

# **CORONARY HEART DISEASE (Arteriosclerotic Coronary Artery Disease; Ischemic Heart Disease)**

**Methodic materials for international students (IV-VI year)**

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## **CORONARY HEART DISEASE (Arteriosclerotic Coronary Artery Disease; Ischemic Heart Disease)**

### **Definition**

IHD is the disease of the heart muscle caused by imbalance between coronary blood flow and metabolic requirements of heart muscle (between oxygen supply and demand) due to local blood flow disturbances more often caused by coronary atherosclerosis.

### **Epidemiology**

The commonest cause of cardiovascular disability and death in industrial countries.

Men:women ratio is 4:1, before age 40 - 8:1, and beyond age 70 it is 1:1.

In men, the peak incidence of clinical manifestations is at age 50–60;

in women, at age 60–70.

**Aethiology. Risk factors.**

The basis of IHD development is insufficient coronary blood flow, which leads to the imbalance of oxygen supply and demand and thus to ischemia or necrosis of heart muscle.

**The most common morphological cause of IHD is coronary arteries atherosclerosis.**

In some cases IHD may be due to coronary arteries spasm (Prinzmetal stenocardia)

**In case if insufficient blood flow is caused by other factors, it is considered as a secondary coronary syndrome, relating to main nosological unit.**

**Following conditions may cause secondary coronary syndrome:**

- Vasculites and connective tissue disorders (Vegener granulomatosis, Nodular periarteriitis etc)
- Ostial narrowing due to luetic aortitis
- Congenital abnormalities – origin of the left anterior descending coronary artery from pulmonary artery, which leads to ischemia and infarctions in infancy
- Aortic stenosis or (more rare) – regurgitation
- Cardiomyopathias (first of all, hypertrophic)
- Rheumatic fever

**Risk factors of IHD are similar to these of other atherosclerosis-associated diseases:**

- positive family history (particularly when onset is before age 50)

- age
- male gender
- blood lipid abnormalities (high LDL level, low HDL level (especially in women, ratio LDL/HDL below 3 – lower risk, over 5 – higher risk; apoprotein “a” presence; growing number of evidences report about elevated TG level as a risk factor)
- hypertension (accelerates atherosclerosis due to caused by local haemodynamic stress endothelium injury; increases the oxygen demands of heart and worsens blood supply due to myocardium hyperthrophia).
- physical inactivity
- cigarette smoking
- diabetes mellitus
- hypoestrogenemia in women
- some authors also mention gout as a risk factor due to its influence on atherosclerosis progression
- stress
- obesity (especial that of the abdominal type)

### **Pathogenesis**

#### **2 groups of factors promote IHD development**

<b>Lowering of myocardium blood supply (mostly morphological)</b>	<b>Increase of myocardium oxygen demands (as a rule, provoke angina paroxysms or acute IHD forms)</b>
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Atherosclerotic changes of coronary arteries and their thrombosis due to instable plaque	Stress and other factors, causing hypercatecholaminemia (smoking, cocaine use) – due to direct hystotoxic action of catecholamines and their physiological effect on cardiovascular system (increase of the heart rate etc)
Coronary arteries spasm	Inadequate physical exertion (catecholamines, haemodynamic changes)
Congenital abnormalities causing insufficient collaterals development	AH (especially crises)
Microcirculation and haemosthesis system disorders (hypercoagulation, increased viscosity), leading to microtrombi formation, worsening of myocardium perfusion and ischemia	Tachycardia, especially tachyarrhythmia
Hypotonia	Hypertensive heart remodeling
Haemodynamically ineffective bradycardia	Endocrine diseases (thyrotoxicosis, pheochromacytoma)
Heart failure	Infections
Low oxygen saturation of blood (diseases of lungs and blood)	
Hypertensive myocardium remodeling (increase of muscle mass with worsening of blood supply)	

### **IHD classification (WHO)**

1. Sudden death (primary heart stoppage)
2. Angina pectoris
  - 2.1. **Exertion-induced angina**
    - 2.1.1. **Exertion-induced angina debut**
    - 2.1.2. Stable angina (1-4 functional classes)
    - 2.1.3. **Progressing exertion-induced angina**
    - 2.1.4. Variant angina (Prinzmetal's)

3. Myocardial infarction

3.1. **Transmural (large foci)**

3.2. **Small foci (мелкоочаговый)**

4. **Post-infarction cardiosclerosis**

5. Rhythm disorders (form is to be mentioned)

6. Heart failure

Atherosclerotic cardiosclerosis (cardiosclerosis due to chronic myocardial ischemia caused by coronary arteries atherosclerosis) is also considered to be a form of IHD but is not mentioned in this classification.

**Other classification, also recommended by WHO experts committee includes following variants of IHD course:**

- angina pectoris
- myocardial infarction
- chronic IHD (asymptomatic myocardial ischemia and ischemic cardiomyopathy)

## **Sudden death**

Primary heart stoppage, more often is caused by ventricular fibrillation, so no signs, giving possibility to state another diagnose, can be revealed.

Section reveals atherosclerotic stenosis (50% and more) of coronary arteries, haemorrhages and ruptures of plaques, thrombosis, focuses of myocardial ischemia.

**Most of authors consider as sudden death which happens no later than 6 hours after symptoms appearing.**

**Risk factors for sudden death**

- risk of myocardial infarction (first hour after symptoms appearance)
- history of myocardial infarction with rhythm disorders and heart failure (moderate and severe left ventricle dysfunction)
- chronic IHD with risk factors of its progression (AH, diabetes mellitus, gout, lipid metabolism disorders, smoking etc)

**However, in ¼ of patients sudden death may be the first clinical manifestation of IHD.**

## **Angina pectoris**

**Definition:**

Angina pectoris is a pain syndrome caused by short time local myocardium ischemia, which can appear either during physical exertion or at rest.

**Epidemiology**

The number of patients suffering from angina is between 30-50 thousand per million of adults in the world. About 0.2-1.2% of new cases are revealed each year (data concerning

males aged 40-59 years old). In general, men: women ratio is 2:1; approximately 80% of patients aged below 50, are males. The gender differences disappear at age over 75.

### **Pathogenesis**

Different variants of angina (see below) have peculiarities of pain syndrome pathogenesis, which will be discussed later.

### **Morphology**

Short-time myocardial ischemia leads to apoptosis activation (natural death of cardiomyocytes); necrosis and necrobiotic changes are not revealed. Condition of coronary arteries depends on angina stability: in instable cases complicated lesions and instable plaques are revealed while in stable angina plaques are usually stable.

### **Clinical picture**

**The only one syndrome is typical for angina – pain syndrome (“angina has two realities – pain and death”). Absence of ischemic ECG signs can’t be a reason to reject angina.**

### **Characteristics of the pain syndrome**

	Typical	Atypical	Excluding angina
Localization	80-90% of cases – behind or slightly to the left of the mid sternum; also may be in upper sternum or precordial region The patient usually shows localization of a pain by a fist	Only in places of pain irradiation (jaw, scapule, along the inner surface of left hand with 4-5 fingers growing numb) Along the right side of sternum, in right side	Place of pain localization could be shown by one finger (the patient point on the pain site by finger) – the pain is not sharply localized. Superficial pain. Pain, localized only in middle

	clenched over the mid chest	In interscapular region Pain in lower sternum can be considered as epigastrium pain	and/or lower abdomen
Character	Heaviness, pressure, aching, bursting, squeezing, smothering, throttling, choking (including sensation of a stake hammered in chest), crushing, gripping, burning, band-like more rare as frank pain. Sensation of a great weight in chest may be present instead of pain. Also feeling of more discomfort than pain may be present. Feeling of “gas”, indigestion or an ill-characterized disorder.	<b>Equivalents of angina (usually in aged people):</b> - sudden dyspnea paroxysm, accompanied by severe weakness sensation - transient dyspnea - tachycardia episodes - rhythmus (extrasistoles, atrial fibrillation paroxysms) and conductivity (transient His bundle branches blocks, AV block) disorders - dizziness episodes, syncopes - weakness paroxysms - asymptomatic ischemia episodes - pain similar to that in spondilosis (cervical and thoracic region) – if angina is associated with cervical and/or thoracic spondilosis	Spasmodic, acute, cutting
Irradiation	Left shoulder and upper arm, moving to elbow, forearm, wrist, 4 and 5 fingers along the inner surface, teeth, back; dermatome C8-T4;	Neck, lower jaw, teeth, interscapular area, right shoulder and distally (characteristics are similar to the left hand)	Irradiation only to lower extremities
Appears	<b>During</b> physical exertion, stress or emotional episodes, cold weather, walking against strong wind, food intake, sexual activity	<b>Angina decubitans</b> (marker of severe deterioration of patient’s condition): appears in lying position, usually at night; provoking factor may be increase in wall stress of the left ventricle caused	During breath (especially deep), cough, while turning the body and head, moving hands, during palpation



		by an increase in end-diastolic volume when lying down. Also tachycardia induced by dreaming, alterations in coronary tone, and diurnal variation in blood pressure which starts to rise from about 4 to 5 a.m. may play a role.	
Dynamics	Paroxysmal with gradual increase of intensity and spreading up to maximal intensity and then quick relief with sensation of “full release”		-
Duration	2-5 minutes, more rare – up to 10-15 min, night paroxysms are usually longer then these caused by exertion		Constant pain, lasting for days, or short-time episodes, lasting for a few seconds
Relieved	Cessation of physical exertion or other above mentioned factors; nitrates intake (after sublingual intake the effect appears in first 1-3 minutes), the effect of nitrates may be delayed in angina, appearing at rest	For angina decubitans – sitting or standing up	Pain, relieved by eating or antacides' intake Pain, relieved by distraction of patient's attention from it
Emotional	Marked emotional characteristics - fear, angst, fear of death, sensation of danger		-

**Atypical pain is usually present in:**

- aged persons
- in combination with cervical and/or thoracic spondilosis
- in patients with stomach, gallbladder, oesophagus diseases
- in women (especially in climacterium)

**Importance of atypical forms diagnostics: in 25% cases of sudden death**

**asymptomatic or atypical angina course is present**

**Thus, in any kind of chest, arms and shoulders, back, neck, lower jaw, teeth, epigastrium pain angina should be suspected. The character of pain, its localization, irradiation, dynamics, provoking and relieving factors should be deeply analyzed from the point of view of similarity to these of angina pectoris.**

**Peculiarities of angina in women:**

- **risk factors:** also menopause and passive smoking; more important than in men are HDL and TG level rise and diabetes mellitus.
- **“X-syndrome”** may be present, when the ischemia is due not to coronary arteries, but microvessels affection. Typical pain syndrome and positive ECG-test with physical exertion are present, but angiographic investigation reveals normal coronary arteries.
- more favorable angina course but worse infarction prognosis (more often heart failure, thromboembolisms, fatal arrhythmias, myocardium ruptures).

**Asymptomatic (silent) myocardium ischemia**

As silent myocardium ischemia are considered asymptomatic (painless) ischemia episodes, **revealed only by Holter’s ECG monitoring (ST depression)**. More common, these episodes occur in the morning. The true prevalence of silent ischemia is unknown because it is revealed only in Holter’s ECG monitoring or exercise functional tests in patients having IHD risk factors; but some authors (Oxford Textbook of Medicine) report about its presence

in 2.5% of male population and in 10% of patients following myocardium infarction; in the last case presence of silent ischemia episodes have significant impact on further prognosis.

*Silent myocardium ischemia can be present:*

- in patients suffering from angina (usually these with diabetes mellitus and/or cardiosclerosis); asymptomatic ischemia episodes in some patients may be even much more frequent than angina paroxysms
- sometimes silent ischemia may occur in patients, having no other signs of IHD
- silent ischemia episodes may accompany by **angina equivalents** (see table: atypic pain), which can be felt by patient as paroxysms of weakness, dizziness, dyspnea, syncope, arrhythmia; painless myocardium infarction is accompanied by all typical symptoms, except pain (weakness, perspiration, heart failure, arrhythmia etc).

**Objective signs, revealed in patients with angina:**

There is no typical angina objective symptoms, so the base of the diagnosis is analysis of patient's complains. Instrumental investigations give an additional help.

**But, following objective symptoms can be found in angina patients:**

- signs of **AH** (palpation, auscultation)
- signs of **atherosclerosis** (xantomias, xantelasmas, arcus senilis; palpable wall of temporal and radial arteries, bruits at aorta and its branches)

- signs of **heart muscle affection** (weak tones, weak 1 tone, appearance of 3 tone, murmurs, heart dilatation)
- **arrhythmic** syndrome (extrasistoles, atrial fibrillation)

**Differential diagnosis:**

**Main diagnostic pathway:**

<b>Connected with heart</b>	<b>Not connected with heart</b>
<b>In general:</b> objective signs of cardiovascular system affection are often present	<b>In general:</b> objective signs of cardiovascular system affection are not typical; objective signs of the other systems diseases, that may cause pain, are present.

**Pain syndromes, connected with heart affection:**

	Angina	Myocardium infarction	Cardialgia (myocarditis; vascular dystonia, mitral valve prolapse)	Dissecting aorta aneurism	Pericarditis
Localization	Sternal region	Usually wider (maybe, spreading to the whole chest)	Left side (not related to sternal region)	Central and left chest. True cardiac pain may appear if dissection is around coronary ostium	May be similar to than in angina
Character	Heaviness, pressure, squeezing etc	Same as angina but very intensive, severe	Not paroxysmal; stitching, aching; more constant	Tearing , very intensive and severe	May be similar to than in angina (acute in dry and sensation of heaviness in

					exudative one)
Irradiation	Typical	Wide irradiation zone	Usually not present	Neck, abdomen, through the back	May be similar to than in angina
Appears	During the exertion	May be related to repeated stress situations or episodes of physical exertion, may not be related	No relation to physical exertion etc; usually gradual appearance	Suddenly	Usually constant
Dynamics	Gradual increase and quick relief	Increasing intensity of pain after appearance may be present	Without marked beginning and end, without typical dynamics; can change during body, head and arms movements	Reaches maximal intensity immediately; the pain may migrate as the dissection extends	Worsening while lying down and deep breathing
Duration	3-5 minutes up to 10-15 min	More than 30 min	More prolonged	Continuous	Prolonged
Relieved	Quick relief after use of nitrates or cessation of physical or emotional exertion	No effect of nitrates (even repeated intake); pain usually is not relieved by itself, only special treatment (usually including narcotics) relieve the pain	No effect of nitrates or exertion cessation; in myocarditis – antiinflammatory treatment lead to gradual relief	Unrelieved by rest or position	Relieved by sitting forward
Other symptoms	Emotional symptoms (fear, angst, fear of death)	Pale skin; perspiration; presence of acute heart failure, arrhythmias; shock	<b>Vascular dystonia:</b> young people; astenic syndrome, trembling, poly-uria; nothing revealed objectively <b>Mitral valve prolapse:</b> objective signs <b>Myocarditis:</b> fever, rhythmus	Shock may be present; pleura symptoms in case of leaking aneurism; paroxysmal dry cough and dysphagia due to compression	Fever may be; objective signs of pericarditis

			disorders, murmurs may be; in severe cases heart failure		
	ECG (exertion test); scintigraphy, ultrasonic and arteriographic signs	ECG; serum enzymes elevation; ultrasonic signs	<b>Dystonia:</b> nothing revealed <b>Prolapse:</b> ultrasonic signs <b>Myocarditis:</b> inflammatory changes in blood; antibodies titer	Ultrasonic, X-ray picture	

**Other causes, related with heart:** hypertrophic cardiomyopathy (symmetric and subaortal stenosis); aorta valve stenosis and insufficiency (auscultation - murmurs); aortitis; hypertensive crises in pulmonary artery system.

**Pulmonary artery embolism may be also present in cardiological patients;** pain is accompanied by cough, dyspnea, haemoptysis, pleural pain. Signs of pleuritis (haemorrhagic) and lung infarction (“infarction-pneumonia”) may be present. Syncope, shock and marked central cyanosis are present in severe cases.

**Pain, not related to the heart**

System	Diseases	Characteristics of pain
Joints, bones and muscles	Spondilosis (thoracic, cervical) – thoracic root pain	Intensive prolonged pain in sternal region and left side with irradiation to left arm, shoulder an intercostal space; often asymmetrical. Radiation from the back or to outer or dorsal aspect of the arm and the thumb and index fingers rather than the ring and little fingers may be present. Dynamics (increase or decrease of intensity) is related to head, body and arms movements, twisting, lateral flexion, straining or lifting, cough.

		Intracostal spaces and paravertebral points palpation is painful. Neurological examination and X-ray confirm the diagnose. No nitrate effect is present.
	M. scaleni anterior syndrome	Compression of nerves and muscles between M. scalenus anterior and 1 <sup>st</sup> rib. Intensive pain in precordial region with irradiation to left part of neck and inner surface of left arm. Not paroxysmal, no nitrates' effect and typical dynamics. Later blood flow, innervation and trophic disorders of left arm skin appear.
	Titze syndrome	Painful thickening of cartilages of ribs (2-4 ribs, uni- or bilateral or isolated); may be present also in patients with chronic respiratory diseases. Body movement lead to more intensive pain; palpation of ribs cartilages is painful.
	Herpes zoster	Pain is intensive, constant; localization and irradiation may mimic angina or infarction; pain is not paroxysmal without exertion provocation and nitrates effect; appearance of rash elements confirm the diagnose
	Other ribs and cartilages diseases	Trauma, periostitis, metastases, myeloma, sarcoma – local pain during palpation; palpation reveals changes of the ribs surface; X-ray picture confirms the diagnose
	Muscles and nerves diseases	Inflammation, trauma, overtension – constant pain without nitrates effect and exertion provocation. Aggravation of pain by body and left hand movements. Painful palpation of muscles or (in case of intercostal neuralgia) intercostal spaces.
Gastrointestinal	Oesophagitis	Pain located in sternal region and lower chest, burning (like that of drinking very hot fluids), irradiation to throat and back. Appears while stooping, lying down, heavy lifting, and straining, bending, especially after eating of excessive food. May be associated with acid reflux, a bitter taste in the mouth, and relieved by alkalis. Radiation radiate down the arms is not typical. Patients may describe regurgitation and occasionally true dysphagia. <b>Reflux</b> may be induced by vigorous exercise which can make the distinction with angina more difficult. <b>Diffuse oesophageal spasm</b> produces quite severe sudden retrosternal pain which may be relieved by nitrates. This can cause particular diagnostic difficulty, but the pain is not effort-related.

		Diagnosis is confirmed by endoscopy and assessment of esophageal motility.
	Oesophagus cancer	Progressive dysphagia, voice disorders, endoscopic examination
	Peptic ulcer	Pain is central, felt in the epigastrium and lower chest, radiating through to the back, may be worse after meals and wake the patient at night. Peptic ulcer pain is episodic, and generally relieved by alkalis but not nitrates. No exercise provocation is observed. Endoscopy confirms the diagnosis.
	Cholecystitis or pancreatitis	Very occasionally the pain of cholecystitis or pancreatitis may be confused with cardiac pain. The pain of cholecystitis is usually in the right hypochondrium with referred pain in the right shoulder tip and right arm. It is associated with nausea, vomiting, and a febrile illness. Objective signs are present (painful palpation in gallbladder region, Mussy symptom), jaundice may be present. Acute pancreatitis produces a severe central and upper abdominal pain radiating through to the centre of the back which may be partially relieved by sitting hunched forward; pancreatic pain can last for several days. The pain is provoked by heavy meals, containing a lot of fats, but not physical exertion (if stones are present, provocation by running or traveling by train may make the diagnosis more difficult). But nitrates' effect is not present.
Neural	Diencephalic syndrome, syringomyelia	Neurological examination
Lungs, pleura	Pleuritis	Pain is aggravated by deep breathing, cough and relieved by chest immobilization; auscultation picture is present
	Spontaneous pneumothorax	Pain is aggravated by breathing; dry cough is present. Objective signs of pneumothorax are revealed and respiratory failure may be present.
	Lung cancer	Haemoptysis, cough in case of central cancer; X-ray and bronchoscopic results. Pain is constant, no effort provocation and no nitrates effect is observed.
	Primary lung artery hypertension (including hypertensive)	Similar pain with nitrates' and stoppage effect, but ECG reveals the overload of right atrium and ventricle



**But: all these conditions may accompany angina pectoris; thoracic root and gastrointestinal disorders (for example, cholecystocardial syndrome) may also provoke angina. So, final diagnosis is based on symptoms, ECG and ultrasonic analysis and, in confusing cases, test-treatment by nitrates (especially if risk factors are present). Special attention: aged patients and women (frequency of atypic angina forms). Indications to invasive investigations (endoscopy) should be carefully analyzed.**

## 2.1. Exertion-induced angina

### 2.1.1. Exertion-induced angina debut.

Pain appears for the first time in life, usually in cases of physical exertion (sports etc), severe stress situation (death of relatives, severe job strain, etc), severe overstrain.

Special attention should be paid to exertion angina debut with progressive course

(Отдельно (в рамках понятия "нестабильная стенокардия") выделяют впервые возникшую стенокардию напряжения прогрессирующего течения).

Rarely disease may begin from the rest paroxysms:

- in patients with angioneurotic disturbances of coronary arteries tone (also in climacterium)

- in patients with chronic digestive disorders (pain appearance during the abdominal pain and may be masked by it). Pathogenesis: hypercatecholaminemia causes coronary spasm and leads to excessive oxygen demands. More often in aged and women. Differential diagnosis: ECG, ultrasonic examination.

## 2.1.2. Stable angina

**The main characteristics is stereotypism of:**

- pain character, localization and irradiation
- provoking factors
- methods of relief (including daily nitrates dose)
- ECG changes during every paroxysm.

**Pathogenesis:** fixed coronary obstruction due to stable plaque leads to normal blood supply at rest, but in case of physical exertion the work of heart is increased and the vessel can't dilate effectively, so the pain appears. While plaque is stable and narrowing – constant, physical exertion tolerance is also stable.

**Functional classes of stable angina**

Class	Clinical criteria	Exercise tolerance
I	Pain is caused by exertion, significantly more intensive than usual	More than 600kgm/min
II	Pain appears in case of quick walking or walking upstairs (3 storeys) or walking 500 m and more; cold weather, going against the wind, emotional stress increase possibility of pain appearance	450-600 kgm/min

III	Pain appears in case of walking in ordinary temp or upstairs (1 storey) or walking 100-500 m	150-300 kgm/min
IV	Pain appears in case of minimal physical activity; at rest; in situations when metabolic demands of myocardium increase (angina decubitis)	<150 kgm/min

**Rare episodes of rest angina in patient with good exertion tolerance can't be considered as criteria of IV functional class of angina.**

### **Rest angina**

Angina appearing at rest.

#### **Patophysiology:**

Several factors can cause angina appearance at rest:

- A. emotional factor (angina caused by emotions): pathogenesis is the same to that in exertion angina (emotions lead to hypercatecholaminemia, causing increase of BP and heart rate and thus – myocardium metabolic demands which can't be compensated adequate blood supply by narrowed artery)
- B. angina appearing at night:
  - BP fall with bradycardia episodes; so perfusion will be maximally reduced in zone supplying by narrowed artery

- Dynamic coronary obstruction – local spasm located at a narrowed site of the artery; the degree of spasm may vary from slight to even complete blood flow block; in rare cases branch of the artery may be involved in spasm.

Presence of rest angina episodes only may be revealed in patients with angioneurotic disturbances or diseases of gastrointestinal system. In these cases, if duration of angina is more than 1-2 months, it may be considered as a stable IHD course.

But appearance of rest angina episodes in exertion angina patients is a sign of severe coronary atherosclerosis.

### 2.1.3. Crescendo angina. Unstable angina

Unstable angina, which is not a nosological form (as nosological form crescendo angina is considered) , is included in separate group because of its prognostic significance: high risk of myocardium infarction and sudden death.

Following conditions are included in this group:

- angina debut (crescendo and non-crescendo) during 4 weeks from the first angina episode
- crescendo angina in patients having stable angina before
- angina remaining or appearing in first day after myocardium infarction
- intermediate coronary syndrome (focal myocardium dystrophy, acute coronary insufficiency)

**Clinical peculiarities:**

- prolonged angina episodes (20-30 min)
- more frequent angina episodes (to evaluate frequency, which often can't be fixed by patient, the number of nitrate tablets or inhalations used for pain relief can be evaluated)
- increase of pain intensity
- incomplete effect of nitrates
- lowering of exertion tolerance and working ability

### **Intermediate coronary syndrome:**

Occupies position between angina and myocardium infarction. **As intermediate coronary syndrome chest pain is considered if it is caused by myocardium ischemia, lasts about 30 min and is accompanied by ECG changes (ST rise or depression), which disappear in 24 hours after attack.** Slight (no more than 50% over the higher border of normal range) increase of myoglobin and enzymes may be present in blood due to dystrophic changes of myocytes in ischemia zone.

**Pathogenesis:** vasospasm, microemboli by circulating platelets aggregates; more rare – severe increase of oxygen demands due to hypertensive crisis, tachysystolic paroxysms, physical exertion etc in patients with coronary atherosclerosis).

**Transformation of unstable angina to myocardium infarction: risk criteria (E.Braunwald, 1994):**

### **High risk**

- prolonged (more than 20 min) rest angina paroxysm
- pulmonary oedema or appearance of **rales**, related to myocardium ischemia
- rest angina with ST changes 1 mm and more
- angina with appearing or growing intensity of mitral regurgitation murmur
- angina accompanying by hypotonia (systolic BP less than 90-100 mm Hg)

### **Medium risk**

- no high risk factors but at least one of following is present:
- relieved prolonged (more than 20 min) rest angina paroxysm in patient with diagnosed IHD or in case of its high risk
- rest angina
- night angina
- angina accompanying by transient T changes at ECG
- debut of angina with history less than 2 weeks
- abnormal Q or ST depression less than 1 mm in several ECG leads (ECG investigation not during pain paroxysm)
- age 65 and more

### **Low risk:**

- Absence of high and medium risk factors but one of following ones is present

- increase of frequency, severity and duration of angina episodes
- angina appears in case of exertion significantly less intensive than before
- debut of angina with 2-4 weeks history
- no ECG changes are revealed

### 2.1.4. Prinzmetal's angina

First described by Prinzmetal in 1959.

**Epidemiology:**

2-3% of patients

**Pathogenesis:**

Spasm of coronary arteries, in some cases reaching the degree of occlusion causing transient or ischemia or even myocardium necrosis. Long-time occlusion leads to progressive bradycardia and ventricles fibrillation. The role of endothelin is considered to be significant (its raised levels have been found in plasma in patients during pain).

### **Clinical peculiarities**

- typical pain syndrome
- pain appears at rest, unpredictably, more often at night or in the morning after waking up
- severe prolonged angina attacks (10-15 and more min)
- attacks are accompanied by pallor, profuse perspiration, palpitation, severe shortness of breath may be present
- paroxysm is not always relieved by nitrates
- paroxysmal rhythm disorders may be present (atrial fibrillation, ventricle extrasystoles and tachycardias, sometimes – ventricles fibrillation).
- emotional component is usually present (frightening pain)
- is accompanied by typical ECG changes - arch-like ST rise – subepicardial or transmural ischemia; more rare – ST depression (subendocardial ischemia). ECG changes disappear spontaneously after relief of pain.

Very occasionally patients appear to have a vasospastic tendency with a history of migraine and Raynaud's phenomenon.

Some patients, however, have good tolerance to physical exertion at the daytime.

### **Examination of patient with angina or suspected angina**



### 1. The aims of examination are following:

- to prove or reject myocardium ischemia diagnosis (including differential diagnosis of pain syndrome)
- to differentiate between IHD forms (stable and unstable angina, myocardium infarction)
- to evaluate functional class of stable angina
- to evaluate presence of other IHD forms (arrhythmia, post-infarction cardiosclerosis, heart failure)
- to evaluate peculiarities of IHD and atherosclerosis in certain patient, including family history of IHD and atherosclerosis, presence of risk factors, history of the disease (age of onset, how quick does IHD develops, treatment efficacy and side effects etc) and thus to evaluate individual prognosis
- to evaluate presence of the diseases, which may accelerate atherosclerosis and/or influence on drugs choice

### 2. Laboratory diagnosis

Investigation	Significance
Haemogram	Absence of changes is typical for angina
Lipid spectrum	In case of suspected IHD presence of atherogenic changes will be an argument In case of confirmed angina it has a prognostic significance To evaluate necessity and character of hypolipidemic treatment
Serum enzymes (creatinophosphokinase and its MB-fraction, lactate-dehydrogenase; glutamic oxaloacetic transaminase (USA) in Russia aspartataminotransferase and ala-	Help to differentiate between angina (first of all, unstable) and myocardium infarction

ninaminotransferase are also used); troponin-test	
Coagulogram	To evaluate presence of blood clotting disorders and assess possible ways of correction

### 3. Instrumental examinations

#### A. ECG (dynamic investigations)

- if at the moment of registration pain is absent, no changes can be revealed (in 60-70% of cases with short angina history it may be normal; also bundle branches blocks may be present, rhythm disorders etc)
- during the paroxysm: in 60-80% the downsloping or horizontal ST depression more than 1 mm with accompanying T changes. More rare the ST rise may be present.

#### B. Holter's monitoring

Reveals symptomatic and asymptomatic ischemia episodes. Can be especially useful in patients with night symptoms or variant angina with good exertion tolerance.

Also can reveal presence and severity of rhythm disorders and is used in patients with unclear syncopes.

In suspected high functional classes of angina, when exercise test is associated with higher complications risk monitoring can be used instead.

#### C. Exercise Electrocardiography

Exercise testing is the most useful noninvasive procedure for evaluating the patient with angina. Exercise testing is often combined with scintigraphic studies or echocardiography (see below).

Exercise testing can be done on a motorized treadmill or with a bicycle ergometer. A variety of exercise protocols are utilized, the most common being the Bruce protocol, which increases the treadmill speed and elevation every 3 minutes until limited by symptoms. At least two electrocardiographic leads should be monitored continuously.

### **1. Indications**

- to confirm the diagnosis of angina
- to determine the severity of limitation of activity due to angina
- to assess prognosis in patients with known coronary disease, including those recovering from myocardial infarction, by detecting groups at high or low risk;
- to evaluate responses to therapy (the investigation is performed initially and after a course of treatment)
- less successfully, to screen asymptomatic populations for silent coronary disease: in high risk patients (usually a strong family history of premature coronary disease or hyperlipidemia), those whose occupations place them or others at special risk (eg, airline pilots), non-specific ECG changes revealed at rest.

#### **Absolute contraindications:**

- myocardium infarction less than 4 weeks from the onset
- pre-infarction or pre-stroke condition (unstable angina, transient cerebral ischemia etc)

- acute trombophlebitis (risk of pulmonary thrombosis)
- Heart failure III and IV functional class
- Severe respiratory failure

**Relative contraindications:**

- chronic aneurisma of heart or vessels
  - severe AH: systolic BP more than 220, diastolic – 130 mm Hg
  - tachycardias of unknown origin (heart rate more than 100 per minute)
  - history of severe rhythmus disorders and/or syncopes
  - bundle branches block (especially left) – due to the difficulties of ECG evaluation
  - low extremities arteries atherosclerosis with severe ischemic symptoms
  - fever and infectious diseases
  - Aortic stenosis
- In spite of the fact that quoted risk of exercise testing is one death and 2 nonfatal complications per 10000 tests (E.Braunwald), individuals with pain paroxysms at rest or minimal activity (IV class) are at higher risk and should not be tested.

**Criteria of test discontinuation:**

*Clinical*

- angina paroxysm

- exacerbation or appearance of heart failure (shortness of breath, dyspnea)
- severe weakness appearance
- appearance of cerebral blood flow insufficiency signs (dizziness, headache, nausea, vision disorders)
- quick increase of heart rate which is not adequate the age and exercise intensity
- BP fall (25-50% fall from the initial level)
- BP rise up to 230/130 and higher
- if patient refuses from test continuation (fear, discomfort, weakness, pain in legs)

### **ECG**

- ST decrease more than 1 mm
- ST rise more than 1 mm.
- Appearance of rhythmus (extrasystoles 1:10 and more frequent, tachycardia, atrial fibrillation etc) or conductivity disorders
- QRS changes: decrease of R height, Q and QS becoming deeper and wider.

### **Criteria of positive test:**

- angina paroxysm
- severe dyspnea or shortness of breath
- BP fall (fall is 25-33% from initial level)

-1 mm (0.1 mV) horizontal or downsloping ST segment depression (beyond baseline) measured 80 ms after the J point.

- ST rise 1 mm.and more

### **Farmacological tests**

Are performed when due to low extremities diseases (ischemia, thrombophlebitis, ortopaedical defect etc) exercise test can't be performed.

### **Main principles:**

- increase of heart work with increase of oxygen demands (isoprenalin) causing ischemia and ECG changes
- lowering of heart work and oxygen demands (beta-blockers)
- influence on coronary vessels tone : ergometrin –spasm, dipiridamol and nitroglycerin – dilatation.

The most informative are tests with dipiridamol, isoprenalin and ergometrin.

### **Caution:**

Pharmacological tests are performed only in a department, where intensive care is available.

Criteria are the same as these for physical exercises.

### **Myocardial perfusion scanning**

Combining of an exercise test with myocardial perfusion imaging using thallium<sup>201</sup> tomography, which reveals the ischemia zones (disturbed perfusion).

Tc (technecium) perfusion scanning reveal necrotized foci as “hot” ones.

Positron-emission tomography with glucose and fatty acids isotopes can reveal the local disturbances of myocardium metabolism.

### **Ultrasonic investigation (echocardiogram)**

During the pain episode – zone of transient dyskinesia is revealed

The investigation becomes more informative if stress-echocardiography is performed (exercise or pharmacological tests); that method also can reveal hibernation zones (relatively normal, but not contracting tissue).

### **Angiography**

Gives possibility to evaluate localization and character of arteries affection and presence of collaterals, so that method of surgical treatment can be chosen. Is used in unclear cases in young and middle-aged patients, but more often precedes surgical treatment in IHD patients.

Contraindications include fever, severe diseases of lungs, liver, kidneys, severe rhythm disorders, cardiomegalia with severe heart failure, stroke, high sensitivity to iodine preparations.

Degrees of vessel narrowing:

1 - 50%

2 - 75%

3 – more than 75%

4 - occlusion.

### **Diagnostic formulas**

- IHD. Exertion-induced angina III functional class.
- IHD. Prinzmetal's angina

### **Natural course:**

Fluctuating with destabilization periods.

### **Prognosis and outcomes**

Outcomes in stable angina (per year): lethal – 2-3%; infarction 2-3%.

In case of unstable course complications rate increases. The most unfavorable prognosis have patients with main stem of left coronary artery stenosis or three-vessels stenosis and Prinzmetal's angina.



## **Criteria of high risk of organic coronary arteries affections and severe IHD prognosis**

### **(USA cardiologists association)**

- EF (ejection fraction) is less than 35% at rest or at physical exercise
- Low tolerance to physical exercise – downsloping ST appearing at heart rate 120 per min or less, ST changes remain 6 min and later after exercise discontinuation and is accompanied by systolic BP fall 10 mm Hg and more and/or ventricular rhythm disorders
- Marked changes revealed by perfusion scintigraphy at rest or at exercise: big numerous defects, big fixed defects with signs of left ventricle dilatation and increase of isotope consumption by the lungs
- Stress-echocardiographically revealed disturbances of more than 2 segments contractility after test with low doses of dobutamin or in case of rare heart rate.

### **Treatment**

**Aim of treatment:** to reduce frequency and severity of attacks and myocardium infarction risk, to improve quality of life and its duration.

#### **I. Way of life changes**

The main principles are the same to these in cases of atherosclerosis. The work and hobbies, connected with intensive overstrain (physical or emotional) should be avoided. In some countries (including USA) some professions are should be given up (at least temporarily) by law: air-line pilots, air traffic controllers, divers, and heavy goods vehicle drivers.

## II. Drug therapy

### 1. Nitrates

- reduce resistance to blood flow in coronary arteries (endogenous vasodilator agent - NO)
- increase coronary blood flow
- improve perfusion of ischemia zone
- reduce peripheral veins and arteriols tone, so less blood amount comes to heart  
(venous blood depot) – decrease of preload and afterload
- positive inotropic action
- improvement of pulmonary blood flow, decrease of tone of a.pulmonalis and pressure in it.

	Short-time of action	Retarded – only for paroxysms prevention
Nitroglycerin	<b>Very short time of action (from 1-2 to 5 min)</b> Tablets (0.3-0.6mg), capsels, aerosol for inhalations (0.4mg), solution for intravenous infusion <b>Used for relief of paroxysm, prevention is possible if a drug is taken just before the exertion, going to cold wind etc</b>	Nitroglycerin depots: - tablets (Sustak, Nitrong etc – 6.25 and 12.5 mg) - patch, paste, plaster, ointment for percutaneous use Used for paroxysms prevention
Isosorbid dinitrate	Nitrosorbide tablets (relief and prevention) – 10 mg; 60-80 mg daily Isoket solution for i.v. infusion	Tablets: Cardiket-retard, Isoket-retard (20-80 mg); 60-80 daily Polymer plates for application on mouth mucosa
Isosorbid mononitrate	Monochinque, Ismo (20 mg tablets) etc 40-60 daily	Monocinque-retard, Imdur (60 mg scored extended release tablets) 40-60 daily

Nitropentone	Erynithis (10 mg; 80 daily)	
Sydnoimines - drugs with action similar to nitrates	Molsidomin=corvaton=sidnopharm (2 mg), acts for 6 hours	

**Side effects:** headache, nausea, dizziness, and hypotension (less marked – mononitrates and nitropenton, the last one is also significantly less active).

**Contraindications:** closed-angle glaucoma, intracranial pressure increase, stroke.

**Sydnoimines**

- peripheral vasodilator
- reduces heart overload without direct action on coronary arteries
- reduces tension of left ventricle wall, so blood flow in subendocardial zones improves

**Beta-receptors blockers**

- reduce the influence of sympathetic neural system on heart: decrease of heart rate, BP, oxygen demands
- improvement of myocardium blood flow if collaterals are present
- proved reduction of sudden death episodes
- regression of LV hypertrophy

Non-selective	Cardioselective (beta-1-selective)	With ISA (intrinsic sympathomimetic activity)
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<p><b>Anaprilin</b>  <b>Nadolol=Corgard</b> – long-acting one (20, 40, 80,120 mg); daily 20 (initial)-240 (maximal)  <b>Sotalol=betapace</b> (80, 160, 240; daily 80-320) with class III antiarrhythmic activity</p>	<p><b>Atenolol</b> (25,50, 100 mg tab); 50-200 daily  <b>Metoprolol; Lopressol</b> (50;100), retard-<b>Toprol XL</b> – 50, 100,200. Daily 50-200  <b>Bisoprolol</b> (2.5; 5,10); Ziac – combined with Hydrochlorothiazide  <b>Nebivolol</b> – superselective with NO-metabolism modulating activity</p>	<p><b>Non-selective:</b>  <b>Pindolol (visken)</b> – 5 and 10 mg tablets; 5-60 mg daily  <b>Selective – Acebutalol (Sectral)</b> – capsels 200; 400 mg; 200-1200 daily; retard</p>
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ISA drugs also have an effect of partly stimulation of beta-receptors in arteriols.

**Side effects:** caused by influence on beta-receptors and more marked in non-selective ones

- bradycardia
- decrease of cardiac output
- conductivity disorders
- progression of heart failure (can be prevented by the use of small doses of selective blockers, or use of ISA drugs and Carvedilol (with  $\alpha$ -blocking activity), which have been shown to improve the course of heart failure)
- bronchospasm
- hyperlipidemia (less in selective ones)
- exacerbation of peptic ulcer
- exacerbation of low extremities ischemia

Absolute contraindications:

- asthma, COPD for non-selective
- weak sinus syndromw
- AV block II-III
- Heart rate less than 50
- Systolic BP less than 100

### Calcium channels antagonists

- Blocking of calcium influx into the cell of myocardium and smooth muscles of vessels
- Normalizes of diastolic relaxation of heart and reduces of diastolic pressure in left ventricle
- Improvement of blood flow in ishemized zones; reduction of coronary spasm in sites of atherosclerotic narrowings, dilatation of collaterals
- Peripheral vasodilatation and postload reduction
- Positive influence on vascular endothelium
- Antiagregant activity and positive influence on lipid methabolism.
- Retard-forms reduce LV hypertrophy

Group	Drugs and doses	Side effects	Indications	contrindications
Niphedipin (dyhydropiridin)	Cordaflex, Corinfar, Nifedipin, Adalat 2 <sup>nd</sup> generation: Felodipin, Isradipin (5- 10 mg daily)	<b>in non-retard forms:</b> - quick BP fall, which can lead to syncope, sympathetic stimu- lation and thus proishemic effect	Angina in patients with arterial hypertension Prinzmetal's angina Contraindications to beta-blockers	- hypotonia - cardiogenic shoke - diabetes mellitus - pregnancy Non-retard forms use in aged patients can

		<b>Retard forms don't have such side effect</b>		cause syncope episodes due to quick BP fall
Amlodipin (3 <sup>rd</sup> generation): 5-10 mg daily				
Verapamil	Isoptin (240 mg daily) 2 <sup>nd</sup> generation – Gallopamil	- heart rate retardation - do not cause significant BP fall - conductivity disorders	Angina with rhythm disorders (extrasystols, supraventricular tachycardia) Angina without hypertension	- Bradycardia - AV block - hypotonia - pregnancy - WPW
Dilthiazem	Dilthiazem (180 mg daily) Cordil, Cordizem 2 <sup>nd</sup> generation - Clinthiazem	- may cause heart rate retardation (less than Verapamil) and conductivity disorders	Same as both groups	Same as Verapamil

### **Antiagregants**

**Aspirin** 100 mg daily

**Heparin:** more often used in unstable angina (subcutaneously 2.5-5 thousands of units 4 times daily or intravenously, control of blood clotting); **heparins with low molecular weight:** fraxiparin, enoxiparin.

**Antitrombin drugs:** Girudin, Girulog – are used in unstable angina but rarely; further investigations are needed to evaluate their efficacy

**Platelets glycoprotein receptors IIb/IIIa antagonists:** unstable angina in combination with Girudin

**Dipyridamol (Curantil) is not used because it leads to reduction of blood flow in narrowed artery and improvement – in unchanged ones (see dipyridamol functional test).**

**Drugs improving myocardium metabolism:**

**Trimethazidin** (Preductal, Preductal MB)– 20 mg (60 mg daily) improves ATP metabolism and increase of glucose utilization instead of that of fatty acids. I

**Riboxin** – also improves myocardium metabolism, but less than trimethazidin (more old variant), can be used per os and i.v. (infusions, injections); is still used in Russia.

**III. Main principles of the modern approach to angina treatment (American association of cardiologists):**

- **Aspirin or other antiagregant drugs:** aspirin 60-125mg daily; Ticlopidin (Ticlid) – 500 mg daily; Clopidogrel (Plavix) – 75 mg daily
- **Beta- blockers and BP control**
- **Cholesterol level normalizing and smoking cessation**
- **Diet and Diabetus mellitus treatment**
- **Education and physical exercises**

Education includes education of patients and relatives how to assess pulse rate, BP measurement, to analyze peculiarities of pain syndrome. Methods of pain relieving, especially necessity of short-time action nitrates but not non-specific drugs (Menthol, Validol, Corvalol etc) use to relief pain

should be underlined. Patient and relatives must know when and how to call for medical care in emergency situations.

**Thus, according to these recommendations, beta-blockers and antiagregans are the first line of drug therapy.**

#### **IV. Surgical treatment: Coronary artery surgery (bypasses between aorta and coronary arteries)**

Indications:

- left main stem stenosis more than 50%
- 2-3 arteries stenosis more than 70% in case of good permeability of distal vessels
- anterior intraventricular arteria stenosis more than 70% in case of good permeability of distal vessels
- severe course of angina (at rest and exertion), refractory to medical treatment, low physical exertion tolerance, loss of working ability
- unstable angina progressing for 24-48 hours in spite of active therapy, including thrombolysis.
- Post-myocardial infarction patients with continuing angina or severe ischemia on noninvasive testing.

Operation is possible if EF fraction is more than 40%.



### Contraindications:

- severe affection of distal and proximal arteries
- EF (ejection fraction) lower than 40%
- Severe diseases of the other systems
- Haemorrhagic syndrome
- Relative contraindication – age over 65.

In addition, many cardiologists feel that patients with less severe symptoms should be revascularized if they have two-vessel disease associated with underlying left ventricular dysfunction, anatomically critical lesions (> 90% proximal stenoses, especially of the proximal left anterior descending artery) or physiologic evidence of severe ischemia (early positive exercise tests, large exercise-induced thallium scintigraphic defects, or frequent episodes of ischemia on ambulatory monitoring). This trend toward aggressive intervention has accelerated as a result of the growing use of coronary angioplasty and stenting. While such patients are at increased risk, it has not been proved that their prognosis is better after coronary revascularization by either surgery or angioplasty.