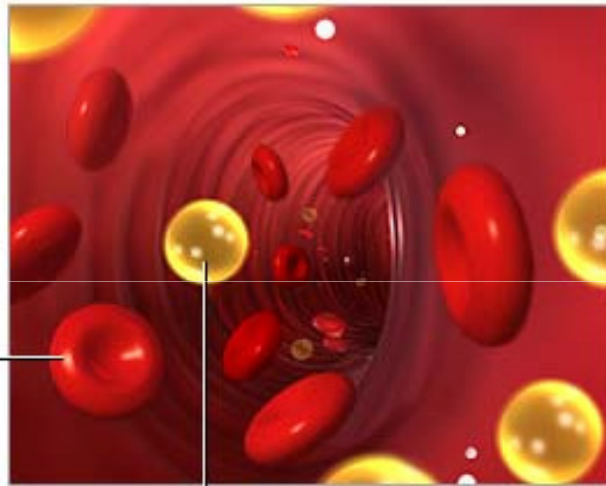


Cholesterol

Normal interior view of artery

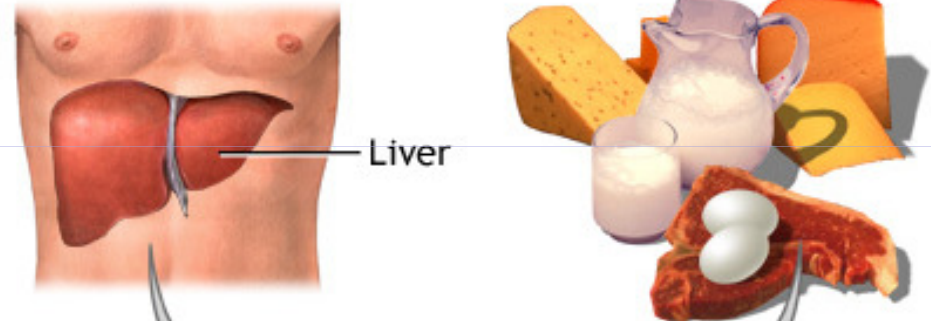


Red blood cell

Cholesterol

ADAM.

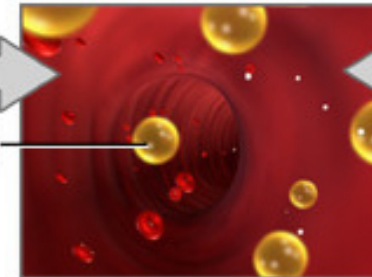
Cholesterol is produced by the liver and we consume it from meat and dairy products



Liver

Cholesterol

ADAM.



Contents of The Lecture

- What is Cholesterol?
- Structure of Cholesteryl Ester
- Normal Cholesterol Level
- Sources of Cholesterol
- What are the Exogenous Sources of Cholesterol?
- Absorption of Exogenous Cholesterol

Contents of The Lecture

- Endogenous Sources of Cholesterol
- The Main Role of the Liver in the Production of the Majority of the Body Cholesterol Pool
- Cholesterol is Transported from Intestine to Liver in Lipoproteins

Contents of The Lecture

- How to Utilize Cholesterol ?
- The Fate of Unused LDL
- HDL (Good Cholesterol)
- What Happens if Cholesterol Gets High?
- How to Treat Hypercholesterolemia?
- Cholesterol Catabolism

Contents of The Lecture

- Cholesterol Recycling and Excretion
- Objective of the Experiment
- Principle of the Test
- Materials
- Method
- Results

□ What is Cholesterol?

- **Cholesterol** is the most prominent member of steroid family of lipids.
- **Cholesterol** is found principally in animals and humans, where it is also the main sterol.

□ What is Cholesterol.....?cont.

- Virtually all human cells and body fluids (including plasma) contain some cholesterol either as free cholesterol or as a storage form: **cholesteryl ester** in which cholesterol is combined with a long chain fatty acid (at C-3), which makes the structure of cholesterol even more **hydrophobic**.

What is Cholesterol?.....cont.

□ Cholesterol is an *amphipathic lipid*, and , therefore, it becomes an essential structural component:

1. Of membranes of cellular organelles.
2. Of the outer layer of plasma membranes.

What is Cholesterol?.....cont.

- Measuring cholesterol concentration is of clinical and analytical importance since:

High levels of plasma cholesterol is associated with

Cardiac Vascular Diseases.

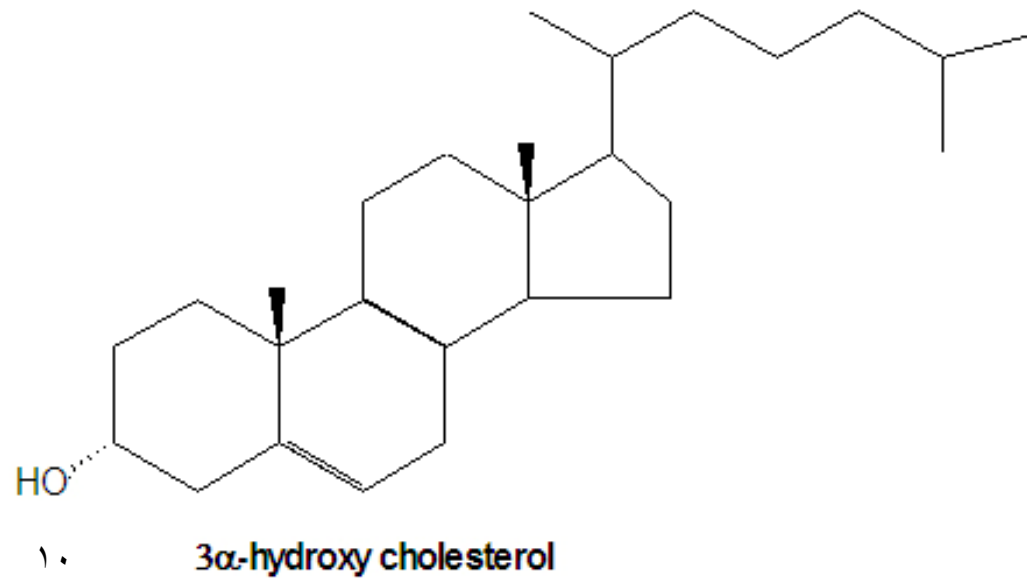
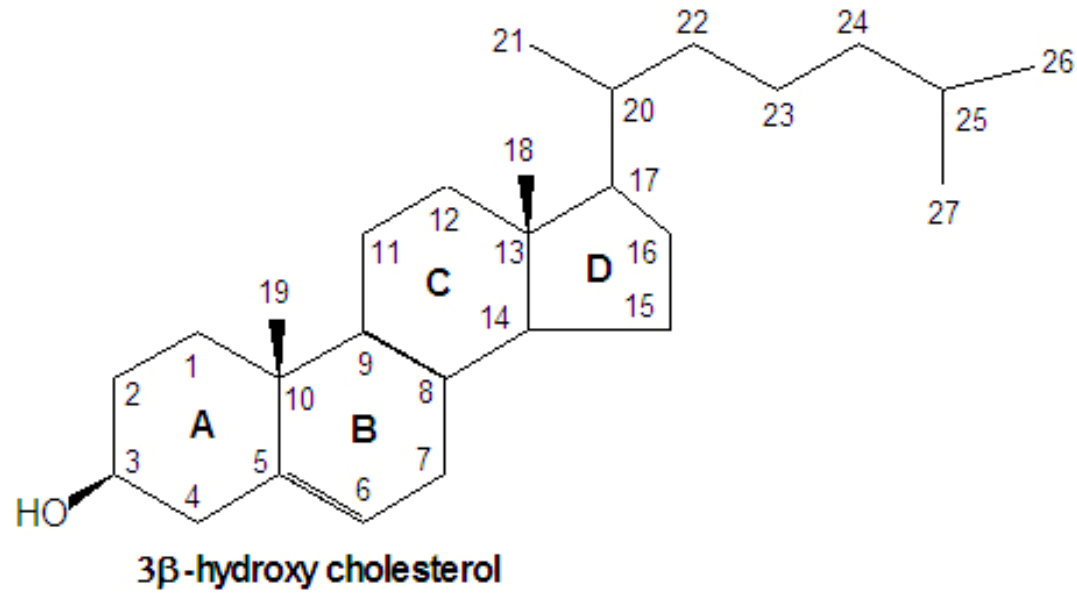
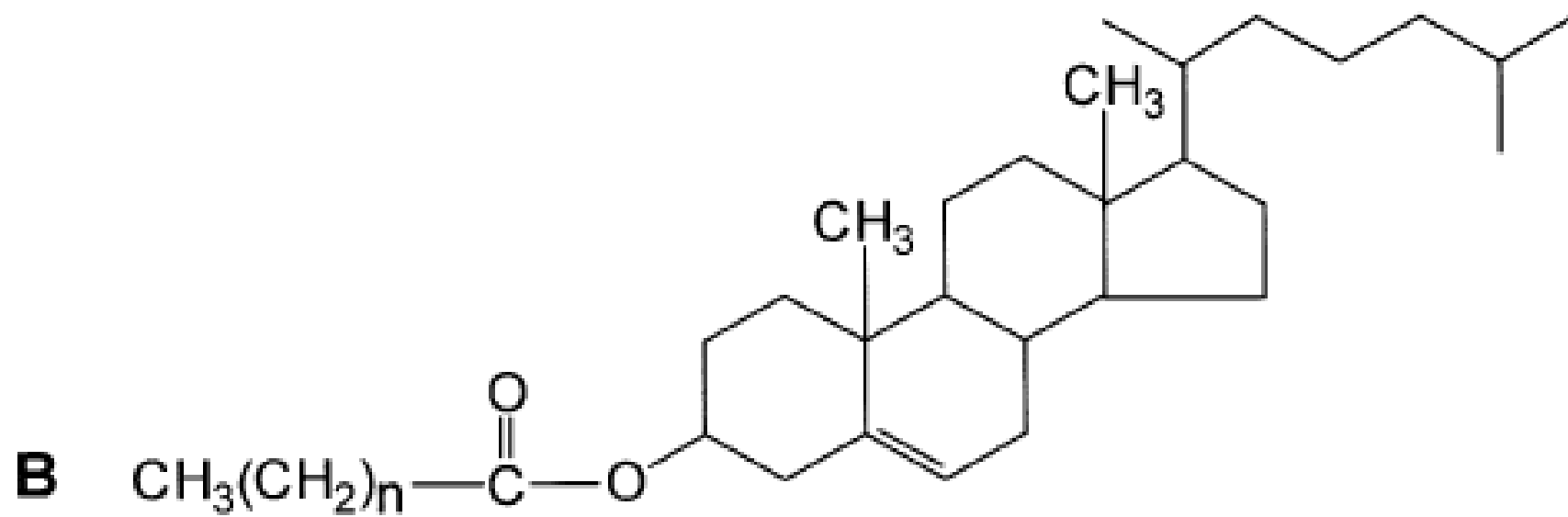


Figure.1.
Cholesterol
Structure

Cholesteryl Ester Structure



Normal Cholesterol Level

- **Desirable total blood cholesterol level less than 200 mg/dL (5.13 mmol/l).** About 50% of all adults fall into this cholesterol level.
- **Borderline high risk total blood cholesterol level 200-239 mg/dL (5.13-6.13 mmol/l).** About 33% of adults fall into this cholesterol level.
- **High risk total blood cholesterol level 240 mg/dL (6.14 mmol/l) and over.** You have twice the risk of coronary heart disease. About 17% of adults are in this cholesterol level.

Sources of Body Cholesterol

Intestine Cholesterol

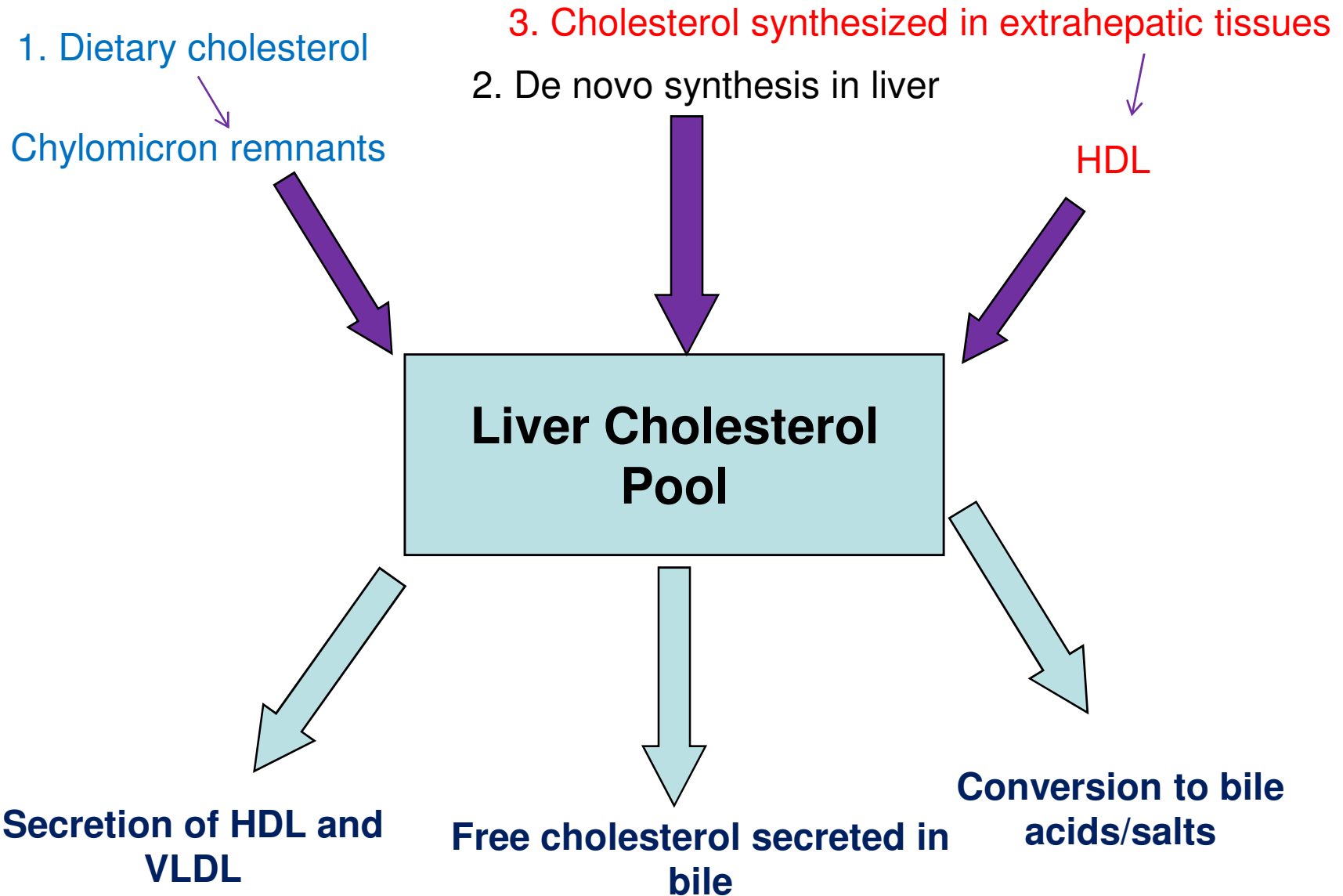
•Cholesterol

in the intestine comes from *diet*, *bile*, and *intestinal secretions*. Therefore **intestine cholesterol** comes from 2 major sources:

(1) Exogenous: (diet)

(2) Endogenous: (bile and intestinal secretions)

Major Sources of Liver Cholesterol



Sources of Body Cholesterol

Liver Cholesterol

- Cholesterol

in the liver comes from 2 major sources:

(1) **Exogenous: (diet)**

(2) **Endogenous: (de novo synthesis in liver and cholesterol synthesized in extrahepatic tissues**

What Are The Exogenous Sources of Cholesterol?

- As a typical product of animal metabolism, cholesterol occurs in foods of animal origin such as egg yolk, meat, liver, seafood, whole fat dairy products and brain.
- These animal products provide the bulk of dietary cholesterol.

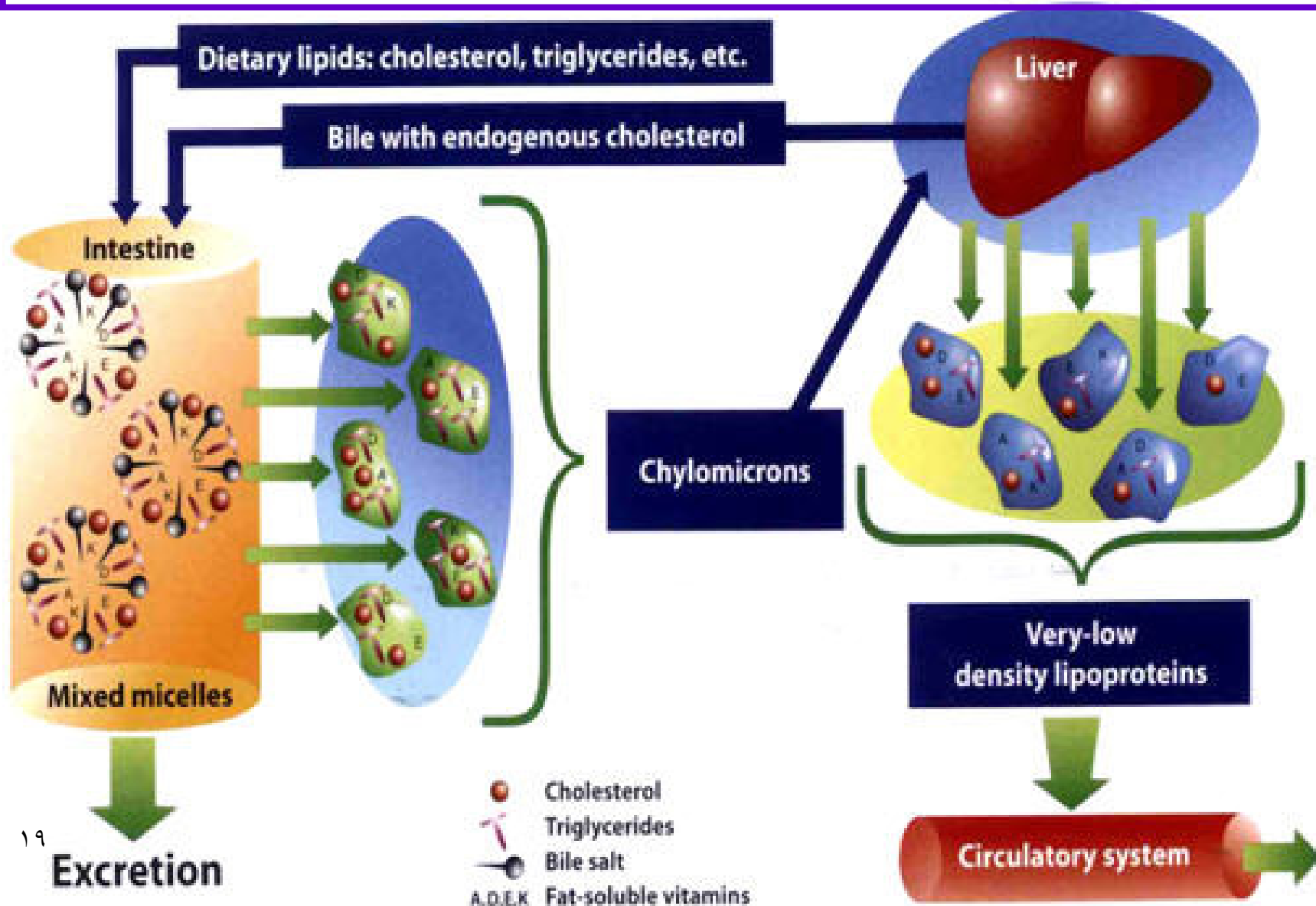
What Are The Exogenous Sources of Cholesterol?.....cont.

- However the fat found in food is composed mainly of triglycerides of about 98 – 99% and only the remaining 1% to 2% of the lipids include **cholesterol** and other lipids.

Intestinal Absorption of Exogenous Cholesterol.....cont

- In order to be absorbed, **cholesterol is solubilized by formation of mixed micelles containing** : (1) **Unesterified cholesterol**
(2) **Fatty acids**
(3) **Monoglycerides (monoacylglycerols)**
(4) **Phospholipids (lysolecithin)**
(5) **Conjugated bile acids.**
- These micelles also facilitate cholesterol transport across the luminal cell surfaces.

Intestinal Absorption of Exogenous Cholesterol.....cont



Absorption of Exogenous Cholesterol....cont.

- In the absence of bile acids, digestion and absorption of both cholesterol and triglycerides are severely impaired.

Endogenous Sources of Cholesterol

- **Cholesterol** is synthesized from acetyl Co.A by virtually all tissues in humans.

 - **Liver** is the major site of cholesterol synthesis.

 - **Intestine** is also a main site of cholesterol synthesis after the liver.

Cholesterol Synthesis

- Similar to ketogenic pathway
- Occurs in cytosol
- Requires NADPH and ATP
- Highly regulated
- 80 % in liver, ~10% intestine, ~5% skin

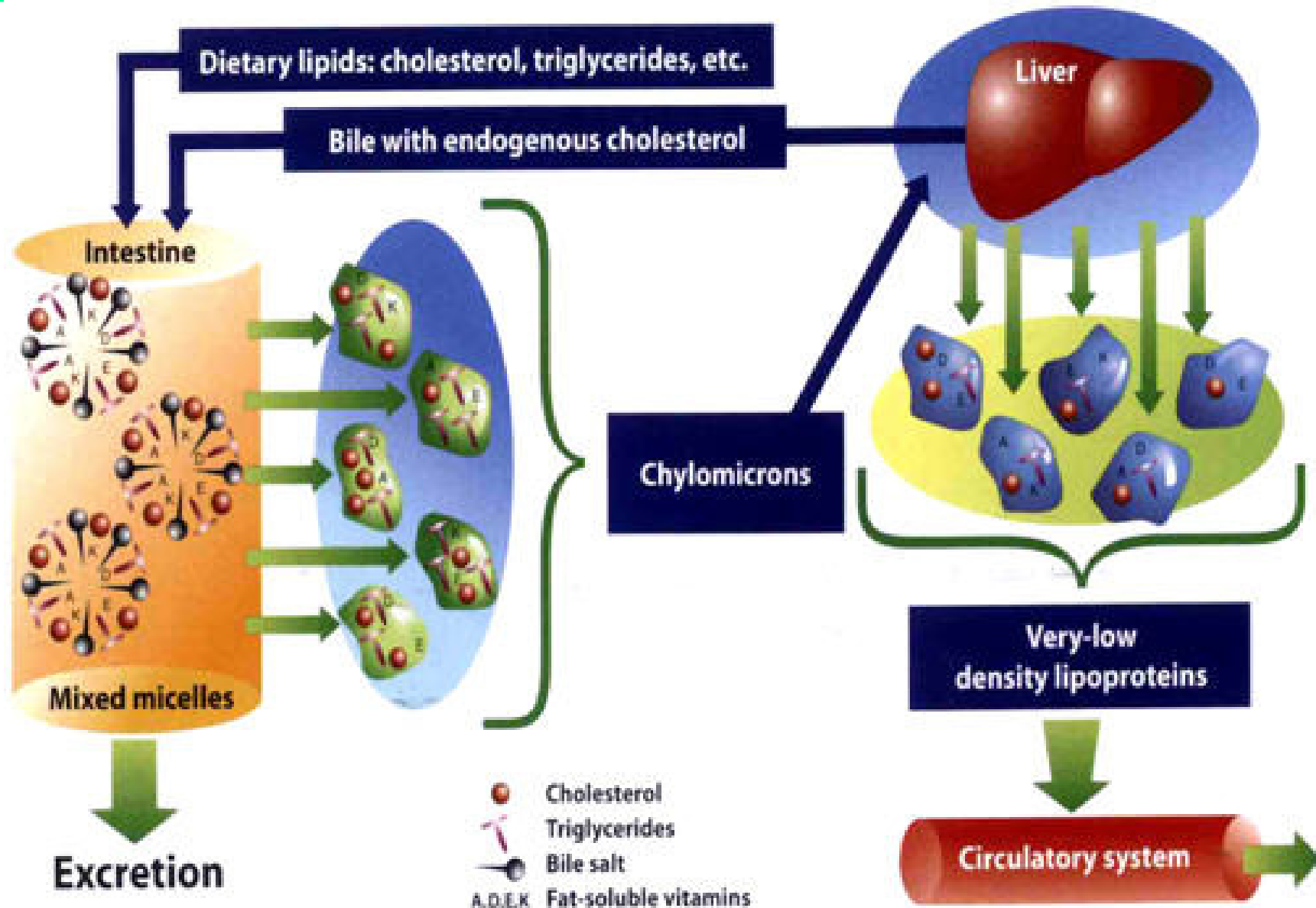
Cholesterol is Transported from Intestine to Liver in Lipoproteins

- **Blood is watery, and cholesterol is fatty.**
- Just like oil and water, the two do not mix. To travel in the bloodstream, cholesterol is carried in small particles called lipoproteins (lip-o-PRO-teens).

Cholesterol is Transported from Intestine to Liver in Lipoproteins

The liver and the gut (intestine) are the two major organs of lipoprotein synthesis and transport.

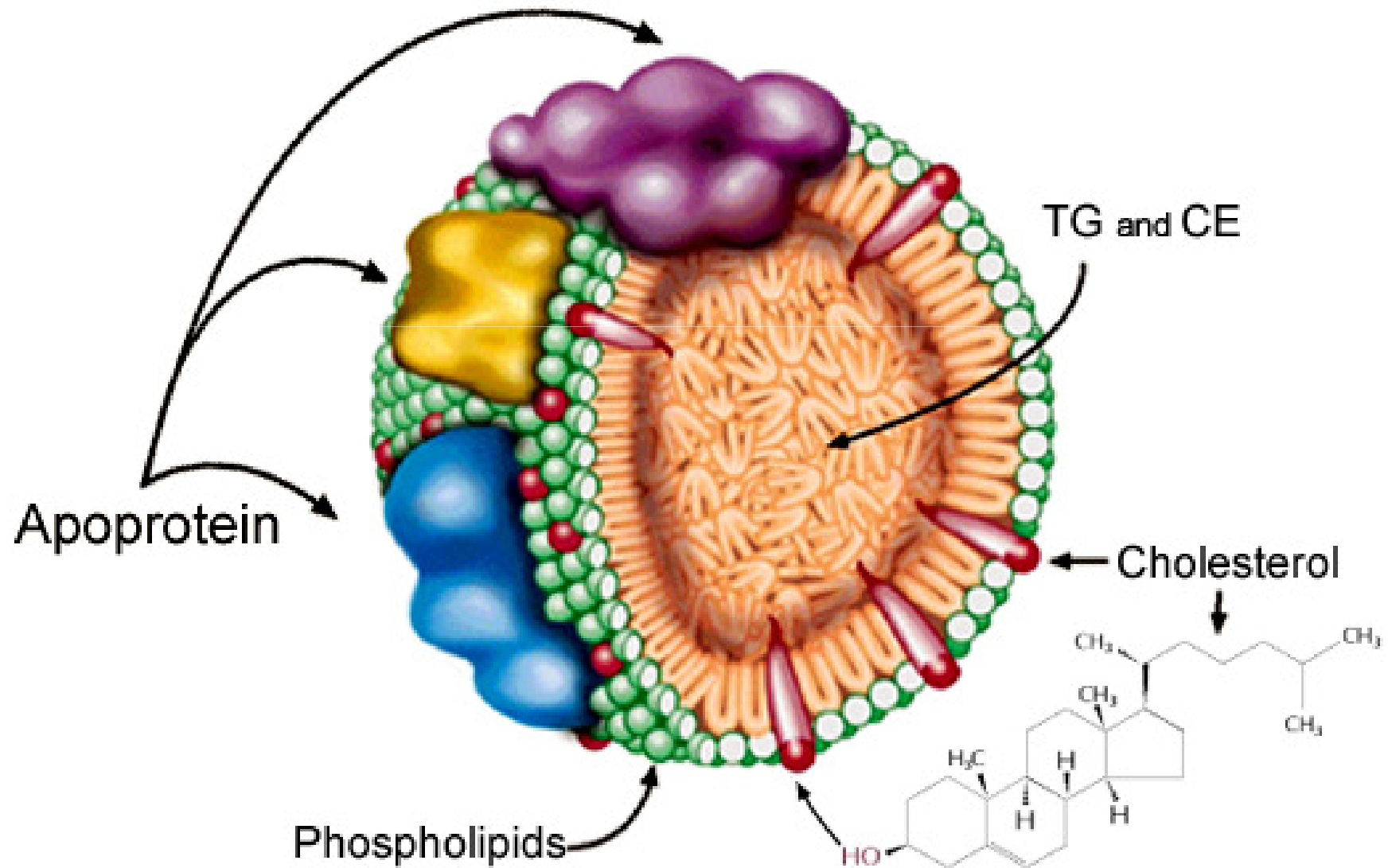
Cholesterol is Transported from Intestine to Liver in Chylomicrons



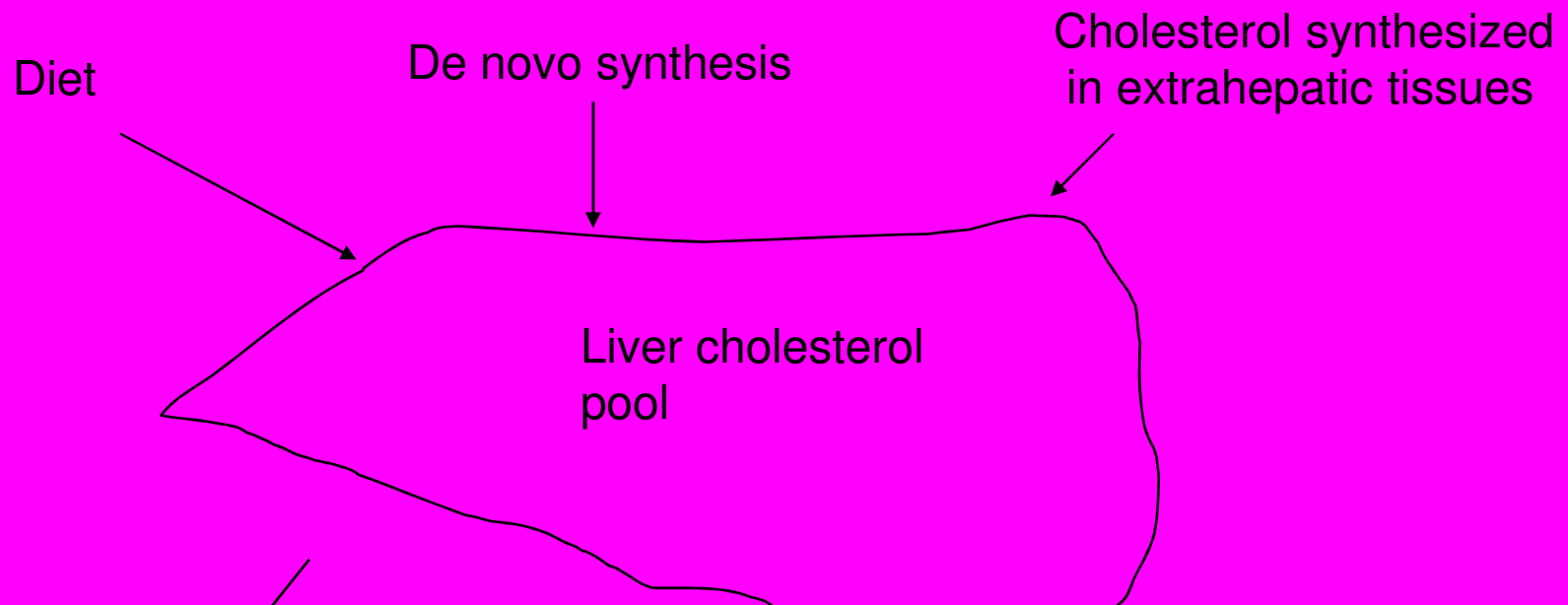
Cholesterol is Transported from Liver to Other Body Tissues by VLDL Lipoproteins

- The use of cholesterol by the liver is to supply cholesterol for the rest of the body's needs.
- In order to do this, **cholesterol** from the liver's pool is combined with **triglycerides** and coated with a **special protein** that makes it soluble in our blood.
- These rather large molecular weight structures are called **very low density lipoproteins** (**VLDL= Cholesterol+ Cholesteryl ester + TG + Additional lipids + Apo-proteins**).

Structure of Lipoproteins: VLDL,IDL,LDL,and HDL



Liver and the Cholesterol

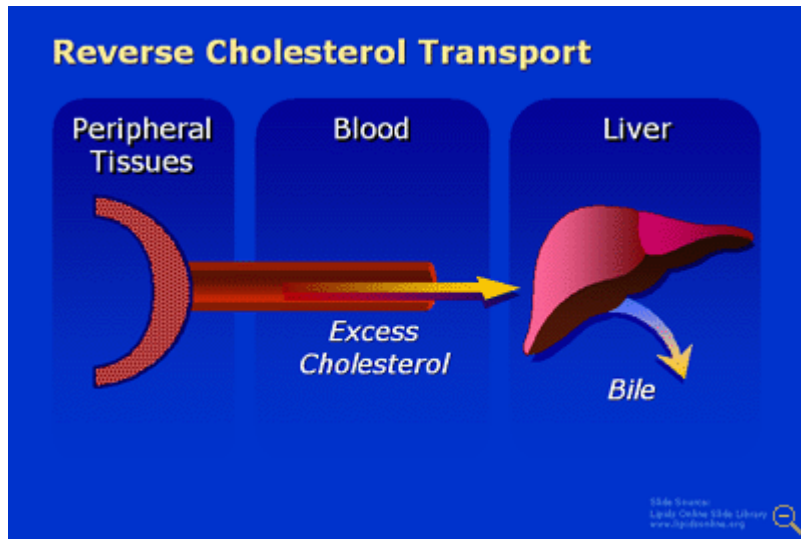


Major routes by which cholesterol leaves liver

(1) Secretion of HDL₂ and VLDL

(2) Free cholesterol in bile

(3) Conversion to bile salts/acids



The Fate of Unused LDL

- The regulated receptors on the liver will help return some of the cholesterol to the liver from unused **low density lipoproteins (LDL)**.
- **LDL** is the so-called “**bad cholesterol**” and genetic differences in these regulated receptors can result in the accumulation of large amounts of LDL in the circulation
(**Familial Hyper-Cholesterolemia**).

HDL

Good Cholesterol

- Another lipoprotein formed by the liver is called **high density lipoprotein (HDL)**, sometimes referred to as the “**good cholesterol**”.
- High density lipoprotein is formed with very small amounts of **cholesterol**, small amounts of **triglyceride** and a special **protein coat** within the liver that makes it distinct from the VLDL.

HDL

Good Cholesterol.....cont.

- The **HDL** in the circulation acts like a **sponge** in picking up excess cholesterol from tissues which normally metabolize cholesterol but are receiving more than they can possibly use.

Classification of Lipoproteins



Chylomicron

**“Bad”
(non-HDL)**

“Good”



VLDL



IDL



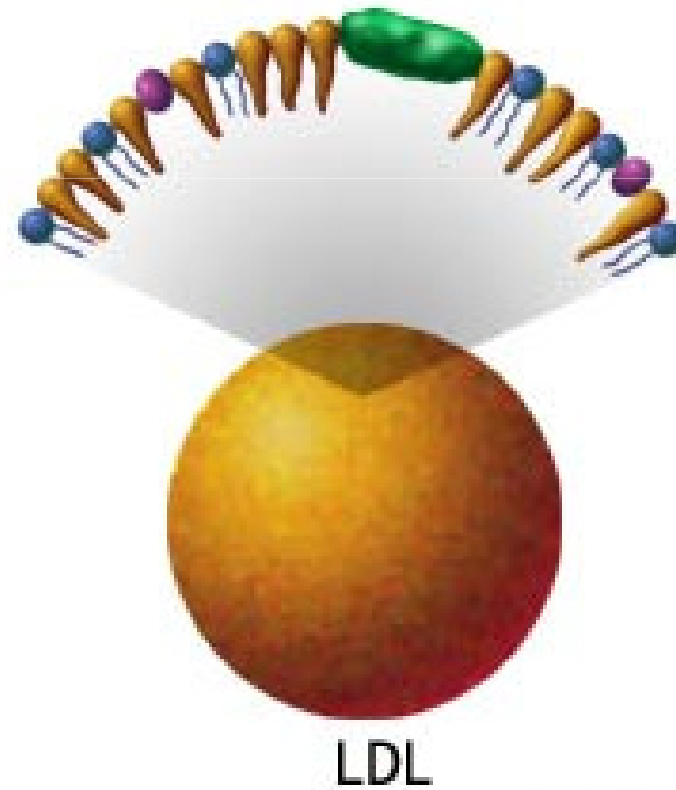
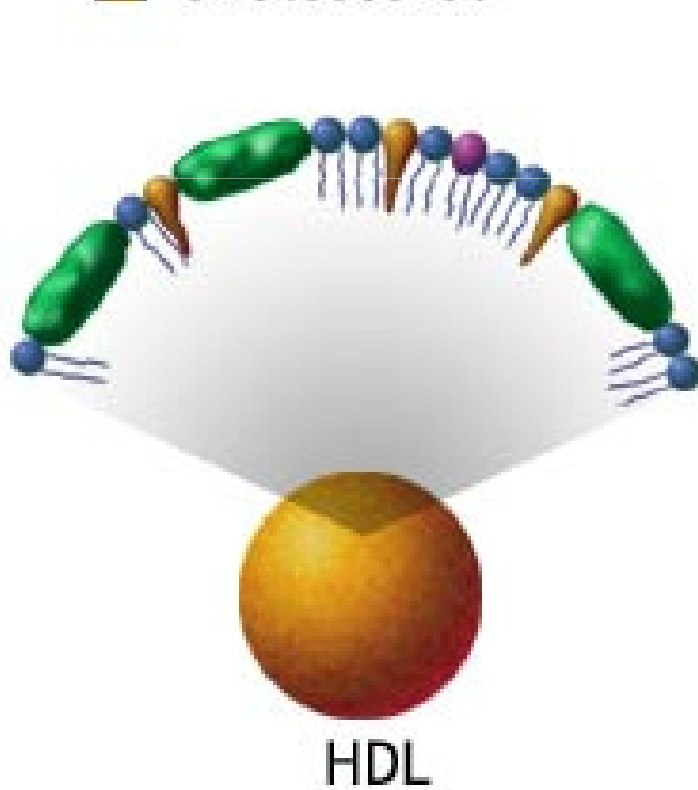
LDL



HDL

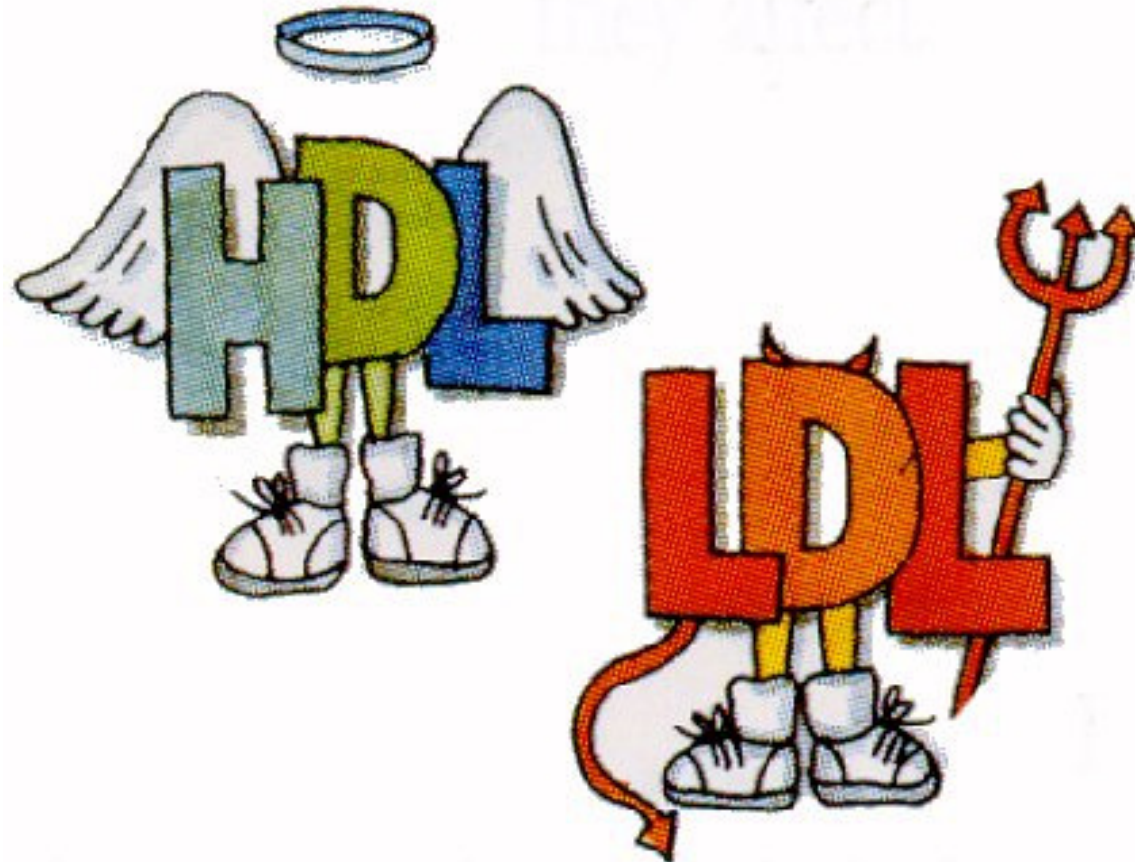
The Difference in Size and Composition between HDL and LDL

■ Proteins
■ Cholesterol



Good Vs. Bad Lipoproteins

- **Plasma Lipoproteins.** There are good and bad forms of lipoproteins in terms of their effect in the formation of **atherosclerotic plaque.**



What Can Cause High Cholesterol Levels?

(I) Hereditary Factors Affect the Cholesterol Level

- ❑ Cholesterol levels can run in families. If the inherited cholesterol levels are very high, this is called Familial Hypercholesterolaemia (FH).

(II) Environmental Factors Affect the Cholesterol Level

- ❑ We know that diet high in saturated fat (cakes, pastry, meat, dairy products) is a major factor that raising cholesterol.

What Can Cause High Cholesterol Levels?

(III) High Cholesterol is Also Seen in Connection with other Diseases Such as:

(1) Reduced metabolism due to thyroid problems

(2) Kidney diseases

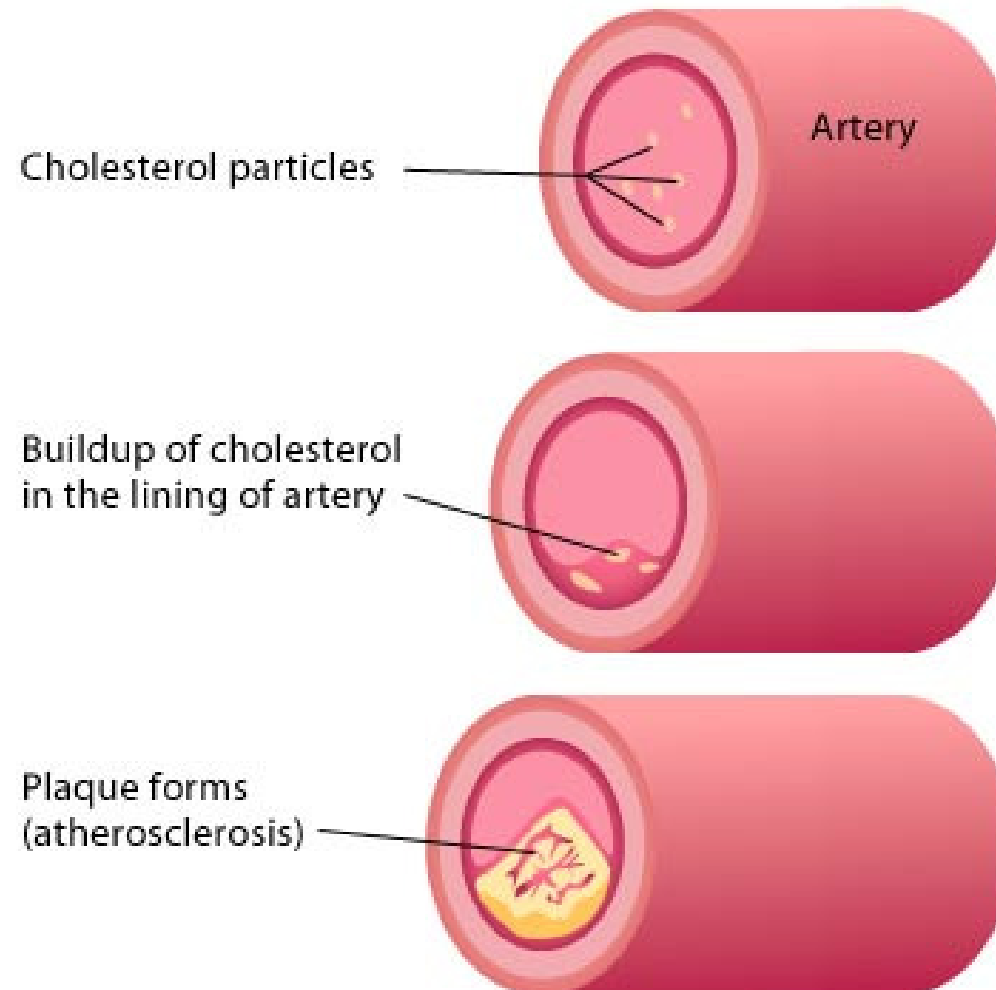
(3) Diabetes

(4) Alcohol abuse.

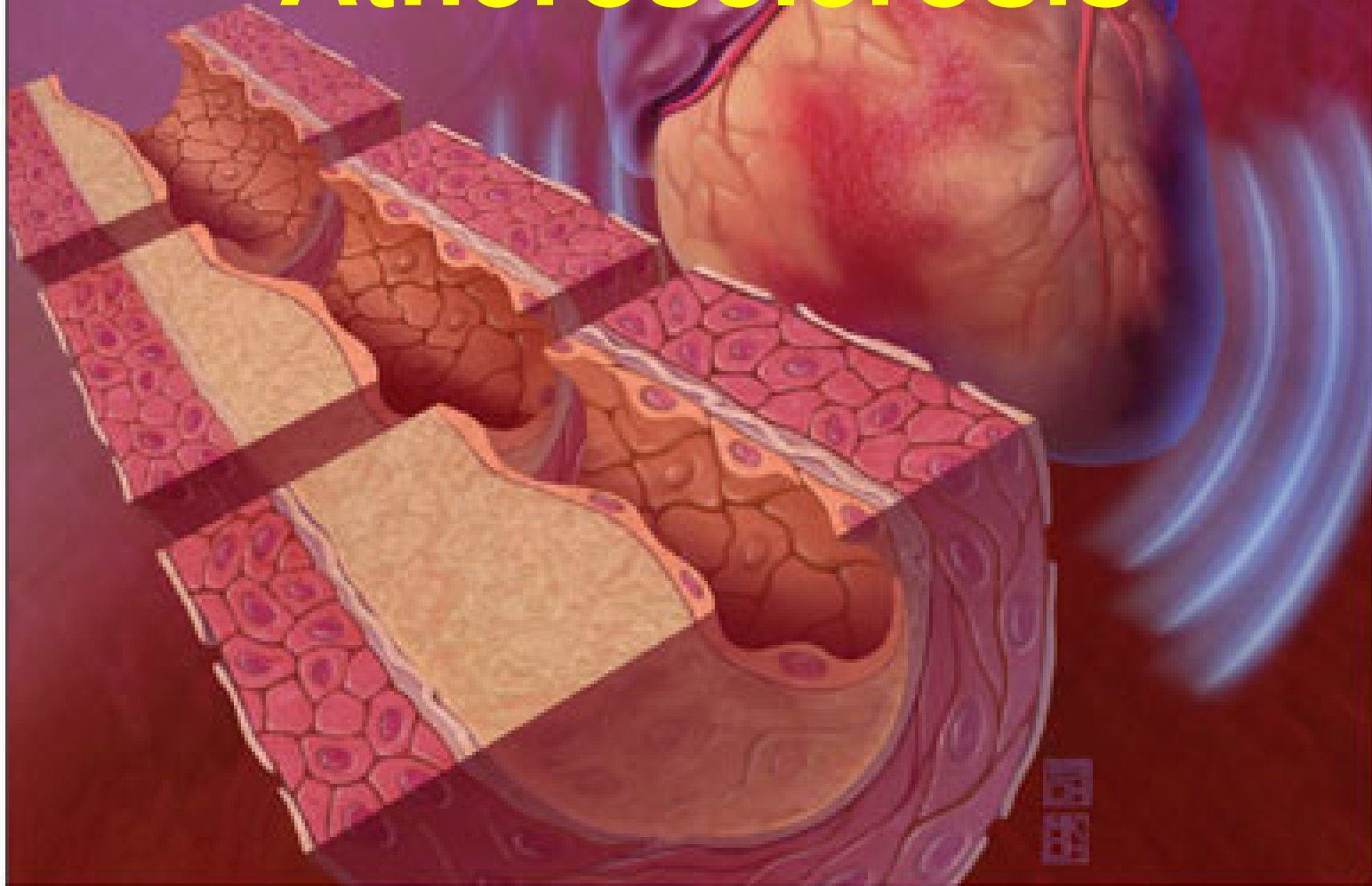
What are the Symptoms of High Cholesterol in the Blood Stream?

- When there is too much cholesterol in the blood, cholesterol is built up in the artery walls, and then the arteries become narrow and hardened, their elasticity disappears and the blood flow through the arteries to the heart is slowed down or blocked and as a result atherosclerosis occurs.
- **If blood can't then flow to a part of the body, the tissue dies.**
- The blood carries oxygen to the heart, and if enough blood and oxygen cannot reach the heart, the patient may suffer chest pain. If the blood supply to a portion of the heart is completely cut off by a blockage, the result is **symptoms of Cardiovascular disease: Heart attack.**

Hypercholesterolemia Causes Atherosclerosis



Hypercholesterolemia Causes Atherosclerosis



HOW TO TREAT HYPERCHOLESTEROLEMIA

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**“An aspirin a day will help prevent a heart
attack if you have it for lunch instead
of a cheeseburger.”**

What Can I Do to Improve My Cholesterol Level?

- If you have high cholesterol, it may be necessary for you to make some lifestyle changes:
 1. If you smoke, quit.
 2. Exercise regularly.
 3. If you're overweight, losing just 5 to 10 pounds can help improve your cholesterol levels.
 4. Make sure to eat plenty of fruits, vegetables, whole grains and fish- all of which promote heart health. Avoid saturated fats, which can raise cholesterol levels, i.e. limit your overall cholesterol intake to less than 300 milligrams per day and 200 milligrams if you have heart disease. **EAT A DIET HIGH IN FIBER:** Fiber, found in oatmeal and whole grains, binds to excess cholesterol in the intestine and removes it from the body.

What Can I Do to Improve My Cholesterol Level?

Choose fruits and vegetables over unhealthy fatty foods



PHYSIOLOGICALLY, IN WHAT WAY THE BODY CAN TREAT **HYPERCHOLESTEROLEMIA?**

- **INCREASE YOUR "GOOD" CHOLESTEROL LEVELS:** High-density lipoproteins (HDL) or "good" cholesterol, carries bad cholesterol away from the arteries and heart and back to the liver where it can be used by the hepatic / extrahepatic tissues. Replacing saturated fats with mono- or poly- unsaturated fats found in nuts and vegetable oils will help raise HDL levels.

How is High Cholesterol Clinically Treated?

- Cholesterol-lowering medicine is needed if the total cholesterol level remains higher than 5mmol/l and the patient already have cardiovascular disease.
- **Statins** (eg simvastatin, atorvastatin, rosuvastatin) are the most effective medicines for lowering cholesterol.
These drugs reduce the production of 'bad' LDL cholesterol by the liver, which decreases LDL cholesterol blood levels by up to 50 per cent.

Cholesterol Catabolism

- The ring structure of cholesterol cannot be metabolized to CO_2 and H_2O in humans.

Cholesterol Catabolism

- After cholesterol enters the cell, the esters are hydrolyzed by the action of specific lysosomal esterases. The lack or malfunction of these lysosomal enzymes results in intracellular accumulation of cholesteryl esters and produces a clinical disorder known as **cholesteryl ester storage disease**.

Cholesterol Recycling And Excretion

- Cholesterol is oxidized by the liver into a variety of bile acids.
- Bile salts are bile acids conjugated with glycine, taurine, glucuronic acid, or sulfate. A mixture of conjugated and non-conjugated bile acids along with cholesterol itself is excreted from the liver into the bile. Approximately 95% of the bile acids are reabsorbed from the intestines and the remainder lost in the feces.↓

Cholesterol Recycling And Excretion

- The excretion and reabsorption of bile acids form the basis of the Enterohepatic Circulation which is essential for the digestion and absorption of dietary fats.
- Under certain circumstances, when more cholesterol is concentrated, as in the gallbladder, cholesterol crystallises and is the major constitute of most gallstones.

OBJECTIVE OF THE EXPERIMENT

- **Estimation of Cholesterol.**

Principle of the Test

- In this experiment cholesterol is estimated by a chemical method rather than an enzymatic method.
- This method is qualitative and quantitative one.

Principle of the Test

.....cont.

- In this method: Cholesterol reacts as a typical alcohol with strong, concentrated acid. The products are green-colored substances, mainly cholestapolyenes and cholestapolyene carbonium ions (**Liebermann – Burchard reaction**)

Principle of the Testcont.

-In this procedure cholesterol reacts with :

1. Acetic acid and acetic anhydride which act as solvents and dehydrating agents.

2. Sulfuric acid that used as a dehydrating and oxidizing reagent.

- The absorbance of the green compound is then measured at 610nm.

Materials

1. Cholesterol reagent (Acetic anhydride + acetic acid)
2. Sulphuric acid 95-97%
3. Standard cholesterol (300 mg/dl)
4. Samples
5. Test Tubes
6. Pipettes
7. Cuvettes
8. Spectrophotometer
9. Water bath

Method

1- Label 7 test tubes for test 1 (A,B) test 2 (C,D) standard (E,F) and blank (O) pipette the following

	(A,B)	(C,D)	(E,F)	(B)
Sample 1	0.1 ml			
Sample 2		0.1 ml		
Standard Cholesterol			0.1 ml	
Distilled Water				0.1 ml
Cholesterol reagent	4 ml	4 ml	4 ml	4ml

Methodcont.

2- Stand for 20 minutes

3- Pipette 1.0 ml of sulphuric acid into each tube running the acid cautiously down the side of the tube.

4- Place the tube in a water bath at room temperature.

5- After around 5 minutes remove from the water bath and shake vigorously to remove any adhered proteins to the walls of the tubes,

6- Stand for 10 minutes then measure the absorbance of the samples against the blank at 610nm.

Results

Sample 1 Absorbance

A =

B =

Sample 2 Absorbance

C =

D =

Standard Cholesterol Absorbance

E =

F =

Results

Absorbance of samples X 300 = ----- mg/dl

Absorbance of standard

- **The average of normal levels of cholesterol is
150-230 mg/dl**

