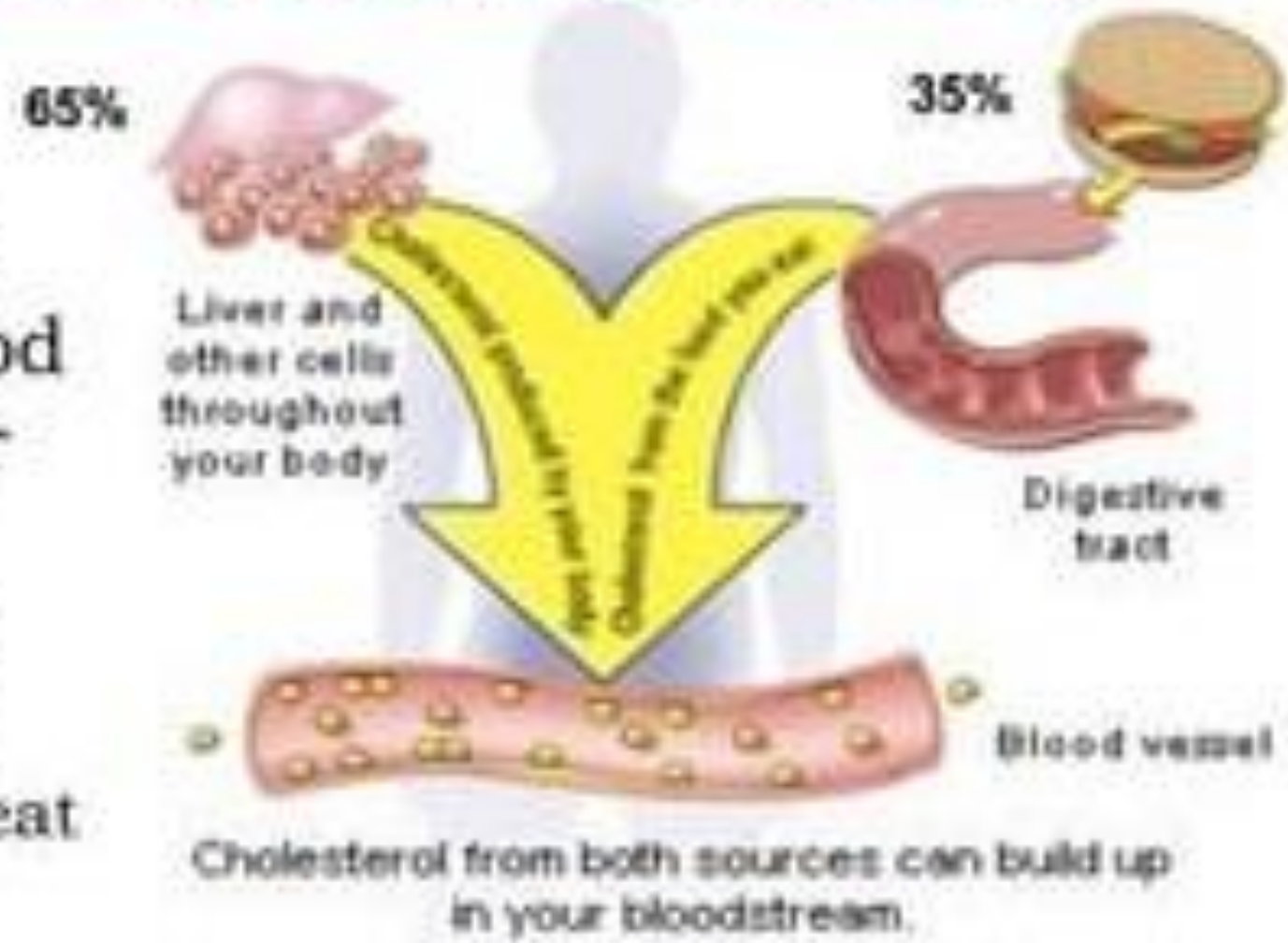
IV	**Basic concepts of Clinical Biochemistry** • A Brief review of units and abbreviations used in expressing concentrations and standard solutions • Specimen collection and processing (Blood, urine, feces) • Anticoagulant and preservatives for blood and urine samples • Transport of specimens	8
V	**Hematology: Blood** • Composition and functions of various components, • Anemia:- classifications, erythrocyte indices • Blood coagulation system, Clotting time, Bleeding time Prothrombin time, RBC count, WBC count,Platelet count Differential count • determination of Hb, PCV and ESR. Hemoglobinopathies, Thalassemia	8
VI	**Disorders of Carbohydrate metabolism** • Regulation of blood sugar • Glycosuria-types of Glycosuria • Oral glucose tolerance test in normal and diabetic condition • Diabetes mellitus and Diabetic insipidus - hypoglycemia, hyperglycemia, Ketonuria, ketosis	4
VII	**Disorders of Lipid metabolism** • Cholesterol: Factors affecting blood cholesterol level • Dyslipoproteinemia, atherosclerosis risk factor and fatty liver. • Involvement of enzymes in diagnostics of heart disease including aspartate transaminase, isoenzymes of creatine kinase and lactate dehydrogenase and troponin	4
VIII	**Liver function test** • Types, differential diagnosis • Liver function test - Icteric index, Vandenberg test, plasma protein changes. Renal function test: Clearance test–Urea, Creatinine • Para- aminohippuric acid (PAH) test, Concentration and dilution test. Enzymology: Clinical significance of SGOT, SGPT, ALP, ACP, CPK and LDH	8

Where does it come from ?

- Two sources of cholesterol: Food & made in your body
- Food sources: All foods containing animal fat and meat products



Blood cholesterol is a fat that is always present in blood cells.

Cholesterol in general is always present in all cell types of the body and is an important component for the structure of cell membranes, a number of hormones and plays many other important functions of body.

Increased level of cholesterol in the blood may cause coronary heart disease (a cause of acute heart attack), stroke (cerebrovascular accident) and peripheral vascular disease. .

Cholesterol can come from two sources: body's synthesis and from the food you eat.

The liver and some other cells of the body make up about 75% of blood cholesterol, the remaining 25% is provided by food.

Cholesterol is insoluble and circulate through the blood stream, along with special protein coat, k/a lipoprotein. There are two important types of lipoproteins:

Low-Density Lipoprotein (LDL) : Specialized in transporting most of the cholesterol in the body's blood. When there is too much LDL in the blood, the artery walls will deposit fat, causing atherosclerosis, which is the cause of dangerous cardiovascular diseases. Therefore, LDL is considered "bad" cholesterol, which needs to be reduced

High-Density Lipoprotein (HDL): In contrast to LDL, HDL is responsible for removing cholesterol from the blood and preventing it from entering the artery walls, thereby limiting the formation of atheroma. Thus, HDL is considered "good" cholesterol, which needs to be increased. There are many different factors that affect the levels of both bad and good cholesterol.

Factors affecting cholesterol

Dietary animal fat, fast food, carbonated water or all foods

that contain too much energy will increase LDL levels and raise total cholesterol. Diet is the main cause of atherosclerosis, myocardial infarction, cerebrovascular accident ... Therefore, to prevent "bad" cholesterol from rising, a reasonable diet should be built. as follows:

Amount of cholesterol ingested: Do not exceed 300mg/day. Use vegetable oil and animal fat in a balanced ratio, suitable for each age group. Eliminate fatty foods, avoid eating animal organs.

Protein: Should account for about 12-15% of the total energy of the entire diet, including beef, pork loin, lean chicken, beans. Fish is a good food for people with dyslipidemia and high cholesterol in the blood. Eat a mix of plant and animal protein.

Carbohydrates: Make up 60-70% of the total energy of the diet. Limit eating too sweet, maximum amount of sugar in the day 10-20g. Use cereal in combination with potatoes. Supplement vitamins, minerals, trace elements, fiber, mainly from green vegetables, fruits, rice.

Overweight, obesity Body mass index (BMI) is used to determine whether a person's body is thin, fat or fit.

The recommended BMI is between 18.5 and 22.9. BMI of 23 or more is considered overweight, easily leading to high cholesterol in the blood.

Lack of physical activity Maintaining a regular exercise regimen will increase HDL and reduce LDL.

Heredity Several genes run in families that govern how cholesterol is digested and processed. This is what affects the cholesterol levels in the blood. There are a number of inherited conditions for high cholesterol.

Age and sex Like genetics, age and sex are factors that affect cholesterol that cannot be changed or influenced. Blood cholesterol in both sexes usually begins to rise at age 20. Most pre-menopausal women will have lower cholesterol levels than men of the same age. After menopause, LDL levels tend to increase, and cardiovascular risk increases accordingly.

Smoking lowers HDL Bad habits like smoking, alcohol, and stimulants are the most common cholesterol-affecting factors that can be avoided. Moreover, quitting smoking and alcohol also helps the body to have better health and eliminates one of the biggest risk factors for cardiovascular disease.

To prevent high blood cholesterol, from the age of 20, it is recommended to perform a blood fat test once a year and from the age of 50 should check every 6 months for total cholesterol, triglycerides, LDL and HDL. Based on the test, the doctor can advise to adjust the diet, increase physical activity or treat with specific drugs if necessary.

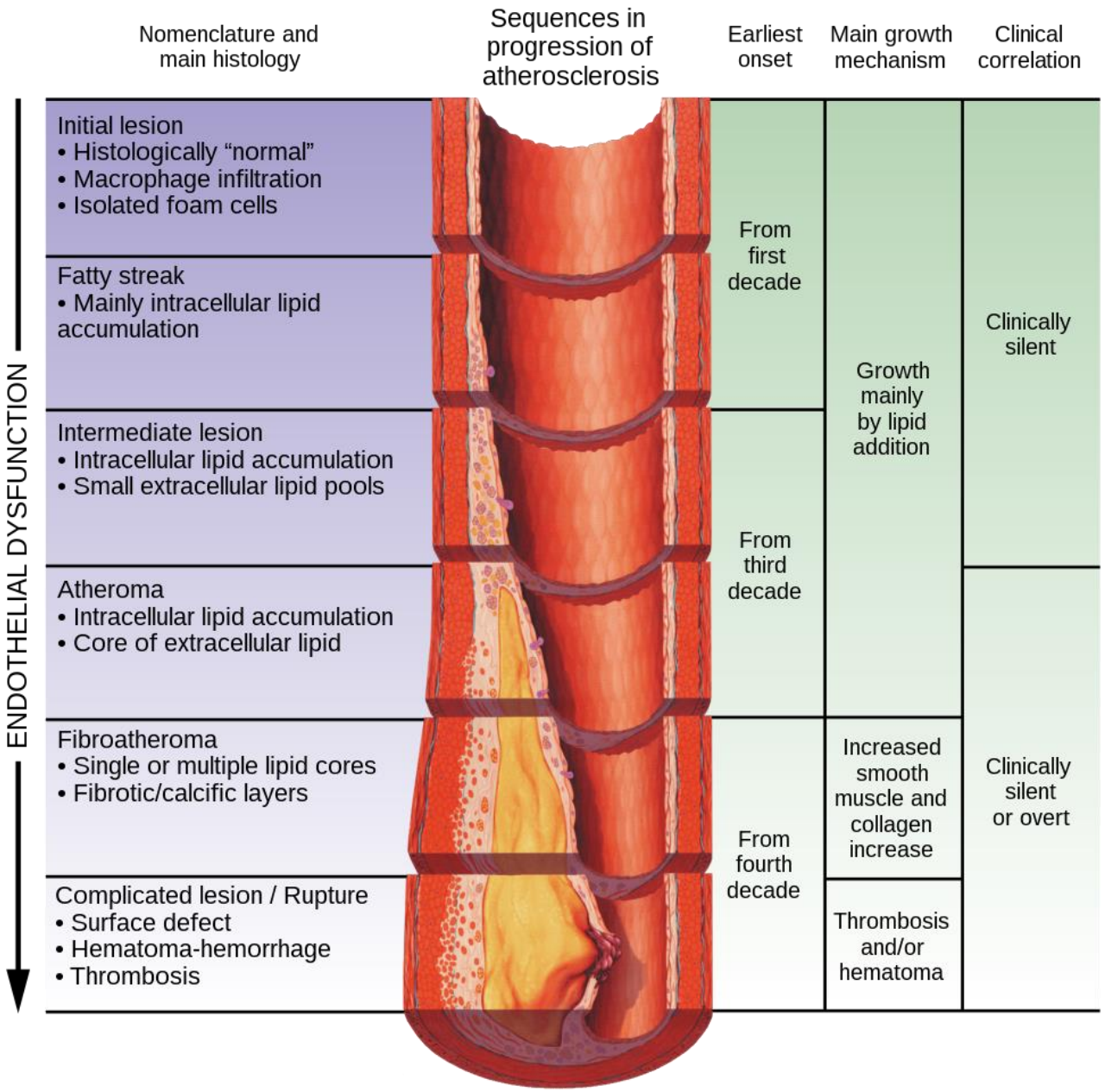
DyslipidemiasPrimary disorders of lipid metabolism such as familial hypercholesterolemia (FH), chylomicronemia, familial combined hyperlipidemia, familial dysbetalipoproteinemia classify according to Fredrickson phenotype.

- Dyslipoproteinemia includes disorders of lipid levels, abnormalities in lipoprotein structure, and abnormal lipoprotein composition or density
- Dyslipoproteinemia is highly prevalent in diabetes, chronic kidney disease (CKD), and diabetic kidney disease
- Dyslipoproteinemia is associated with the development of CKD and renal function impairment in the general population and in diabetic patients

Arteriosclerosis occurs when the blood vessels that carry oxygen and nutrients from the heart to the rest of the body (arteries) become thick and stiff — sometimes restricting blood flow to the organs and tissues. Healthy arteries are flexible and elastic. But over time, the walls in the arteries can harden, a condition commonly called hardening of the arteries.

Atherosclerosis is a specific type of arteriosclerosis.

Atherosclerosis is the buildup of fats, cholesterol and other substances in and on the artery walls. This buildup is called plaque. The plaque can cause arteries to narrow, blocking blood flow. The plaque can also burst, leading to a blood clot.



Atherosclerotic Cardiovascular disease (ASCVD)
Coronary heart disease presents as myocardial infarction, angina pectoris, heart failure, or coronary death
Cerebrovascular disease presents as a stroke or transient ischemic attack
Peripheral artery disease, such as intermittent claudication
Aortic atherosclerosis and thoracic or abdominal aortic aneurysm, the diseases as mentioned earlier are often generalized as the term cardiovascular disease(CVD)
Atherosclerosis is the major culprit in most of the coronary heart disease.[19] Lipids and lipoproteins are established risk factors for developing atherosclerotic cardiovascular diseases(ASCVD). Large clinical trials reported lipid-lowering therapy to reduce the risk of ASCVD events.[20][21]

Several factors are taken into account in 10-year risk cardiovascular assessment as following,

The 10-year risk for ASCVD falls into the following categories:

Low-risk (less than 5%)
Borderline risk (5% to 7.4%)
Intermediate risk (7.5% to 19.9%)
High risk (greater than or equal to 20%)
Risk-enhancing factors such as family history of premature ASCVD, metabolic syndrome, chronic kidney disease, premature menopause, chronic inflammatory disorders, high-risk ethnic groups (e.g., South Asian), persistent elevations of LDL-C greater than or equal to 160 mg/dL or triglycerides greater than or equal to 175 mg/dL, high-sensitivity C-reactive protein greater than or equal to 2.0 mg/L, and ankle-

Nonalcoholic fatty liver disease (NAFLD) is a condition in which fat builds up in your liver. Nonalcoholic fatty liver (NAFL) and nonalcoholic steatohepatitis (NASH) are types of NAFLD. If you have NASH, you have inflammation and liver damage, along with fat in your liver.

Symptoms & Causes

Usually, nonalcoholic fatty liver disease (NAFLD) is a silent disease with few or no symptoms. Certain health conditions and diseases—including obesity, metabolic syndrome, and type 2 diabetes—make you more likely to develop NAFLD.

Diagnosis

Doctors use your medical history, a physical exam, and tests to diagnose nonalcoholic fatty liver disease (NAFLD). Doctors may use blood tests, imaging tests, and liver biopsy to diagnose NAFLD and tell the difference between nonalcoholic fatty liver (NAFL) or nonalcoholic steatohepatitis (NASH).

Treatment

Doctors recommend weight loss to treat nonalcoholic fatty liver disease (NAFLD), which is either nonalcoholic fatty liver (NAFL) or nonalcoholic steatohepatitis (NASH). Weight loss can reduce fat, inflammation, and fibrosis in the liver. No medicines have been approved to treat NAFLD or NASH.

BIOMARKER

- Is a substance used as an indicator of a biologic state
- It is characteristic and found only in tissue of interest
- It is objectively measured
- It is elevated as an indicator of normal biologic processes, pathogenic processes, or pharmacologic responses to a therapeutic intervention
- Detection of marker must enable intervention that prevent or minimize effects of disease

CARDIAC MARKERS

- Intracellular macromolecules (proteins) released from a heart muscle when it is damaged as a result of myocardia infarction (MI).
- They found in the blood.
- They are normally present at all times, however, they are significantly elevated during a damage of the heart muscle.
- **They include:** aspartate aminotransferase (AST or GOT), troponin I & T (TnI, TnT), creatine kinase MB (CK-MB), myoglobin (Mb), lactate dehydrogenase (LDH), B-type natriuretic peptide (BNP), C-reactive protein (CRP), myeloperoxidase (MPO) and ischemic modified albumin (IMA).

ASPARTATE TRANSAMINASE (AST)

- Also called **Glutamic Oxaloacetic Transaminase** (GOT or SGOT, as serum GOT).
- It is widely distributed in tissues but **highest levels** is found in liver, heart, skeletal muscles and RBCs.
- It catalyzes the **reversible transfer** of an α-amino group between aspartate and glutamate and, as such, is an important enzyme in amino acid metabolism (it provide a source of oxaloacetate for Krebs cycle).

- Normal values (8 – 20 U/ L).
- Raised by 6 – 8 hours.
- Peak by 18 – 24 hours.
- Returned to normal by 4 – 5 days.

LACTATE DEHYDROGENASE (LDH)

- Lactate dehydrogenase (LDH, or LD) is an enzyme that is found in almost all body tissues but only a small amount of it is usually detectable in the blood.
- It usually stays contained within the tissues cells. When cells are damaged or destroyed, however, they release LDH into the bloodstream, causing blood levels to rise.
- For this reason**, LDH is used as a general marker of injury to cells.**

LACTATE DEHYDROGENASE (LDH)

Function

- Lactate dehydrogenase catalyzes the interconversion of pyruvate and lactate with concomitant interconversion of NADH and NAD^+.
- It converts pyruvate, the final product of glycolysis to lactate when oxygen is absent or in short supply. This reaction is known as anaerobic homolactic fermentation and is an important way to regenerate NAD^+ to allow glycolysis to continue .

LDH ISOENZYMES

- LDH functions as a **tetramer** and is made of two kinds of subunits, H and M, each of which are encoded by a different gene. This results in 5 different isoenzymes (2 homotetramers and 3 heterotetramers).
- The M subunit is found predominantly in anaerobic tissues including skeletal muscle and liver. The H subunit is more commonly found in tissues with a ready source of oxygen and that metabolize lactate including the heart and the brain.

LDH ISOENZYMES

1. **LDH-1 (4H)** – in the heart
2. **LDH-2 (3H1M)** – in the reticuloendothelial system
3. **LDH-3 (2H2M)** – in the lungs
4. **LDH-4 (1H3M)** – in the kidneys
5. **LDH-5 (4M)** – in the liver and striated muscle

- Usually LDH-2 is the predominant form in the serum. A LDH-1 level higher than the LDH-2 level (a "flipped pattern"), suggests myocardial infarction.

LDH MEASUREMENT

Sample:

- Serum sample is used

Source of error:

- Strenuous exercise can cause temporary elevations in LDH
- Hemolysis of blood can cause false positives

Interpretation:

- Elevated levels of LDH and changes in the ratio of the LDH isoenzymes usually indicate some type of tissue damage. Usually LDH levels will rise as the cellular destruction begins, peak after some time period, and then begin to fall.

LDH RESULT INTERPRETATION

Cardiac disease:

- It can be used as a marker of myocardial infarction. Following a myocardial infarction, levels of LDH will **rise within 24 to 48** hours, **peak at 3-4 days** and remain elevated for up to 10 days.
- In this way, elevated levels of LDH can be useful for determining if a patient has had a myocardial infarction if they come to doctors several days after an episode of chest pain.
- LDH level is directly proportional to the infraction size.
- **Note:** *LDH level can be elevated in other cardiac disease such as Myocarditis and rheumatic fever*

- **Troponins are contractile proteins found within muscle fibres that help regulate contractions.**
- **There are 3 troponins that work as a complex. They are:**

Troponin C (ca- binding component)

Troponin I (Inhibitory component)

Troponin T (Tropomyosin- binding component)

- **During the process of muscle necrosis, Troponins I and T are released from the dying muscle fibres into the blood stream.**

Increases in the concentration of troponins I and T above the reference levels in serum indicate heart muscle fibre and necrosis.

- **Measurement of troponin assays has been a tremendous boon to clinical diagnosis.**

Troponins released from heart muscle remain in the blood stream from 1 to 14 days after the onset of AMI.

- **Troponins as cardiac markers, appear to have many advantages primarily due to their quick release following heart muscle damage and their longevity in the blood stream following heart attack**

- **The risk of death from an Acute Coronary Syndrome (ACS) is directly related to troponin level.**