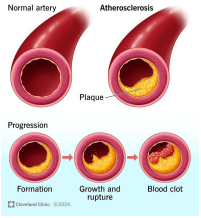
1

Cardiovascular Module

1st Year MBBS (CBL)

Atherosclerosis



H.O.D
Department of Biochemistry
Rawalpindi Medical University
Rawalpindi

Presenter: Dr. Sana Latif
(Senior Demonstrator)

updated Date: 25-02-25

2

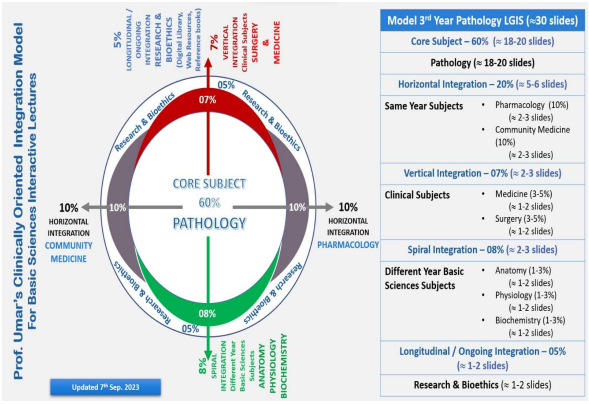
Motto, Vision, Dream

- To impart evidence based research oriented medical education
- To provide best possible patient care
- To inculcate the values of mutual respect and ethical practice of medicine

3

3

Professor Umar Model of Integrated Lecture



4

4

CBL-MCQ Assessment

1. **The primary lipid deposited in atherosclerotic plaques is:**
   A. Triglyceride
   B. HDL
   C. LDL
   D. Phospholipid
   E. VLDL

2. **Oxidized LDL is taken up by macrophages via:**
   A. LDL receptor
   B. Glucose transporter
   C. Transferrin receptor
   D. Scavenger receptor
   E. Insulin receptor

3. **Foam cells seen in atherosclerotic lesions are derived from:**
   A. Endothelial cells
   B. Platelets
   C. Smooth muscle cells
   D. Macrophages
   E. Fibroblasts

4. **The key antioxidant enzyme that helps prevent LDL oxidation is:**
   A. Pepsin
   B. Catalase
   C. Superoxide dismutase
   D. DNA polymerase
   E. Glycogen synthase

5

5

CBL-MCQ Assessment

5. **The major apolipoprotein present in LDL is:**
   A. ApoA-I
   B. ApoB-48
   C. ApoC-II
   D. ApoE
   E. ApoB-100

6. **High levels of which lipoprotein are considered protective against atherosclerosis?**
   A. Chylomicron
   B. LDL
   C. VLDL
   D. HDL
   E. IDL

7. **Atherosclerosis begins with damage to which structure?**
   A. Tunica adventitia
   B. Myocardium
   C. Endothelium
   D. Pericardium
   E. Epicardium

8. **Nitric oxide helps prevent atherosclerosis by:**
   A. Enhancing platelet aggregation
   B. Promoting LDL uptake
   C. Inhibiting endothelial repair
   D. Causing vasodilation
   E. Stimulating smooth muscle proliferation

6

6

CBL-MCQ Assessment

9. **The key biochemical change in LDL that promotes atherogenesis is:**
   A. Oxidation
   B. Glycosylation
   C. Denaturation
   D. Dehydration
   E. Acetylation

10. **Which vitamin has antioxidant properties that may reduce LDL oxidation?**
    A. Vitamin D
    B. Vitamin E
    C. Vitamin C
    D. Vitamin B6
    E. Vitamin K

7

7

CBL-MCQ Assessment

1. C
2. D
3. D
4. C
5. E
6. D
7. C
8. D
9. A
10. B

8

8

Learning Objectives

At the end of the CBL, students will be able to:

1. Discuss the structure and functions of cholesterol
2. Recall normal plasma Cholesterol level
3. Explain causes and effects of hypercholesterolemia
4. Integrate Physiological, Biochemical and Clinical aspects
5. Correlate and build core knowledge on the basis of latest Research, Family Medicine, Artificial Intelligence & Bioethics.

9

9

Interactive Session

- A 55 years old man presented in ER of District Headquarter hospital with complaints of sudden onset pain in chest and left arm. He was diabetic for last 10 years. He had sedentary lifestyle. His serum cholesterol level was found to be very high (360mg/dl). He had disturbed LDL/HDL ratio.
- His CKMB level was found to be raised and ischemic heart changes were noted on ECG. He was diagnosed as a case of Myocardial Infarction.

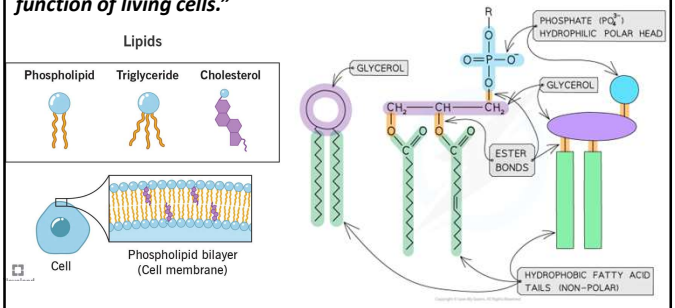
Core Concept 10

10

Core Concept

Lipids

"Lipids are organic compounds that contain hydrogen, carbon, and oxygen atoms, which form the framework for the structure and function of living cells."



11
Core Concept

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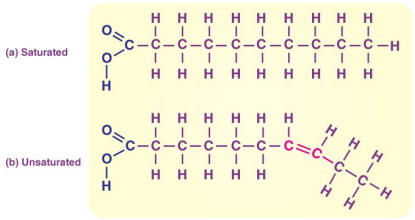
Core Concept

Lipid Structure

- Lipids are the **polymers of fatty acids** that contain a **long, non-polar hydrocarbon chain** with a **small polar region containing oxygen**.

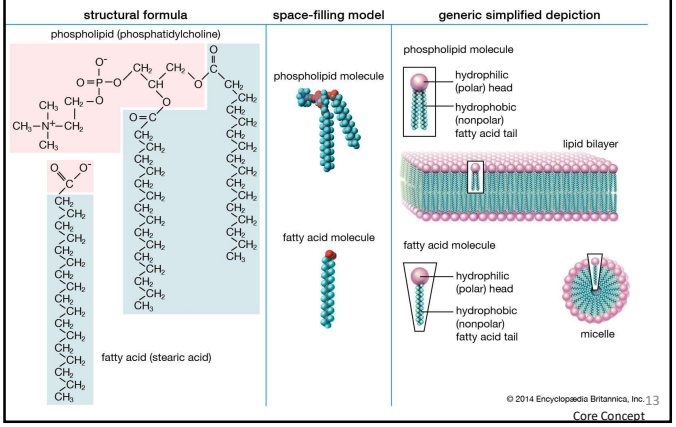


Core Concept 12

12

Core Concept

Lipid Structure

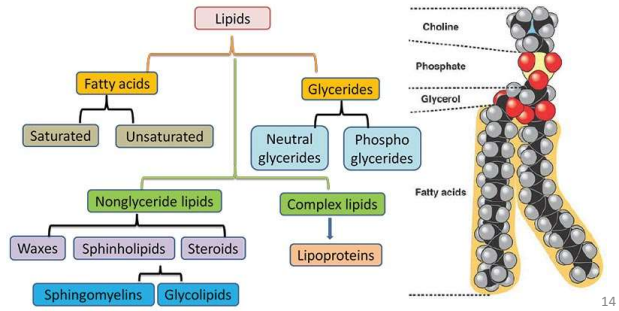


13

Core Concept

Properties of Lipids

- These **organic** compounds are **nonpolar** molecules, which are **soluble only in nonpolar solvents** and **insoluble in water i.e Hydrophobic** because **water** is a **polar** molecule. The substances that are soluble in water are **Hydrophilic**. Those exhibiting both hydrophilic & hydrophobic properties are **Amphipathic**



14

Core Concept

Cholesterol

- Cholesterol is a structural component of cell membranes and serves as a building block for synthesizing various steroid hormones, **vitamin D,** and **bile acids**.
- Provide **stability** and **fluidity.** Cholesterol also plays a crucial role in **regulating cell function**.
- Cholesterol is a **waxy, fat-like substance,** which the body needs for good health, but in the right amounts. Unhealthy, high levels of cholesterol can lead to a condition called **Hypercholesterolemia** (high blood cholesterol).
- Cholesterol in the blood is carried on lipoproteins:
- **Low-density lipoprotein (LDL),** sometimes called **"bad" cholesterol**
- **High-density lipoprotein (HDL),** sometimes called **"good" cholesterol**.

DIFFERENCE BETWEEN HDL & LDL CHOLESTEROL

Characteristic	HDL Cholesterol	LDL Cholesterol
Density	High	Low
Function	Removes cholesterol from arteries to the liver for disposal (known as "good" cholesterol)	Deposits cholesterol in arteries, contributing to plaque buildup (known as "bad" cholesterol)
Associated with	Reduced risk of heart disease and stroke	Increased risk of heart disease and stroke
Levels	Higher levels are desirable	Lower levels are desirable
Normal Range	Above 60 mg/dL is considered protective	Below 100 mg/dL is considered optimal, but exact values depend on individual risk factors
Composition	Contains more protein and less cholesterol	Contains more cholesterol and less protein

15

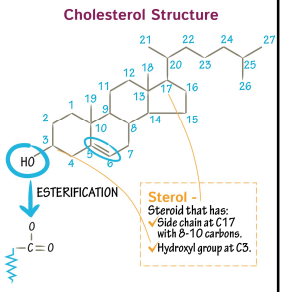
Core Concept

Chemical Structure of Cholesterol

- The chemical formula of cholesterol is $C_{27}H_{46}O$.
- Structure of Cholesterol consists of:

1. A **Central Sterol Nucleus** of four hydrocarbon rings, which are hydrogen and carbon atoms with a circular arrangement. These rings join together in the middle of the compound.
2. A **Hydrocarbon Tail**, a chain of hydrogen and carbon atoms at one end of the molecule
3. A **Hydroxyl Group**, which is one hydrogen atom bonded to one oxygen atom and this hydroxyl group attaches to the other end.

- Both the sterol nucleus and hydrocarbon tail do not mix with water, so this structure cannot travel through the bloodstream alone. For this reason, cholesterol combines with proteins to create **Lipoproteins**, which can travel through the blood to reach cells that need them.



16

Core Concept

Properties of Cholesterol

Properties Of Cholesterol

IUPAC name	(3β)-cholest-5-en-3-ol
Molecular formula	$C_{27}H_{46}O$
Molecular mass	386.664 g/mol
Melting point	148 to 150°C
Boiling point	360°C
Density	1.052 g/cm^3
Solubility	Soluble in acetone, benzene, ether, hexane
Solubility in water	1.8 mg/L at 30°C
Appearance	White crystalline powder

17

Core Concept

Functions Of Cholesterol

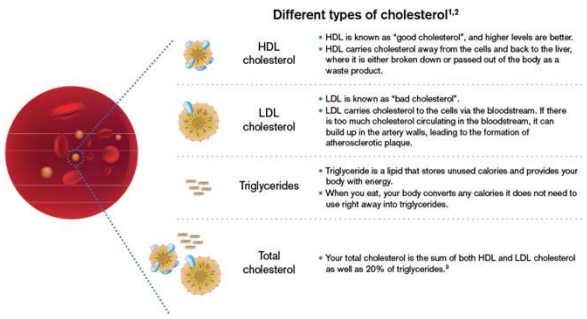
Although people generally believe cholesterol is harmful, it has several important roles, including:

- A **Cell Membrane Component**: Cholesterol is an important part of the cell membrane **structure**. It changes the fluid in the membrane, which can affect the internal cell environment. It also fosters **transportation** within the cell.
- A **Digestive Aid**: Cholesterol is a component of **Bile Salt**. The digestive system uses this to **Absorb Fat-soluble Vitamins A**, **D**, **E**, and **K**.
- A **Precursor** for important bodily substances: The body uses cholesterol to make:
  1. **Vitamin D**, which plays a role in bone health
  2. **Steroid Hormones**, such as **Cortisol**, which help the body respond to stress
  3. **Reproductive System Hormones** such as **Estrogen** and **Testosterone**
- Cholesterol also plays a role in the **Immune System** and **Brain Synapses**. These are points of contact between nerve cells in the brain.

18

Core Concept

Types of Cholesterol



19

Core Concept

Cholesterol Levels

- High cholesterol—also known as **Hyperlipidemia**—is a common condition where the body has unusually high level of fats in the blood.
- These fats include low-density lipoprotein (**LDL**) **Cholesterol** and **Triglycerides**.
- They are absorbed into the body from **cholesterol-rich foods** such as **red meat** and **dairy**.
- **Triglycerides** are also made in the body when **excess calories are converted into fat.**

Anyone age 19 or younger:

Type of Cholesterol	Healthy Level
Total Cholesterol	Less than 170mg/dL
Non-HDL	Less than 120mg/dL
LDL	Less than 100mg/dL
HDL	More than 45mg/dL

Men age 20 or older:

Type of Cholesterol	Healthy Level
Total Cholesterol	125 to 200mg/dL
Non-HDL	Less than 130mg/dL
LDL	Less than 100mg/dL
HDL	40mg/dL or higher

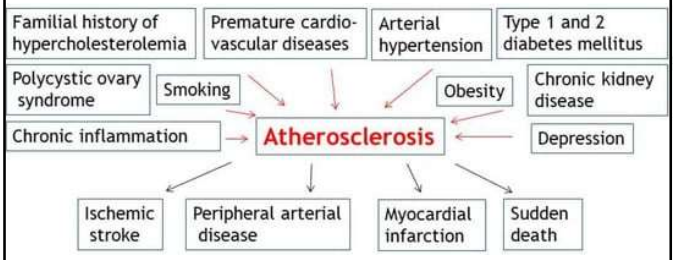
Women age 20 or older:

Type of Cholesterol	Healthy Level
Total Cholesterol	125 to 200mg/dL
Non-HDL	Less than 130mg/dL
LDL	Less than 100mg/dL
HDL	50mg/dL or higher

20

Core Concept

Atherosclerosis – Causes & Effects

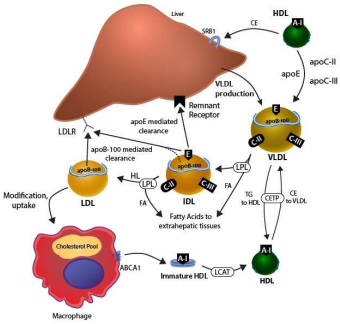


21

Core Concept

Role of Lipoproteins in Atherosclerosis

- Cholesterol is circulated in the blood attached to transport proteins, a combination referred to as lipoproteins.
- **Low-density lipoprotein (LDL)** carries cholesterol **from the liver to various parts of the body**. If there is an excess of LDL, cholesterol can accumulate in the walls of arteries and lead to atherosclerosis. LDL is therefore sometimes called **"bad cholesterol."**
- **High-density lipoprotein (HDL),** carries excess cholesterol **away from cells to the liver**, where it is broken down and treated as a waste product. This lipoprotein is referred to as **"good cholesterol."**

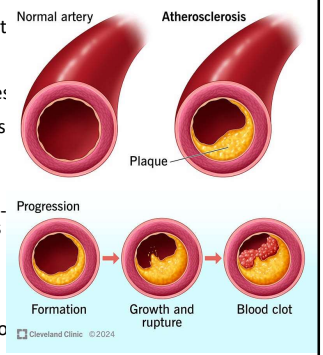


22

Core Concept

Effects of Atherosclerosis

- **Excess cholesterol** present in the **blood** forms fatty deposits in the walls of the **coronary arteries**, the blood vessels that supply the heart with blood.
- As the cholesterol **accumulates**, it causes **atherosclerotic plaques** to form, which narrow and harden the artery walls. This is referred to as **Atherosclerosis**.
- Eventually, these plaques can **block the arteries** and limit the amount of oxygen-rich blood that can reach the heart. This increases a person's risk of **CAD – Coronary Artery Disease** leading to **Angina** and **Myocardial Infarction**
- If the arteries that supplies blood flow to the **brain** i.e the **Carotid Arteries** become narrowed and hardened due to Atherosclerosis, then a person is at an increased risk of suffering a **Stroke**.



23

Core Concept

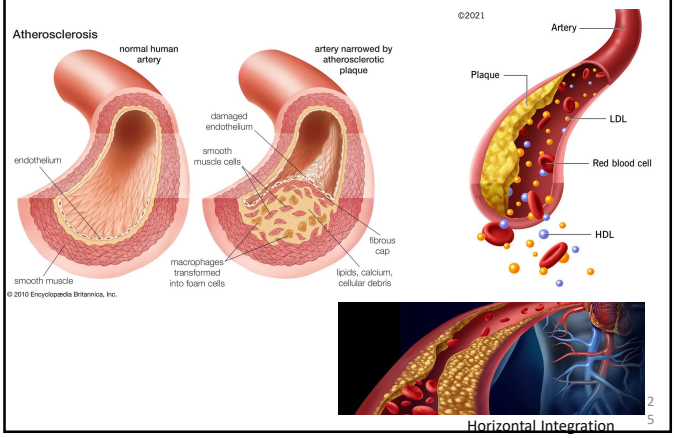
Clinical Conditions Due to Atherosclerosis/Hypercholesterolemia

- When atherosclerosis affects the arteries in the **limbs**, often the **legs**. It can lead to pain, cramping, and reduced blood flow to the extremities known as **Peripheral Artery Disease (PAD)**
- **High Blood Pressure (Hypertension):** High cholesterol levels causing Atherosclerosis can contribute to high blood pressure, which is a risk factor for heart disease and stroke.
- **Type 2 Diabetes**: High cholesterol can be associated with insulin resistance and the development of type 2 diabetes, which can lead to various health complications if not managed properly.
- **Gallstones**: Excess cholesterol in the bile can lead to the formation of gallstones, which can cause abdominal pain and other digestive issues.
- **Non-Alcoholic Fatty Liver Disease (NAFLD):** Elevated cholesterol levels can contribute to the accumulation of fat in the liver, leading to NAFLD, which can progress to more severe liver conditions.

24

Horizontal Integration

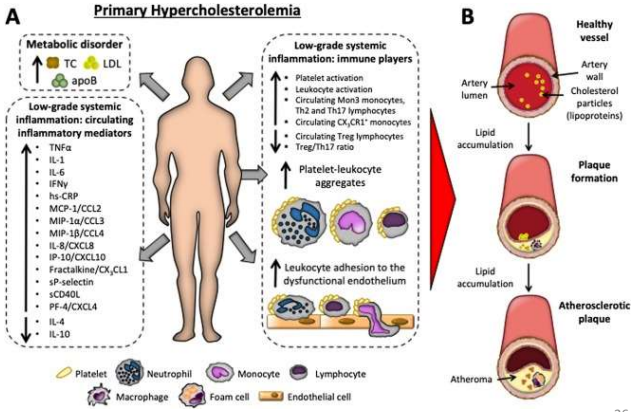
Anatomy



25

Horizontal Integration

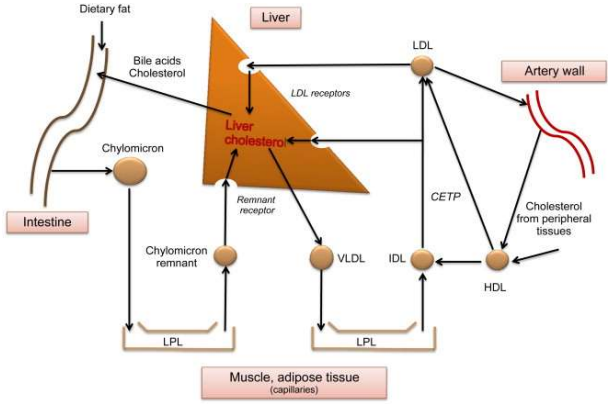
Physiology



26

Horizontal Integration

Related Physiology

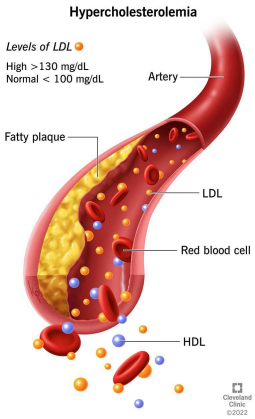


27

Vertical Integration **Clinical Correlation**

Hypercholesterolemia

- Hypercholesterolemia is a lipid disorder in which low-density lipoprotein (**LDL**), or **bad cholesterol**, is **too high**.
- This causes fat to collect in the walls of arteries **Atherosclerosis**, which causes a higher risk of cardiac disease and stroke.
- Atherosclerosis is the main cause of **Cardiovascular Disease**, which is the leading cause of death in the world.



28

Vertical Integration **Clinical Correlation**

Symptoms of Hypercholesterolemia

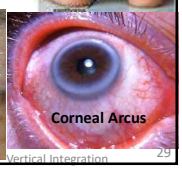
- There are no symptoms of hypercholesterolemia in most people.
- However, in case of severe hypercholesterolemia, there may be cholesterol deposits in the eyelid skin- **Xanthelasma** or connective tissue-**Xanthoma**.
- Cholesterol deposit in the Corn of eye is called a **Corneal Arcus**

Xanthelasma (Xanthoma)

- Collection of macrophages containing lipid droplets
- Associated with
  - Familial hyperlipidemias
  - Nephrotic syndrome
  - Myeloma
  - Pancreatitis
  - Thyroid disease
  - Primary biliary cirrhosis

May be isolated finding

Always check lipids



29

Vertical Integration **Clinical Correlation**

Causes of Hypercholesterolemia

- Genetic Predisposition (pure or familial hypercholesterolemia).
- Regular intake of Diet containing saturated and/or trans fats.
- Lack of exercise/physical activity.
- Using Tobacco products.
- Obstructive liver disease.
- Diabetes Mellitus.
- Hypothyroidism.
- Anorexia nervosa.
- Chronic kidney failure.
- Nephrotic syndrome.
- Amiodarone
- Rosiglitazone.
- Cyclosporine
- Hydrochlorothiazide

30

Spiral Integration **Family Medicine**

Management of Atherosclerosis

Family Medicine plays important role in following manner:

- Diagnosis
- Education
- Dietary Guidance
- Monitoring
- Refer to Specialists

31

Spiral Integration **Artificial Intelligence**

Role of AI in Management

Artificial Intelligence plays role in following aspects:

- Personalized Nutrition
- Diagnostic Tools
- Food Recommendations
- Drug Development

32

Spiral Integration Bioethics

Ethical Consideration

- Informed Consent
- Equal Access to healthcare
- Resource Allocation
- Confidentiality & Privacy

33

33

Spiral Integration Research Article

Atherosclerosis: Pathogenesis, Genetics and Experimental Models

Roberto Ivan, Mota Alvidrez, Jonathan W. Homeister, Monte S. Willis, Edward Suarez Moreira Bahnson

Encyclopedia of Life Sciences (pp.1-10), Chapter: Genetics and disease, Publisher: John Wiley & Sons Ltd, Chichester, Editors: David N. Cooper
https://www.researchgate.net/publication/321335718_Atherosclerosis_Pathogenesis_Genetics_and_Experimental_Models

Abstract:

- Atherosclerosis is a progressive disease of the arteries that results in the development of heart disease and stroke – the most common causes of death in developed countries and a growing socioeconomic burden in developing countries.
- Atherosclerosis results from an initial injury to the artery endothelium caused by mechanical and environmental factors, resulting in an inflammatory response in the vessel wall. The location and morphology of the atherosclerotic lesions predict the nature of the resulting vascular disease.
- Many risk factors for the disease are well known, and current therapies are largely directed at modifying them; however, the large array of poorly understood polygenetic factors affects the development of atherosclerosis.
- Recent developments in genetic studies have been applied to atherosclerosis and are beginning to rapidly reveal the genetic factors that modulate the pathogenesis of this disease.

34

CBL --- Questions /Assessment

1. What is normal plasma cholesterol level?
2. List the causes of hypercholesterolemia?
3. Which vitamin is synthesized from cholesterol in the body?
4. What are the salient features of cholesterol structure?
5. What are the functions of cholesterol?

35

35

Learning Resources

- Textbook of Biochemistry, Lippincott 8th edition, chapter no. 18 , page no. 243, 257, 258
- Google scholar
- Google images

36

36

37