3.22 Ischaemic heart disease

Low blood flow through the large coronary vessels can be expressed clinically only when their narrowing exceeds 75 %. Here the blood pressure decrease behind the obstruction, and the blood flow becomes lower. In such a case ischemia develops in the supplied area of the myocardium. Under the term ischemia we understand a low perfusion of tissues, which most important outcome is inadequate oxygenation, caused by the inadequate perfusion.

Ischemic heart disease is a condition having **the most variable causes**. Yet each and every time the cardiac function is disturbed as a result of the loss of balance between the oxygen supply and its requirements. The most common cause of ischemia is **atherosclerosis** of the coronary epicardial arteries. Their low translucence due to the atherosclerotic process leads to a low myocardial perfusion during the normal requirements for cardiac function, possibly it allows a small blood flow increment when the functional requirement becomes higher. The coronary flow may suffer further lowering of blood flow due to the formation of thrombi, a spasm, and occasionally an embolus. Rarely we may find an abnormal branching of the coronary artery from the pulmonary artery. Myocardial ischemia may occur even in cases where the requirement for oxygen are abnormally high. This happens is case of **excessive left ventricular hypertrophy as a result of hypertension or aortic stenosis**. The signs of angina pectoris will appear and these cannot be differentiated from angina pectoris that resulted from coronary arteries atherosclerosis. In cases of an extreme drop of the transport capacity of blood for oxygen myocardial ischemia may also occur. Yet the combination of high oxygen requirement caused by the left ventricular hypertrophy and the simultaneous presented of atherosclerosis of the coronary arteries very common.

As we mentioned previously, the size of the coronary blood flow is subjected to the myocardial control, and its metabolic level. This is mainly because, that the myocardium can obtain a higher O2 supply when needed by a higher blood flow but not by an increased oxygen extraction because the oxygen extraction is already at its maximum during rest.

The epicardial coronary arteries in the human organism are the site where atherosclerotic process loves to occupy. The dysfunction of vascular endothelium and an abnormal interaction with the circulating monocytes and thrombocytes that leads to abnormal storage of fat in the subintimal space, as well as some cells and other substances. The result is the formation of atherosclerotic plaques in different segments of the coronary arteries and narrowing of their translucency. In translucency decrement to 25 % the coronary arteries no more can provide the increasing myocardial demand for blood and oxygen. When the translucency drops to only 20 % its original level or more, the coronary blood flow will reduce. This reduction results in myocardial ischemia with clinical manifestation. The atherosclerotic process doesn't always progress so much to cause a prominent decrement of the translucency of the vessels. The preformed atherosclerotic plaque may be disturbed, or sloughed and at this site the formation of a thrombus begins. It is only natural that the clinical manifestation and the patient's state as well as the condition of his heart depends on the localization of the affected artery and on its degree of narrowing. The progressing narrowing of the coronary artery is usually connected with the development of the collateral vessels, which provide a better coronary blood flow at least in the resting patient.

In the post stenotic area the resistant vessels are dilated. In case of maximal dilatation the coronary blood flow depends upon the pressure, which is distal to the stenosis. In that case the state of hypoxia depends on the myocardial requirement, possibly the tendency for arterial spasm, but not their dilatation which is already in its maximum.

Low supply of oxygen caused by the coronary atherosclerosis will lead to transitional disturbances of the mechanical, biochemical and the electrical function of the myocardium. A fast developing ischemia usually causes an immediate disturbance of contraction, and relaxation of the myocardium in a certain section. A decreasing perfusion of the subendocardial area leads into a prominent ischemia in the corresponding area of the heart ventricle. Ischemia of a large area can reveal a condition of a transitional left ventricular failure. When ischemia affects the region of papillary muscles, mitral regurgitation may result. Coronary atherosclerosis is not equally distributed. Due to this reason the change in contrac-

tility may affect only a certain segment of the left ventricle. In case of a long lasting ischemia necrosis may result, that is represented as an acute myocardial infarction. The typical clinical picture yet is not necessarily present.

With normal oxygen supply of the heart fatty acids and glucose are metabolized into CO_2 and H_2O. **In case of a prominent drop of oxygen supply**, fatty acids cannot be oxidized. The only left metabolic event that supplies energy is the anaerobic glycolysis, during which glucose is broken down to lactate and a relatively small number of ATP is formed. The intracellular pH becomes low. The oxygen insufficiency is then changing the membrane function. Kalium escapes out of the cells and sodium is accumulated intracellularly in large amounts. The difference between the needs of the myocardium for oxygen and the oxygen supply and length of hypoxia determines the extent of myocardial injury.

Ischemia affects the transport of ions via membranes and the course of the electrical activation in individual myocytes in the heart as whole. Changes the electrical function of the heart during ischemia is shown on the electrocardiogram on the T wave and ST segment. A transitional depression of the ST segment is a picture of a subendocardial ischemia. Elevation of the ST segment is usually caused by a prominent transmural ischemia. Ischemia in any heart segment can produce a marked electrical instability, a result of which is usually ventricular tachycardia or fibrillation. Patients who died of sudden cardiac death due to myocardial ischemia are through to suffer from malignant ventricular arrhythmia.

3.22.1 Angina pectoris

Angina pectoris means anxiety (pain) on the chest. This name was used prior to the knowledge about the association of pain with the diseased coronary vessels. Angina pectoris is actually a syndrom provoked by a transitional myocardial ischemia. Chest pain is commonly the only symptom of the disease. It is of short duration and is typically localized retrosternally. Depending on other symptoms we may differentiate two main forms of angina pectoris and their further more specific types.

3.22.1.1 Chronic stable angina pectoris

Is basically a syndrom caused by a **transitional myocardial ischemia**. Patients complain of a chest pain with different shadowing. In the typical case the pain is retrosternal. That might radiate to the upper limbs and even to some less usual sites such as the neck, or teeth. According to the type of the predisposing factors we may describe different types of stable angina pectoris.

- Angina d'effort – evoked by physical activity
- Postprandial angina – after eating
- Emotional angina pectoris – during excitement
- Angina decubitus – after laying in bed
- Angina pectoris inversa (Prinzmetal) – stenocardia occurring at rest, physical activity is not a causative agent
- Status anginosus – is the commutation of attacks.

Nearly half the patients with angina pectoris have normal ECG at rest. The other half have some nonspecific ECG changes at rest such as changes of the ST segment and the T wave, these changes can be evoked by loading test.

During the treadmill test we control the electrocardiogram and blood pressure prior the test, during it, and after finishing the physical load. ST segment depression that is larger than 0,1 mV compared with the primary ECG reading is considered to be the sign of the induced ischemia. The ST depression last for more than 0,08 seconds and it has a horizontal or a descendant course. It is logical that even the T wave changes or the appearance of ventricular extrasystolies, or paroxysmal tachycardia are a proof of myocardial ischemia. Similarly the drop of blood pressure is an indicator of ischemia and a non overcomed load. In this case a drop in the ejection fraction during the loading test is a prominent indicator of myocardial ischemia, and usually even a sign of the affection of more tan one coronary artery.

The anatomy of the coronary vessels has a very important place in understanding the ischemic disease of the heart. Viewing the coronary arteries can provide us with information about, of or to what extent are the **coronary arteries narrowed** by the effect

of the atherosclerotic process. The coronary arteriography can show of it is possible to perform the percutanneous transluminal coronary angioplasty as a treatment for the condition, whether we have to perform an aortocoronary bypass. Cardiac catheterization is performed to find out any increase in the end diastolic pressure and the enddiastolic volume and mainly of there is any reduction of the ejection fraction. These three parameters are very important from the prognostic point of view in cases of ischemic diseases of the heart. A high enddiastolic pressure with a high enddiastolic volume and a low ejection fraction carries a very bad prognosis. Sclerosis of the left coronary artery root is considered to be the highest risk for patients suffering from the ischemic disease of the heart.

A high end diastolic volume and pressure render the coronary blood flow unfavorable. The application of nitrates causes vasodilatation. And that is why there will be lowering in the left ventricular wall tension during diastole and the flow is improved. Apart from this nitrates are know to cause dilatation of the epicardial coronary vessels. The result is an improvement of the coronary blood supply even via the collateral in the left ventricular wall.

Blocking β–adrenoreceptors is another important factor to influence the ischemic disease of the heart. Substances with such effect decrease the myocardial requirement for oxygen, they inhibit increasing heart rate and contractility that is caused by the adrenergic stimulation. Lowering the heart rate, the ejection volume and pressure at rest are only partially edged by these substances. Sometimes we may notice a prominent bradycardia, disturbances of electric activation and signs of left ventricular failure.

Calcium chanel antagonists have vasodilatatory effect on the coronary arteries. Apart from this they decrease the myocardial requirement for oxygen, decrease the contractility, and the arterial blood pressure. Yet they might lead into some conduction disturbances in the heart and hence bradyarhythmia. A negative inotropic effect and worsening of the left ventricular function or even its failure can appear when use β–adrenergic blockers.

Ischemic heart disease is the problem of oxygen requirement and supply. Improving the blood and oxygen supply might be solved not only pharmacologically but even by mechanically by revascularization. Recently the mechanical revascularization is performed by the percutaneous transluminal coronary angioplasty (PTCA). This method is quite suitable for stenosis of the coronary roots or the proximal stenosis of its main branches. The more distal stenosis are necessarily solved by other techniques.

Revascularization can be provided even by a surgical formation of a new vascular junction between the aorta and a section of a coronary artery which lies distally to the stenosis. In patients with ischemic disease of the heart, the aortocoronary bypass do not decrease the risk of myocardial infarction occurrence. Yet it improves the vascularisation and the actual state of the myocardium. It decreases the mortality in patients with left coronary artery lesion that is affecting all the three main vessels.

3.22.1.2 Unstable angina pectoris

Is another painful form of the ischemic heart disease. It has a very marked beginning of the attack and the spasm occurs at least 3 times per day. Under this type of angina we may put patients suffering of the chronic stable angina pectoris, in whom a worsening of attacks occurred with an increase of their number. The attacks usually last for more than 20 min.

A primary unstable angina pectoris represents a condition, in which we do not find any factors that may lead into worsening of ischemia in patients suffering from this angina. Among the factors that cause worsening of myocardial ischemia are anemia, fever, infection, tachyarhythmia, emotional stress, and hypoxemia. Unstable angina may develop shortly after the occurrence of myocardial infarction. The unstable angina pectoris with attacks occurring at rest is a sign of risk for acute myocardial infarction.

The unstable angina pectoris with evident electrocardiographic changes during the attacks is always combined with the stenosis of one or more coronary arteries. During the attack spasm might cause some microscopical changes of the endothelial surface of the atheromatous plate and hence might lead to a thrombocytic plug. This is why we usually give heparin in case of such attack.

In patients with unstable angina pectoris cathetrisation is necessary as well as coronarography. Then a decision for PTCA or a surgical revascularization takes place.

3.22.1.3 Asymptomatic (silent) ischemia

During the treadmill test in patients with various circulatory disturbances we may uncover patients with ischemic heart disease. Apart from the treadmill test results these patients are usually diagnosed by the use of longitudinal ECG examination with judging the ST segment shape on the ECG. It is a fact that these patients have no symptoms of the ischemic heart disease. Their long lasting monitoring showed that the occurrence of sudden death is common in this group, as well as myocardial infarction or the manifestation of non stable angina pectoris. The progression might be judged only individually. About the prognosis the decisive factors are the left ventricular function, the state of the coronary arteries, the effect of pharmacological therapy, and the possibility of revascularization and even its contraindication

3.23 Acute myocardial infarction

Acute myocardial infarction is a dynamic state, in which a stopped myocardial perfusion leads to myocardial irreversible injury. Acute myocardial infarction **is an anemic necrosis most commonly caused by a closure of a coronary artery** or one of its branches affected by an atherosclerotic process. The causes of the coronary artery closure might be some obvious morphological changes (thrombus based on the atherosclerotic changes), it might also be coronary artery spasm that occurred with or without the presence of the atherosclerotic changes in the affected vessel. The area affected by necrosis can not be changed or drown smaller. It is surrounded by a hypoxic myocardial area of various sizes. In experimental conditions necrosis (death) of the myocytes occur within 15–40 min following the stop of blood flow and a complete coronary artery or its branch occlusion.

The cause of myocardial infarction is most commonly an acute thrombotic closure of the coronary artery affected by atherosclerosis. Sometimes stenosis is not very prominent and the occurrence of myocardial infarction is caused by a rupture of an atherosclerotic plaque or the formation of a thrombus (plug) in this locality. In some cases we are dealing with a coronary spasm (what is known as obstructive form). It is usually compelled with coronary sclerosis. In what is known as the non obstructive form we noticed an increased tone of the large coronary artery, or an increasing tonus of the distal coronary field. An important factor for coronary artery closure is an intimal injury. In the following years it was found out that the endothelium plays a very important role in the coronary artery obstruction. The endothelium modulates the function of the vascular smooth muscle via the liberation of substances that control local constriction and relaxation of the vessels. Haemodynamics factors (increasing the coronary blood flow) and some substances (serotonin, acetylcholin) can activate the liberation of some endothelial relaxing factors - EDRF Endothelium Derived Relaxing Factor. In a normally functioning artery with intact endothelium, the release of EDRF causes vasodilatation. Apart from this it has an antithrombotic effect on the luminal surface of the endothelium. In the presence of the atherosclerotic plaque or an injured endothelium no EDRF is formed or released and so its mentioned functions do not appear. When thrombocytes aggregate on the endothelial surface they will release thromboxan that cause further vasoconstriction and further thrombocyte aggregation. **Endothelial dysfunction** occurs quite often due to some minor insults. It might be an activation of the vascular smooth muscles, that is not so prominent so that to cause a serious arterial occlusion. The endothelial injury is the most probably due to a faster flood flow in the area of the partial functional stenosis. Later on there will be a deposition of thrombocytes on the injured endothelium and a formation of non occlusive micro thrombi. The atherosclerotic process doesn't only lead into a lower translucency of the coronary vessels. During this process a monocellular infiltration, foam cells and leukocytes can release many factors (thromboxan, leukotriens, 5-hydroxytryptamin), these result into thrombocyte aggregation, an increased predisposition for blood coagulation, stimulation of migration and proliferation of other cells. Apart from this they have other affects on the distal segments of the coronary system. The clinically known triggering factors