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 №5

Diseases of the cardiovascular system. Heart attack. Enzymatic diagnostics of myocardial infarction.

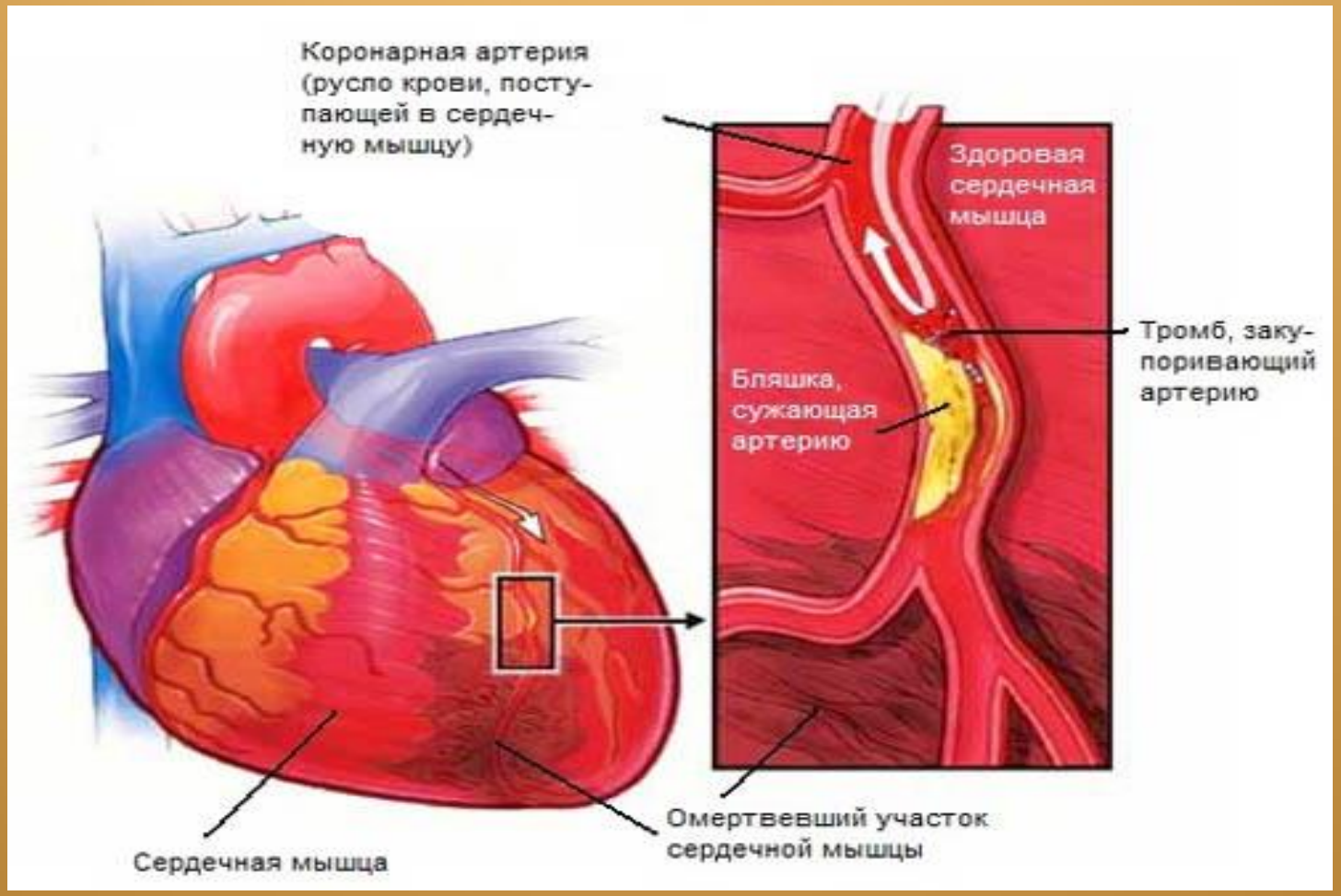
In the group of cardiovascular disease (CVD) usually include:

- Coronary heart disease
- Cerebrovascular disease,
- Lesion of the peripheral arteries

- The leading role in the pathogenesis of CVD plays atherosclerosis.
- In the structure of CVD mortality of about 85-90% accounted for brain stroke and coronary artery disease. Worldwide annually from CVD causes nearly 17 million people.

- **The vast majority of deaths from cardiovascular disease (80%) - people from middle-and low-income areas.**
- **In Western Europe in the last quarter-century cardiovascular mortality decreased by 32% due to the prevention, timely diagnosis and treatment.**
- **At the age of 35 to 59 years in the U.S. 100,000 people die each year 116 people, in India - more than two times, and in Russia in this age dies 5 times (!) more people than in the U.S.**

Complete or partial blockage of the coronary arteries leads to myocardial infarction



Diagnosis of myocardial infarction is based on:

- The patient's complaints (pain symptoms),
- Electro-cardiogram,
- The study of blood cardiac markers

Diagnosis of myocardial infarction is made in the presence of two of three signs

Imbalance between the actual blood supply to the myocardium and its needs in the blood supply may be due to the **following reasons**:

Intravascular reasons:

- Atherosclerotic narrowing of the coronary arteries;
- Thrombosis and thromboembolism of the coronary arteries;
- Spasm of the coronary arteries.

Extravascular reasons:

- Tachycardia;
- Myocardial hypertrophy;
- Hypertension.

As a result of defects occurring in the cytoplasmic membranes of myocardial cells, proteins and enzymes localized in their cytoplasm enter the blood of patients with MI:

- **Creatine kinase,**
- **Aspartate aminotransferase,**
- **Alanine aminotransferase,**
- **Lactate dehydrogenase,**
- **Myoglobin**
- **Troponins**
- **NT-PRO-BNP**

Lactate dehydrogenase (LDH 1,2,3,4,5)

Glycolytic enzymes involved in the final stages of the conversion of glucose. Zinc-containing enzyme, is localized mainly in the cytoplasm.

- **Considered to be a specific marker for acute myocardial infarction.**
- **By Acute MI at the level increases rapidly for 2-4 day, and normalized only 2 to 3 week.**
- **Other factions and LDG3, LDG4 - enzymes lung tissue LDG5 - liver.**

ALT, AST

Aminotransferase liver, muscle, myocardium.

- **Levels are elevated in liver and myocardium.**
- **Normally, the ratio of AST / ALT (de Ritis coefficient) is 1,33 ± 0,42.**
- **In acute myocardial infarction, this ratio increases. Increase in serum AST observed in 6-12 hours from the onset.**
- **The maximum increase observed at 2-4 days and 5-7 days to the level of the enzyme comes to normal.**

MB-fraction of creatine kinase (CK-MB)

General CK consists of three isoenzymes:

CK-MM (muscle)

CK-BB (brain)

CK-MB - dimer composed of two subunits:

M (muscle) and B (brain).

CK-MB is considered relatively cardiac. Skeletal muscles contain up to 3% of the protein.

Increase in serum levels of the enzyme is observed after 4-8 h after acute myocardial infarction, and reaches a maximum after 12-24 h on the third day of the enzyme activity returns to normal (in patients with uncomplicated MI)

Myoglobin

- Is a protein that carries oxygen in the skeletal muscle and myocardium.
- Increasing in the blood 2-3 hours after the onset of pain and preserved for 2-3 days.
- Increase of myoglobin in the first 2 h is detected in 50%, for the 3rd time at the - at 92%, the 5 th hour - 100% of patients with MI.
- Myoglobin level in MI may increase 4-10 times or more, depending on the area of myocardial damage.

Myoglobin.

When an increase in myoglobin concentration is detected:

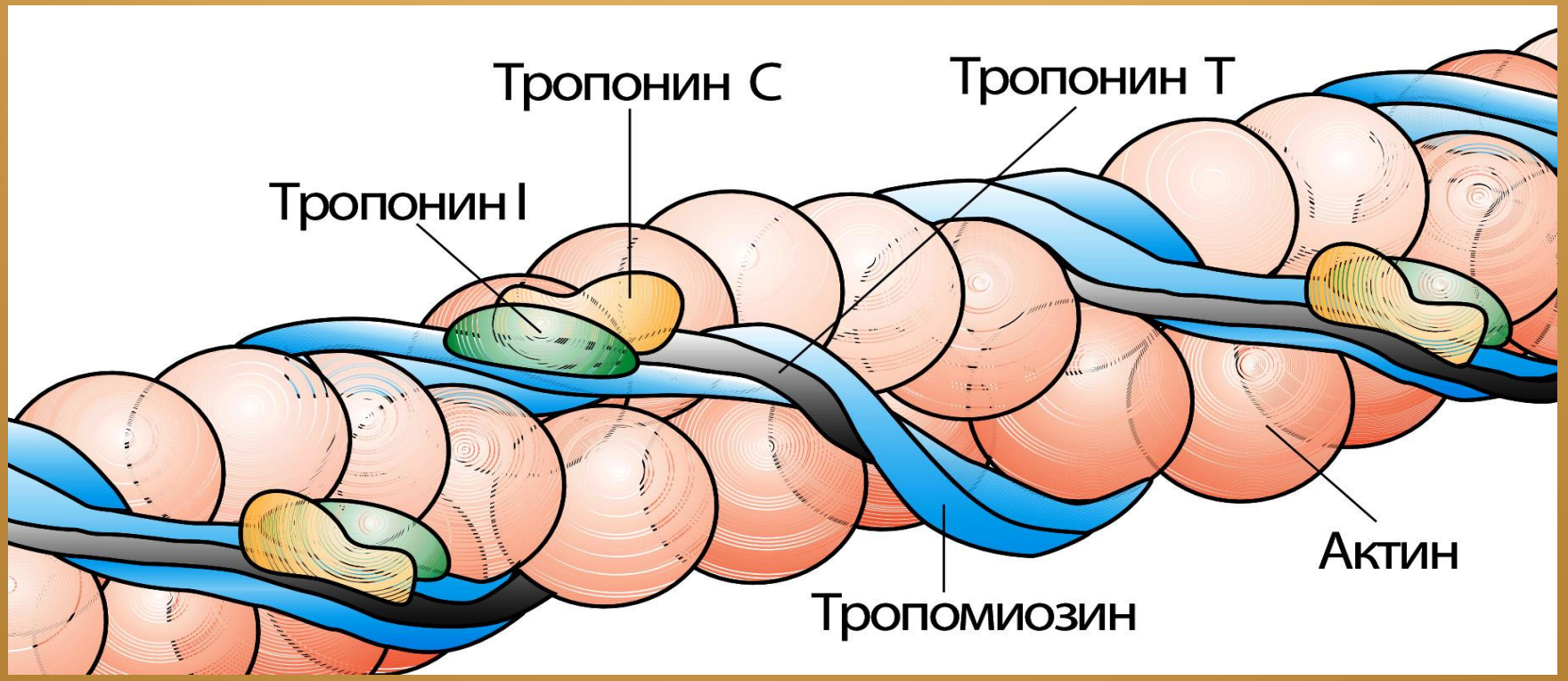
- **in patients with the syndrome of prolonged compression,**
- **in patients with long-term compression syndrome,**
- **with extensive muscle damage,**
- **in case of severe electric shock,**
- **thermal burn,**
- **arterial occlusion of the ischemic muscle.**

Determination of *total creatine kinase (CK), lactate dehydrogenase (including isoforms), aspartate aminotransferase (AST)* as markers of myocardial infarction in the present not recommended due to their low specificity.

In recent years, the definition used in the serum troponin complex components myocardium - troponin I and T.

Troponin.

Regulatory globular protein composed of three subunits, which is involved in the process of muscle contraction. Found in skeletal muscle and cardiac muscle, but not in the smooth muscle.



Troponins

Are part of the contractile myocytes.

Troponin C (mol m 20 thousand) binds Ca2 +, changes troponin I. Similar to the structure of calmodulin.

Troponin T (mol m 37 thousand) binds to tropomyosin.

Troponin I (mol m 25 thousand) binds to actin in thin filaments, thereby keeping tropomiozin troponin-complex on the site, prevents the interaction of actin and myosin.

Troponins

- Troponin T and I, there are three isoforms in:
- heart-muscle type,
- slow skeletal muscle type and
- fast skeletal muscle type.

A cardiac isoform of troponin T was detected:

when recovering from a skeletal muscle injury,

in patients with polymyositis or for Duchenne Muscular dystrophy,

in the epithelial cells of the renal tubules.

Troponins

Cardiac troponin I isoform presents only in cardiac muscle.

- **If the damage of myocardial troponin complex disintegrates and troponin molecules migrate into the blood.**
- **Within 4-6 hours after the incident, the concentration of troponin in the blood can be measured with modern laboratory techniques.**

Troponins I and T

- The process of release of troponin I has a single-phase nature, and troponin T - biphasic.
- Increasing levels of troponin determined within 8-10 days after the onset of MI.
- Interval of absolute diagnostic sensitivity troponin in patients with AMI is 125-129 hours.
- Determine the specificity of troponin in MI was 90% and specificity superior to CK, LDH too.

Troponin I

The high specificity of troponin makes them particularly valuable in the diagnosis of myocardial infarction after cardioversion, resuscitation, surgery.

Readings to determine troponin:

- **Diagnosis of MI**
- **Assessment of reperfusion after thrombolytic therapy**
- **Selection of groups of high coronary risk in patients with acute coronary syndrome without ST elevation,**
- **Selection of patients treated with the greatest effect of low molecular weight heparins**

Norma troponin I

Acute MI	**0,5 мкg/l**
boundary exceptions	
Acute MI	**2,0 мкg/l**
Border confirm	

Norma troponin T

Acute MI excluded (after 3-8 hours after the onset of)	**< 0.4 мкg/l**
Acute MI is not excluded (Requires further diagnostic)	**0,4-2,3 мкg/l**
Acute MI confirmed	**> 2.3 мкg/l**

Protein that binds fatty acids, heart shape (H-FABP)

- FABPs - class of cytoplasmic proteins that bind long chain fatty acids.
- They are well represented in the various cell types and play an important role in intracellular catabolism of fatty acids. Known, at least 6 of tissue-specific forms of FABP.
- In the heart muscle FABP found in high concentrations - 10-20% of the cytoplasmic proteins.

Protein that binds fatty acids, heart shape (H-FABP)

- **H-FABP (FABP3) - a small protein with MM 15 kDa, FABPs - class of cytoplasmic proteins that bind long chain fatty acids.**
- **They are well represented in the various cell types and play an important role in intracellular catabolism of fatty acids. Known, at least 6 of tissue-specific forms of FABP.**
- **In the heart muscle FABP found in high concentrations - 10-20% of the cytoplasmic proteins.**

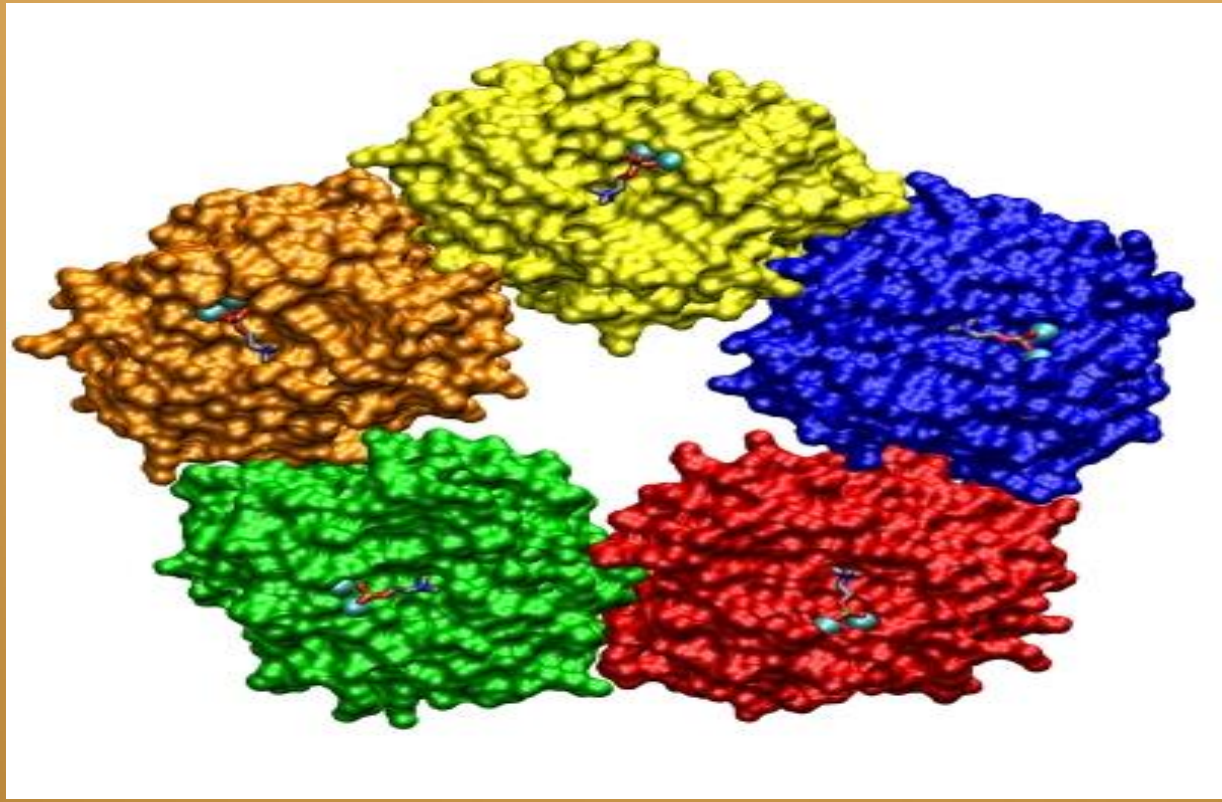
- **In patients with AMI is released into the blood.**
- **The highest concentration of H-FABP was observed after 3 h after MI, for 12-24 hours, it returns to the normal range.**
- **Thanks to these properties, H-FABP is used as a sensitive marker for early diagnosis of acute myocardial infarction and to monitor its flow.**

Protein that binds fatty acids, heart shape (H-FABP)

- **Elevated levels of H-FABP can detect individuals with high risk of adverse events, even in patients with normal levels of troponin I.**
- **In addition, the concentration of H-FABP can be judged on the vastness of MI.**
- **In the plasma of healthy human serum is present about 1.6 ng/ml H-FABP, with the age limit of normal concentration slightly increasing.**

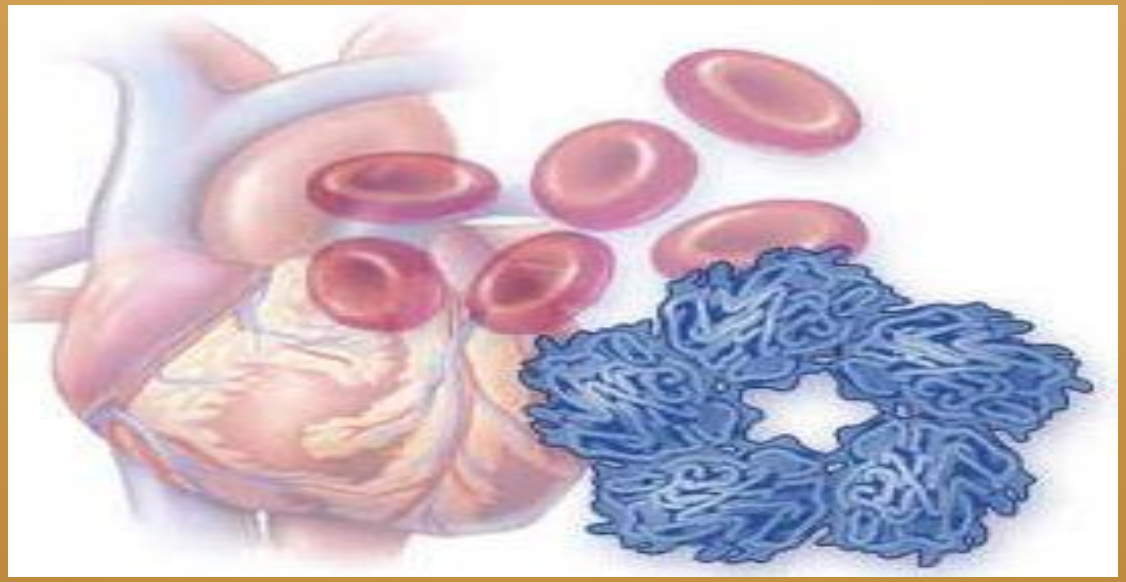
C-reactive protein

- Its detection indicates the presence of inflammation in the body or necrotic process.
- He refers to proteins so-called "acute phase".



C-reactive protein.

Sharply positive for CRP indicates the severity of the inflammation. Measurement of baseline CRP to evaluate the risk of acute myocardial infarction (AMI), stroke, and sudden cardiac death in patients not suffering from cardio-vascular diseases.



C-reactive protein

At concentrations of CRP:

- **less than 1.0 mg/l**

the risk of vascular complications (myocardial infarction, stroke) - the minimum

- **at 1.1-1.9 - low,**
- **at 2.0-2.9 - moderate,**
- **with more than 3 mg/L - high.**

For values> 10 reason for raising CRP - infectious

Homocysteine

- An amino acid that is formed during the metabolism of the essential amino acid methionine.
- Homocysteine in plasma is mainly bound to proteins. Elevated homocysteine levels are cytotoxic. Homocysteine can damage the blood vessels, making them with loose surface.
- On the damaged surface deposited cholesterol and calcium, forming atherosclerotic plaque. Elevated levels of homocysteine increases thrombosis.

Homocysteine

- In patients with elevated HC increases the risk of MI in all age groups, regardless of smoking, cholesterol and hypertension.
- HC is an independent risk factor for AC coronary, peripheral and cerebral vessels.
- Each increase in HC to 5 mmol/l is accompanied by an increased risk of disease of the cerebral arteries by 1.5 times and peripheral arteries in 6.8 times.

Homocystein

- In men with HC level only 12% higher than normal, there is a threefold increase in the risk of heart attack.
- With hyperhomocysteinemia may be due to 10% of the risk of coronary heart disease in the general population.
- Additional administration of vitamin B6 and folic acid reduces the number of MI within 14 years by 45%.

Homocystein

It is recommended to check the level of HCs in all patients with arterial or venous thrombosis, coronary heart disease, all preparing for pregnancy women with relatives who were infarction and thrombosis at the age of 45-50 years.

NT-pro BNP

Diagnosis and monitoring of heart failure

Chronic heart failure (CHF) - a syndrome characterized by the inability of the heart muscle to provide adequate blood flow for the metabolic and functional needs of the organism.

A key part of the pathogenesis of chronic heart failure - ventricular dysfunction, adequate emission levels.

Causes:

- Ischemic heart disease, cardiomyopathy, congenital heart
- Hypertension
- Lung
- Anemia
- Obesity
- Multiple organ pathology
- Endocrine disease
- Kidney disease
- Alcoholism, drug use

Symptoms:

- Heart attack (may be painless)
- Sudden Death
- Rapid breathing (dyspnea)
- Frequent cough, especially when lying down
- Swelling of the legs, knees and feet
- Ascites
- Dizziness or fainting
- Fatigue

Natriuretic peptides (NP)

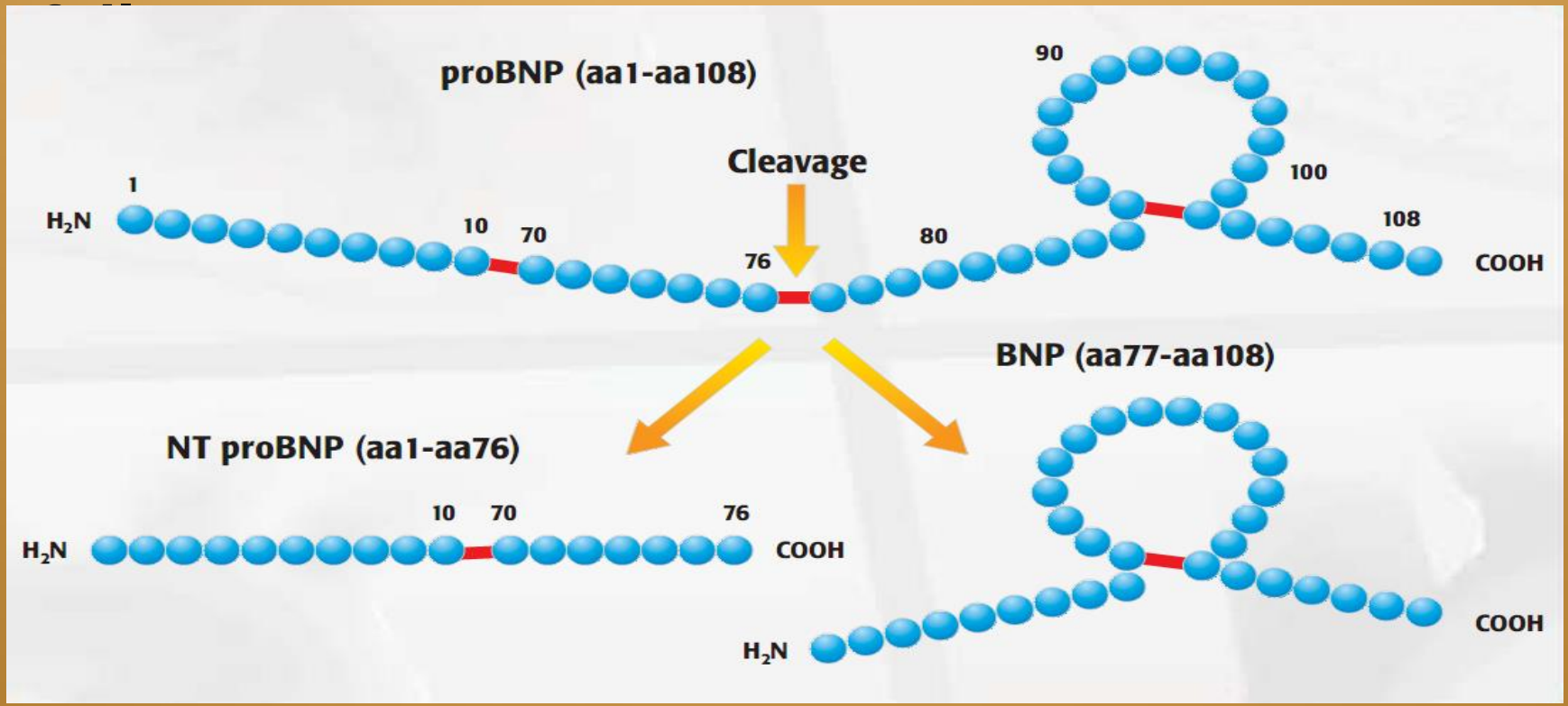
Atrial (ANP), brain (BNP) and C-natriuretic (CNP) peptides - members of the family of hormones secreted by the atrium, ventricle and the endothelial cells of blood vessels.

NP cause range diuretic, natriuretic and antihypertensive effects.

In cardiovascular diseases, an increase in the level of SNP is combined with a violation of the contractile function of the heart.

NT-pro-BNPNT-pro-BNP (inactive N-terminal peptide) - a marker of left ventricular dysfunction.

- The content of the analyte in the blood increases in the early stages of myocardial dysfunction and the development of heart



The clinical significance of BNP and NT-pro-BNP:

- Identification of patients with heart failure (screening);
- Confirm severity of heart failure;
- Directed monitor patients with heart failure;
- Monitoring of therapy and its optimization;
- Identification of risk among patients with acute; coronary syndromes and prognosis of the disease (complications and recurrent attacks).

Antibodies to cardiolipin (ACA)

Play a significant event in the primary abnormalities of the coronary arteries at a young age, they are detected in more than 70% of patients with coronary artery disease.

Is a basis to antiphospholipid syndrome (APS)

One of the most common cardiac symptoms of APS is a valvular heart disease

Leads to recurrent thrombosis intrakardial small coronary vessels.

PAPP-A

- **PAPP-A - zinc-MMP cleaves IGFBP-4, thereby facilitating the release of the active insulin-like growth factor (IGF-1).**
- **PAPP-A synthesis is increased in response to tissue damage**
- **With CVD PAPP-A acts as a sensitive marker of inflammation and damage than troponins.**
- **(> 10 mIU / L) levels of PAPP-A in the blood is highly sensitive and specific test for the diagnosis of acute coronary syndrome.**


Thanks for your a t on