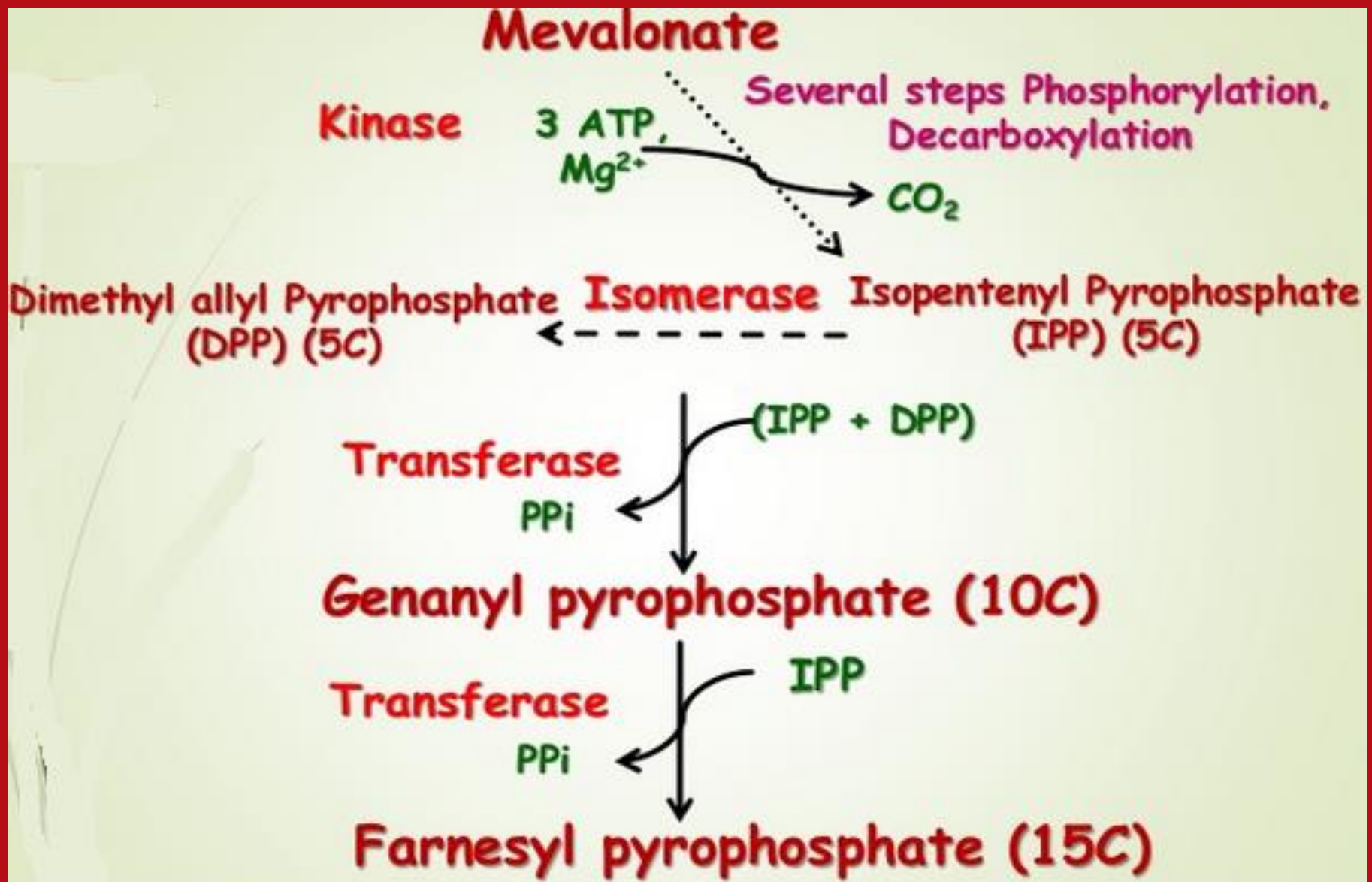
— 2 NADPH + 2H$^+$

HMG-CoA Reductase → 2 NADP$^+$ + CoA-SH$^+$

Mevalonate

BIOSYNTHESIS OF CHOLESTEROL

BIOSYNTHESIS OF CHOLESTEROL

3. Production of isoprenoid units : In a three-step reaction catalysed by kinases, mevalonate is converted to 3-phospho 5-pyrophospho-mevalonate which on decarboxylation forms isopentenyl pyrophosphate (IPP). The latter isomerizes to dimethylallyl pyrophosphate (DPP). Both IPP and DPP are 5-carbon isoprenoid units.

4. Synthesis of squalene : IPP and DPP condense to produce a 10-carbon geranyl pyrophosphate (GPP). Another molecule of IPP condenses with GPP to form a 15-carbon farnesyl pyrophosphate (FPP). Two units of farnesyl pyrophosphate unite and get reduced to produce a 30-carbon squalene.

BIOSYNTHESIS OF CHOLESTEROL

5. Conversion of squalene to cholesterol : Squalene undergoes hydroxylation and cyclization utilizing O_2 and NADPH and gets converted to lanosterol. The formation of cholesterol from lanosterol is a multistep process with a series of about 19 enzymatic reactions. The following are the most important reactions

- Reducing the carbon atoms from 30 to 27.
- Removal of two methyl groups from C_4 and one methyl group from C_{14}.
- Shift of double bond from C_8 to C_5.
- Reduction in the double bond present between C_{24} and C_{25}.

BIOSYNTHESIS OF CHOLESTEROL

2 Farnesyl pyrophosphate (15C)

Squalene synthetase

NADPH + H⁺

2 Farnesyl pyrophosphate combines

2PPi

NADP⁺

Squalene (30C)

Epoxidase
Hydroxylase
Cyclase

O2

NADPH + H⁺

O2, Several steps

NADP⁺

H2O

Lanosterol

NADPH + H⁺

O2, Several steps

NADP⁺

CO2,
COOH

CHOLESTEROL

BIOSYNTHESIS OF CHOLESTEROL

The enzymes (about 19?) involved in the conversion of lanosterol to cholesterol are associated with endoplasmic reticulum. 14-Desmethyl lanosterol, zymosterol, cholestadienol and desmosterol are among the intermediates in the cholesterol biosynthesis. *The penultimate product is 7-dehydrocholesterol which, on reduction, finally yields cholesterol.*

DEGRADATION OF CHOLESTEROL

Cholesterol undergo degradative reactions in humans with conversion of cholesterol to physiologically important products like,

Bile acids & Bile Salts
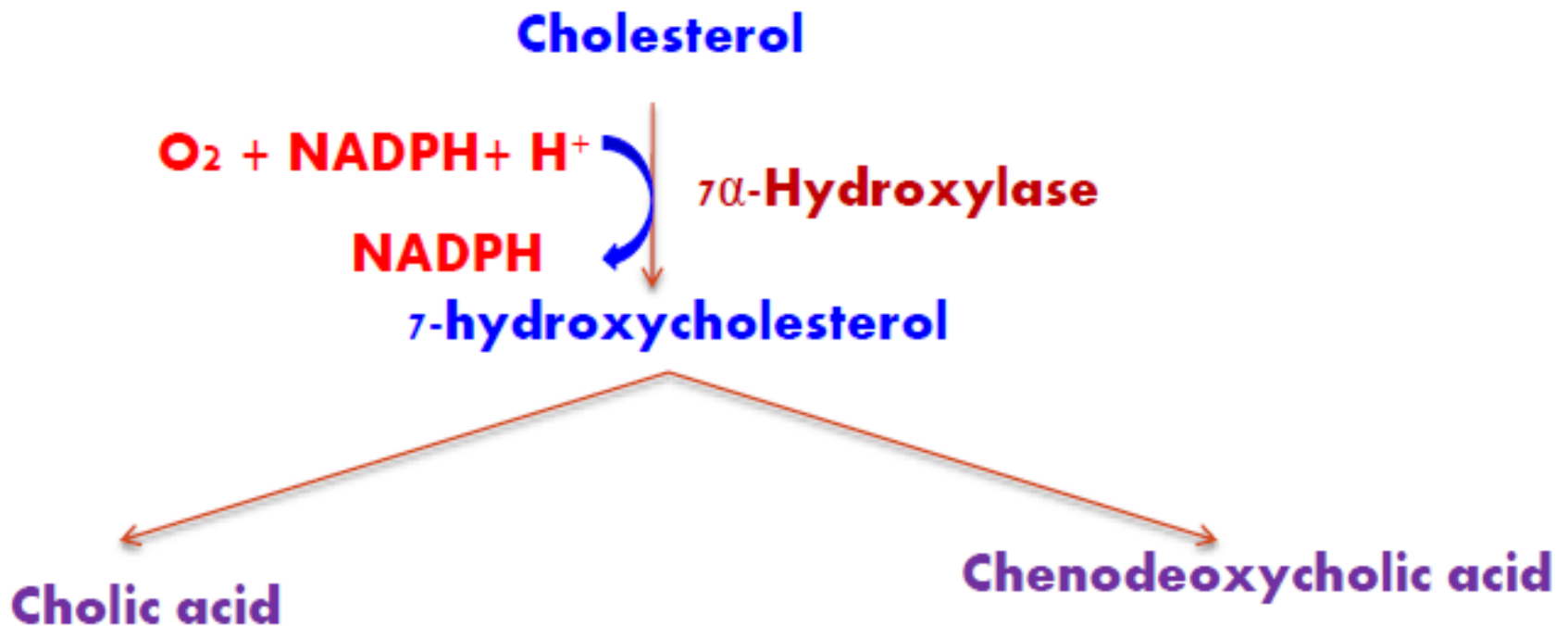
Steroid Hormones

Vitamin-D

CONVERSION OF CHOLESTEROL TO BILE ACIDS

- The primary bile acids are
  - ✓ Cholic acid
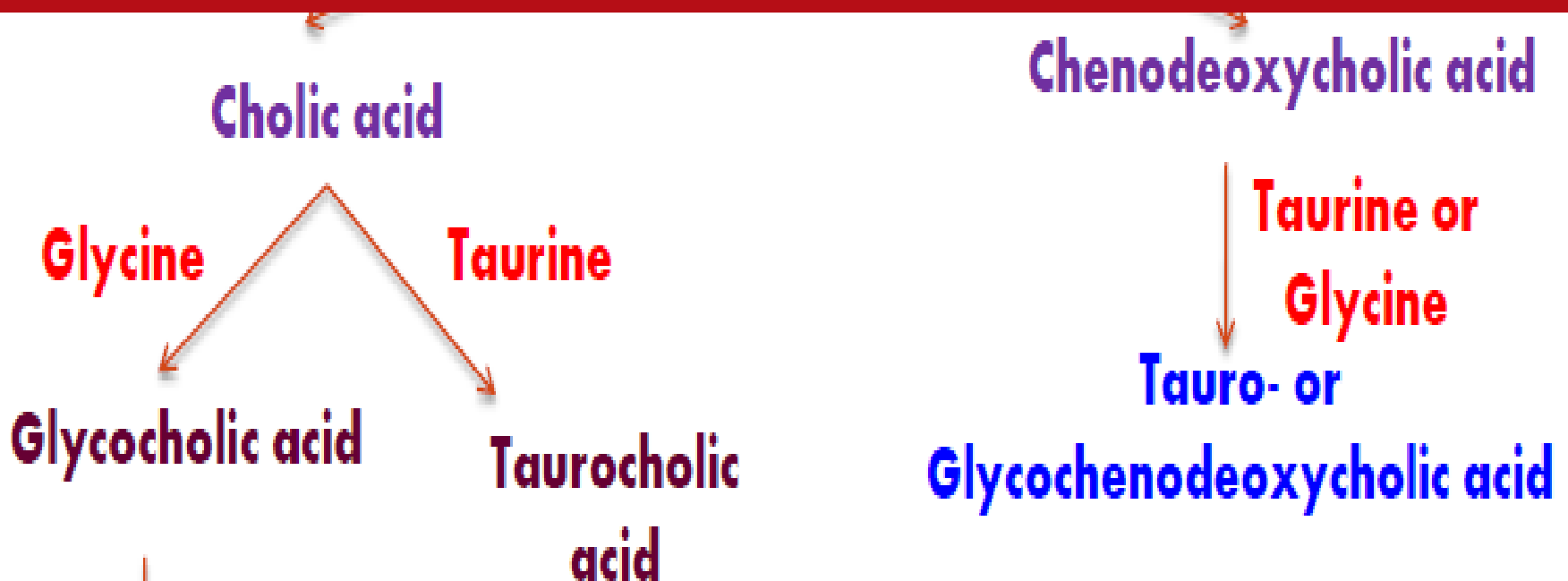 - ✓ Chenodeoxycholic acid
- synthesized in the liver from cholesterol by multistep pathways

Cholesterol

$O_2 + NADPH + H^+$

7α-Hydroxylase

NADPH

7-hydroxycholesterol

Cholic acid

Chenodeoxycholic acid

CONVERSION OF CHOLESTEROL TO BILE ACIDS

The primary bile acids are conjugate with glycine and taurine to form

❖ Glycocholicacid
❖ Taurocholic acid
❖ Glycochenodeoxycholic acid
❖ Taurochenodeoxycholic acid

Cholic acid

Glycine   Taurine

Glycocholic acid   Taurocholic acid

Chenodeoxycholic acid

Taurine or Glycine

Tauro- or Glycochenodeoxycholic acid

CONVERSION OF CHOLESTEROL TO BILE ACIDS

- The **primary bile acids are acted upon by the intestinal bacteria**, which results in deconjugation & decarboxylation to form secondary bile acids.

Glycocholic acid

Glycochenodeoxycholic acid

↓ Intestinal Bacteria

Intestinal Bacteria ↓

Deoxycholic acid

Lithocholic acid

CONVERSION OF CHOLESTEROL TO BILE ACIDS

Bile acid Synthesis

Cholesterol

O_2 + NADPH+ H^+
NADPH
7α-Hydroxylase

7-hydroxycholesterol

Cholic acid

Glycine — Taurine

Glycocholic acid

Taurocholic acid

Intestinal Bacteria

Deoxycholic acid

Chenodeoxycholic acid

Taurine or Glycine

Tauro- or Glycochenodeoxycholic acid

Intestinal Bacteria
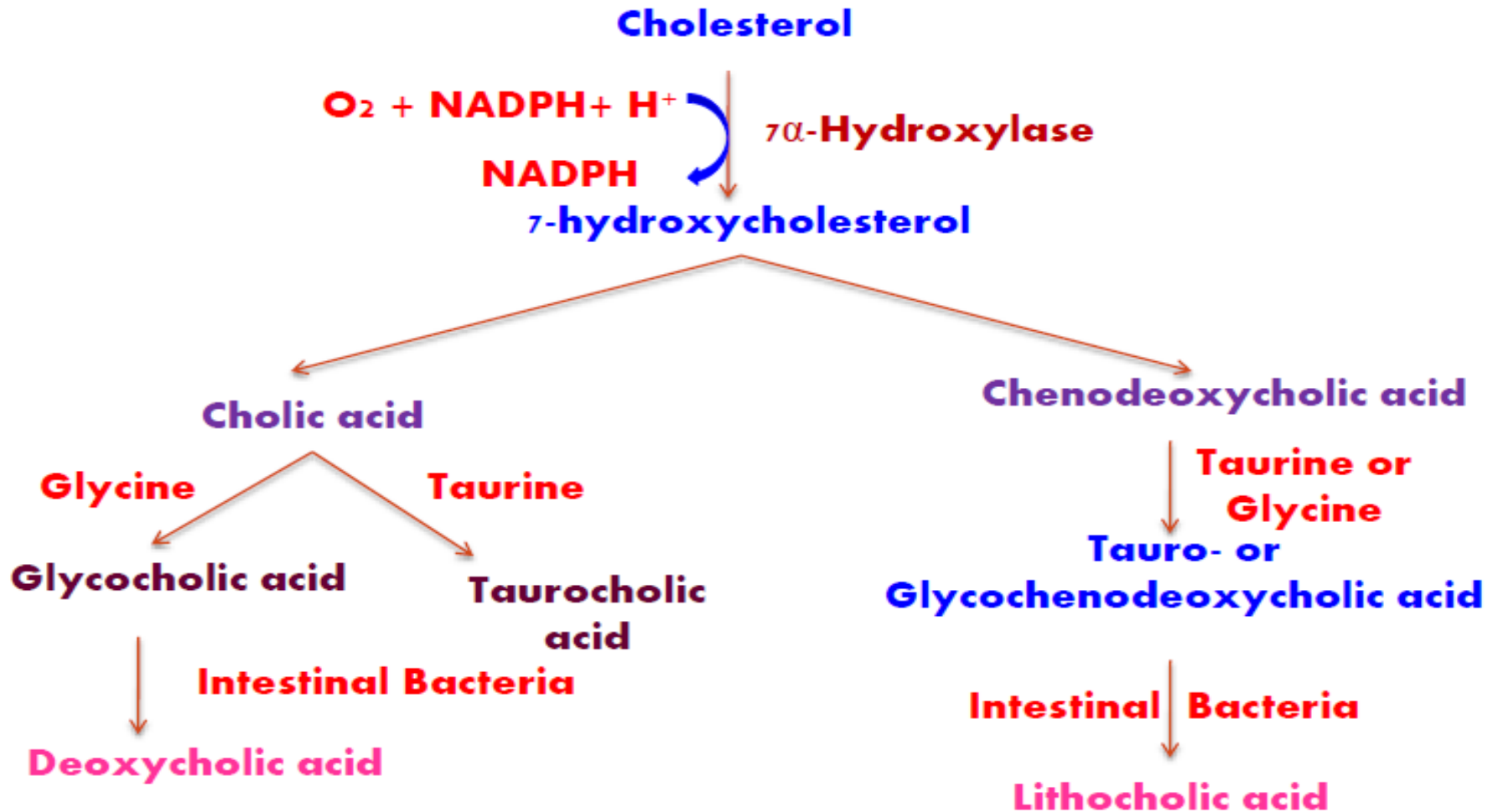
Lithocholic acid

BILE SALTS

Primary bile acids on conjugation with glycine or taurine, conjugated bile acids (glycocholic acid, taurocholic acid etc.) are formed which are more efficient in their function as surfactants.

In the bile, the conjugated bile acids exist as sodium and potassium salts, sodium taurocholate and sodium glycocholate, which are known as bile salts.

BILE SALTS

ENTEROHEPATIC CIRCULATION

➡ The conjugated bile salts are synthesized in liver and accumulated in the gall bladder.

➡ From there they are secreted into the small intestine where they are serve as a emulsifying agents for digestion and absorption of fat.

➡ A large portion of the bile salts are reabsorbed and returned to the liver through portal vein.

➡ Thus bile acids are recycled and reused several times in a day.

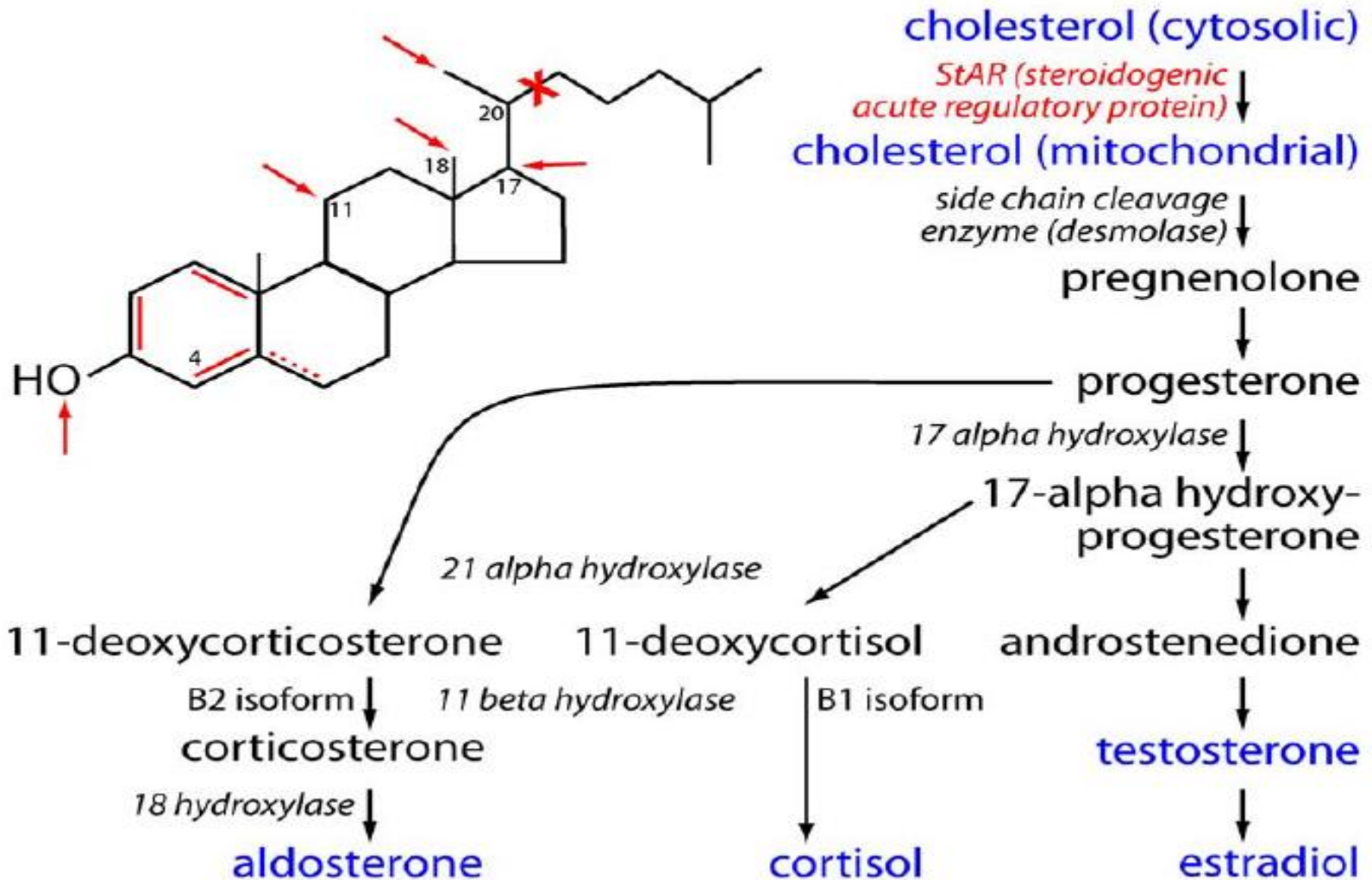➡ This is known as **Enterohepatic circulation**.

BILE SALTS

Cholelithiasis

- Bile salts & phospholipids are responsible for keeping the cholesterol in bile in a soluble state.

- Due to bile salts & phospholipids deficiency (particularly bile salts), cholesterol crystals precipitate in the gall bladder often resulting in cholelithiasis- cholesterol gall stone disease.

- Cholelithiasis may be due to defective absorption of bile salts from the intestine, impairment in liver function, obstruction of biliary tract etc.

CONVERSION OF CHOLESTEROL TO STEROID HORMONES

- Cholesterol is the **precursor** for the synthesis of all the five classes of **steroid hormones**

- Glucocorticoids (Cortisol)

- Mineralocorticoides (Aldosterone)

- Progestins (Progesterone)

- Androgens (Testosterone)

- Estrogens (Estradiol)

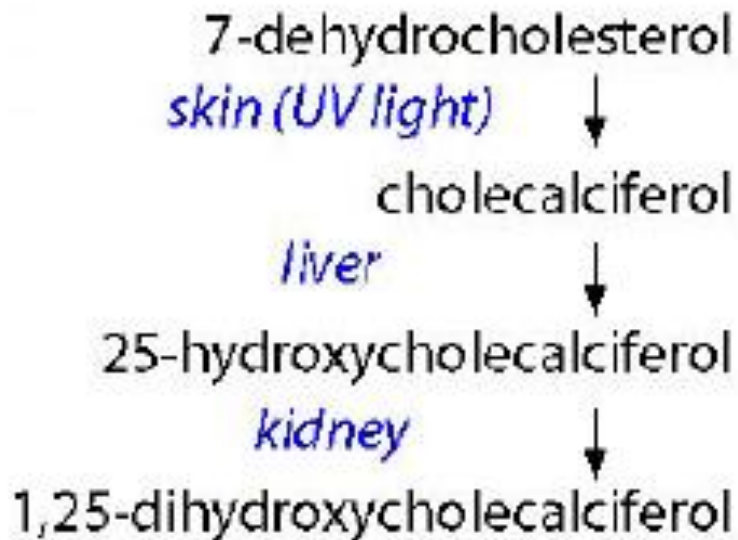# CONVERSION OF CHOLESTEROL TO STEROID HORMONES

Steroid hormones. This diagram is an overview of the process of steroid hormone biosynthesis in the human body, highlighting a key regulated step, several enzymes useful for understanding normal tissue specificity of these events, and several key products.

cholesterol (cytosolic)

StAR (steroidogenic acute regulatory protein)

cholesterol (mitochondrial)

side chain cleavage enzyme (desmolase)

pregnenolone

progesterone

17 alpha hydroxylase

17-alpha hydroxy-progesterone

21 alpha hydroxylase

11-deoxycorticosterone   11-deoxycortisol   androstenedione

B2 isoform   *11 beta hydroxylase*   B1 isoform

corticosterone   testosterone

18 hydroxylase

aldosterone   cortisol   estradiol

CONVERSION OF CHOLESTEROL TO VITAMIN-D

Synthesis of vitamin D

- **7-Dehydrocholesteroal,** an intermediate in the synthesis of cholesterol, is **converted to cholecalciferol** (vitamin D$_3$) UV rays in the skin.

7-dehydrocholesterol
skin (UV light) ↓
cholecalciferol
liver ↓
25-hydroxycholecalciferol
kidney ↓
1,25-dihydroxycholecalciferol

7-Dehydrocholesterol is Converted to vitamin D through various Enzymatic reactions occur in liver and kidney.

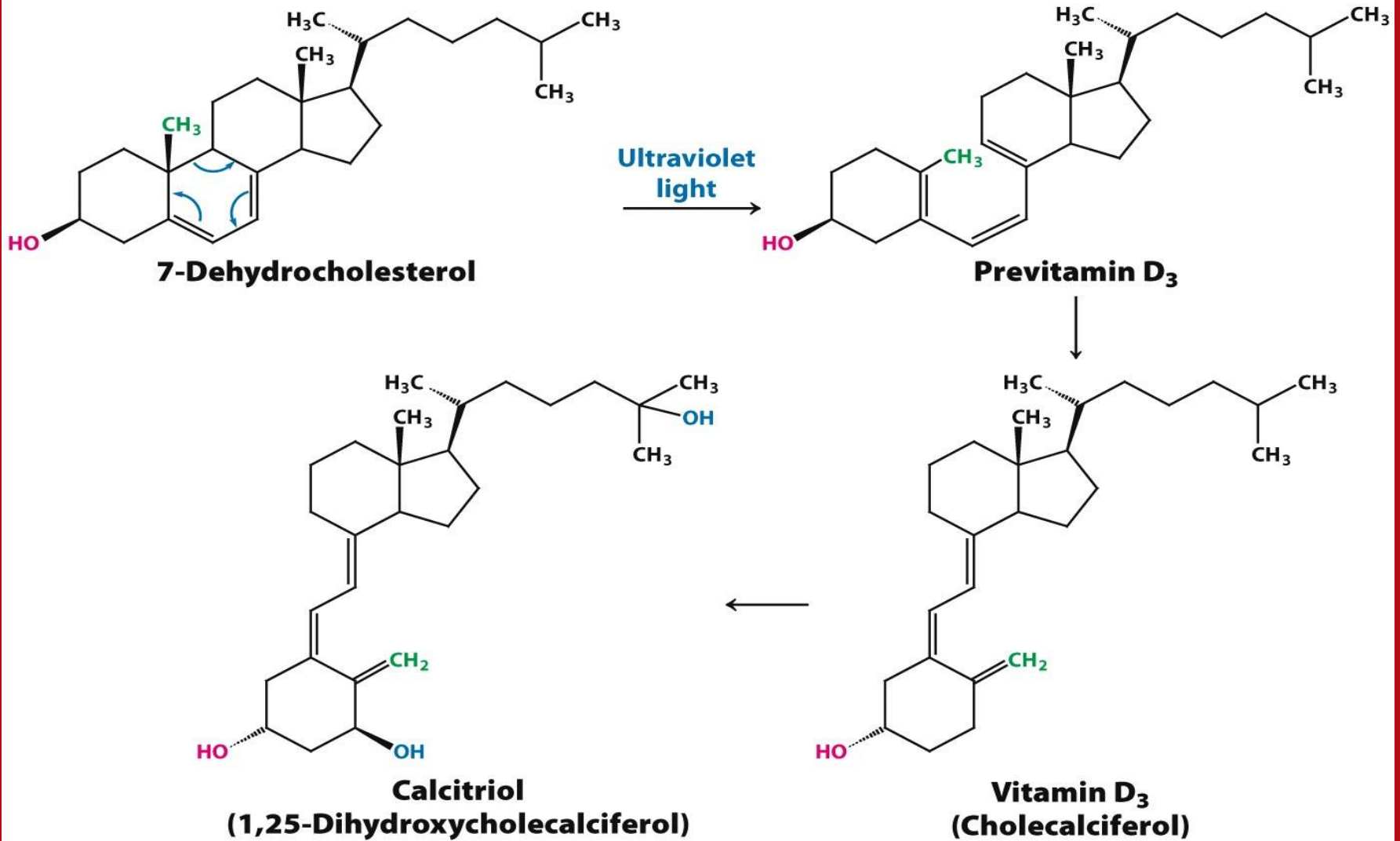# CONVERSION OF CHOLESTEROL TO VITAMIN-D

Figure 26.32
Biochemistry, Seventh Edition
© 2012 W. H. Freeman and Company

TRANSPORT OF CHOLESTEROL

- Cholesterol is present in the plasma lipoproteins in **two forms**

- About 70-75% of it is in an esterified form with long chain fatty acids.

- About 25-30% as free cholesterol.

- Free cholesterol readily exchanges between different lipoproteins & also with the cell membranes.

# TRANSPORT OF CHOLESTEROL

Role of LCAT

- **High density lipoproteins** (HDL) **& the enzyme lecithin-cholesterol acyltransferase** (LCAT) **are responsible for the transport & elimination of cholesterol from the body.**

- **LCAT is a plasma enzyme, synthesized by the liver.**

- It catalyses the transfer of fatty acid from the second position of phosphatidyl choline (lecithin) to the hydroxyl group of cholesterol.

- HDL-cholesterol is the real substrate for LCAT & this reaction is freely reversible.

- LCAT activity is associated with apo-A$_1$ of HDL.

TRANSPORT OF CHOLESTEROL

Reaction catalyzed by LCAT

Phosphatidylcholine   Cholesterol

Lecithin cholesterol acyltransferase (LCAT)

Lysophosphatidylcholine   Cholesterol ester
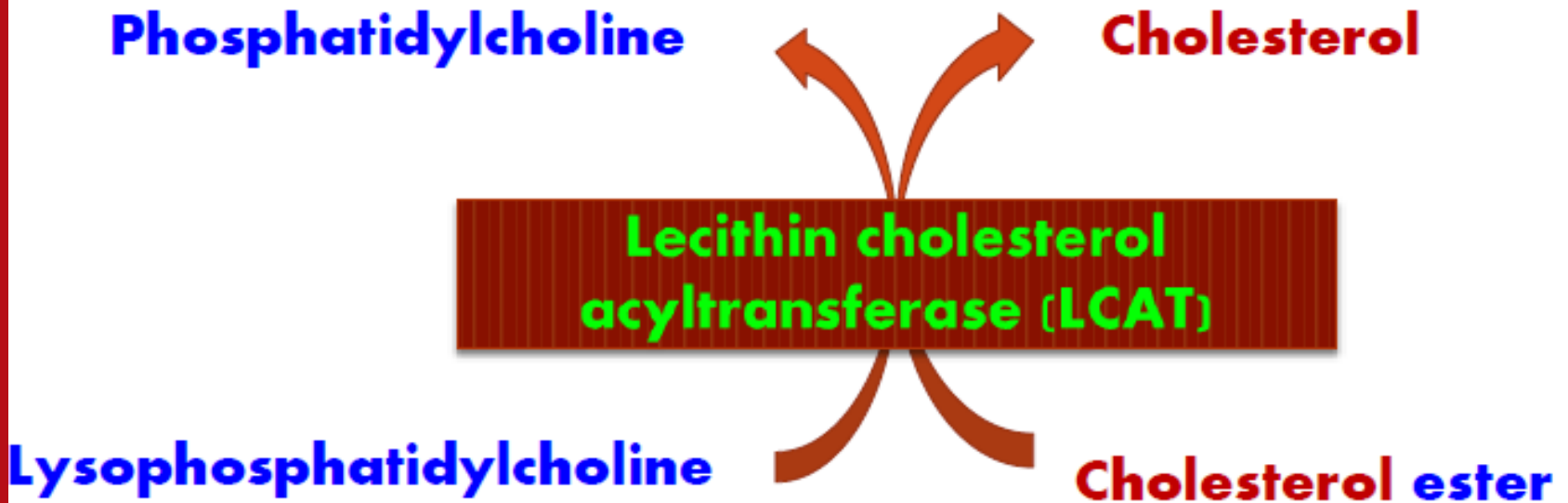
Cholesterol contains

a)30 carbon atoms
b)17 carbon atoms
c)27 carbon atoms
d)15 carbon atoms

ANSWER: 27 Carbon atoms   (c)

Isomer of Isopentrnyl pyrophosphate is

a) Geranyl pyrophosphate
b) Farnesyl pyrophosphate
c) Dimethyl allyl pyrophosphate
d) None of the above

ANSWER: Dimethyl allyl pyrophosphate (c)

Number of molecules of acetyl COA needed for The synthesis of one mole of cholesterol

a) 18 molecules
b) 17 molecules
c) 15 molecules
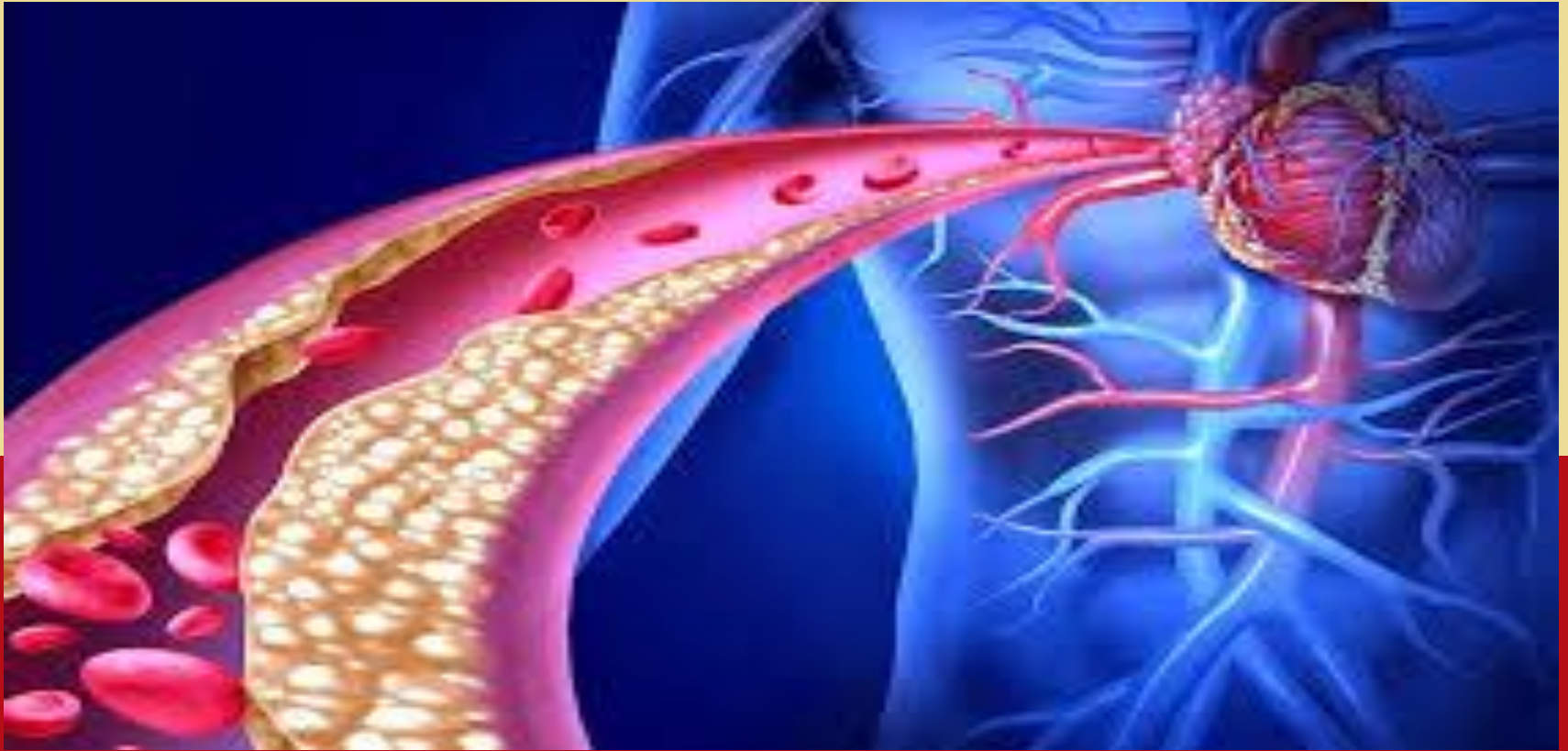d) 21 molecules

ANSWER: 18 molecules   (a)

Which intermediate of cholesterol synthesis is used as the starting material for the syntheis of Vitamin D

a) Squalene
b) Lanosterol
c) Zymosterol
d) 7-Dehydro chloesterol

ANSWER: 7-Dehydro chloesterol   (d)

DISORDERS OF LIPID METABOLISM

BY
A.CAROLINE GRACE

INTRODUCTION

❀ **Lipids are insoluble in aqueous solutions.**

❀ **Hence lipids (mainly cholesterol) are transported in a protein capsules called lipproteins.**

❀ **Cholesterol is a waxy, fat-like substance made in the liver and other cells. It's also found in certain foods, such as dairy products, eggs, and meat.**

❀ **Human body needs some cholesterol to function properly**

INTRODUCTION

❀ cell walls, also known as membrane, it's major structural component is cholesterol, and also cholesterol is needed to produce hormones, vitamin D, and the bile acids that helps you to digest fat.

❀ But the body needs a limited amount of cholesterol.

❀ In healthy individuals, the total plasma cholesterol is in the range of 150-200 mg/dl.

❀ Cholesterol travels through the blood after attached to a protein. The combination protein and cholesterol is called a lipoprotein.

INTRODUCTION

* Plasma cholesterol is associated with different lipoprotein fractions (LDL, VLDL and HDL).

* There are three types of lipoproteins in your blood: high density, low density, and very low density.

* The specific type depends on how much protein there is in relation to fat.

INTRODUCTION

Lipoproteins are *molecular complexes* that consist *of lipids and proteins* (conjugated proteins). They function as transport vehicles for lipids in blood plasma. Lipoproteins deliver the lipid components (cholesterol, triacylglycerol etc.) to various tissues for utilization.

Structure of lipoproteins

A lipoprotein basically consists of a neutral lipid core (with triacylglycerol and/or cholesteryl ester) surrounded by a coat shell of phospholipids, apoproteins and cholesterol `. The polar portions (amphiphilic) of phospholipids and cholesterol are exposed on the surface of lipoproteins so that lipoprotein is soluble in aqueous solution.

INTRODUCTION

* **Low density lipoproteins (LDL) are also called "bad" cholesterol because it can deposit buildup a coat on the walls of arteries. The more LDL there is in the blood, the greater the risk of heart disease.**

* **High density lipoproteins (HDL) are also called "good" cholesterol. It helps the body get rid of LDL. Maintaining a higher level of HDL is good. If your HDL level is low your risk of heart disease goes up.**

* **Very low density lipoproteins (VLDL) are similar to LDL in that it contains mostly fat and not much protein.**

* **Triglycerides, another type of fat, are carried in the blood by VLDL. Excess calories, alcohol, or sugar in your body are converted into triglycerides and stored in fat cells throughout your body.**

INTRODUCTION

❀ **In adults, the normal LDL-cholesterol is about 80-150 mg/dl**

❀ **while HDL-cholesterol is around 30-60 mg/dl.**

❀ **Elevation in plasma HDL cholesterol is beneficial to the body, since it protects the body from atherosclerosis and coronary heart diseases (CHD).**

❀ **On the other hand, increase in LDL-cholesterol is harmful to the body as it may lead to various complications, including CHD.**

Hypercholesterolemia

Hypercholesterolemia or hyperlipidemia or dyslpidemia is the presence of increased or abnormal levels of lipids or lipoproteins in blood

Increase in plasma cholesterol (> 200 mg/dl) concentration is known as hypercholesterolemia and is observed in many disorders

1. **Diabetes mellitus** : Due to increased cholesterol synthesis since the availability of acetyl CoA is increased.

2. **Hypothyroidism (myxoedema)** : This is believed to be due to decrease in the HDL receptors on hepatocytes.

3. **Obstructive jaundice** : Due to an obstruction in the excretion of cholesterol through bile.

Hypercholesterolemia

Bad cholesterol and good cholesterol :

The cholesterol in high concentration, present in *LDL*, is considered *bad* due to its involvement in altherosclerosis and related complications. Thus, LDL may be regarded as *l*ethally *d*angerous *l*ipoprotein. Small dense LDL (*sdLDL*) is considered to be the *most dangerous fraction of LDL* associated with CHD. On the other hand, *HDL cholesterol* is *good*

Hypercholesterolemia

LIFE STYLE FACTORS INLUENCES CHOLESTEROL LEVEL

DIET

Saturated fat and cholesterol in the food you eat increase cholesterol levels. To lower your cholesterol level, try to reduce the saturated fat and cholesterol in your diet.

WEIGHT

In addition to being a risk factor for heart disease, being overweight can also increase cholesterol. Losing weight can help lower your LDL and total cholesterol. And it can also increase the level of HDL.

EXERCISE

Regular exercise can lower LDL and raise HDL. You should try to be physically active for at least 30 minutes on most days.

Hypercholesterolemia

LIFE STYLE FACTORS INLUENCES CHOLESTEROL LEVEL

AGE AND GENDER
As you get older, cholesterol levels rise. Before menopause, women tend to have lower total cholesterol levels than men. After menopause, though, women's LDL levels tend to rise.

DIABETES
Poorly controlled diabetes increases cholesterol levels. Having control of your diabetes can cause your cholesterol levels to fall.

HEREDITY
Your genes partly determine how much cholesterol your body makes. High blood cholesterol can run in families.

OTHER FACTORS
Certain medications and medical conditions can cause high cholesterol.

Hypercholesterolemia

Control of hypercholesterolemia

Several measures are advocated to lower the plasma cholesterol level

Consumption of PUFA : Dietary intake of polyunsaturated fatty acids (PUFA) *reduces the plasma cholesterol level*. PUFA will help in transport of cholesterol by LCAT mechanism (described earlier) and its excretion from the body. The oils with rich PUFA content include cottonseed oil, soya bean oil, sunflower oil, corn oil, fish oils etc. Ghee and coconut oil are poor sources of PUFA.

Plant sterols : Certain plant sterols and their esters (e.g. sitostanol esters) *reduce* plasma cholesterol levels. They inhibit the intestinal absorption of dietary cholesterol.

Hypercholesterolemia

Hypercholesterolemia

Dietary fiber : Fiber present in vegetables decreases the cholesterol absorption from the intestine.

Avoiding high carbohydrate diet : Diets rich in carbohydrates (e.g. sucrose) should be avoided to control hypercholesterolemia.

Impact of lifestyles : Elevation in plasma cholesterol is obseved in people with smoking, abdominal obesity, lack of exercise, stress, high blood pressure, consumption of soft water etc. Therefore, adequate changes in the lifestyles will bring down plasma cholesterol.

Use of drugs : Drugs such as *lovastatin* which inhibit HMG CoA reductase and decrease cholesterol synthesis are used. Statins currently in use include atorvastatin, simvastatin, fluvastatin and pravastatin.

FATTY LIVER

The normal concentration of lipid (mostly phospholipid) in liver is around 5%. Liver is not a storage organ for fat, unlike adipose tissue. However, in certain conditions, lipids—especially the *triacylglycerols—accumulate* excessively in liver, resulting in fatty liver

This causes

impairment in metabolic functions of liver. Fatty liver is associated with fibrotic changes and cirrhosis, Fatty liver may occur due to two main causes.

1. Increased synthesis of triacylglycerols

2. Impairment in lipoprotein synthesis.

FATTY LIVER

1. **Increased triacylglycerol synthesis** : Mobilization of free fatty acids from adipose tissue and their influx into liver is much higher than their utilization. This leads to the overproduction of triacylglycerols and their accumulation in liver. *Diabetes mellitus, starvation, alcoholism* and *high fat diet* are associated with increased mobilization of fatty acids that often cause fatty liver. Alcohol also inhibits fatty acid oxidation and, thus, promotes fat synthesis and its deposition.

FATTY LIVER

2. Impaired synthesis of lipoproteins : The synthesis of very low density lipoproteins (VLDL) actively takes place in liver. VLDL formation requires phospholipids and apoprotein B. Fatty liver caused by impaired lipoprotein synthesis may be due to :

- a defect in phospholipid synthesis;
- a block in apoprotein formation;

- a failure in the formation/secretion of lipo-protein.

Among the three causes, fatty liver due to impairment in phospholipid synthesis has been studied in some detail. This is usually associated with the dietary *deficiency of lipotropic factors* such as choline, betaine, inositol etc.

FATTY LIVER

Certain chemicals (e.g. puromycin, ethionine, carbon tetrachloride, chloroform, lead, phosphorus etc.) that inhibit protein synthesis cause fatty liver. This is due to a blockade in the synthesis of apoprotein B required for VLDL production.

Lipoprotein synthesis and their secretion require ATP. Decrease in the availability of ATP, sometimes found in pyridoxine and pantothenic acid deficiency, impairs lipoprotein formation. The action of ethionine in the development of fatty liver is believed to be due to a reduction in the availability of ATP. Ethionine competes with methionine and traps the available adenosine (as adenosylethionine)—thereby reducing ATP levels.

OBESITY

- A life-long, progressive, life-threatening, costly, genetically-related, multi-factorial disease of excess fat storage with multiple co-morbidities

OBESITY

- **WHO Definition**: Obesity and overweight are defined as an accumulation of excess body fat, to an extent that may impair health.

- A crude population measure of excess fat is the body mass index (BMI), a person's weight (in kilograms) divided by the square of his/her height (in metres).

- WHO defines overweight as a BMI of 25 or more, and obesity as a BMI of 30 or more.

OBESITY

Body mass index (BMI)

Clinical obesity is represented by body mass index. BMI is calculated as the weight (in kilograms) divided by the height (in meters^2).

$$BMI\ (kg/m^2) = \frac{Weight\ (kg)}{[height\ (m)^2]}$$

Healthy reference range for BMI is between 18.5–24.9 kg/m^2.

- Grade I obesity or overweight – BMI 25–30 kg/m^2
- Grade II or clinical obesity – BMI > 30 kg/m^2
- Grade III or morbid obesity – BMI > 40 kg/m^2

Obesity is associated with many health complications e.g. type II diabetes, CHD, hypertension, stroke, arthritis, gall bladder disease.

OBESITY

This formula will give you your body mass index (BMI). the obesity is diagnosed when the (BMI) is 30 or more. now look to this table below to know more about the (BMI).

BMI	Result
Less than 18.5	Underweight
18.8-24.9	Normal
25-29.9	Overweight
30-40	Obese
More than 40	very obese

OBESITY

What are the complications of obesity?

Now is obesity dangerous, the answer is yes, and if you are obese you are at risk to have one or more of a great number of obesity health problems. including:

- Type 2 diabetes.
- High blood pressure.
- Stroke.
- Heart disease.
- Gallbladder disease.
- Osteoarthritis.
- poor wound healing.
- Sleep apnea,(dangerous sleep disorder in which breathing repeatedly stops and starts).
- High cholesterol and triglycerides.
- Metabolic syndrome.
- Cancer.
- Depression.

OBESITY

So the causes of obesity is a combination of states and risk factors that work together to store more fat in our bodies, and these factors include:

•**Inactivity:**
 without activity you don't burn as much calories. and you need to have more exercise to burn the excessive calories.

OBESITY

•**Diets:** some bad eating habits like high calories diets epically in the night, or skipping a healthy breakfast, and replace it by junk fast food, all of that increase the body fat .

•**Pregnancy:** some women after the baby is born have an increasing in their weight, and if they don't lose that weight, with many pregnancies after that, they may become obese.

OBESITY

•**Lack of sleep:** this cause disturbances in the body hormones, and increase the appetite. you also may crave to height calories food.

•**Drugs:** some medications lead the body to gain more weight, these drugs include, diabetes medications, steroids and beta blockers, anti-seizure medications, antipsychotic medications and antidepressants drugs.

OBESITY

•Medical conditions: some diseases and syndromes lead the body to store more fat and gain weight like Cushing syndrome. some disease low the metabolic rate in the body and low the amount of burned calories every day such as the hypothyroidism. And some diseases lead the patient to low his activity, such as the arthritis or maybe the patients with paraplegia

Cush synd: high levels of the hormone cortisol for a long time

•Genetics: genes affect the amount of body fat we store and where to store,

•Family lifestyle: not because of the genes we find the obesity runs in the families, it also because of their life style and the food they eat. We can notice that some countries such as USA, have more obese people than others countries like Japan and this is because the culture and the life style.

OBESITY

•**Age:** obesity could occur at any age, but when we get age we lose more amount of muscles built. more amount of muscles give higher rate of metabolism and calories burning. When we lose them we reduce the calories burning and tend to fill the body with fat.

ATHEROSCLEROSIS

Definition:

- Arteriosclerosis occurs when the blood vessels that carry oxygen and nutrients from your heart to the rest of your body (arteries) become thick and stiff — sometimes restricting blood flow to your organs and tissues.

- Healthy arteries are flexible and elastic, but over time, the walls in your arteries can harden, a condition commonly called hardening of the arteries.

NORMAL BLOOD FLOW

BLOCKED ARTERY due to atherosclerosis
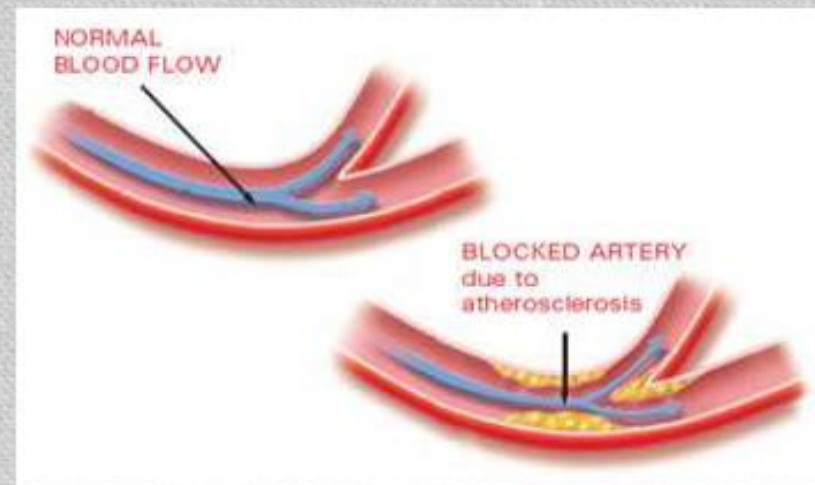
ATHEROSCLEROSIS

- Atherosclerosis is a specific type of arteriosclerosis, but the terms are sometimes used interchangeably.

- Atherosclerosis refers to the build-up of fats, cholesterol and other substances in and on your artery walls (plaques), which can restrict blood flow.

- These plaques can burst, triggering a blood clot. Although atherosclerosis is often considered a heart problem, it can affect arteries anywhere in your body.

- Atherosclerosis usually is preventable and is treatable.

Plaque Buildup on Artery Walls

1   2   3   4

ATHEROSCLEROSIS

Causes of atherosclerosis and CHD : The development of atherosclerosis and the risk for the coronary heart disease (CHD) is directly correlated with plasma cholesterol and LDL. On the other hand, plasma HDL is inversely correlated with CHD.

Disorders that may cause atherosclerosis

Certain diseases are associated with atherosclerosis. These include diabetes mellitus, hyperlipoproteinemias, nephrotic syndrome, hypothyroidism etc. Many other factors like obesity, high consumption of saturated fat, excessive smoking, lack of physical exercise, hypertension, stress etc., are the probable causes of atherosclerosis.

ATHEROSCLEROSIS

Relation between HDL and CHD

The increased levels of plasma HDL (good cholesterol) are correlated with a low incidence of cardiovascular disorders. *Women* have higher HDL and are *less prone to heart diseases* compared to men. This is attributed to *estrogens* in women. Strenuous physical exercise, moderate alcohol intake, consumption of unsaturated fatty acids (vegetable and fish oils), reduction in body weight—all tend to increase HDL levels and reduce the risk CHD

Antioxidants and atherosclerosis

Antioxidants, in general, decrease the oxidation of LDL. There is some evidence, based on the epidemiological studies that taking of antioxidants (vitamins E and C or β-carotene) reduces the risk of atherosclerosis, and CHD.

ATHEROSCLEROSIS
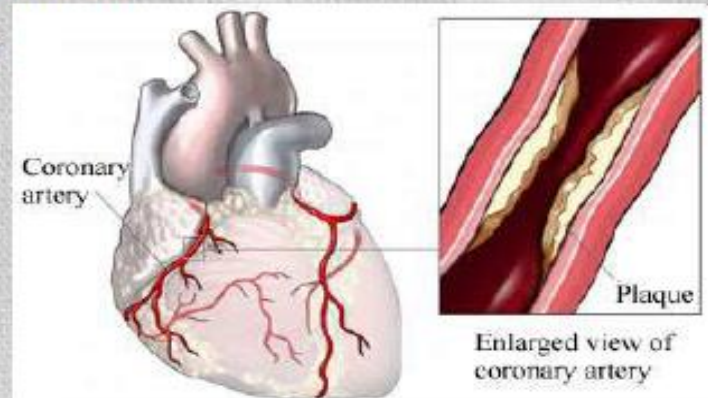
Types of atherosclerosis:

- Atherosclerosis can occur anywhere in the body, including the heart, legs, and kidneys.

Coronary Artery Disease

- This condition occurs when the coronary arteries of the heart become hard. The coronary arteries are blood vessels that provide the heart's muscle tissue with oxygen and blood. Plaque prevents blood flow to the heart.

Carotid Artery Disease

- The carotid arteries are found in your neck and supply blood to your brain. These arteries may be compromised if plaque builds up in their walls. The lack of circulation may cause a decrease of blood and oxygen to the brain's tissue and cells.

Coronary artery

Plaque

Enlarged view of coronary artery

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Symptoms:

Most symptoms of atherosclerosis do not show until a blockage occurs. Common symptoms include:

- chest pain (angina)
- pain in the leg, arm, and anywhere else that an artery is blocked
- shortness of breath
- fatigue
- confusion (if the blockage affects circulation to the brain)
- muscle weakness in the legs from lack of circulation

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- Blood tests: used to evaluate kidney and thyroid function as well as to check cholesterol levels and the presence of anemia.

- Chest X-ray: shows the size of your heart and whether there is fluid build up around the heart and lungs.

- Echocardiogram: shows a graphic outline of the heart's movement

- Ejection fraction (EF): determines how well your heart pumps with each beat.

- Treatment:

  - Lifestyle changes

  - Medications

  - Angiography and stenting

  - Bypass surgery

SUMMARY

Hypercholesterolemia or hyperlipidemia or dyslpidemia is the presence of increased or abnormal levels of lipids or lipoproteins in blood

☞ Hypercholesterolemia is associated with atherosclerosis and coronary heart diseases. Consumption of polyunsaturated fatty acids and fiber decreases cholesterol in circulation. Drugs—such as lovastatin, cholestyramine, compactin and clofibrate—reduce plasma cholesterol.

☞ Excessive accumulation of triacylglycerols causes fatty liver which can often be prevented by the consumption of lipotropic factors (choline, betaine, methionine).

☞ Obesity is an abnormal increase in body weight due to excessive fat deposition (>25%). Overeating, lack of exercise and genetic predisposition play a significant role in the development of obesity.

SUMMARY

☞ Atherosclerosis is characterized by hardening of arteries due to the accumulation of lipids and other compounds. The probable causes of atherosclerosis include hyperlipoproteinemias, diabetes mellitus, obesity, high consumption of saturated fat, lack of exercise and stress.

☞ Atherosclerosis and coronary heart disease are directly correlated with plasma cholesterol and LDL, inversely with HDL. Elevation of plasma lipoprotein a suggests increased risk of CHD.

☞ Alcoholism is associated with fatty liver, hyperlipidemia and atherosclerosis.

What is atherosclerosis

a. A weakening of the heart muscle
b. The narrowing and hardening of arteries
c. The formation of blood clots in veins
d. All of the above

ANSWER: The narrowing and hardening of arteries   (b)

The classes of dietary fatty acids which have the most beneficial effect on plasma LDL cholesterol levels?

a) polyunsaturated fatty acids
b) Saturated and trans unsaturated fatty acids
c) Monounsaturated fatty acids
d) Both a and c

ANSWER: polyunsaturated fatty acids   (a)

The supplementation of diet with which fat soluble vitamins has been shown to reduce cardiovascular disease?

a) Vitamin A and D
b) Vitamin A and K
c) Vitamin D and E
d) None of the above

ANSWER: **Vitamin D and E** **(c)**

Besides high cholesterol, which of these can make it more likely that you will get heart disease?
a. Cigarette smoking
b. High blood pressure
c. Family history of heart disease
d. Age
e. All of the above

ANSWER: All of the above   (e)

LDL cholesterol is called "bad" cholesterol because:

a. It causes low blood counts
b. It can cause blockage in the arteries
c. It changes heart rhythm
d. None of the above

ANSWER: It can cause blockage in the arteries   (b)

What is the main site of lipid transformation and absorption?
a. Mouth
b. Stomach
c. Small intestine
d. Large intestine

ANSWER: **Small intestine**   **(c)**