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DISORDERS OF LIPID METABOLISM. HYPERLIPOPROTEINEMIA. DYSLIPIDEMIA.

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SERUM LIPOPROTEINS

Lipids are one of the most important classes of complex molecules, present in the cells and tissues of animals as part of adipose tissue, playing an important physiological role. The term lipids combines substances with a general physical property of hydrophobicity.

Lipids are divided into classes, in which they combine molecules that have similar chemical structure and general biological properties. Variety and level of lipids in cells, tissues and organs determined by the processes of lipid metabolism, including their transport, absorption, use by cells, synthesis de novo, destruction and excretion. Lipid metabolic processes take place with the participation many proteins with different functions, which, as well as encoding them genes are also components of the lipid metabolism system.

Lipid metabolism is one of the most complex metabolism of the body. The importance of lipids in the body is great: they form the basis central nervous system, form the lipid matrix of cellular membranes and organelles of cells play an important role in energy metabolism.

Some lipids are complex enzyme complexes, taking part in immunological reactions, processes digestion, blood clotting.

Lipid metabolism can be divided into the following stages: cleavage ingested fats and their absorption in the gastrointestinal tract intestinal tract; transformation of the absorbed fat breakdown products intotissues leading to the synthesis of fats specific to a given organism; fatty acid oxidation processes accompanied by release biologically useful energy; the release of metabolic products from the body.

Lipids and lipoproteins

Lipids

Plasma lipids are composed mainly of fatty acids (FA), cholesterol, triglycerides and phospholipids. The bulk of lipids are triglycerides, which are an important energy substrate, and cholesterol is the main component of cell membranes and intracellular organelles.

Fatty acids (FA) have the general formula:

CH3 (CH2) nCOOH.

At the early stages of phylogenesis, the transfer of all FAs took place (and passes) in the composition of high density lipoproteins (LP) (HDL) in the form of polar lipids (phospholipids - PL and diglycerides - esters with alcohol glycerin); from HDL, the cells absorbed lipids only passively.

At later stages of phylogenesis, the formation of LP of low density (LDL). They began to transfer FAs to cells in the form non-polar lipids: saturated fatty acids (EFAs), monoene fatty acids (FFAs) and unsaturated fatty acids (unsaturated fatty acids) in the form of ethers with trihydric alcohol glycerol, and essential polyene FA (ESPUFA) in the form of esters with monohydric cyclic alcohol cholesterol (CS). From the composition of LDL cells have absorbed EFA, FFA, UUFA and ESPUFA already actively, by receptor apoB-100 endocytosis. Much later, during the formation the biological function of locomotion and the insulin system occurred the formation of very low density LP (VLDL). They became in large quantity to transfer to cells only EFAs and MFAs as substrates for cell production of energy, ATP synthesis, and insulin-dependent cells they began to be absorbed by apoE / B-100 receptor endocytosis.

The improvement of the LP system at the stages of phylogenesis is dictated by biological necessity, development and improvement organism, the formation of new biological functions and biological reactions.

The human body contains both saturated and unsaturated fatty acids with different roles: saturated fatty acids in cells are an energetic material, unsaturated FAs perform plastic function. Fatty acids in mammals - major energy supplier. In blood plasma, they are found mainly in esterified form: in the composition of mono-, di - and triglycerides; phospholipids and cholesterol esters. Lipases that break down TG into digestive tract, hydrolyze esters at a high rate glycerol formed by unsaturated FA and slowly break down TG, formed by saturated fatty acids. With a high content of unsaturated FA in the composition of TG, its esters are faster hydrolyzed and removed from blood flow. In this regard, it is recommended to eat vegetable oils rich in polyene unsaturated FAs, possessing antiatherogenic action, instead of animal fats, containing mainly saturated fatty acids. Normal values the content of fatty acids in the blood serum is 0.4–0.8 mmol / l.

Triglycerides have a general formula:

CH2-O-R1

|

CH-O-R2

|

CH2-O-R3, where R1, R2 and R3 are fatty acid residues.

Triglycerides are trihydric alcohol glycerol, esterified with long-chain FAs, including in the body in humans, unsaturated fatty acids predominate: oleic, stearic, palmitic.

The classification of TG is determined by which FA is esterified in the second the (middle) position of the trihydric alcohol glycerol (sn-2); From 16: 0 palmitic saturated

FA (EFA), C 18: 1 oleic monoenic FA (mono-LC), C 18: 2 linoleic or C18: 3 linolenic ES, unsaturated (not) NLC.

Form hepatocytes and C18: 0 stearic triglycerides - intermediate between palmitic and oleic. Due to the physicochemical differences between TG apoB-100 structures them separately into palmitic, oleic,

linoleic and linolenic VLDL and secretes all four subclasses VLDL into the bloodstream.

Triglycerides make up about 90% of all lipids, and their intensity metabolism is the largest among other lipids: conversion of 75–150 g of TG. Therefore, after eating fatty foods, the level of TG rises significantly and remains high for several hours. Everything is normal TGs are removed from the bloodstream within 12 hours. Long-chain FAs, included in the TG, are the optimal source of macroergs, formed during β-oxidation of FAs in mitochondria, therefore, most organs for energy needs uses exactly TG, the exception is the brain, the energy supply of which occurs due to glucose metabolism.

Cholesterol

Cholesterol is a monohydric secondary alcohol and is not a lipid, however, when FAs interact with it and form the transport form of FA and the deposited form of cholesterol in the cytosol (cholesterol arahidonate), the cholesterol esters become lipids. In organism a person has about 80% of free cholesterol; in blood serum - 30% free and 70% CS ethers. About 1.5 g of exogenous is absorbed from food CS, which is 35-40% of its total amount that got into the body with food during the day, another 1 g of cholesterol is synthesized in the body.

Part of the cholesterol is oxidized to bile acids, part is removed with feces. After consumption of food, the level of cholesterol in the blood serum is practically not changes.

Phospholipids (PL) - unsymmetrical diesters of phosphoric acid general formula: RO (O) P (OH) OX, where R is alkyl (acyl, alkenyl) derivatives of polyhydric alcohols - glycerol (diols, sphingosines), X is the remainder of the amino alcohol, amino acid, myoinositol, or glycerin. Phospholipids are compounds similar to TG, in which one of residues of FA is replaced by phosphate with a nitrogenous base. Molecules phospholipids contain non-polar hydrophobic "tails" and polar hydrophilic "head", due to which non-polar LC circuits are capable of interact with lipids, and polar phosphate "heads" - with water surroundings. In lipoproteins, PL is maintained in a dissolved state non-polar lipids such as TG and CS esters. Normal values of PL in serum levels are 2–3 mmol / l in men and slightly higher in women.

Lipids are insoluble in water, they are transported in the blood to complex with proteins. The main carrier of free LCDs is albumin, while other lipids circulate in complexes, known as lipoproteins.

Lipoproteins

Lipoproteins are water-soluble complexes with a high molar mass, consisting of lipids and one or more proteins called apolipoproteins (apoLP). All LP are formed in the liver and / or in intestines, their main function is the transport of lipids. LP complex contains a non-polar core composed of triglycerides and esters cholesterol surrounded by a polar layer of phospholipids, non-esterified cholesterol and apolipoproteins. Depending on the the role of apoLP, they can be conditionally divided into two classes.

The first of them should include apoLP, which form the micellar structure of LP complexes and serve as the nucleus of LP particles. In this the group includes apoB (apoB-100 and apoB-48) and apoA (A-1 and A-11), responsible for the implementation of lipid transport. ApoB – structural LP protein, rich in triglycerides, does not leave the micellar complex in the process of sequential metabolic transformations of very low lipoprotein density (VLDL) in the intermediate density LP (IDP) and further in the LP low density (LDL), the accumulation of which in the vascular wall is a pathogenetic link in the atherosclerotic process.

Apoproteins AI and A-II are the main proteins of high density LP (HDL).

Another class includes apoLP, which regulate lipid metabolism. These apoproteins are contained in LP in significantly smaller amounts and in the process of LP conversions in the bloodstream move between LPs of different classes in the form of protein-lipid complexes. The main representatives of this group are apoE (with isoforms E2, E3, E4) and apoC (C-I, C-II, C-III). ApoLP play a major role in metabolism LP, being ligands of particles interacting with cellular receptors for specific drugs.

Lipoproteins have been classified based on density, detected in electrophoresis or ultracentrifugation, and by its size are divided into 5 fractions: chylomicrons (HM), VLDL, IDL, LDL, HDL .

In phylogeny, LDL was formed earlier than VLDL; between them many millions of years. To understand the conversion of VLDL to LDL it is rational to consider them not by the difference in density, but on the basis of their functions, reasonably believing that VLDLP implement energy supply cells, and LDL provides cells with structural materials.

Density of VLDL when transferring energy substrates to cells (palmitic EFA + stearic + oleic mono-FA) lower, than LDL in the transfer of non-EFA and ES-poly-FA. Quantity palmitic and oleic TGs in VLDL in the bloodstream are ten times more, than linoleic and linolenic LDL. When, during the hydrolysis of TG, linoleic and linolenic VLDL acquire the hydrated density of LDL - it is physiological. If palmitic and oleic VLDL instead of their absorption by cells in the form of ligand VLDLP remain in the blood and when Continuation of lipolysis acquire the density of LDL - this is non-physiological.

Having acquired the density of LDL, they functionally remain palmitic and oleic carriers of substrates for energy production . V intercellular environment ligand-free palmitic and oleic VLDL with density LDL are biological "waste"; it is called absorb the "sedentary" macrophages of the intima as a local pool of PCT for collection and disposal of biological "waste" from the intravascular pool intercellular environment.

Chylomicrons are the largest drugs rich in triglycerides. After entering the bloodstream, they decay to remnant (residual) particles that are captured by the liver. In the physiological state of HM are present in the blood serum only after ingestion of fatty foods, but not on an empty stomach. Triglycerides are synthesized in the liver and enter the bloodstream in the form of VLDL, which disintegrate to LDD and then partially converted to LDL. Under certain metabolic conditions, remnants VLDL and LDL accumulate in the blood and contribute to the risk of coronary heart disease; LDL contain 60-70% of total serum cholesterol (TC) and are the main atherogenic class of drugs; HDL contains 20-30% total cholesterol blood serum. It was shown that there is an inverse dependence of the CS level HDL with risk of coronary artery disease.

Very low density lipoproteins (VLDL) are large and "Loose" drugs containing about 55% TG, 19% cholesterol and only 8% protein (apoproteins B-100, E, C-1 and C-II). This drug class is the main the transport form of endogenous TGs synthesized in the liver. By entering blood, VLDL are also exposed to lipoprotein lipase, localized including on the surface of the vascular endothelium. V as a result, TG is split into glycerol and NEFA, which also used by adipose tissue, myocardium and skeletal muscles in as an energy substrate. Remains of VLDL turn into LP intermediate density (BID), which are then partially removed by the liver from the bloodstream, and partially transformed into low-density LP (LDL) and are also removed from the bloodstream.

There are 6 main stages of VLDL assembly in the ER: 1-broadcast apoB on membrane bound ribosomes; 2-extension of protein on the cytoplasmic side of the ER membranes. Subsequently formed the protein is either destroyed , or passes through the ER membrane and associates with its outer side . The assembly of the VLDL particle occurs in a kind of pocket that forms in the outer layer of the ER. Pocket is a place where TAGs penetrate for the formation of VLDL .

At the last stage, the formed VLDL particles are split off from membranes and secreted from the cell . Intermediate density lipoproteins (IDLs) are formed from HM and VLDL. LDDs are removed from the bloodstream by liver cells, where most of them part degrades. From 5 to 50% of the DOP is converted to LDL.

Low density lipoproteins (LDL) represent more than small particles, which are the main transport form of CS. They contain about 6% TG, the maximum amount of cholesterol (50%) and 22% protein. Approximately 2/3 of the rapidly exchanging pool of cholesterol is synthesized in the body, mainly in the liver (endogenous cholesterol), entering organism with food (exogenous cholesterol). It should be remembered that the key the

enzyme that determines the rate of synthesis of endogenous cholesterol is hydroxyl methyl glutaryl-CoA reductase (HMG-CoA reductase).

Further LDL metabolism can occur in two ways. The first of them in the norm significantly prevails and consists in the capture of LDL specific receptors of hepatocytes with an affinity for apoproteins B and E located on the LDL surface. Captured by the hepatic cell, the particles are absorbed by hepatocytes and undergo hydrolysis with the formation of free cholesterol, protein and fatty acids, which then utilized by cells.

1. It is characteristic that the level of intracellular free cholesterol is the most important factor regulating the activity of HMG-CoA reductase and the rate of synthesis of specific LDL-receptors of hepatocytes, using which captures new LDL particles circulating in the blood.

So, with a decrease in the content of intracellular cholesterol, the activity of HMG-CoA reductases and, accordingly, the rate of synthesis of endogenous cholesterol.

At the same time, the synthesis of LDL-receptors of the hepatocyte and uptake and absorption of LDL from the bloodstream and their intracellular catabolism. As a result, the content of cholesterol inside the cell is recovering. On the contrary, at high intracellular concentration free cholesterol slows down the synthesis of endogenous cholesterol and LDL receptors and the level of intracellular cholesterol is gradually normalized. Described the principle of feedback between the intracellular concentration of cholesterol and the rate of metabolic processes is successfully used at present time to treat certain lipid disorders.

2.The second pathway of LDL catabolism is free radical LDL peroxidation. Free radicals formed in the human body in the process of metabolism, are, as you know, highly active and unstable molecules that easily oxidize LDL cholesterol. As a result, the so-called modified (oxidized) LDL, which are poorly recognized by B and E receptors hepatocytes and therefore do not participate in the normal physiological pathway of LDL catabolism. Oxidized LPs are captured macrophages, which are transformed into foam cells, included in atherosclerotic plaques. Moreover, modified LDL cause damage to the vascular endothelium, launching a whole cascade of pathological reactions from the vascular walls. Normally, the processes of lipid peroxidation are poorly expressed.

They are significantly enhanced by various cardiovascular diseases vascular system, in particular, with atherosclerosis, being one of important etiological factors contributing to the emergence and the progression of the disease. Thus, LDL belongs to the most atherogenic fraction of LP. Increase in total LDL content, especially modified oxidized LP, is associated with a high risk of atherosclerosis and its complications.

High-density lipoproteins (HDL) - the smallest and densest LP particles. They contain only 5% TG, 22% cholesterol and the largest the amount of protein (40%) - apoproteins A-I, A-II and C and belong to the drug, possessing antiatherogenic properties. The latter

are determined the participation of HDL in the catabolism of all other drugs, since with the help of HDL reverse transport of cholesterol from peripheral organs is carried out, including including from the arterial wall, from the surface of chylomicrons and VLDL, macrophages and smooth muscle cells, to the liver, where it occurs utilization and conversion to bile. The synthesis of "mature" HDL particles is just is carried out due to the addition of free cholesterol from other drugs and peripheral tissues to the initial forms of HDL disc-shaped.

The synthesis of full-fledged spherical HDL occurs, therefore, when mandatory participation of HM, VLDL and LDL. In addition, HDL in the process metabolism, CM, VLDL and LDL attach to themselves their apoproteins A and C, influencing the activity of numerous enzyme systems, involved in lipid metabolism.

The very transformation of the initial (nascent) discoid forms of HDL, synthesized in the liver, into "mature" spherical particles occurs in as a result of absorption from the surface of CM, VLDL and peripheral tissues free cholesterol and its esterification. Formation of CS esters absorbed HDL, carried out with the obligatory participation of the enzyme lecithin cholesterol acyltransferase (JIXAT) present in primary discoid forms of HDL. Subsequently, part of the esterified cholesterol transferred from HDL to the remnants (remnants) of VLDL, XM and DIL, which captured and absorbed by hepatocytes.

Characterization of lipoproteins

Parameters	LP fractions				
	HM	LPVLD	LPID	LPLD	LPVHD
Density g / ml	<0.95	0.960-1.006	1.007-1.019	1.021-1.063	1.64-1.21
Average diameter, nm	500	43	27	22	8
Place education	Small intestine	liver	Catabolism LPVLD	Catabolism LPVLD thorough LPID	Liver, small intestine, catabolism LPVLD
The main function	Transport exogenous TG, delivery to	Transport endogenous TG	Predecessor of LPLD	Ether transport HS	Source of apoproteins, HM, VLDL; return

	the liver food cholesterol				transport XC
Medicinal product LP,%					
TG	90	65	20	5	5
HS	5	15	25	50	20
PL	4	10	35	25	25
Protein	1	10	20	20	55
apoprotein	A.B-48.C.E	B-100.C.E	B-100.E	B-100	A.C.E

Apolipoproteins A and B

Apolipoprotein A (ApoA) is the main protein a component of lipoproteins that transport cholesterol from cells of peripheral tissues in the liver, which is called the reverse cholesterol transport. ApoA protein is present in the body in two forms: ApoA-I and ApoA-I. ApoA synthesis occurs in the intestinal wall and in the liver. Apolipoproteins A are transported from the intestine to composition of chylomicrons and then accumulate in high lipoproteins density (HDL).

The physiological function of ApoA-I is to activate lecithin cholesterium acyltransferase (LCAT) - an enzyme that is involved in removing free cholesterol from cells of peripheral tissues. At contact with HDL cells extract cholesterol from cell membranes.

The enzyme LCAT catalyzes the esterification of cholesterol found on the surface of the HDL, the polarity of which changes in this case. Esterified cholesterol moves into the HDL particle, as a result, in the surface layer of HDL cholesterol concentration decreases, making room for new cholesterol molecules.

The physiological role of ApoA-P is not fully understood, but it is believed that that this protein can activate hepatocyte lipase and inhibit LHAT. By suppressing the activity of LCAT, ApoA-P prevents esterification cholesterol, thereby reducing the efficiency of transport of cholesterol in composition of HDL, which can be interpreted as the indirect participation of ApoA-P in violation of lipid metabolism.

There is currently no direct correlation of content ApoA-H with cardiovascular risk. However, since ApoA-1, activating LCAT, helps to remove cholesterol from peripheral tissues, and ApoA-P, inhibiting LCAT, prevents elimination of cholesterol, it is assumed that a certain clinical the ratio of ApoA-I / ApoA-P may matter. Apoliproprotein B (ApoB) is part of lipoproteins, trans- porting lipids to peripheral tissues. Receptors for it are present in almost all tissue cells, with the exception of cells nervous system and erythrocytes. The ApoB protein comes in two forms:

ApoB-48 having a molecular weight of 241 kDa and ApoB-100 s molecular weight 513 kDa. ApoB-48 is synthesized in the gastrointestinal intestinal tract. It is the most important structural protein very low density lipoproteins. Increasing the level of ApoB-48 in serum can occur with hyperlipoproteinemia I, III and V types. ApoB-100 is synthesized in the liver and is present in all atherogenic fractions of lipoproteins. Fragments of ApoB-100 and related with them, reactive aldehydes are included in the group of compounds that received the general name "oxidized lipids and lipoproteins". To the same a heterogeneous group of atherogenic substances include oxidized free fatty acids, lipid peroxidation products, oxidized cholesterol, lysophosphatidylcholine, etc.

Functions of major apolipoproteins:

• Apo B-100 - the main apoprotein of chylomicrons;

 Apo C-II - LP-lipase activator;

 Apo E - a protein that interacts with cell receptors;

 Apo A - LKHAT activator (lecithin cholesterol acyltransferase).

Figure 1.7. shows a general overview of the functions of lipoproteins.

The exogenous pathway of dietary fats goes through the formation stage chylomicrons , endogenous - through the formation of VLDL formation.

Chylomicrons contain apoprotein B-48 and blood receive apo C II and apo E from HDL.

All lipoproteins of the endogenous pathway instead of apo B-48 contain white B-100, synthesized in the liver. Lipoprotein lipase acts in both pathways (reactions 4 and 6), forming residual chylomicrons (HM resid.), lipoproteins

intermediate density and LDL, which are captured by receptors hepatocytes (reaction 7 and 10) and other tissues. HDL predecessors are formed in the liver (reaction 11). HDL3, enriched in blood cholesterol, reversibly converted to HDL 2 (reaction 8 and 9) by enzymes

LCAT (lecithin-cholesterol-acyltransferase) and hepatic triglyceride lipase. Cholesterol Carrying Protein Carrying Esters cholesterol from HDL to VLDL, HDL and LDL, which deliver it to the liver.

Thus, HDL plays a major role in the transport of cholesterol from peripheral tissues to the liver, where it becomes available for synthesis bile acids and subsequent excretion from the body.

Characterization of the main serum apolipoproteins

apolipoprotein	lipoprotein	Place of education	The main function
A-1	**LPVD**	**Intestines, liver**	**Structural protein, activator LHAT, receptor ligand**
A-2	**LPVD**	**Intestines, liver**	**HDL Structural protein, lipase activator hepatocyte, ligand**
B-48	**HM**	**Intestines**	**HDLPT , an inhibitor Structural protein chylomicrons, Lipid absorption**
B-100	**LPLD, LPVLD**	**Liver**	**Participates in synthesis and secretion of VLDL, structural protein LDL, LDPP,**
APO(A)	**LP(A)**	**liver**	**LV / PEORNetsPe, pltiograonvd for Inhibitor fibrinolysis**

Lipoprotein metabolic disorders are widespread and are the causes or manifestations of 30 different diseases. Everything dyslipoproteinemia are divided into 5 classes. There is a detailed characteristic of primary (genetically determined) dyslipoproteinemia and secondary, resulting from other diseases. Changes in blood composition for each class dyslipoproteinemias, both primary and secondary, have common characteristic signs.

Hyperlipoproteinemia

Hyperlipoproteinemias are diseases in which in the body, the formation, transport or cleavage of lipoproteins is impaired theines, as a result of which plasma triglyceride levels increase and / or cholesterol. Hyperlipoproteinemias in developed countries are one of the most common metabolic pathologies.

Hyperlipoproteinemia, by the mechanism of occurrence, are divided into primary and secondary.

Primary hyperlipoproteinemias include:

• Hyperlipoproteinemia associated with genetic features of lipid metabolism, or family, which are due to congenital disorders of lipid metabolism. Family diagnosis hyperlipoproteinemia is placed in cases where similar lipid metabolism disorders are found in at least two close relatives.

• Hyperlipoproteinemia caused by environmental factors, because lipid metabolism can be disrupted under the influence of unfavorable factors, such as unhealthy diet.

In addition, there are a large number of intermediate forms.

With secondary hyperlipoproteinemia, an increase in lipid levels lead to metabolic disorders associated with the main disease. Secondary hyperlipoproteinemia in various diseases: diabetes mellitus, liver disease, kidney disease or hormonal disorders, some autoimmune diseases, multiple myeloma, lymphosarcoma, in clinical practice are much more common than primary.

• In diabetes mellitus, all types of metabolism are impaired, including number and lipid metabolism, resulting in a significant increase the level of chylomicrons and triglycerides. In addition, a significant contribution to the development of hyperlipoproteinemia in diabetes mellitus is caused by diabetic nephropathy.

• With nephrotic syndrome, there is a pronounced loss of albumin in the urine and analbuminemia develops. For supporting oncotic pressure compensatory increase in liver synthesis proteins, including lipoproteins.

• Acute and chronic pancreatitis is often combined with hyperlipoproteinemia.

• Disrupted lipid metabolism in liver diseases, which takes a direct part in this process. Cholestasis in obstructive jaundice leads to a decrease in HDL levels and the appearance

special low-density lipoprotein LDL-C. Violation of secretion lipids leads to an increase in their level in the blood serum. At alcoholic cirrhosis increases the synthesis of lipoproteins. Primary biliary cirrhosis of the liver is accompanied by a significant increase serum cholesterol.

• An increase in serum lipids is accompanied by hypothyroidism and pituitary insufficiency, in which there is reducing the level of metabolism and, in particular, slowing down oxidation cholesterol in the liver.

Based on changes in the concentration in blood plasma of cholesterol and triglycerides, as well as the ratio between individual fractions lipoprotein Fredrickson et al. in 1965 proposed the classification hyperlipoproteinemia. This classification in 1979 after the introduction some changes were accepted by WHO and approved for use in clinical practice.

Classification of hyperlipoproteinemias D. Fredrickson's classification Hyperlipoproteinemia is characterized by abnormally high the content of lipids and / or drugs in the blood. Since their normal levels change with age, in order to identify DHP it is necessary to decide on the concept of normal values. In newborns, the concentration of cholesterol and cholesterol LDL in the blood does not exceed 2.6 and 1.0 mmol / l, respectively. In the first year the child's life, the level of cholesterol increases and remains unchanged until sexual maturation, making up, as a rule, 4.1 mmol / l. Then the concentration of CS increases with age from 4.25 to 6.50 mmol / l and above: moreover, up to 55 years its concentration is higher in men, after 55 years - in women. Normal cholesterol levels vary significantly in different populations.

To establish the type of hyperlipoproteinemia, clear biochemical criteria. There are currently two approaches to classification of SDP: the first is to establish a normal level lipids and drugs according to the results of epidemiological studies, the second the approach is based on the determination of different levels of LP, depending on risk of developing coronary artery disease.

In the first approach to classifying SDP for each population determine their criteria for the rate of indicators of lipid metabolism, discarding 5 to 10% of the minimum and maximum content values

lipids in the sample with Gaussian distribution. Wherein hyperlipidemia is such a concentration of cholesterol and triglycerides that exceeds the level of 90 or 95% of the specified concentration values lipids according to sex and age in this study. At this definition of the "norm" criteria, the upper limit of the normal values for cholesterol is 6.5 mmol / l, and this concentration is very high, since the risk of developing coronary artery disease increases even at a cholesterol level of 5.2 mmol / l.

Thus, in fact, the “normal” CS values are higher than the concentration, contributing to the development of atherosclerosis. These criteria for the values of the norm and

pathology of lipids and form the basis for the classification of DHP, proposed D. Fredrickson.

Using electrophoresis and preparative ultracentrifugation, D. Fredrickson et al. described five types hyperlipoproteinemia, each of which is characterized by a certain GLP phenotype (mobility in electrophoresis and quantitative ratios different lipoproteins). Attempts to classify SDP were undertaken repeatedly and earlier, but did not find application in practice due to their imperfection.

However, the classification proposed by D. Fredrickson turned out to be insufficient to cover the entire variety of types: its main drawback - inconsistency of lipoprotein phenotypes with genetic defects, determining these phenotypes (the same phenotype can be found for various diseases). In addition, the severity of HFD depends on gender, age, diet and many environmental factors. GLP type may be affected by diet, weight changes, and treatment.

Finally, any type of hyperlipoproteinemia may be primary. (genetically determined, hereditary) and secondary (acquired), what this classification did not allow to reveal.

Later, experts from the World Health Organization (WHO), taking the classification of D. Fredrickson as a basis, revised it by adding additional phenotype. WHO classification is based on phenotypic characteristics of blood serum in case of lipid metabolism disorders and contains five types, and the most common of them, II, is subdivided into two more subtypes: II a and II b. The advantage of this classification is that it describes the entire LP spectrum at the most common SDPs. The main drawback (as well as

D. Fredrickson's classification) - with its help it is impossible to establish, primary or secondary SODI has caused metabolic disorders. She also does not take into account the concentration of HDL cholesterol, although this value significantly affects the likelihood of developing coronary artery disease in patients with HFD.

Despite these shortcomings, this typing system had is of great importance for identifying metabolic disorders that cause GLP, and allowed a rational approach to the diagnosis of disorders lipid metabolism and treatment of patients. The WHO system is still widely used by clinicians.

Type I – hyperchylomicronemia

Hyperchylomicronemia due to decreased cleavage chylomicrons and can be both congenital and acquired.

Congenital form in which there is a congenital lipoprotein defect lipase is inherited in an autosomal recessive manner. Secondary form observed in alcoholism, diabetic acidosis, dysglobulinemia, hypothyroidism and pancreatitis. The disease is rare. Congenital form clinically manifests itself only in the homozygous type. The first manifestations of the

disease found in childhood and adolescence. To the main symptoms include hepato- and splenomegaly, intestinal colic, xanthomatosis. Frequent a complication is repeated pancreatitis, which are the main cause of death of patients. Restriction of dietary fat leads to normalization of the general condition and laboratory parameters. Development atherosclerosis in persons with the described disorder of lipid metabolism is not is accelerating.

This pathology is characterized by normal or insignificant elevated serum cholesterol with sharp elevated triglyceride levels, as a result of which the ratio cholesterol triglycerides is less than 0.1. External changes lipoproteins are expressed in a decrease in the content of a- and β-lipoproteins due to a violation of the catabolism of high lipoproteins triglycerides with normal or slightly elevated pre-β-lipoproteins (VLDL).

II Type It is characterized by an increase in the level of β -lipoproteins, which in some patients is combined with an increase in the content of pre-β-lipoproteins, in this connection, two variants of hyper-β-lipoproteinemia are distinguished: IIa and II6. Both type can be found in representatives of the same family. It is considered that the congenital form is inherited in an autosomal dominant manner with incomplete penetrance.

Type IIa hyper-β-lipoproteinemia

Hereditary form of hyper-β-lipoproteinemia (or familial hyper-cholesterolemia) is associated with a slowdown in the breakdown of LDL due to violation of their absorption by cells. The manifestation of the disease is facilitated a diet high in fat and cholesterol. In patients with this type, the formation and secretion of bile acids are impaired. Have homozygous individuals develop the first signs already in childhood, in heterozygous - after 20 years. Hypercholesterolemia can develop with regular excessive intake of lipids from food and especially cholesterol. The secondary form may be due to hypothyroidism, liver diseases, nephrotic syndrome, porphyria, hypercalcemia. A typical clinical manifestation is the tendon xan. volumes (deposition of cholesterol in tendons), which are most common appear in the area of the Achilles tendon and extensor tendons palms and feet, as well as periorbital xanthomas. In homozygous individuals xanthomatous changes take place in the endocardium and heart valves.

The main clinical manifestations are early signs atherosclerotic changes in blood vessels, mainly coronary, in connection with which death from myocardial infarction can occur even in children age. Patients with this type, as a rule, have a lean physique without a tendency to diabetes.

The disease is characterized by an increase in the content of β-lipoproteins (LDL) with normal levels of pre-β-lipoproteins (VLDL) and a liporoproteins. Serum cholesterol concentration is increased with heterozygous form up to 9-11, with homozygous - up to

18-20 mmol / l. The triglyceride content in the blood is normal. Ratio cholesterol / triglycerides more than 1.5.

Type II hyper-β -lipoproteinemia with hyperpre- β -lipoproteinemia

This type of hyperlipoproteinemia can also be hereditary, and develop against the background of diseases such as liver disease, diabetic acidosis, Tenji's disease.

Clinically, type II is manifested by disorders characteristic of atherosclerosis, and changes in the vessels are the most severe character. Patients are usually overweight, impaired glucose tolerance and signs of fatty liver disease.

In the blood serum, the content of β-lipoproteins (LDL) is sharply increased and pre-β-lipoproteins (VLDL), as well as cholesterol and triglycerides.

Type III - dys-β -lipoproteinemia

The disease is usually hereditary and rare. Family type III hyperlipoproteinemia is presumed to be inherited by autosomal recessive type and is due to delayed decay VLDL.

The first signs of the disease are observed already in early childhood age. Typical clinical manifestations are yellowish brown lipid deposits in the skin of the palmar lines and tendons xanthomas. Changes in the walls of the arteries, both coronary and peripheral. Obesity developing in young people is common age, diabetes mellitus, fatty liver. Diet food quickly leads to a decrease in cholesterol and triglyceride levels in serum.

Cholesterol and triglyceride levels are elevated, most often in the same degree. The cholesterol / triglyceride ratio is about 1. Type IV - hyperpre-β-lipoproteinemia (endogenous hypertriglyceridemia)

The disease can be either hereditary or secondary, which develops in persons suffering from diabetes mellitus, pancreatitis, Cushing's syndrome, gout, hypofunction of the pituitary gland, glycogenosis, dysglobulinemia, as well as alcohol abuse. Maybe develop with prolonged use of oral contraceptives. With a hereditary type, the disease manifests itself at a young age.

The type of inheritance is not clear. This type of hyperlipoproteinemia is based on impaired hydrolysis triglycerides in VLDL. Patients have atherosclerotic changes in blood vessels, mainly coronary, less often - cerebral. Patients with type IV are usually overweight, moreover, fat deposits are most pronounced on the face and in the neck. Often this type of lipid metabolism disorder is combined with diabetes mellitus.

Overweight and excessive carbohydrate intake. Eating a reduced diet carbohydrates leads to the normalization of blood lipids.

Changes in the blood are characterized by an increase in the level of pre-β-lipoproteins (VLDL) and triglycerides. The content of β -lipoproteins in within the normal range. Triglyceride levels are elevated and cholesterol - can be normal or slightly elevated.

The cholesterol / triglyceride ratio is generally less than 1.

Type V - hyperpre- β -lipoproteinemia and chylomicronemia.

The reasons for this violation have not been established. The secondary form can ound in diabetes, nephrotic syndrome, pancreatitis, alcoholism. In this type, the level of pre-β-lipoproteins is increased and chylomicrons.

Clinically, the disease manifests itself after the age of 20 years. Have overweight patients, pancreatitis, angiopathy.

Atherosclerotic changes are most pronounced in the coronary vessels.

Often combined with diabetes mellitus. The level of triglycerides in the blood is high and moderatecholesterol. The cholesterol / triglyceride ratio is 0.2-0.6.

Primary hyperlipoproteinemia

0	Other names illness	Genetic form	[Cholesterin] v plasma	[TAG] v plazme	Risk development atherosclera oza	Clinical manifestations
1	Exogenous hypertriglyceridemia Family hypertriglyceridemia (hyperchylomicronemia) Fat-Induced Hyperlipoproteinemia	Autoimmune recessive (rare)	↑↑↑	↑↑↑	-	Pancreatitis xanthomatosis, hepatosplenomegaly
2	Family hypercholesterolemia	Autoimmune	↑↑↑	A)N B) ↑	Very high,	Early atherosclerosis,

		dominant			especially coronary arteries	xanthomatosis
3	Family dysbetalipoproteinemia Floating betalipoproteinemia	Dominant; a type inheritance indefined (quite common)	↑↑↑	↑↑↑	Very high (coronary and peripheral arteries)	Early atherosclerosis xanthomatosis
4	Endogenous hypertriglyceride i Family hyperprepalipoproteinemia Carbohydrate-Induced Triglyceridemia	Genetically heterogeneous (common)	↑↑↑	↑↑↑	↑↑↑	Available early atherosclerosis, decline tolerance to glucose, hyperuricemia
5	Family hypertriglyceridemia Combined exogenous and endogenous hypertriglyceridemia	Genetically heterogeneous (enough common)	↑↑↑	↑↑↑	-	Pancretatitis, xanthomatosis, sensory neuropathy, hyperuricemia, decline tolerance to glucose

Secondary hyperlipoproteinemia

The change	Cholesterol	TAG	The Cause	Mechanism

composition				hyperlipemia
Type 1	N or ↑	↑↑↑	Systemic erythematous lupus	Linking with glycosalipoglycans capillary endothelium
Type 2	↑↑↑	N	Diseases liver, hypothyroidism	↑catabolism of LPLD
Type 3	↑↑↑	↑↑	Nephrotic syndrome Syndrome Cushing's	↑ VLDL secretions → ↑ formation of LDL
Type 4	↑↑↑	↑↑	Monoclonal gammopathy	Education complexes of Ig with VLDL or with reminants particles that violates them metabolism VLDL secretion ↑
Type 5	↑↑↑	↑↑↑	Monoclonal gammopathy Sugar diabetes Alcohol Oral contraceptives	

Modern classification of HLP

Given the accumulated data on the relationship of increased content Cholesterol and the risk of developing coronary artery disease, expert groups of the National Cholesterol Education Program in the United States (National Cholesterol Education Program, NCEP) and the European Society for the Study atherosclerosis, a different classification of HLP has been proposed. Depending on from the risk of coronary artery disease experts recommend:

1. Allocate several levels of cholesterol: desired - <5.2 mmol / l,borderline high - 5.2-6.2 mmol / l and high -> 6.2-6.5 mmol / l

2. Change (lower) the normal values for LDL cholesterol and leave the same "norms" for TG and HDL cholesterol. Based on these criteria it is customary to distinguish moderate hypercholesterolemia - the level of cholesterol is 6.2-7.5 mmol / l - and severe - cholesterol level> 7.8 mmol / l.

Later, on the basis of data obtained in the course of extensive research on primary and secondary prevention of coronary artery disease, European Society for the Study of Atherosclerosis published the developed diagrams for determining the risk of coronary artery disease and "target" values of indicators lipid metabolism. Researchers use the term "target values" since it is believed that at these values, the risk of developing coronary artery disease significantly decreases and, consequently, the achievement of the proposed rigid criteria for indicators of lipid metabolism is the goal lipid-lowering therapy. The choice of lower values of the lipid norm is justified from the point of view of primary and secondary prevention of coronary artery disease. Application of uniform criteria for the diagnosis of HFD allows comparing its prevalence in populations with different mean levels of cholesterol, since 95% of individuals in whom DHP was detected according to epidemiological criteria, have hereditary conditioned form. Accordingly, as the normal lipid values, the proportion of persons whose HFD is due to only by environmental factors.

Reconsidering lipid levels to lower "normal" values that determine the degree of risk of coronary artery disease occur regularly: in 1998 the second was published [13–15], and in 2001 - the third Expert reports

NCEP. The third NCEP USA Expert Report focuses on identifying and assessment of high levels of cholesterol in adults (Adult Treatment Panel III, ATP III).

What's new in the Asia-Pacific region III in comparison with the previous ones Reports?

1. Changed (toughened) normal levels for LDL cholesterol, cholesterol HDL and TG (Table 4).

2. The main risk factor for CHD is the level of LDL cholesterol (and not levels of cholesterol and HDL cholesterol, as previously thought). LDL cholesterol classification offers 5 levels with a very narrow gradation of its concentration.

3. For the first time, triglyceridemia is recognized as an independent risk factor IHD: according to the proposed classification, 4 levels of TG concentration were identified.

Normal values for TG became lower - 1.70 instead of 2.26 mmol / l.

The difference between levels 1.70 and 2.26 mmol / L is so small that require significant improvement in the analysis procedure and reduction of the coefficient of variation of measurement results.

Hypertriglyceridemia is essential in the formation of pathology peripheral and cerebral vessels. TG concentration over 11.30 mmol / L is associated with pancreatitis and requires immediate medical intervention.

4. Introduced a new indicator of lipid metabolism - non-HDL Cholesterol (non-HDL Chol). Non-HDL Chol is a HS, which is included in all factions of the LP, for excluding the HDL fraction. It is recommended to consider it as secondary marker of risk of coronary artery disease and take into account in the case when the level of cholesterol LDL is "optimal" or "close to optimal", and the level of TG - "High" (> 2.26 mol / l). Non-HDL Chol indicates the content of cholesterol in atherogenic fractions: LDL and VLDL and is calculated as the concentration XC + 0.78. Data on the level of cholesterol in these fractions allow for more reliable identify the degree of risk of coronary artery disease.

5. It is recommended to consider the "normal" level of HDL cholesterol concentration 1.03 mmol / l (instead of 0.90 mmol / l). HDL cholesterol concentration less than 1.03 mmol / l indicates an increased risk of coronary artery disease in patients, even if the total cholesterol is not increased. Based on the results population studies have shown that currently about 40% men and 15% of women have a high risk of coronary artery disease for this very reason indicator. Low HDL cholesterol - the most common lipid pathology among men with cholesterolemia and may be associated with other risk factors such as high TG concentration, diabetes, sedentary lifestyle, smoking, diet, certain medications. At HDL cholesterol level of more than 1.55 mmol / l, there is an inverse relationship with risk of ischemic heart disease.

6. All adults over 20 are advised every 5 years perform a complete study of the lipid spectrum: cholesterol, triglycerides, LDL cholesterol, cholesterol HDL and non-HDL Chol.

The values of lipid metabolism indicators recommended by ATP III, are close to those proposed in 1998 by the European Society for the study of atherosclerosis. In both documents, LDL cholesterol levels are less than 3.0 mmol / l and total cholesterol less than 5.0 mmol / l, are called not "normal", but - "Optimal" and "desired", respectively. In addition, low the level of cholesterol is as undesirable as high: it may indicate about various pathologies: anemia, hyperthyroidism, liver cell necrosis, oncological diseases, etc. In this regard, in the order form for the analysis must indicate the upper and lower limits of the norm XC.

With a change in the level of "normal" values for lipids taken ATP III, the number of patients who can be classified as persons with an increased risk factor for coronary artery

disease. in the report APR III as in the reports of the European Society for the Study of atherosclerosis, emphasizes the need for individual work with every patient. Each person's lipid content varies from day to day and from week to week, therefore, when choosing a treatment, even in good equipped laboratory, it is necessary to determine the lipid profile at least twice at different times (with an interval of 2 weeks) and take into account the results of two or more measurements. Serum lipid level blood changes also during pregnancy, physical activity, infectious diseases, surgery, heart attack myocardium, hormone therapy.

Clinicians in Europe and the US Unanimously Recognize the Importance of Control indicators of lipid metabolism for primary and secondary prevention Ischemic heart disease. This approach requires the expansion of lipid research, the introduction of new methods for diagnosing lipid metabolism disorders, improving accuracy and reproducibility of analysis results, strict implementation quality control programs for research in the CDL. In this regard, it is necessary change the order format in the CDL for lipid research: order form should contain a list of lipids and drugs with an indication of their classification by levels corresponding to the APR III recommendation.

Alipoproteinemia

Alipoproteinemias are diseases caused by disorders lipid metabolism, which are accompanied by a decrease in the level serum lipoproteins. Alipoproteinemias are primary, or congenital and secondary.

An-α-lipoproteinemia (hypo-α-lipoproteinemia), or Ten's disease li - characterized by a deficiency of α -lipoproteins and develops as a result of congenital impairment of the synthesis of apolipoproteins AI and All. Transmitted by autosomal recessive type. In homozygous individuals in the blood serum there is practically no normal α -lipoprotein, instead of which in the bloodstream circulates an altered a-lipoprotein called "Tenji lipoprotein", which can be identified using immunochemical methods. In heterozygotes, the serum contains both normal and altered α-lipoproteins.

Clinically manifested by hepatosplenomegaly, an increase in lymph nodes and tonsils, which turn orange, neurotic disorders, retinitis and corneal opacity. The disease is not associated with an increased incidence of atherosclerosis. In the blood serum of patients, in addition to α-lipoprotein deficiency levels of phospholipids and cholesterol are significantly reduced, and the level triglycerides are elevated even in fasting serum.

A- β -lipoproteinemia (hypo-β -lipoproteinemia) or Bazin's disease Kornzweig (acanthocytosis) is a hereditary disorder of the formation of P-lipoproteins, pre-β-lipoproteins and chylomicrons associated with decreased ability of the liver to synthesize apolipoprotein B. Disease is rare. It is inherited in an autosomal dominant manner.

The secondary form is due to liver or gastrointestinal diseases intestinal tract. In addition, a reduced level of β-lipoproteins has place with hyperfunction of the thyroid gland, when an accelerated breakdown of lipoproteins.

Clinically manifested by severe malabsorption syndrome with steatorrhea and progressive dystrophy. As a result of serious deficiency in the body of lipoproteins, there are changes in cellular membranes that lead to severe disruption of many systems organism. As a result of shortening the life of erythrocytes, anemia. The defeat of the myelin sheaths causes disorders from peripheral nerves and central nervous system: extinction tendon reflexes, which manifests itself in early childhood, ataxia, nystagmus, impaired spatial orientation, phenomena myopathy and cardiopathy, retinopathy pigmentosa. Serum levels of triglycerides, cholesterol, phospholipids.

Hyperchylomicronemia

Physiological hyperchylomicronemia is observed within 10-12 hours after eating fatty foods. If in a hungry state, concentration TAG of chylomicrons is increased, then hyperchylomicronemia occurs. he disappearance of chylomicrons from the bloodstream depends on many factors:

The presence of normal LP-lipase (the enzyme is localized in the endothelium capillaries);

he presence of HDL in the blood supplying apo C II and apo E; The normally functioning transfer mechanism of these apolipoproteins on chylomicrons, which is necessary for the activation of LP-lipase and hydrolysis of TAG in lipoproteins;

The presence of a sufficient amount of apolipoproteins.

Violation of any of these factors leads to the development hyperchylomicronemia. Indeed, there are hereditary forms hyperchylomicronemia due to a defect in LP-lipase, Apo C proteins II and apo E.

Hyperchylomicronemia is manifested by an increase in concentration TAG (more than 200 mg / dl) on an empty stomach. If the blood plasma of such patients is kept at a temperature of 4 ° C during the day, then fatty cream-colored flakes formed by chylomicrons. With pronounced hyperchylomicronemia, xanthomas develop, which are TAG deposits, early memory loss occurs, pain in stomach. If the concentration of TAG exceeds 4000 mg / dl, then it develops retinal lipemia (lipaemia retinalis), in which lipids are deposited on retina and further deteriorates vision. Regardless of etiology relief of the condition occurs with a sharp restriction of dietary fats and such a diet prolongs the patient's life.

Hypercholesterolemia

The most common type of hyperlipidemia is hypercholesterolemia, leading to the development of atherosclerosis.

Atherosclerosis is the progressive accumulation of excess lipoproteins and other blood components, accompanied by reactive the formation of fibrous tissue mainly in the inner membrane arteries of elastic and muscular-elastic type, as well as a complex other changes to them.

Numerous disorders of LP metabolism are characterized by an increase in lipids and LP in the blood (hyperlipoproteinemia), a decrease (hypoliproteinemia) or a change in the ratio of drug classes (dyslipoproteinemia).

The main purpose of the study of lipid metabolism is to identify violations lipid metabolism as a risk factor for cardiovascular diseases. In this regard, the study of the lipid spectrum should be carried out in patients with: ischemic heart disease with cerebrovascular accident and blood flow in large arteries; family predisposition to early the development of ischemic heart disease (in persons under 60 years of age); other risk factors: sugar diabetes, arterial hypertension, etc .; local lipid deposits (xanthomas, xanthelases, lipid striae, lipid arch of the cornea) at age up to 50 years old; as well as in the case of lipidimic blood serum. Diagnostics lipid metabolism disorders should be carried out in three stages .The first step is to determine the content of total cholesterol and triglycerides; in case of detection of hypercholesterolemia or hypertriglyceridemia, the second stage of the study should be carried out.

The second stage is the determination of the lipid spectrum: total cholesterol, triglycerides, HDL cholesterol, cholesterol LDL; electrophoresis of drugs; calculation of the atherogenic index (AI) and the level of cholesterol LDL, if not measured. LDL cholesterol level is calculated by Friedwald's formula:

LDL cholesterol = TC - (HDL cholesterol + TG / 2.2).

The formula can be used if the concentration of TG is less than 4.5 mmol / l, and the blood for the study was taken on an empty stomach. Atherogenic index for assessment the ratio of atherogenic and antiatherogenic drugs is calculated by formula:

IA=GHS-HS LPHD/ HSLPHD

The atherogenic index is ideal in newborns (no more

1), reaches 2.2-2.5 in healthy men and women aged 25-30 and increases by 4-6 units in persons with coronary artery disease. The third stage is the differentiation of primary and secondary HLP, which carried out by the method of excluding all diseases, which are characterized by secondary DHP: diabetes mellitus, nephrotic syndrome and others lesions of the renal parenchyma, liver pathology with the phenomenon of cholestasis, a decrease in albumin in the blood, the presence of an acute or chronic phase inflammatory

process, etc. Typing of HLP at the present time carried out at a level of cholesterol and TG exceeding 6.2 and 2.3 mmol / l, respectively. Comprehensive laboratory research allows make a diagnosis of primary HLP and then engage in clarification specific mechanisms of lipoprotein metabolism disorders in order to correction.

The mechanisms of formation of primary HLP can be clarified only in specialized laboratories (lipid centers) equipped with high-tech equipment and having highly qualified staff.

LIPOPROTEIN (A).

NEW IN BIOCHEMICAL DIAGNOSTICS OF ATHEROGENESIS

LP (a) [Lp (a)], or "lipoprotein a small", as already mentioned, "Dangerous relative of the bad" LDL-C. Actually LP (a) is X-LDL with "makeweight" - a large glycoprotein called Apo (a) - apolipoprotein (a) and which, using one disulfide bond covalently linked to apolipoprotein Apo B, which is part of LDL-C. Like LDL-C, the LP (a) particle consists of cholesterol, triglycerides, Apo B, phospholipids and apolipoprotein Apo (a) LP (a) is synthesized in the liver by combining LDL-C and Apo (a) due to the disulfide bond. LP (a) catabolism, in contrast to other lipoproteins, occurs in the kidneys, not the liver .. Apo (a) structure. Apo (a) is a glycoprotein that has homology to plasminogen human and consists of domains called "kringle", (pretzel, eng.), which, in fact, are similar to analogous domains of plasminogen. Apo (a) consists of an inactive protease domain, one domain. kringle V and a different number of kringle IV domains. In different individuals in the gene, encoding Apo (a), there can be a different (from 12 to 51) number of fragments DNA encoding the apo (a) domain. As a result, protein size and the size of the particles of LP (a) in the population, significant polymorphism is observed. The number of "kringle" domains in apo (a) is thus predetermined genetically and can vary from 12 to 51. And therefore the molecular weight protein Apo (a) in different individuals can range from ~ 280 to 800 kDa, now 34 isoforms of LP (a) are known.

In Apo (a), the kringle domains are organized into a specific protein "motif", consisting of three loop-like structures, stabilized three disulfide bonds. This "motive" is also contained in a large number of proteins encoded by genes of the prothrombin family, including prothrombin, plasminogen, hepatocyte growth factor, urokinase, factor XII, tissue plasminogen activator. (see reviews 1-4).

Recall that plasminogen is a precursor (proenzyme) of plasmin - the main enzyme that breaks down fibrin clots. How unexpected it turned out that the size of apolipoprotein (a) determines the concentration of LP (a) in plasma.

The smaller the size of Apo (a), the higher the level of LP (a).

Indeed, as has been established in many studies, the less the size of Apo (a), that is, the fewer "kringle IV" domains in it, the higher the level of LP (a) in plasma and vice versa,

the longer the Apo (a) molecule, the lower concentration of LP (a). In general, the level of Apo (A) synthesis is determined by by how quickly its isoforms are secreted. Lesser isoforms of Apo (a) is secreted faster and therefore the level of LP (a) in the plasma back proportional to the size of Apo (a) (5.6). Thus, the level of LP (a) in the blood is determined genetically - the length of the gene encoding apo (a). As indicated, in human population, there are many alleles (different variants) of the gene Apo (a), which encode a different number of kringle IV domains. Generally, the concentration of LP (a) in different individuals can range from <0.1 to > 200 mg / dl and vary by 1000 times. LP (a) levels <14 mg / dL are considered normal. But different alleles gene Apo (a) differ not only in the number of regions encoding domains of kringle IV, but also according to the nucleotide sequences of these domains. In other words, not only the number of domains can be different, but also their "quality". At the moment, about 100 alleles of the gene have been discovered Apo (a).

The composition of the drug (a), as mentioned, includes X-LDL and its central apolipoprotein B. In general, it is generally accepted that the level of LP (a) in plasma is more than than 90% is determined genetically and depends mainly on speed biosynthesis of Apo (a), which is inversely proportional to the size of Apo (a). Starting from early childhood, the concentration of LP (a) increases, reaches a plateau to maturity and then remains practically unchanged. Further increase the level of LP (a) is observed only in postmenopausal women. Unlike most lipid risk factors, the risk of associated with increased levels of LP (a), does not depend on either age or gender, diet and living conditions. However, it turned out that factors that can increase the level of lipoprotein (a) do exist. How it was said that LP (a) catabolism occurs in the kidneys.

Physiology of LP (a)

Despite decades of hard research, normal the physiological role of LP (a) has not yet been precisely clarified. It is assumed that LP (a) or is somehow involved in the metabolism of cholesterol and triglycerides (because it is similar to X-LDL), or takes some part in the processes coagulation, because Apo (a) is similar to plasminogen .. Or "both" together. As for the pathophysiological role, there is more clarity on this issue. LP (a) can cause cardiovascular disease due to proatherogenic nature inherent in LDL-C, and stimulate thrombus formation due to the prothrombotic properties of apolipoprotein Apo (a). Both are convincingly shown. LP (a) really is present in atherosclerotic plaques and takes part in thrombotic events that occur there. Presence is associated with increased concentrations of LP (a) and they, in turn, are determined by the characteristics of the gene encoding apolipoprotein (a).

Proatherogenic activity of LP (a)

Convincing evidence that elevated LP (a) levels are associated with CVD shown in at least 18 prospective studies.

Numerous data indicate that a high level of LP (a) - an independent risk factor for atherogenesis and thrombogenesis. According to the opinion American Heart Association, elevated LP (a) levels increase the risk of acute coronary events by 70%. (1-6,13-15). And here's how to summarize briefly the result of the perennial studies of the "pathogenetic" properties of drugs (a):

1) LP (a) has a high affinity for fibronectin and forms complexes with proteoglucans and glucose gluaminglucans extracellular matrix;

2) this leads to the selective accumulation of LP (a) in the walls vessels and to the induction of the inflammatory process;

3) moreover, LP (a) is an adhesive substrate for monocytes and activates inflammatory cells by interacting with integrin beta 2 - Mac-1. Recall that integrins are transmembrane glycoproteins that function as cell-substrate and intercellular adhesive receptors that bind cells to their environment;

4) the interaction between the Mac-1 integrin and LP (a) increases in the presence of elevated levels of homocysteine;

5) as a result of the interaction between LP (a) and Mac-1, activation of a transcription factor, which in turn activates the expression of genes involved in the induction of the inflammatory process and expression of prothrombotic tissue factor (tissue thromboplastin, factor III) .

Moreover, LP (a), like LDL-C, is very sensitive to oxidative processes.

And phagocytosis of oxidized forms of LP (a) and LDL-C leads to the accumulation of foam cells and atherosclerotic plaques. It has been shown that increased the ratio of oxidized phospholipids / Apo B and oxidized phospholipids / LP (a) are associated with coronary artery disease (17,18).

It was also found that the mitogenic effect of LP (a) on smooth muscle human cells, stimulating their growth. And the higher the LP (a) level, the above is such a stimulating effect. In this case, the oxidized LP (a) stimulates cell proliferation stronger than native .. Essentially, that the antioxidants probucol and fluvastatin inhibited the oxidation of LP (a). The authors believe that oxidized forms LP (a) are more atrogenic than native ones.

 The atherogenic effect of LP (a) is enhanced by its ability transfer oxidized phospholipids. Atherogenicity of LP (a) related to his ability:

1) activate the integrin Mac-1 and, thus,

2) stimulate the attraction of inflammatory cells to atherosclerotic plaques and,

3) stimulate the formation of oxidized phospholipids, which are inflammation induction mediators that induce penetration monocytes into the walls of blood vessels.

 LP (a) is an independent prothromobotic factor. Particles

LP (a) due to the presence in Apo (a) of the kringle IV domains:

1) inhibits the binding of plasminogen, thereby,

2) reduce the formation of plasmin, which, in turn,

3) reduces fibrinolysis, and this leads,

4) to increased thrombogenesis.

 LP (a) and progression of atherosclerotic plaques.

According to retrospective studies, increased levels of LP (a), namely 30 +/- 26 mg / dL versus 14 +/- 9 mg / dL, are associated with the progression of plaque in coronary arteries that have not previously had stenosis. It was found that the plaques accumulate mainly small particles of LP (a) containing short versions of Apo (a).

This was discovered when it was determined which isoforms of Apo (a) and Apo B are present in atherosclerotic plaques from patients who have undergone endarterectomy of the carotid (removal of the endothelium from the carotid artery) according to for severe stenosis. At the same time, the levels of LP (a) were higher in women. (37 mg / dL, control 19.3 mg / dL) than men, while concentrations Apo B in women was lower. It is important that LP (a) deposits in plaques were more than deposits of Apo B. Moreover, in plaques smaller isoforms of LP (a) were found than in plasma. However, in women with unstable plaques, LP (a) levels were elevated as in plaques and in serum (44, 0 mg / dl vs 22.3 mg / dl): In general, both in both men and women, plaques selectively accumulate more small isoforms of LP (a), ratio: small particles of LP (a) / large LP particles (a) in carotid plaques was 1.2, and in serum - 0.5.We emphasize that this pattern is valid for both women and for men.

The diagnostic value of elevated LP levels (a).Epidemiological studies related to clinical the usefulness of routine determination of the plasma LP (a) level is very are numerous. A large number of studies have shown a positive the relationship between the levels of LP (a) and CVD. Using the method immunoturbidimetry with latex enhancement, the results are independent of the size of apolipoprotein (a).

Thanks to advances in the standardization of methods for the determination of drug (a) and more correct statistical processing of data, the provision that increased levels of LP (a) levels - a risk factor for cardiovascular, cerebrovascular diseases, as well as peripheral diseases vessels is considered to be clearly established and generally accepted.

 Elevated LP (a) - the most common genetically mediated impairment of lipid metabolism in persons with early cardiovascular diseases: increased LP (a) concentrations increase coronary risk in particular in men with high levels of LDL-C and

low levels of XHDL. LP particle size (a) and is independent genetica predictor of CVD in patients with hypercholesterolemia;

 LP (a), angioplasty and coronary artery bypass grafting: an increased level of LP (a) is a risk factor for clinical relapse after percutaneous transluminal balloon angioplasty;

 LP (a) and cerebrovascular diseases: increased level of LP (a) is a risk factor for ischemic stroke, in particular stroke caused by atherosclerosis of a large artery;

 LP (a) during hemodialysis: high levels of LP (a) after hemodialysis and the predominant content of small isoforms of LP (a) predominantly associated with subsequent cardiovascular events, while the small sizes of the Apo (a) isoforms were more than stronger predictor characteristics than elevated levels LP (a);

 LP (a) for renal pathologies: nephrotic syndrome really leads to an increase in LP (a); level measurement LP (a) for renal pathologies, as well as before and after hemodialysis allows you to assess the risk of subsequent vascular events;

 LP (a) and type 1 diabetes mellitus: with diabetes mellitus 1, the levels of LP (a) above 30 mg / dL are associated with a doubled risk of cardiovascular complications, including coronary and peripheral arteries, as well as cerebrovascular diseases. Moreover, this correlation was not affected by increased LDL-C levels, nor decreased HDL-C levels;

 LP (a), DM 2 and microvascular diseases: LP (a) higher than 19.5 mg / dl and the dominance of its small particles -predictor of peripheral arterial disease in type 2 diabetes;

 LP (a) is a predictor of mortality in type 2 diabetes peripheral arterial disease: in patients with insulin - is dependent on diabetes mellitus 2 and peripheral arterial diseases with LP (a) levels above 36 mg / dL strongly increase the risk of mortality. Have patients with insulin-independent diabetes type 2 diabetes and LP (a) equal to 36 mg / dL, the risk of mortality is the same as in patients with peripheral arterial disease, but no diabetes.

BIOCHEMICAL ASPECTS OF ATHEROSCLEROSIS

Atherosclerosis - a pathological change in the internal (intima) and partially middle (media) membranes of the arteries. The word is derived from the Greek.

"Athere" - gruel, the main component of which is cholesterol esters (ECS) included in the hardened sclerosed plaque.

The clinical manifestations of atherosclerosis are various widespread vascular diseases of various organs: heart, aorta, brain, kidneys, lower extremities. Atherosclerotic plaque obstructs blood flow and causes ischemia and hypoxia of the organ, and when complete blockage of the vessel with plaque or a thrombus induced by it there are myocardial infarction, stroke, gangrene of the extremities.

Pathological processes in the vascular wall develop in humans with aging: heterogeneity of the endothelium and other cells occurs inner shell, as a result of the accumulation of "foamy" cells under endothelium, lipid spots appear on the inner surface of the vessels and strips, and then in their place - atherosclerotic plaques. Part plaques include, in addition to ECS, TAG, glycosaminoglycans, collagen, elastin, calcium, macrophages, mSMC, dead cells. In atherosclerotic plaques with a high frequency of herpesvirus DNA (cytomegalovirus and herpes simplex), as well as chlamydia. The role of these microorganisms remains unclear. At rupture of fibrous capsules are exposed under the influence of mechanical and toxic factors cholesterol gruel and such a "malignant" plaque becomes the center of platelet aggregation, deposition of fibrin clots and thrombus formation.

Atherosclerosis is a multifactorial vascular disease. Therefore, according to With the accumulation of experimental data, various hypotheses arose about its etiology and pathogenesis: cholesterol or infiltration, thrombogenic, clonal ("vascular myoma"), autoimmune and peroxide.

All hypotheses are related to the transport of LP and cholesterol (CS) into the vascular the wall. An increased level of cholesterol is an indisputable pathogenetic a factor in the development of atherosclerosis, and its etiological role is clearly manifests itself in young patients with a hereditary nature of the pathology: mutational change in the primary structure of apo B-100 (LDL protein) or LDL - receptor. In both cases, the complementarity between LDL and LDL-receptor of hepatocytes and other organs, as well as receptor endocytosis of LDL cells and increases the content of LDL and cholesterol in the blood.

For the elderly and, to a lesser extent, for the young, an essential role other risk factors also play a role: chemical and physicochemical modification of LDL (glycosylation, especially in diabetes mellitus, peroxidation of cholesterol and polyunsaturated fatty acids in LDL, desialation, partial proteolysis, aggregation), damage factors endothelium (infections, inflammation, hypertension, toxic factors, e.g. nicotine, high concentrations of LDL and VLDL), increased blood clotting, hemodynamic factors (plaques occur in places of bends, branching, vascular stenosis) and changes in the contenthormones.

Factors that increase the risk of diseases associated with atherosclerosis.

Modifiable factors		Non-modifiable factors
Lifestyle	biochemical and physiological factors	personality parameters
High-calorie food with increased	Hypercholesterolemia due LDL	Age Floor

keeping an animal fat and cholesterol Smoking Excess consumption alcohol Decreased physical activity	Arterial hypertension Low blood levels of HDL Hypertriglyceridemia Obesity Diabetes Thrombogenic factors	The presence of loved ones relatives of clinical manifestations of atherosclerosis (for men - up to 55 years old, for women - under 65) Family history patient with hyperlipidemia

1. Age for men - over 45;

2. For women over 55 or early menopause without estrogen therapy;

3. A family history of coronary artery disease;

4. Smoking;

5. Arterial hypertension;

6. Diabetes mellitus.

Integral model of arterial wall atherosclerosis, taking into account the listed etiological and pathogenetic factors, shown in Figure 3.1. In a healthy person, blood LDL is transported to endothelium and other cells of the CS vessel, necessary for them to form membranes. With hypercholesterolemia due to increased levels LDL, or when modifying LDL, the main flow of CS into the inner wall vessels are carried out by monocytes. The latter phagocytose LDL, modified LDL (mLDL), autoimmune complexes of mLDL with antibodies and transfer cholesterol to the subendothelial site of the intima. LDL are destroyed in the endolysosome, releasing cholesterol, which accumulates in cytosol of macrophages in the form of ECS drops, giving the cells a foamy appearance ("Foamy" cells). CS esterification is catalyzed by acyl-CoA cholesterol acyltransferase (ACAT) activated by free cholesterol.

"Foamy" cells, dying, release cholesterol into the intercellular space to form plaques.

Another source of plaque cholesterol is smooth muscle cells (SMCs).

Activated macrophages produce cytokines in the intima (interleukin 1, etc.), which stimulate the migration of MMC from the media of the vessel to the intima, and also their proliferation and transformation into synthesizing type SMC ("Myoma of the vessel"). The latter produce collagen and other structures connective tissue fibrous plaque. Modified GMK (mMMC) also phagocytose LDL and MLDL, turning into "foamy" cells.

In areas of endothelial damage, LDL, especially oxidized LDL, interacting with platelet receptors, induce their aggregation with thrombus formation and their synthesis of platelet growth factor, which, like the cytokines of macrophages, it transforms the SMC in the intima. In aggregation platelet activation factor is also involved, synthesized in platelets, endothelium, macrophages, and thromboxane A_3, formed in platelets from arachidonic acid. Moreover, damaged endothelium produces less nitric oxide (NO). V as a result, the paracrine effect of NO on platelets and SMC decreases arteries, which leads to the activation of the inositol phosphate regulation system, an increase in the calcium content in these cells and, accordingly, to platelet aggregation and vasoconstriction, i.e. to atherogenic effect. About 70% of blood cholesterol is found in LDL.

Therefore, hypercholesterolemia is the main risk factor for the development of atherosclerosis, usually associated with an increase in blood LDL and their predecessors VLDL - two atherogenic drugs. Therefore, more not hypercholesterolemia, but dilipoproteinemia - quantitative predominance of LDL, VLDL and qualitative changes in the structure of LDL (MLDL).

Atherogenicity of excess LDL and especially MLDL due to their ability to interact with monocyte receptors, SMC, platelets and cause the formation of "foam" cells and atherosclerotic plaques (Figure 3.1). LDL-HDL antagonists, possessing a special mechanism for the extraction of cholesterol from cells and other drugs with the participation of lecithin-cholesterol acyltransferase (LCAT), carry out the reverse transport of "excess" cholesterol from organs and blood to the liver, where it is mainly turns into bile acids. Antiatherogenic HDL with about 10 times lower molecular weight than LDL, easily pass between endothelial cells and through the vascular wall, removing from intima cells excess cholesterol. Then, through the paravasal vessels, HDL is transported Cholesterol in the liver (Fig. 3.2.). HDL in human blood is heterogeneous in composition apo A.

HDL with apo A-1 are more antiatherogenic than HDL, containing both apo A-1 and apo A-II. Apo A-1 is the strongest activator of LCAT in comparison with other HDL proteins. Therefore HDL, containing only apo A-1, are especially important for diagnostics and control of treatment of atherosclerosis.

Antiatherogenicity of HDL is also associated with their high content of phospholipids (25-40,%) - antioxidants.

Another minor type of superaterogenic drugs is known - LP (a). They differ from LDL in the presence of an additional protein - apo (a), one the molecule of which is linked to one molecule of apo B-100 disulfide connection on the surface of the LP. The concentration of LP (a) in human blood is low changes during the life of an individual, unlike other drugs. Between by some people, the concentration of drug (a) can differ up to 1000 times.

An increased level of LP (a) is considered to be severe hereditary a deterministic marker of a high risk of developing atherosclerosis. LP (a) binds to fibrin through special domains in apo (a), and also with collagen, elastin, fibronectin in the vessel wall, etc. by way of cholesterol it is deposited in the vessel normally or if it is damaged. Excessive amounts of LP (a) and apo (a) block fibrin, competing with plasminogen (primary structures of the latter and apo (a) highly homologous), which increases thrombosis and inhibits fibrinolysis. So is the mechanism of high atherogenicity of LP (a). Known isoforms apo (a), due to different alleles of the same gene on the 6th chromosome. For patients with coronary heart disease are more characterized by a high level of LP (a) in the blood and the predominance of low molecular weight apo (a) isoforms.

There are ethnic differences in the concentration of LP (a) and the spectrum of isoforms apo (a).

The interaction of LP with cells occurs with the participation of various types of receptors. In the cells of the parenchymal organs and connective LDL tissues are transported normally by receptor multistage regulated endocytosis by means of LDL-receptor (apo B, E-receptor).

This receptor is a transmembrane domain glycoprotein, containing galactose and sialic acid. N-terminal domain binds the ligand is LDL. On the surface of hepatocytes is about 50-70% of all LDL receptors in the body. With a high content of cholesterol in the liver represses the synthesis of LDL receptors on the principle of negative feedback communication. On the contrary, estrogens, iodothyronines and hypocholesterolemic drugs - statins activate their synthesis.

With a variety of mutations (more often deletions) in the LDL receptor gene, located in the short arm of the 19th chromosome, a hereditary familial hypercholesterolemia of the homo- or heterozygous type (frequency in populations 〖10〗 ^ (- 6) and 2 * 〖10〗 ^ (-3), respectively). Especially early and severe, not amenable to dietary and pharmacotherapy forms of coronary atherosclerosis is characteristic of homozygous pathology. Mutations disrupt complementarity between apo B-100 LDL and LDL receptor or associated with violation of synthesis and other stages of the functioning of the receptor in the process of endocytosis. As a result, the patient has a sharp hypercholesterolemia (up to 1000 mg / dL in homozygotes and up to 500 mg / dL in heterozygotes), an increase in LDL levels, an increase in the time of their circulation in blood, which contributes to the formation of atherogenic MLDL. Another hereditary form of atherosclerosis, clinically similar to previous, but milder - familial hypercholesterolemia, due to a structural defect in apo B-100 LDL. It occurs when dominant mononucleotide mutations in several codons of the apo B gene 100 (2nd chromosome), corresponding to the C-terminal half of the protein. Such apo-protein does not bind to LDL-receptor, which increases the content of LDL and cholesterol in the blood. Mutations can also lead to an atherogenic effect in the gene for constitutive

endothelial isoform of NO synthase (eNOS) with decrease in NO production. Other forms of hereditary (primary) dyslipoproteinemia associated with atherosclerosis.

With glycosylation of the LDL receptor in a patient with diabetes mellitus glycosylation of apo B-100 LDL also occurs. Violated by them complementary interaction and secondary dyslipoproteinemia and atherosclerosis. In monocytes (macrophages) and in the vascular endothelium, the main role in LDL absorption is not played by LDL receptors, but by special unregulated scavenger receptors, which are particularly involved in the seizure MLNP with their subsequent transport into the vessel wall.

The level of cholesterol in the blood depends on a huge number of hereditary and non-hereditary factors associated with its intake into the body with food, synthesis and regulation, with transport, expenditure on synthesis bile acids and other compounds and with excretion. About 80% cholesterol synthesized in the liver. With an increase in the amount of cholesterol in food (more 300-500 mg / day) in a healthy person, its synthesis in the liver decreases, so how cholesterol and cholesterol oxidative derivatives inhibit the activity and synthesis of the regulatory enzyme HMG-CoA reductase. Conversely, vegetarians have synthesis endogenous cholesterol is very intense. With pathological processes, the dynamic equilibrium between the indicated factors that can lead to hypercholesterolemia and the occurrence "Vicious circle" in the circulation of cholesterol and drugs.

Exogenous and endogenous cholesterol (Fig. 3.4) comes, respectively, from intestines and liver into the blood as part of VLDL, which are converted to LDL. Part of LDL in excess is absorbed by liver cells with the participation of LDL receptors. In cholesterol-enriched hepatocytes, LDL synthesis is inhibited receptors, therefore, the transport of LDL and cholesterol to the liver decreases, but their level in the blood and the duration of circulation increase.

Inhibition of the flow of cholesterol from the blood to the liver enhances the synthesis endogenous cholesterol and the release into the blood of new portions of VLDL, again in LDL. Such a "vicious circle" occurs when mutational modification or glycosylation of LDL or LDL receptor proteins. At high concentration of LDL in the blood and their modification is enhanced transport of LDL and cholesterol into the vessel wall with the participation of mainly monocytes macrophages and their scaring receptors. Such a "vicious circle" is impossible interrupt by restricting food cholesterol or glucose. When heterozygous familial hypercholesterolemia decrease in the level of cholesterol in the blood can be achieved by using statins that inhibit HMG-CoA reductase and inducing the expression of a single normal allele gene of LDL-receptor in hepatocytes. With homozygous familial hypercholesterolemia, only extracorporeal therapy is effective (removal of LDL from the blood), partial liver transplantation and gene therapy.

Hormones such as iodothyronines and estrogens reduce blood levels the content of cholesterol and LDL. Iodothyronines induce at the level of transcription formation of

LDL receptors and liver 7α-hydroxylase – regulatory enzyme for the synthesis of bile acids from cholesterol. Estrogens inhibit the formation of the last enzyme, but activate the synthesis of LDL receptors and HMG-CoA-reductases of the liver (regulatory enzyme for the synthesis of cholesterol). So with hypothyroidism (hypothyroidism) develops hypercholesterolemia and secondary - atherosclerosis. In women before during the climacteric period, the level of total cholesterol in the blood is slightly lower, the HDL content is higher, which inhibits the development of atherosclerotic vascular lesions compared to men. However, the content of CS in hepatocytes and bile of women are higher. Therefore, they are more often formed in biliary tract cholesterol stones (gallstone disease). After menopause in the absence of estrogen replacement therapy indicated differences between men and women are being leveled.

Laboratory diagnostics of atherosclerosis is based on analysis in blood lipids, LP and assessment of other risk factors. In the presence of loved ones relatives of clinical manifestations of hereditary atherosclerosis in young and middle age, it is advisable to early assessment of risk factors in children in order to correct their lifestyle and possible early treatment. Not it will be superfluous here to note the role of iridology in early detection risk of atherosclerosis. Informativeness of iridological symptoms is large enough.

When biochemical analysis, one should focus on the following markers of risk of atherosclerosis: high blood levels of cholesterol, LDL, MLNP, LP (a), apo B, and also calculate the derived quantities - coefficients of atherogenicity:

Markers of resistance to atherosclerosis - low content in blood LP (a), apo B-100 (protein LDL and VLDL) and high - apo A-1 and apo A-4 (HDL proteins).

The content in the blood of total cholesterol, cholesterol and severity

Hypercholesterolemia

Hypercholesterolemia	HS LEVEL	GENERAL HS		HS LLD
		Mg/dl	Mmol/l	
Heavy	Very high	>300	>7.8	-
Moderate	high	250-300	6.5-7.8	>155
benign	Borderline	200-250	5.2-6.5	135-155
Missing	Desirable	<200	<5.2	<135

Methods of non-invasive laboratory diagnostics are being developed, in

which for the analysis of CS are used the intact skin of patients, their saliva and tears. For health prediction, diagnosis, prevention and treatment algorithms for examining patients are applied, taking into account risk factors and developing recommendations for adjusting lifestyle, treatment and the frequency of repeated laboratory control. Prevention of atherosclerosis is based on a healthy lifestyle, correcting non-hereditary and hereditary risk factors development of pathology.

LIPID EXCHANGE IN PATIENTS

ONCOHEMATOLOGICAL DISEASES

Lipid metabolism disorders are not only the cause of the development a number of diseases, but can also be a consequence of various pathological processes. The most studied changes in lipid metabolism in patients with cardiovascular diseases, in particular, atherosclerosis. But the fact that lipids are involved in the mechanism of oncogenesis is not is in doubt. It is known that both normal and pathological, including oncohematological, lipids not only ensure the functioning effector proteins, but they themselves are effectors that are involved in signaling processes, up to the regulation of gene expression.

With oncological diseases, systemic disorders occur lipid metabolism. When studying the lipid composition of blood in 146 women with breast cancer (BC), ovarian cancer and other oncogynecological diseases, a reliable an increase in serum LDL cholesterol in breast cancer and a decrease in other gynecological tumors. HDL levels are reduced in all patients.

Modern medicine pays great attention to identifying and correction of HCS, which, by all accounts, is a threat to life. At the same time, low levels of cholesterol are considered a positive sign. But, considering that this compound plays a key role in proliferation cells, it should be assumed that a low level of cholesterol in the blood is associated with a high the need for it of neoplastic cells. It has been established that the content and the rate of CS biosynthesis increases in proliferating cells normal tissues as well as many tumors. So, with prostate cancer and glioma showed a significant increase in the content of cholesterol in tumor cells and normal tissues surrounding the tumor. These changes are associated with by several mechanisms: an increase in its absorption from the circulation, stimulation of endogenous synthesis, as well as blocking the release excessive cholesterol from cells during malignant transformation. Metabolism fat in the tumor is always accelerated, which is associated with high intensity cell division, a prerequisite for which is the synthesis lipid components of the cytoplasmic membrane. With favorable the outcome of the disease, these changes disappear. Thus, the study of lipid metabolism in patients with AL can provide new data on the biology of these neoplasias, and to identify additional criteria for the activity of the neoplastic itself process, prognosis of treatment results and early diagnosis of complications.