Federal state budgetary educational institution of higher education "Volgograd state medical University" of the Ministry of health of the Russian Federation

Department of clinical laboratory diagnostics

LECTURE №4
Cardiovascular system diseases. Atherosclerosis. Disorders of lipids metabolism.

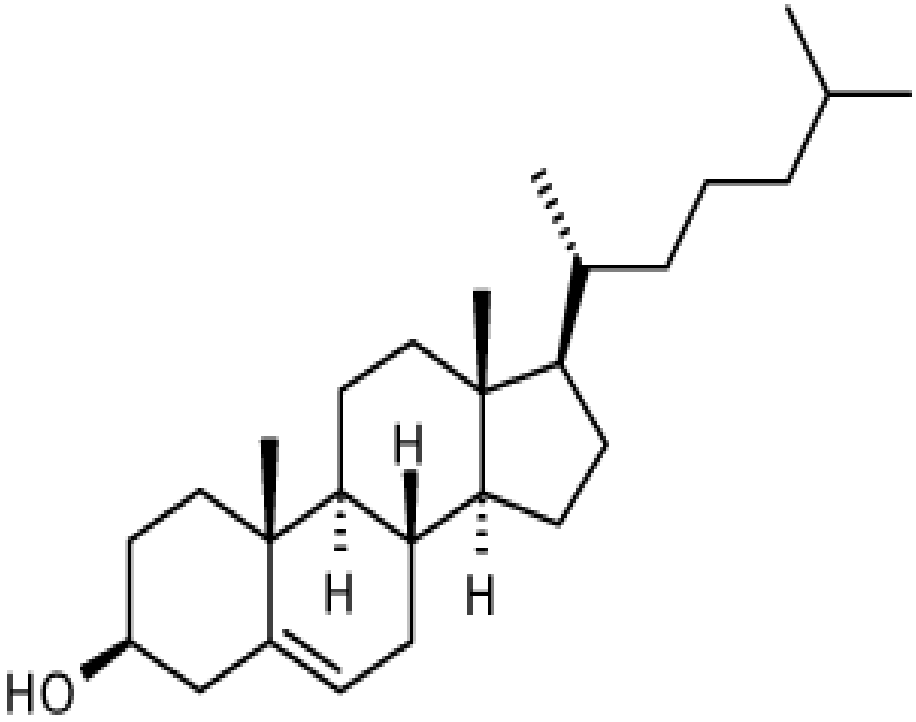
Lipids are organic compounds, water-insoluble, but soluble in organic solvents (air, gasoline, chloroform).

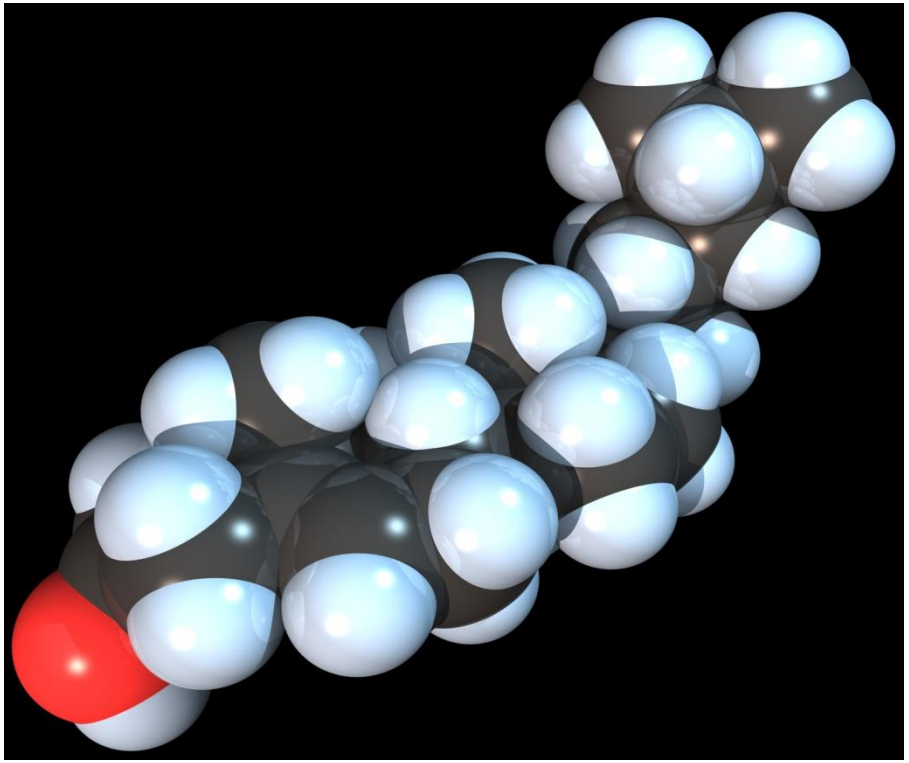
simple	composite	steroids
triglycerides (neutral fats) wax	phospholipids glycolipids lipoproteins	cholesterol sexual hormones bilious acids

Functions of lipids

- **1. Structural: phospholipids, glycolipids, cholesterol are as a part of membranes**
- **2. Power: when splitting 1g of fat, 38,9 kJ of energy is allocated.**
- **3. Reserving: a reserve energy source (a fat drop in a cage, a fatty body of insects, a hypodermic fatty tissue).**
- **4. Protective:**
- **- physical protection against bruises;**
- **- water repellency: wax: cuticle, feathers, wool;**
- **- electric isolation: glycolipids (myelin);**
- **- prostaglandins (causing fever, stimulate reduction of muscles of an internal).**
- **5. Thermoregulatory:**
- **- thermal isolation (hypodermic fat);**
- **- «brown fat» is a biological heater.**
- **6. Source of endogenous water: oxidation of 100 g of fat gives 107 ml of water.**
- **7. Regulatory: lipids are predecessors of synthesis of steroid hormones, liposoluble vitamins A, D, E**

Cholesterol

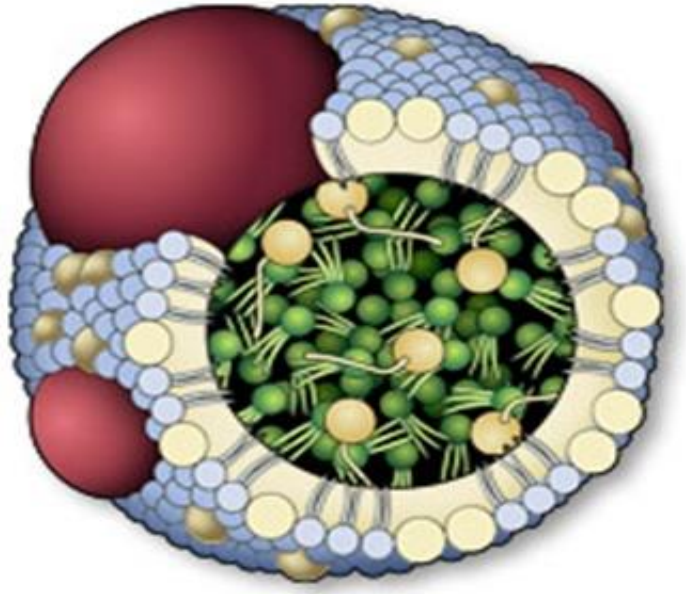




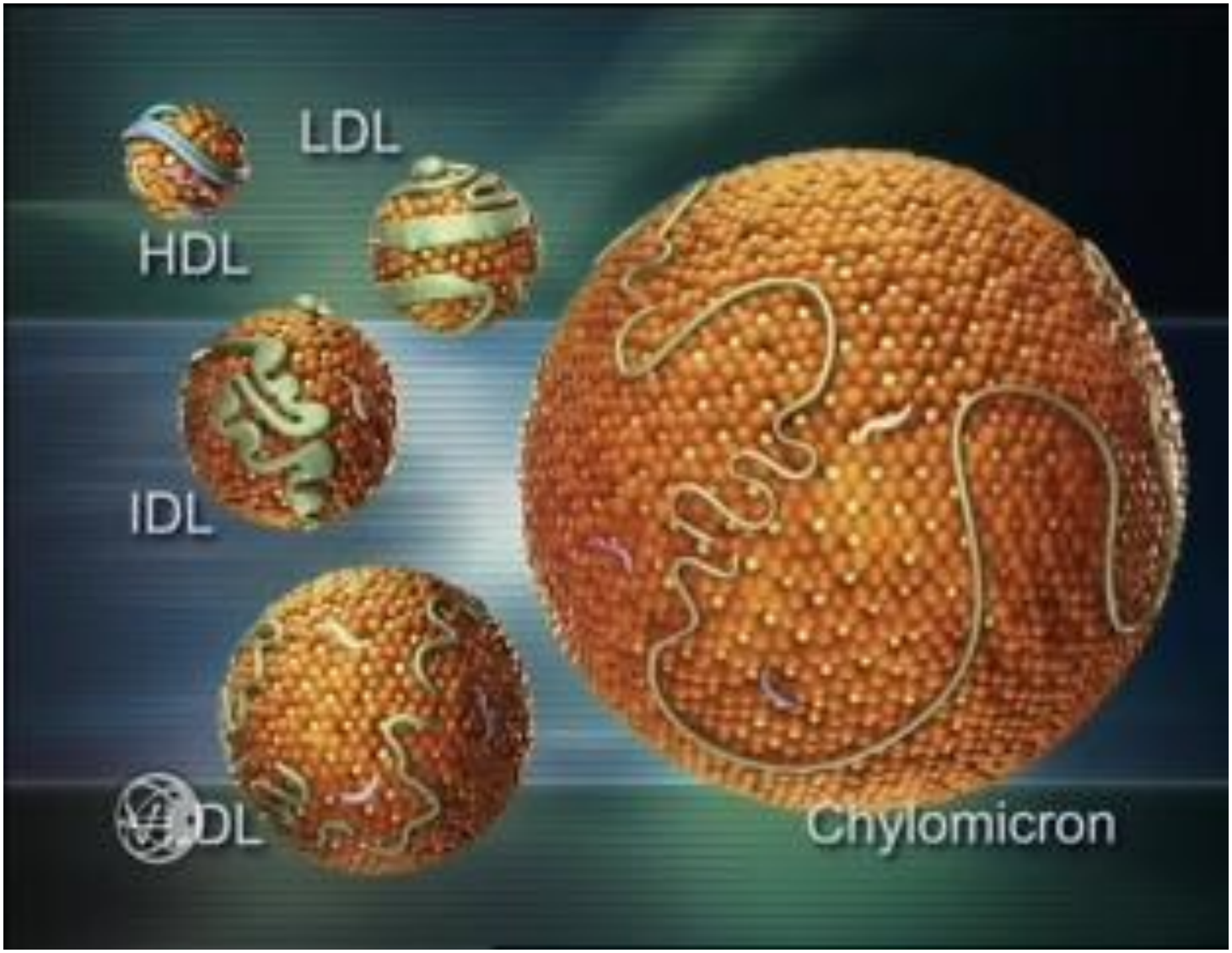
Cholesterol functions

- • lowers fluidity and a transmittivity of biological membranes
- • participates in ensuring barrier function of membranes
- • influences activity of membranous enzymes
- • excess of cholesterol in a cytoplasmatic membrane complicates operation of calcium pumps
- • is the predecessor of steroid hormones of adrenal glands and sexual hormones, vitamin D
- • being oxidized, turns into bilious acids and it is deduced from an organism
- • the lack of a cholesterin of an organism promotes the increased risk of development of tumoral and virus diseases

Lipoproteins

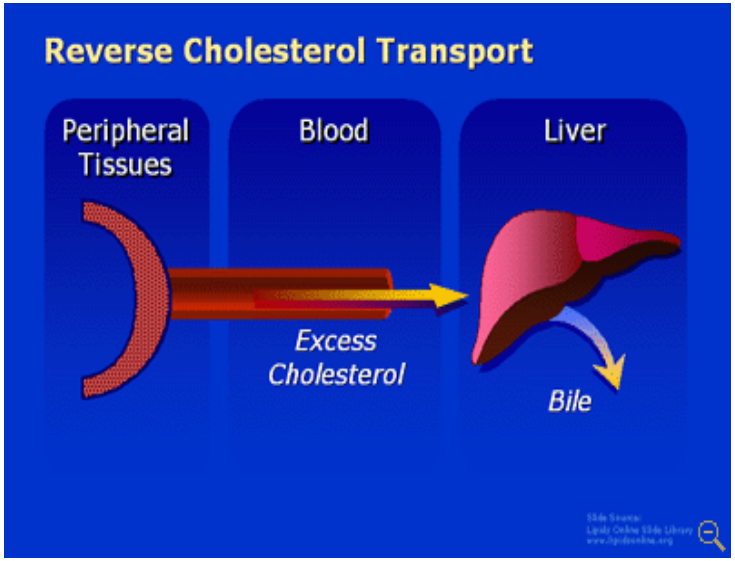


Particles of lipoproteins have a spherical form and consist of a hydrophilic envelope and a hydrophobic core. The hydrophobic core is presented by non-polar triacylglycerides and cholesterol air. The hydrophilic envelope is the top tessellated monolayer consisting of phospholipids, cholesterol and apoproteins. The hydrophilic envelope provides solubility of lipoproteins and defines paths of a metabolism and destiny of each lipoproteins (due to apoproteins).

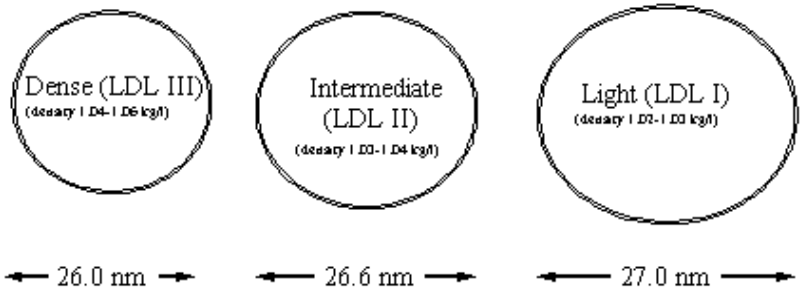

LDL
HDL
IDL
Chylomicron

- **The less size of the LDL particle is the higher is the atherogenesis.**

- **HDL deletes an exuberant cholesterin from fabrics and from a blood-groove and promotes its transportation in a liver.**
- **HDL are anti-atherogenous since are interfaced to decrease in risk of an atherosclerosis and connected with it diseases**



LDL Subfractions



Apolipoproteins

Apolipoproteins are the protein constituents of lipoproteins and they have three main functions:

- **1. They facilitate lipid transport by interacting with the phospholipids, thereby helping to stabilise cholesterol esters and triglycerides.**
- **2. They regulate the interaction of these lipids with the enzymes lecithin cholesterol acyltransferase (LCAT), lipoprotein lipase (LPL) and hepatic triglyceride lipase (HTGL).**
- **3. They bind to cell surface receptors.**

Hyperlipoproteinaemia types

- **Type I– hyperchylomicronaemia**
- **Type IIa– hypercholesterolemia**
- **Type IIb– hypercholesterolemia + hypertriglyceridemia**
- **Type III– hyper intermediate density lipoproteinemia**
- **Type IV– hypertriglyceridemia**
- **Type V – hyperchylomicronaemia + hyper very low density lipoproteinemia**

Laboratory diagnostics of dyslipidemia

- **Screening**

Its purpose is identification of dyslipidemia (determination of cholesterol level in the serum; in case of hyperlipidemia lipids spectrum analysis)

- **Diagnostic investigation**

Its purpose is identification of dyslipidemia types, assessing the total risk of ischemic heart disease (primary, secondary, dyslipidemia phenotyping, atherogenicity index definition, apo B/AI, LP (a), phenotype of apo E)

- **Therapy monitoring**

Its purpose is estimation of therapy effectiveness, diagnosing complications.

Calculation of cholesterol

Total cholesterol = LDL + VLDL + HDL

Calculation of the LDL

- **VLDL=TG/2.2, mmol/l**
- **VLDL=TG/5, mg/dl**
- **Calculation of the LDL**
- **LDL=cholesterol-TG/2.2-HDL, mmol/l**
- **LDL=cholesterol-TG/5-HDL, mg/dl**
- **LDL = chol – (HDL +TG*/2,2)**

***if TG level does not exceed 4,5 mmol/l (Friedvald's Formula)**

Investigation of lipid metabolism

- **1. The first stage is definition of the content of total cholesterol and triglycerides; if hypercholesterinemia or hypertriglyceridemia is detected, it is necessary to go on the second investigation phase.**

- **2. The second stage is definition of lipid spectrum: cholesterol, TG, HDL-cholesterol, LDL-cholesterol; LP electrophoresis; calculation of atherogenicity index (AI) and the LDL content if it wasn't measured before.**

- **3. The third stage is differentiation between primary and secondary GLP which is made by elimination of all diseases for which the secondary GLP are characteristic: diabetes mellitus, nephrotic syndrome and other lesions of renal parenchyma, liver diseases with manifestations of cholestasis, decreased blood albumin, acute or chronic phase of inflammatory process, etc.**

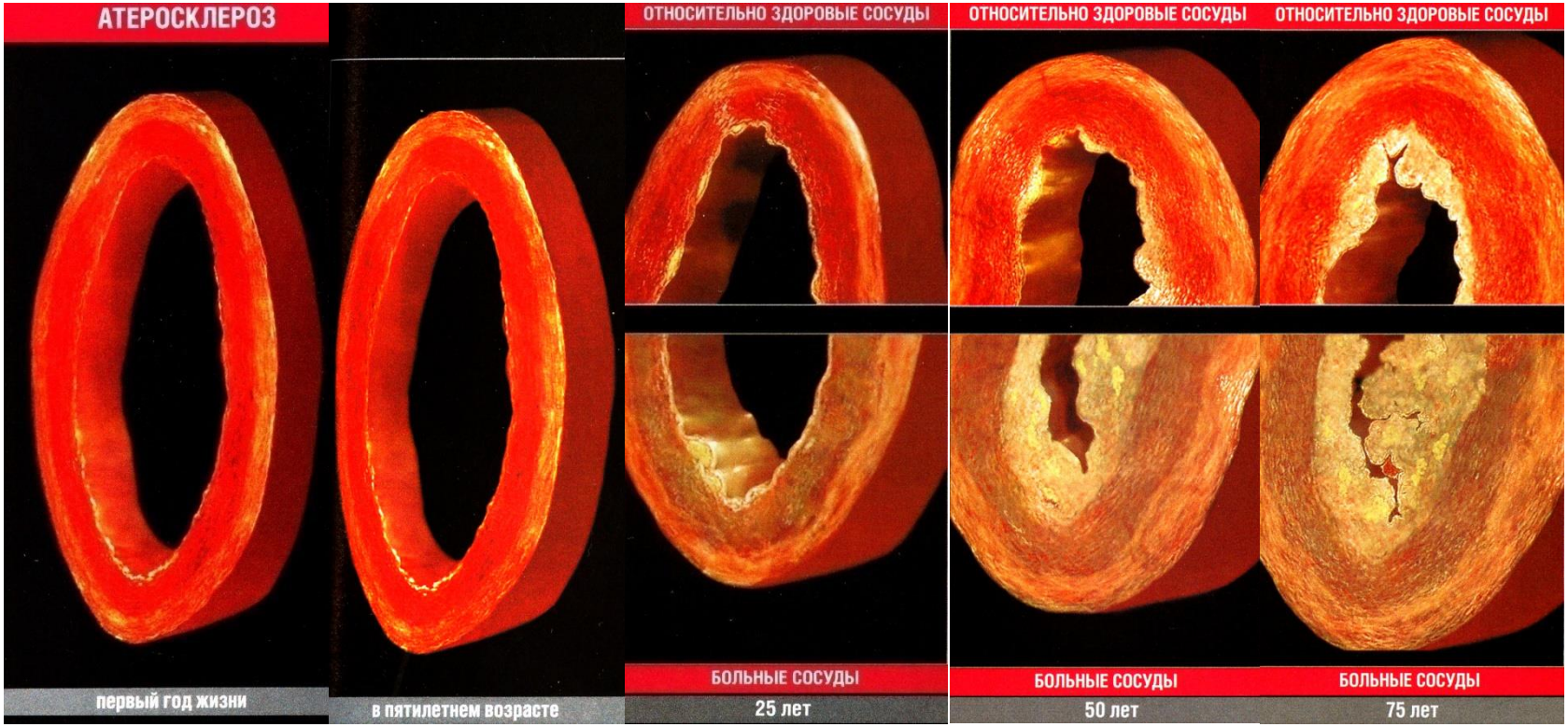
Procedure of blood sampling for investigation of lipid metabolism

1. **The blood should be taken in the morning on an empty stomach (for definition of TG and the LDL), 12–14 h after meals.**
2. **Separation of serum (plasma) from corpuscular elements of blood should be carried out within the first 3 h from the moment of blood withdrawal.**
3. **The samples should be stored at temperature of 0-4 °C for no longer than 3 days.**
4. **Lipid profile should be studied no less than twice at different times (at an interval of two weeks), take into account the findings of no less than 2 measurements.**

- **Ischemic heart disease is atherosclerotic lesion of the coronary arteries system resulting in coronary failure. It is manifested as angina pectoris, dystrophy, necrosis (heart attacks), myocardial sclerosis, as well their consequences and complications including sudden death.**

- **Hyperlipoproteinemia is a major risk factor of ischemic heart disease characterized by elevated lipid and LP content in blood serum.**

ATHEROSCLEROSIS is the result of infringement of the active transport of polynonsaturated fatty acids, development of a syndrome pathological compensation, the broken synthesis of eicosanoids, the chronic progressing disease of large and average elastic and is muscular-elastic arteries characterized by the proliferative-synthetic answer of some cages of a vascular wall and blood on pathological lipoproteins, with formation of atheromas in intima.


АТЕРОСКЛЕРОЗ
первый год жизни
в пятилетнем возрасте
ОТНОСИТЕЛЬНО ЗДОРОВЫЕ СОСУДЫ
БОЛЬНЫЕ СОСУДЫ
25 лет
ОТНОСИТЕЛЬНО ЗДОРОВЫЕ СОСУДЫ
БОЛЬНЫЕ СОСУДЫ
50 лет
ОТНОСИТЕЛЬНО ЗДОРОВЫЕ СОСУДЫ
БОЛЬНЫЕ СОСУДЫ
75 лет

ATHEROSCLEROSIS

Atherosclerosis is a result of disorder of the active transport of polyunsaturated fatty acids, development of pathological compensation syndrome, disturbed synthesis of eicosanoids.

Traditional modificational risk factors of atherosclerosis include: arterial hypertension, dyslipoproteidemia, diabetes, smoking, obesity, physical inactivity.

- **In deficiency of fatty acids, mainly Ω-3 fatty acids, two processes dominate:**
- **• change of structure and properties of cellular membranes and chemical structure of biologically active eicosanoids.**
- **• pathological indemnification aimed at establishing aphysiological active transport of fatty acids into cells.**
- **Necrosis of mesenchymal cells begins sets off an inflammation syndrome.**

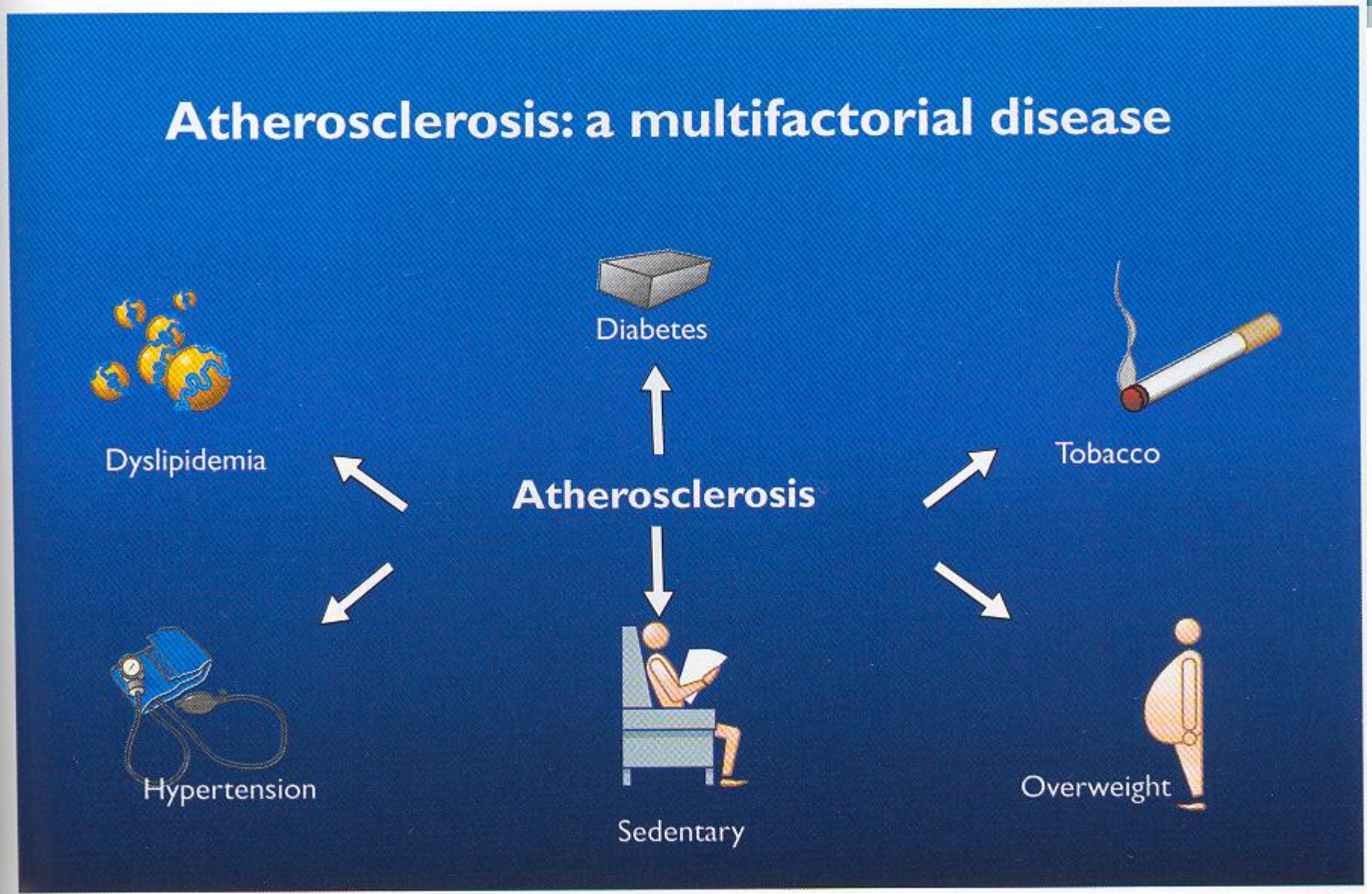


Figure 3 Traditional risk factors include age, male sex, dyslipidemia, hypertension, smoking, and diabetes. More recently identified risk factors include obesity and a sedentary lifestyle.

Target values of lipid content in the blood according to the European recommendations, 2003

Indicator	Patients without coronary heart disease or diabetes	Patients with coronary heart disease and diabetes
Cholesterol	< 5 mmol/l	< 4.5 mmol/l
LDL-cholesterol	< 3 mmol/l	< 2.5 mmol/l

Markers of a higher risk of death of cardiovascular diseases are also as follows:
- HDL <1.0 mmol/l in men and <1.2 mmol/l in women,
- TG >1.7 mmol/l

Coronary heart disease is the narrowing or blockage of the coronary arteries, usually caused by atherosclerosis.

- **Diagnosis of heart attack is based on symptoms of disease, ECG diagnostics, laboratory diagnostics (increase of the enzymes level in the blood).**

The development of the myocardial ischemia causes suppression of oxidative phosphorylation, activation of glycolysis and declining of the assimilation of glucose.

As a result of defects arising in the cytoplasmic membranes of myocardiocytes, proteins and enzymes of the cytoplasm enter the blood. It depends on molecular size and the speed of their elimination from the blood flow.

Risk factors

Biological factors:

- **old age**
- **male**
- **genetic factors**

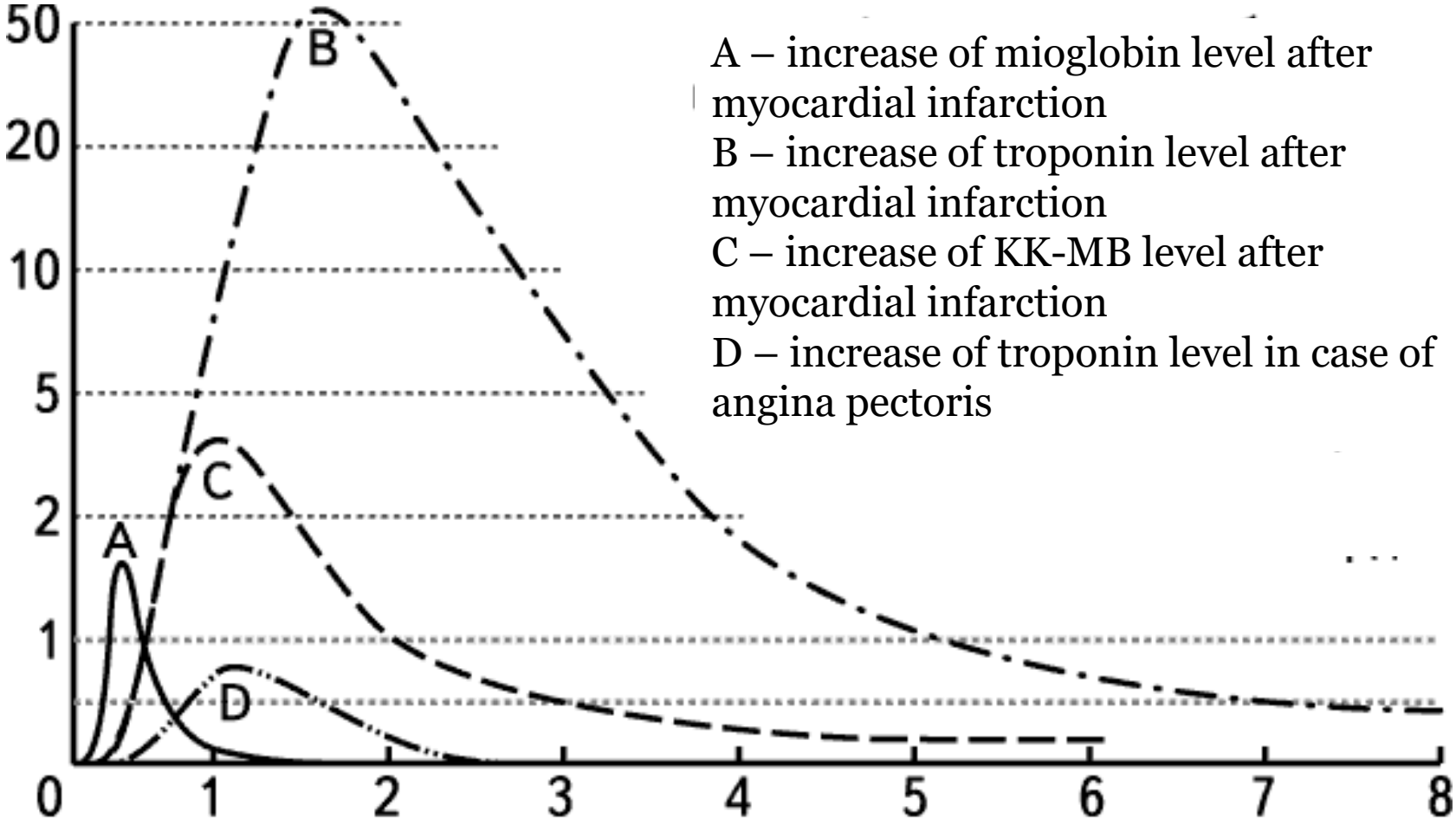
Anatomical, physiological and metabolic factors:

- **dyslipidemia**
- **arterial hypertension**
- **obesity**
- **diabetes**

Risk factors

Behavioural factors:

- **dietary habits**
- **smoking**
- **alcoholism**
- **low physical activity.**



A – increase of mioglobin level after myocardial infarction
B – increase of troponin level after myocardial infarction
C – increase of KK-MB level after myocardial infarction
D – increase of troponin level in case of angina pectoris

Markers of heart attack

Marker	Structure	Pathology	Value
KK-MB	3 isoenzymes: MM (muscle), BB (brain), MB.	• heart attack • the heart operation • myocarditis and myocardiodystrophy • chest radiotherapy • stress • muscle damages	Increase of the KK-MB level is 4-8 hours after the acute attack and lasts 12-24 hours, on the third day the activity of the enzyme returns to normal values. The magnitude of improvement is corresponding to the affected areas of the myocardium.

Troponin I	Contractile protein	• heart attack diagnostic • assessment of the reperfusion after thrombolysis treatment • selection of high coronary risk groups among patients with acute coronary syndrome without ST segment elevation	Increase of the troponin I level in the blood is 4-6 h after acute attack, it reaches its maximum on the 2-nd day and returnes to normal between 6 and 8 days.

Myoglobin	Chromoprotein, the transporter of oxygen in the muscles.	• heart attack • electric shock • crash-syndrome • muscle damages • burn	Increase of the protein level in the blood is 2-3 h after the pain and lasts 2-3 days. Repeated increase of the myoglobin level in the blood may indicate the expansion of the heart damages zone.

LDH	Isoenzymes: LDH 1, 2 – heart, LDH 3, 4 – lung, LDH 5 – liver.	• cardiovascular diseases • diseases of the liver • anemia • oncology diseases	Level of enzyme increases rapidly in 2-4 hours, it reaches its maximum on the 2-nd day and is normalized by only 2-3 weeks.

ALAT, ASAT	Aminotranspherases of liver, heart, muscles.	Damages of heart and muscles. De Ritis coefficient = AST/ ALT (1,33±0,42)	Level of enzymes increases in 6-12 hours, and is normalized by only 5-7 days.

CRP	Protein of inflammation acute phase	Tissue damage (inflammation, trauma)	The concentration of CRP in the blood serum or plasma increases within 24-48 h after acute tissue damage, reaches a peak in the acute phase and is reduced after the resolution of inflammation or injury, a basic level of C-reactive protein reflects inflammation in vessel's intima and prospectively determines the risk of the development of vascular complications.

Other markers:

- **Natriuretic peptides (brain, atrial)**
- **Protein that binds fatty acids, the cardiac form of (H-FABP)**
- **Homocysteine**
- **Cytokines**
- **Hemostatic factors**
- **Adhesion molecules**
- **Caspase**
- **Lipid spectrum**

- **Thank you for your attention!**