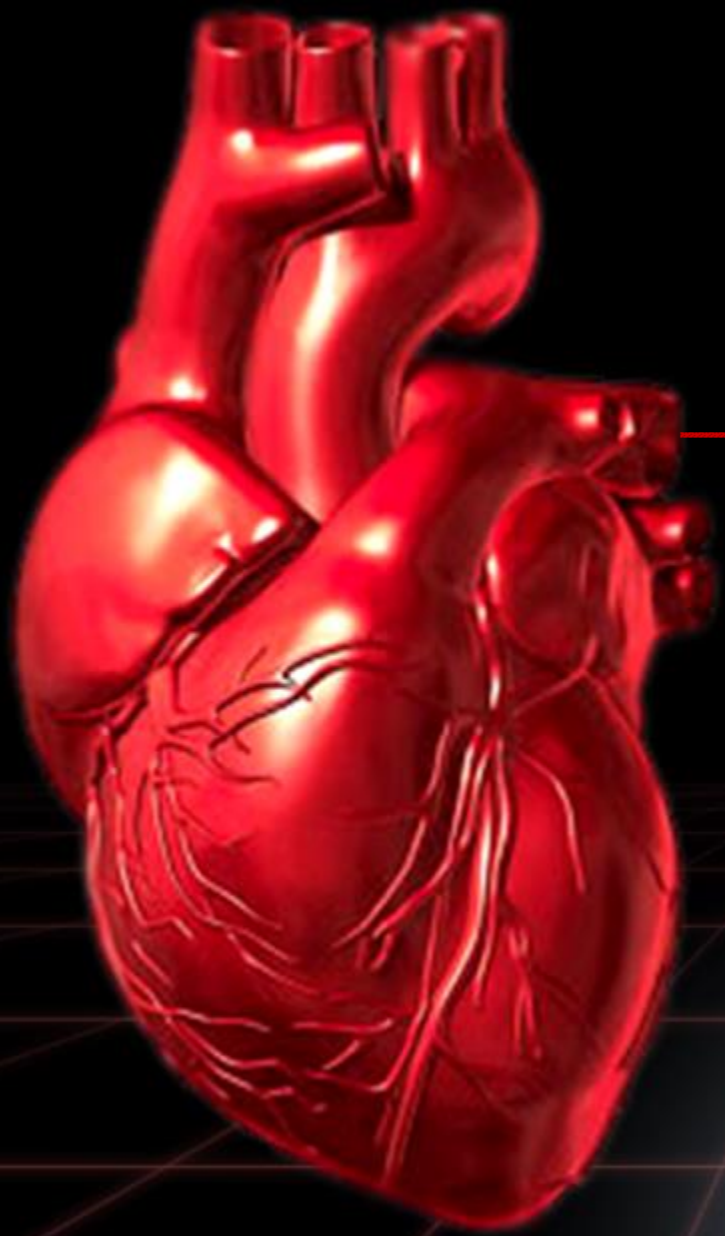


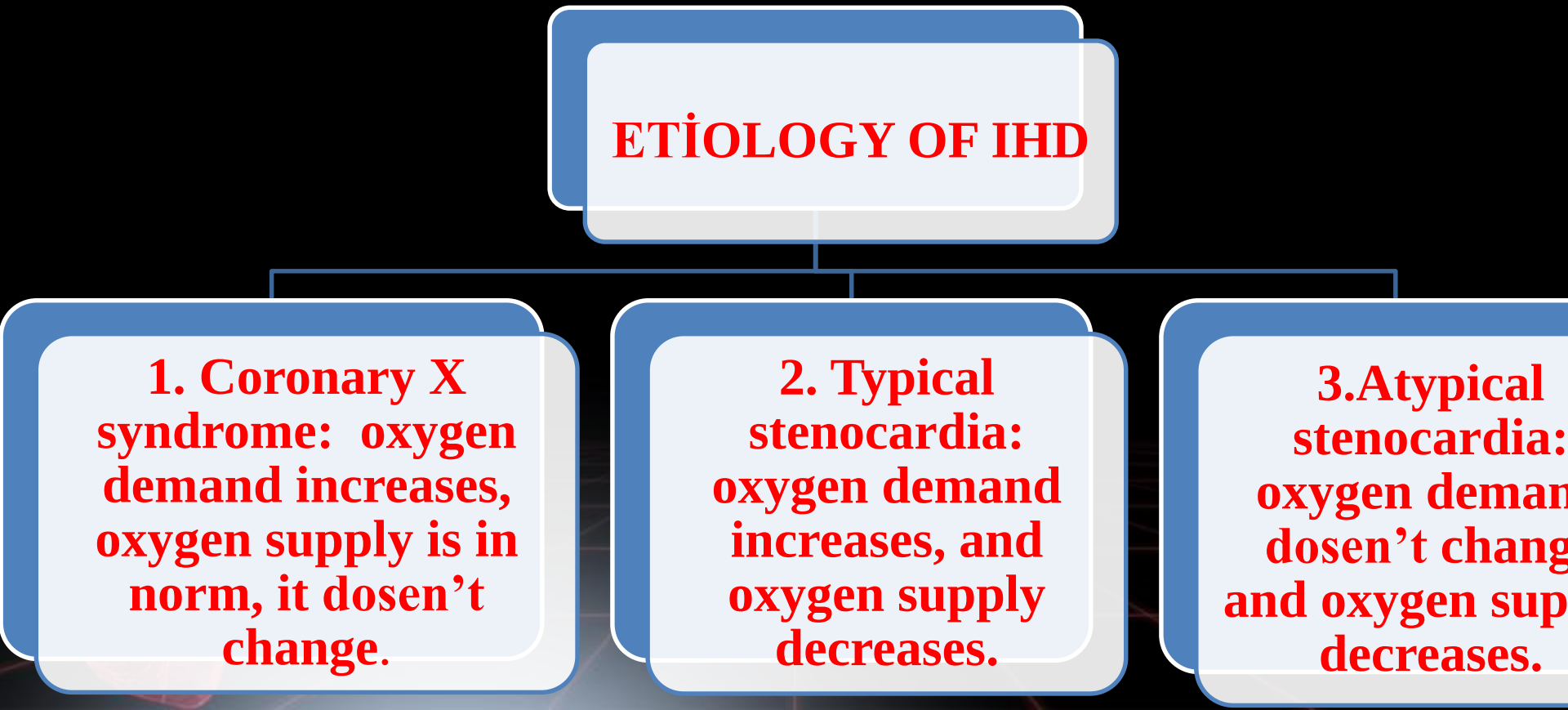
Azərbaycan
Tibb Universiteti

LABORATORY DIAGNOSTICS OF CORONARY DISORDERS. ISCHEMIC HEART DISEASES

Department of Pathological Physiology

GENERAL ETIOLOGY OF ISCHEMIC HEART DISEASES

The etiology of ischemic heart diseases are associated with disbalance between the oxygen demand and the oxygen supply of the heart muscle. It can express in 3 versions:



ETİOLOGICAL FACTORS OF IHD

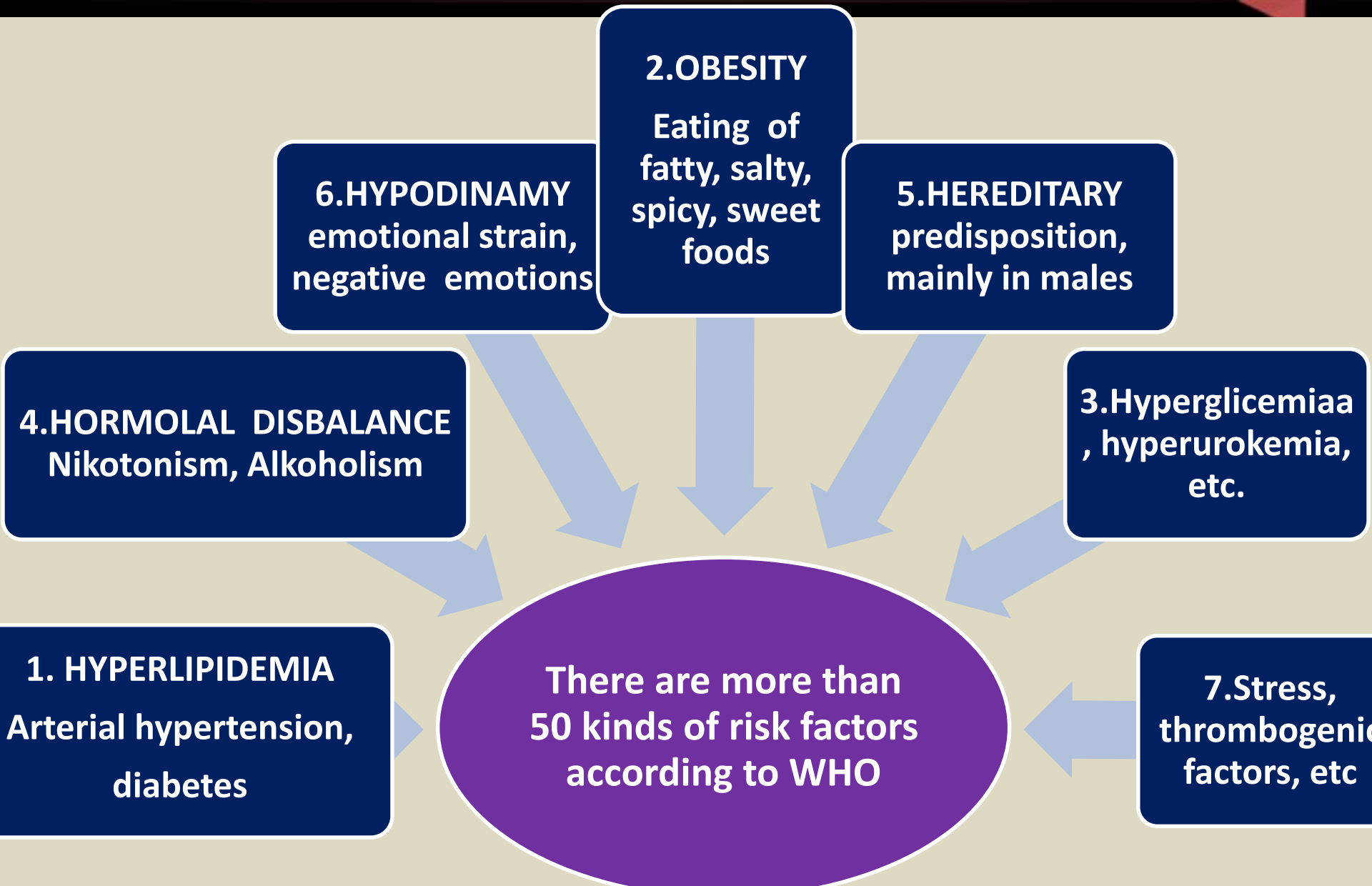
1. ATHEROSCLEROSIS OF CORONARY ARTERY

2. SPASM OF CORONARY ARTERY

3. THROMBOCYTIC AGREGATES INSIDE OF CORONARY ARTERIES

4. MİCROVASCULAR DYSFUNCTION

RİSK FACTORS OF IHD



HIGH LEVEL OF RİSK FACTORS ACCORDING USA CARDIOLOGY ASSOCIATION

1. Hypercholeste-rolemia – more than 6,7 mmol/l
2. Trygliserid emia – more than 2,9 mmol/
3. A/P- higher than 160/95 mm Hg.
4. Body weight more than 30%-of norm
5. Hyperglice mia- fasting glucose more than 6,6 mmol/l, decreasing of glucose tolerance test

ETİOLOGICAL FACTORS OF IHD

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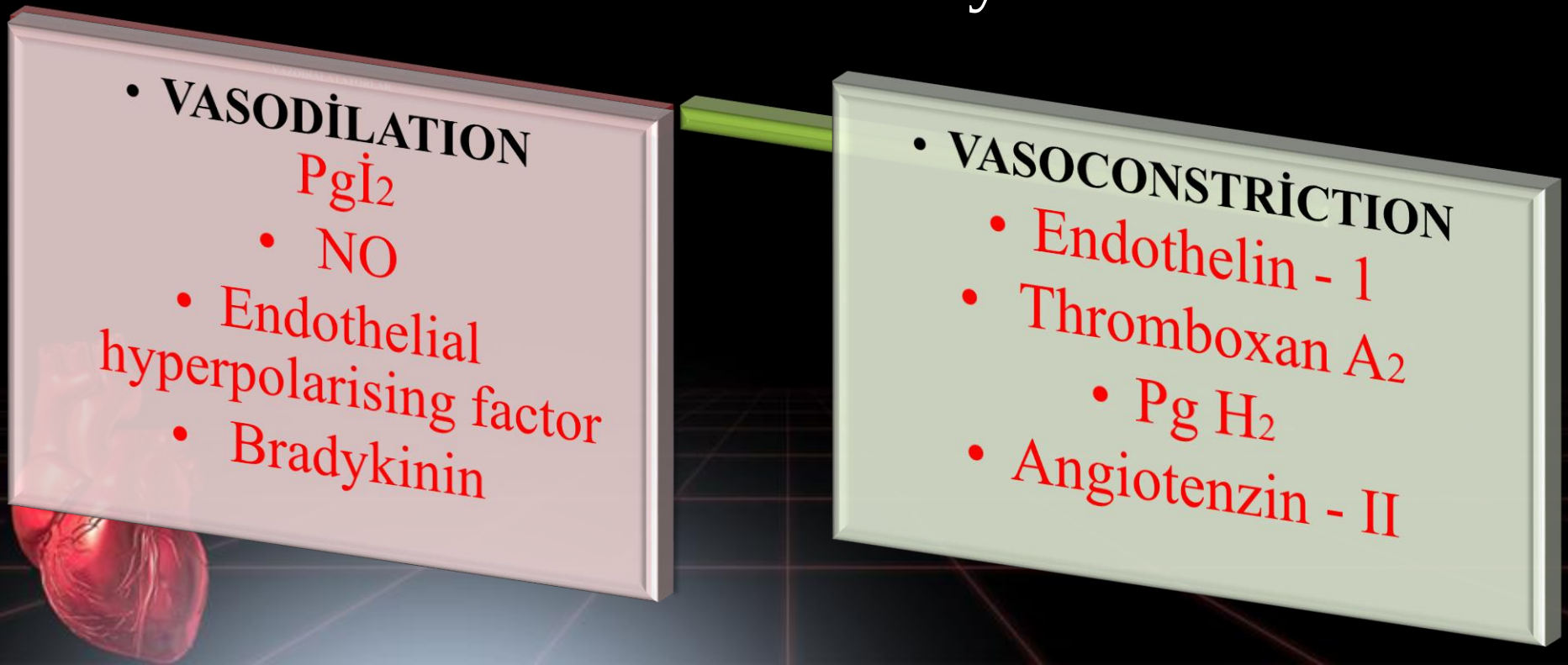
ATHEROSCLEROSIS OF CORONARY ARTERY

Etiological factors of coronary insufficiency in 90-95% of cases linked with atherosclerosis.

The role of “endothelial factors” in the regulation of vascular tonicity:



SPASM OF CORONARY ARTERY

Normally, adenosine, bradykinin, substance P, acetylcholine, etc. dilates coronary vessels and improves perfusion. In atherosclerosis of coronary vessels, arterial hypertension, diabetes and risk factors reduce production of NO and PG I_2. These decrease endothelium-dependent relaxation and spasm occurs.

Endothelial vasoconstrictors – Ag II, thromboxan A2, endothelin cause spasm of coronary vessels and decreases perfusion. Activation of symphatoadrenal system – releasing of catecholamines –α_1 adrenoreceptors also increase the spasm of coronary vessels.

A-CORONARY THROMBOCYTIC AGGREGA

ACTIVATION of VASCULAR-THROMBOCYTİC MECHANİSMS of COAGULATION

3 main components of vascular-thrombocytic hemostasis takes role:

1.Specific receptors of platelets

(glycoprotein Ib, IIb, IIIa)

2. Collagen;

3. Willebrand factor.

Vascular-thrombocytic hemostasis s activated by Willebrand factor, which is released during damage of vessel wall.

ADF, catecholamines, collagen increases blood coagulability. Activated platelets releases clotting factors:

- Thromboplastic factor – III;

- Antiheparinic factor – IV;

Willebrand factor –VIII;

factor V, thromboglobulin;

- Alpha 2- antiplasmin, fibrinogen, etc.

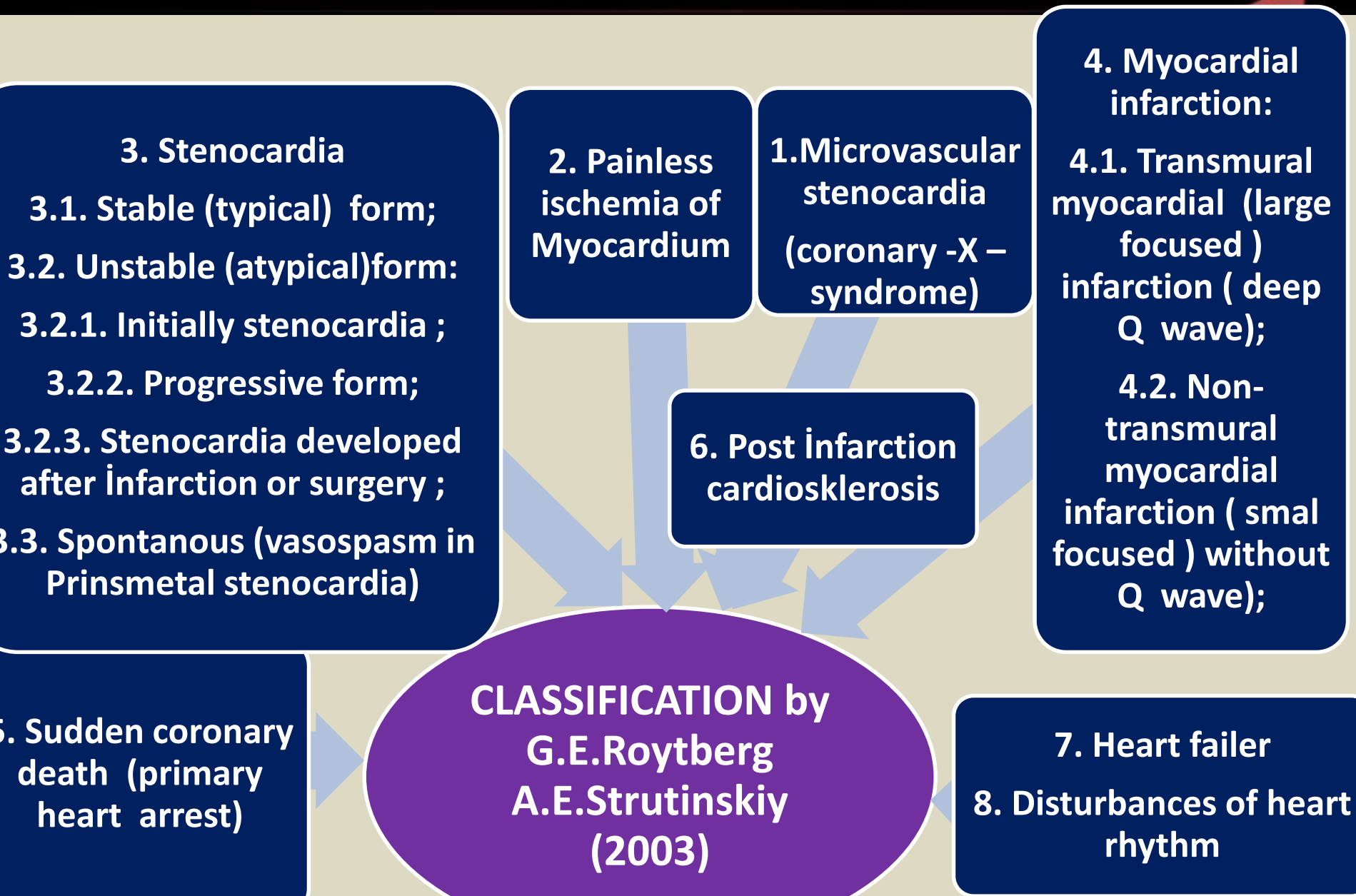
MİCROVASCULAR DYSFUNCTİON

«CORONARY X» SYNDROME

The changes are recorded mainly in the small coronary vessels, the size of which doesn't' t exceed 150-350 μm. Narrowing of the small coronary vessels is observed due to hypertrophy in smooth muscle of vessels.

These changes are associated with increased production of endothelin and neuropeptide Y on the background of the endothelial dysfunction. Reduction of vasodilators - NO and protocyclin is of great importance.

CLASSIFICATION OF IHD

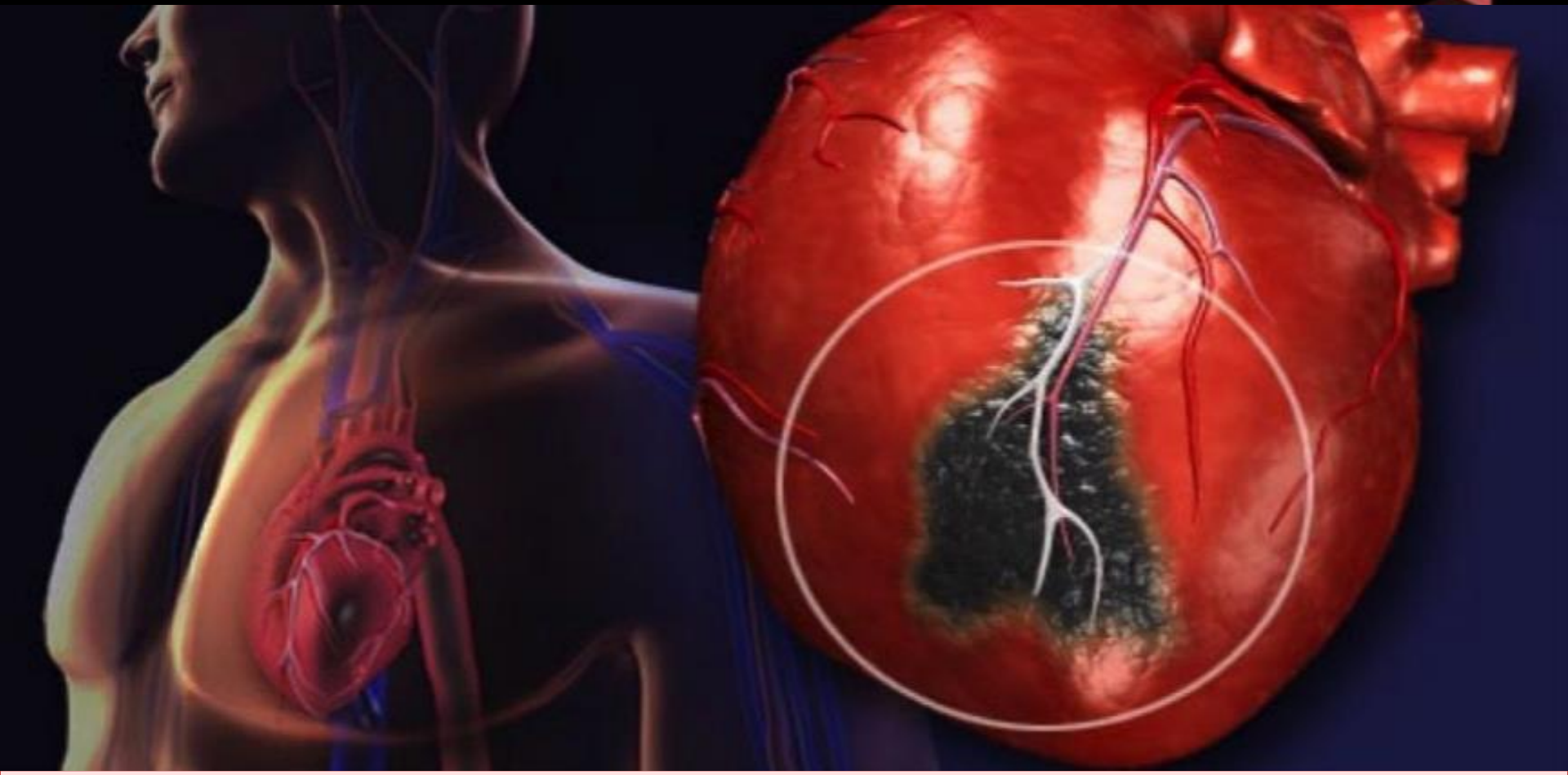


ACUTE CORONARY SYNDROME

Acute coronary syndrome is a group of symptoms that give reason to suspect the development of myocardial infarction or unstable angina due to IHD, the pathogenetic basis of which is acute occluding thrombosis of the coronary artery. Clinical forms are as follows:

1. Unstable stenocardia
2. Small focused myocardial infarction with non-elevated ST segment
3. Myocardial infarction with elevated ST segment
4. Relapsing myocardial infarction
5. Complete blokade of left leg of Hiss bandle

MİOCARDIAL İNFARCTION



Ischemic necrosis of heart muscle due to acute coronary insufficiency.

ETİOLOGY OF MİOCARDIAL İNFARCTION

MİOCARDIAL İNFARCTION

- ATHEROSKLEROSIS of CORONARY VESSELS (90-95%)
- **CORONARY SPASM and THROMBOSIS of CORONARY ARTERY (5%)**
- OTHER DISORDERS of CORONARY ARTERİES (1-3%)
  - SYSTEM VASCULİTES
  - EMBOLISM of CORONARY ARTERY
  - DISURBANCES I N BLOOD CIRCULATION
  - HEART TRAUMA
  - METABOLIC DISORDERS
  - DISTURBANCES of COAGULATION SYSTEM
  - CONGENITAL DEFECTS of CORONARY ARTERIES

MİOCARDIAL İNFARCTION

Ischemic necrosis of heart muscle that occurs as a result of acute coronary insufficiency.

- the area of atherosclerotic plaque, all-fixed thromb is formed, which doesn't stop blood circulation;
- the thromb doesn't dissolve due to he fibrinolytic system, it gradually grows and completely closes the vessel lumen (occlusion)
- Transmural infarction with deep Q-wave develops.

- If the thrombus doesn't completely occludes the vessel, then subendocardial or intramural myocardial infarction occurs without a Q-wave;
- In 70-80% of cases, complete occlusion takes 2-3 days to 2-3 weeks;
- This period is manifested by symptoms of unstable stenocardia (pre-infarct condition);
- In 20-30% of cases, the thrombus is formed very quickly.

Stages and forms of Myocardial infarction

1. (I stage) – ischemia leads to the formation of necrosis. From 30 min. to 2 hours;
2. (II stage) – formation of necrosis and myomalation, till 10 days;
3. (III stage) sub-acute period from10-days to 4-8 weeks;
4. (IV stage) post-infarction period - scar formation , coagulation of scar, 2-6 monthes.

1. Typik-angious form;
2. Asthmatic form;
3. Abdominal form;
4. Arrhytmic form;
5. Serebrovascular form;
6. Asymptomic form.

DIAGNOSIS of MI BASED ON:

-CLINICAL MANIFESTATION
-ECG CHANGES
-LABORATORY TESTS OF BLOOD

CLINICAL MANIFESTATION

---Severe persistent chest pain radiates to the left arm, neck and lower jaw;

----Numbness, coldness of the extremities;

----Dyspnea, nausea and vomiting;

----Changes in blood pressure;

ECG changes

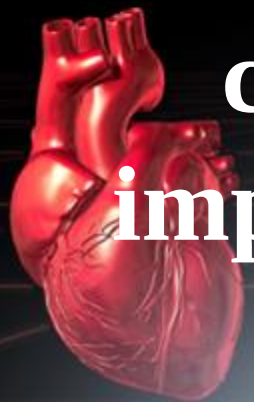
ST-segment elevation

T-wave inversion

Q-wave formation

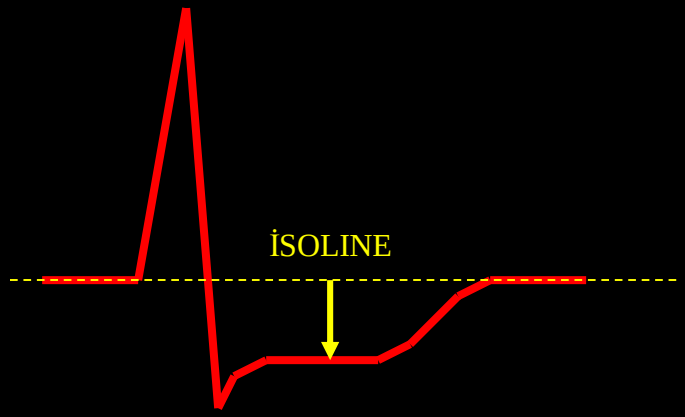
In 30% of cases, the typical changes of ECG are not enough to diagnose MI.

Determination of the activity of cardiospecific enzymes is very important to make the diagnosis of acute myocardial infarction.



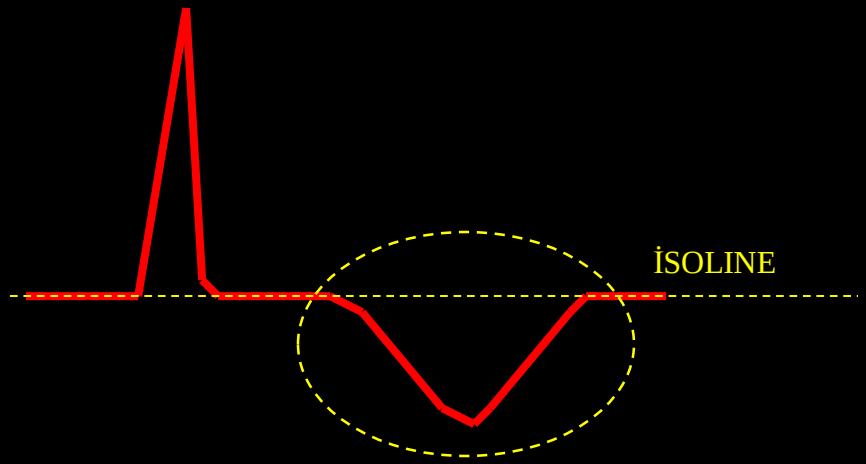
ECG CHANGES IN İSCHEMİA AND MYOCARDIAL İNFARCTION

SUBENDOCARDİAL İSCHEMİA



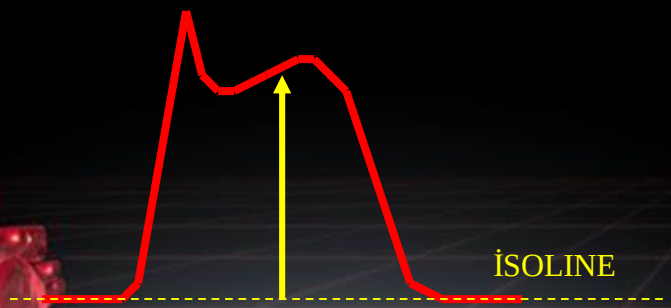
ST SEGMENT DEPRESSİON

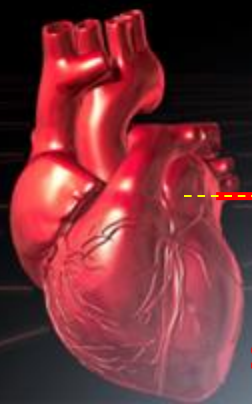
ACUTE SUBENDOCARDİAL İSCHEMİA



«CORONARY» T WAVE

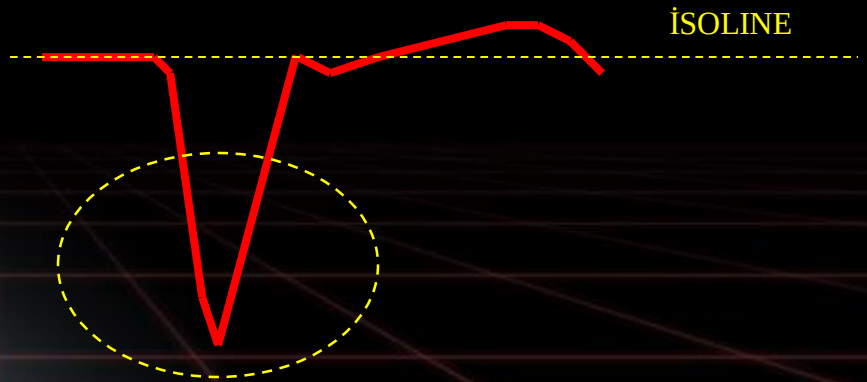
TRANSMURAL İSCHEMİA





ST SEGMENT ELEVATION

TRANSMURAL İNFARCTION



PATHOLOGICAL QS WAVE

LABORATORY INDICES FOR DİAQNOSIS OF IHD

1. Laboratory indices for IHD Risk ;

2. Laboratory indices for differensial diagnosis of acute coronary syndrome;
3. Laboratory indices for chronic heart failer

Laboratory indices for IHD Risk

Determination of the following sensitive laboratory indicators for the risk of IHD :

-C-reactive protein (CRP);

-Lipoproteins (LDLP);

-Lipoprotein-associated phospholipase A2 (LP – PLA2);

-ApoB/ApoA1 ratio;

High-sensitivity C-Reactive Protein – increased level of high-sensitivity CRP is an indicator of the initial stage of endothelial dysfunction.

CRP-more than 3 mg/l – high risk of acute coronary changes and stroke (at least in the next 5 years);

CRP- between 2.0 – 2.9 mg/l – moderate risk;

CRP-between 1.1 – 1.9 mg/l – low risk;

CRP-less than 1.0 mg/l indicates minimal risk.

The level of high-sensitivity CRP is considered the main indicator of cardiovascular risk even in practically healthy people with low ChM and LDLP. Thus, in cases of normal LDLP (less than 3.36 mmol/l) and high-sensitivity CRP is more than 2.0 mg/l, the usage of statins reduces the risk of myocardial infarction and heart stroke during 4 years.

Lipoproteins are considered important risk factors not only IHD, but also for acute coronary syndrome.

The level of lipoproteins 0.3 g/l indicates a low risk of cardiovascular diseases,

0.3-0.5 g/l is a high risk,

more than 0.5 g/l is a very high risk.

Epidemiological studies have shown that people with normal olesterol levels, but lipoproteins above 0.3 g/l, have at least a 2-f creased risk of IHD. If LDLP is elevated at the same time, the ris ischemic heart diseases increases up to 8 times.

Lipoprotein – associated PhospholipazeA_2

(thrombocyte activating factor) – is the specific indicator of ves
wall injury, myocardial infarction and ischemic insult of brain

LP – PLA2 is combined with circulating LDLP. When LDLP enters the vascular endothelium, LP-PLA2 is synthesis is stimulated (according to the degree of progression of atherosclerotic plaque) and it passes into the bloodstream.

The level of LP-associated PLA2 in blood ranges from 0.29 to 50 ng/ml. Increasing of CRP and also LP – PLA2 , the high risk of development acute coronary syndrome.

ApoB/ApoA1 RATIO

ApoB/ApoA1 ratio – predicts MI risk even in people with normal lipid levels. Each lipoprotein contains a specific proteins- (Apo).

ApoB - is a major component of LDLP, which transports TG from the intestine to adipose tissue.

ApoA1 – is the main component of HDLP, it plays a role in transporting chylomicrons from the periphery (including the vessel wall) to the liver by participating in the transport of triglycerides and chylomicrons.

Ratio of ApoB / ApoA is greater than 1, the risk of ischemic heart disease is considered high.

LABORATORY DIAGNOSTIC INDICES FOR Acute Coronary Syndrome

Determination of differential diagnostic indicators of acute corona
syndrome - myocardial infarction, unstable angina, stable angina a
minimal damage of the myocardium is of particular importance i
practical medicine.

Biochemical indicators of damage in the myocardium are called

cardiomarkers.

The main biochemical cardiomarkers of acute myocardial infarction

T and I troponins;

CK-MB isoenzyme;

AsAT; Myoglobin; LDH -1 isoenzyme.

CARDIAL TROPONINS T and İ

Cardial troponins T and I are cardiospecific proteins. Tropo
T and I concentration increases early after myocardial necrosi
Therefore, the determination of cardiospecific troponin T and I
important for the diagnosis of MI.

3 isoenzymes of troponins T and I are distinguished. Only o
isoenzyme of troponin T and I is considered specific for the
myocardium. Normally, these isoenzymes are not detected in t
blood, but after MI they are transferred from the damaged
cardiomyocytes to the blood and their level increases. Unlike
myoglobin, the detection of these isoenzymes is highly specif
("gold standard") for myocardial damage.

Troponin T

Increasing of troponin T (norm: 0-0.2 mg/l) is observed twice .

I wave is recorded 3-8 hours after the injury, and the peak level is recorded 12-18 hours later.

II wave is registered on the 3-4th day after the injury.

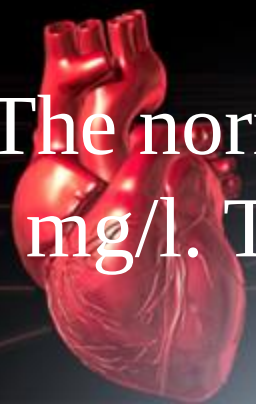
On the 7-10th day of myocardial necrosis, the level of Troponin T decreases becomes completely normal.

he degree of increase of this indicator depends on the are of the necrosis.

CARDIAC TROPONINS I and T in MI

Troponin I is more cardiospecific compared to Troponin T, especially when the patient suffers from IHD and renal failure at the same time, this indicator is of greater diagnostic importance.

The dynamics of troponin I changes in the blood during myocardial necrosis are similar to troponin T, but there is no second rising phase.



The normal concentration of this indicator is up to 3.1 mg/l. Troponin T and I both provide similar clinical information.

MİOGLOBİN

Myoglobin is considered a more sensitive cardiomarker specially in the first hours of MI this protein is already detected in the blood.

The norm of myoglobin in the blood is up to 40 ng/ml. During myocardial necrosis, the concentration of myoglobin increases 10 times or more after 0.5-2 hours. But disadvantage of this indicator is that, its low cardiospecific. Thus, myoglobin is detected in both cardiac and sceletal muscle. In clinical practice, the determination of myoglobin is important to rule out MI (if myoglobin does not rise after an acute pain attack, it rules out myocardial damage).

CREATİNKİNAZE (CK)

Creatine kinases – 3 different isoenzymes are distinguished.

CK-BB is found in brain tissue

CK-MM in skeletal muscles

CK-MB in heart muscle.

For diagnosis of MI, not the total activity of CK, but the CK-MB isozyme plays an important role.

4-6 hours after the development of MI, the level of CK-MB rises and reaches a maximum in 24 hours. 2-3 days after the MI, returns to normal. The level of elevation of this isoenzyme depends on the size of the necrosis site. To rule out a myocardial infarction, the activity of CK-MB should be determined every 8 hours (at least 3 negative results should be obtained).

Aspartate aminotransferase AST –

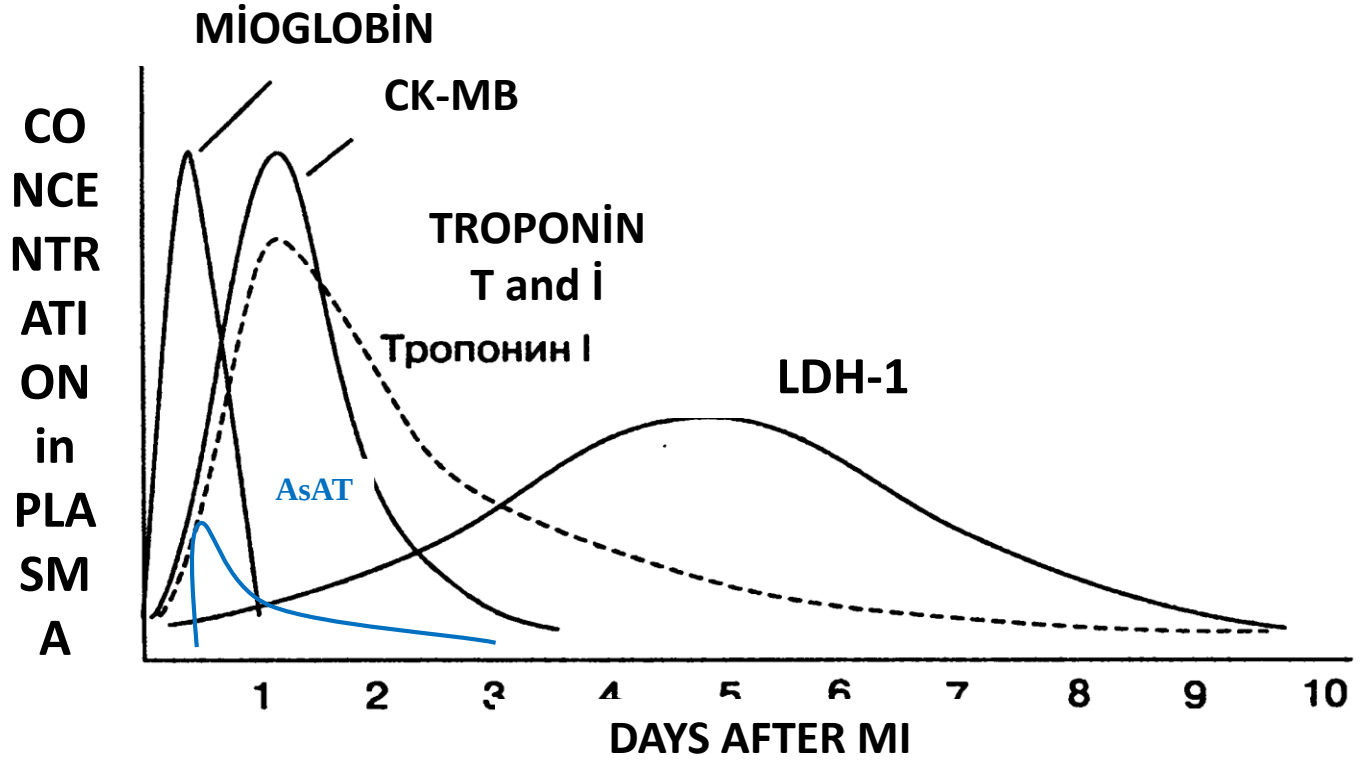
the enzyme catalyzes the transfer of amine groups from asparagine to ketoglutaric acid. Since this reaction is the main component of amino acid metabolism, it is carried out in any metabolically active cell.

AST is widely distributed in the tissues of the body, especially in the myocardium, skeletal muscles, and the liver. This enzyme is found in kidney cells and erythrocytes. The level of the AST begins to rise approximately 8 hours after the onset of MI, reaches its maximum level in 24 hours, and the normalization of the enzyme activity occurs in 2-3 days.

LDH- 5 isozymes of LDH are identified. Like CFCs, they are also organospecific. While LDH5 is mainly accumulated in the liver and skeletal muscles, more LDH1 is detected in the heart muscle. In many cases, the total activity of LDH (the sum of LDH1 + LDH2 + LDH3, etc.) is determined, and in some laboratories, the activity of LDH1, which is specific for the heart muscle, is determined.

LDH1 isozyme begins to rise 6-12 hours after the MI. At this time, the total level of LDH is still within the norm. An increase in the activity of LDH1 is not considered an absolute criterion of MI, the activity of this enzyme can be increased during acute coronary ischemia even without the focus of necrosis in the myocardium. However, at this time, the maximum activity of LDH1 can increase more than 2 times the normal level, and its normalization occurs in 10-12 hours.
This indicator is used as an auxiliary criterion for diagnosing CMI.

CARDİOMARKERS n MI



THE LEVEL OF CK-MB IS DIRECTLY PROPORTIONAL WITH THE SIZE OF THE INJURY (INCREASES AFTER 4-6 HOURS, REACHES A MAXIMUM AT 24 HOURS, IS HIGH UP TO 3 DAYS), MYOGLOBIN IS INCREASED IN THE FIRST HALF HOUR, BUT IS NOT CARDIOSPECIFIC, TROPONINS ARE INCREASED CARDIOSPECIFICLY MAXIMUM IN APPROXIMATELY 24 HOURS, REMAINS AT CERTAIN LEVEL UP TO 7-10 DAYS).

The Main Characteristics of Cardiomarkers

Troponin I	Specific marker of Acute Coronary Syndrome
Troponin T	Specific marker of Acute Coronary Syndrome Less Specific than Troponin İ
Mioqlobin	High sensitive marker in Acute Coronary Syndrome, but not completely specific. It can increase during damages of skeletal muscles and in diseases that is not associated with heart pathology.
CK - MB	Cardio-specific marker in AMI. But an increase of its concentration can also be observed in diseases of skeletal muscles and other

A new marker H-FABP (Heart-Fat Acid Binding Protein) a myocardial protein that binds fatty acids associated with myocardial necrosis. It is a cytoplasmic protein that binds the chain of fatty acids. This indicato increases in the blood after 1.5-3 hours during AMI, and returns to norm after 24 hours. It shows the same growt dynamics as myoglobin, it has significantly greater specificity. The European Society of Cardiology recommends determining the amount of H-FABP in the blood to prevent early myocardial necrosis when acute coronary syndrome is suspected.

LABORATORY INDEXES Determined in CHF

Natriuretic peptides are– atrial NP, brain NP and C –NP

They are synthesized in the atria, ventricles and endothelium vessels. The stimulus for their secretion is the increase of pressure in the left ventricle.

ANP - is an antagonist of the renin-angiotensin-aldosterone system. It accelerates renal blood circulation and filtration, slows down the reabsorption of sodium and water and increases diuresis. It causes vasodilator effect, reduces the concentration of renin, aldosterone, noradrenaline and endothelin-1 in the blood.

Brain NP – secreted by ventricular cardiomyocytes, has a diuretic and vasodilator effect. This peptide was named as such because it was first detected in the brain extract of animals.

C-NP is mainly synthesized in the CNS, has a limited diuretic and vasodilator effect

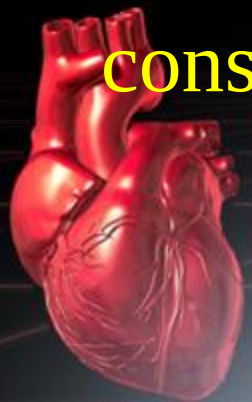
NP concentration increases during heart failure.

Determination of precursor form of pro-BNP, its inactive form

NT-pro BNP of great importance.

NT-pro BNP has some advantages over BNP. This marker circulates more in the blood at a relatively high concentration (the elimination time of BNP is 20 minutes, and for NT-pro BNP, this time is 60-100 minutes).

An increase of BNP and NT-pro BNP over is considered an indicator of chronic heart failure.



Methods for Determination of Myocardial Enzymes

No special preparation of the patient is required. Intramuscular injections may increase CK levels. Therefore, it is necessary to take the blood before the injection or 1 hour after the injection.

Blood is usually taken when the patient enters the hospital and during the next 2 days. If a patient has a suspicion of a myocardial infarction, it is important to do a blood test immediately. Myocardial enzymes may be at normal levels 4-8 hours after myocardial infarction. If the blood test is taken too late, a false result can be obtained.

5 ml of blood is enough for the determination of myocardial enzymes. The research is carried out in blood plasma or serum. If the examination is carried out in blood plasma the blood is collected in a test bottle containing the anticoagulant-lithium. If serum is used for analysis, the blood is collected in a simple test tube without any impurities.

PRINSIPLES OF PATHOGENETİC TREATMENT

ANALGETİCS

CORONARY DİLATATORS

ANTİCOAGULANTS and THROMBOLYTİCS

CARDIA-SURGERY

β-ADRENOBLO-CATORS

AG -RESEPTORS BLOCKATORS

ANTİARRHYTMİC

ELEKTRO-İMPULS

CALSİUM BLOCKATORS

DİQQƏTİNİZƏ GÖRƏ TƏŞƏKKÜR EDİRƏM !