

PATHOPHYSIOLOGY OF THE CARDIOVASCULAR SYSTEM

Jan Barcal

Department of Pathophysiology, Faculty of Medicine Pilsen, Charles University

The main function of the cardiovascular system is to ensure sufficient perfusion of all tissues and organs by the blood supplying oxygen and nutrients and removing metabolic products.

The existence of a pressure gradient in the circulation (ΔP) and resistance (peripheral resistance, R) is crucial. The blood flow (Q) is directly proportional to the pressure gradient and indirectly proportional to the resistance – i.e.: $Q = \Delta P / R$

The resulting blood pressure in the circulatory system is thus determined by the interdependence of the volume of circulation, vascular compliance and the volume of circulating blood.

HYPERTENSION

It is a disorder in the regulation of the relationship between the amount (flow) of blood and the resistance to its flow, i.e. cardiac output on the one hand and peripheral resistance (resistance) on the other.

Increasing the value of blood pressure in the systemic (or pulmonary) circulation is possible by 3 mechanisms:

- increasing the amount of blood that flows through the bloodstream
- increasing the resistance of the blood vessels, which is placed in the flowing fluid (blood)
- combination of both of previous

The established boundaries between still "normal pressure" and hypertension are artificially established and sometimes differ:

140/90 mmHg (in systemic circulation) - for outpatient measurements (for 24-hour monitoring 130/80), 30/12 mmHg (in pulmonary circulation)

In this context, it is good to know that the main determinant of systolic pressure is the work of the relevant ventricle (dependence on venous return, myocardial contractility, heart rate, or aortic elasticity in the systemic circulation); for diastolic pressure, the most important is the "value" of peripheral resistance.

Systemic arterial hypertension is a condition where the pressure is higher than the above-mentioned limit values and according to the type of cause we divide it into:

1. Primary = essential (95% of cases) – with unknown etiology and poor clarified pathogenesis
2. Secondary hypertension (5% of cases)

Essential hypertension

- Basic cause unknown, diagnosis by exclusion of secondary hypertension
- Initially a latent development, often an accidental finding on another examination
- Relatively often already systemic involvement (complications) - brain, heart, kidneys, retina

Probable etiopathogenetic mechanisms:

- Genetics - 50 - 70% positive family history; polygenic heredity - the predisposition to the disease is inherited
- Neurogenic - cortico-visceral and cortico-subcortical dysfunction (type of neurosis), effect of stress (increased SAS activity, affect - increase in blood pressure, tranquilizers - decrease in blood pressure)

- Lifestyle influence - excessive salt intake, inappropriate diet, stress...

The term mosaic theory of hypertension is sometimes used - so there are a number of complementary factors.

Pathophysiological consequences and complications of essential hypertension

- Increased pulsations, mechanical irritation of the endothelium, predisposition to atherosclerosis
- Risk of bleeding (including arterial) - epistaxis, brain, retina (hypertensive retinopathy), etc.
- Increase in cardiac pressure work (afterload is increased), concentric hypertrophy, myocardial infarction, impaired oxygenation, predisposition to heart failure
- Hyperfiltration in the glomeruli, sclerotization of nephrons, predisposition to chronic renal failure (hypertensive nephropathy)

Secondary hypertension

= hypertension in the systemic circulation. There is a primary disease that is complicated by hypertension; it is a heterogeneous group of diseases.

Pheochromocytoma

- Tumor of the adrenal medulla or ganglia, a source of catecholamines (in 90% noradrenaline)
- Seizure hypertension (up to 300/150) or persistent

Renal artery stenosis (renovascular hypertension)

- Activation of renin secretion, renin-angiotensin-aldosterone axis
- Primarily vasoconstriction, then hypervolemia

Primary hyperaldosteronism (Conn's syndrome) - sodium and water retention

Cushing's syndrome = increased level of glucocorticoids, which also have mineralocorticoid effects (see adrenal pathophysiology)

Chronic renal failure - fluid retention

Pregnancy hypertension

- New placental circulation
- Affects 5 - 15% of women, sometimes proteinuria, edemas - (pre) eclampsia (EPH gestosis = edema + proteinuria + hypertension)
- Influence of hypervolemia and placental metabolites causing vasoconstriction

Hypertension during pharmacotherapy - oral contraceptives, sympathomimetics, ATB - allergic reactions with hypertension

Pulmonary hypertension

= increase of pressure in the pulmonary circulation

- Formation by identical mechanisms - imbalance between blood volume and bloodstream resistance
- It is a low-pressure system - hypertension can easily occur acutely (pulmonary embolism)

Basic division according to etiology:

- **HYPERKINETIC HYPERTENSION** - Left-right heart shunts - increased flow through the pulmonary system - part of the blood with pathological communication (defect of the atrial septum or ventricles, ductus arteriosus persistens) returns to the right heart and from there back to the pulmonary circulation. Compensation by morphological reconstruction of arterioles - muscle thickening, the result is total increase of resistance.

- **POSTCAPILLAR HYPERTENSION** - pressure increase in the left atrium (physiologically there is a very small pressure gradient between the pulmonary artery and the left atrium) - left heart failure, mitral stenosis and insufficiency, cardiomyopathy, etc.
 - **REACTIVE HYPERTENSION** - consequence of vasoconstriction of arterioles as a reaction to hypoxia (physiological mechanism of optimization of perfusion of individual parts of the lungs according to their ventilation); this reaction is caused by conditions with reduced pO₂ in the alveolar air - chronic bronchitis, emphysema, obesity, neuromuscular diseases, sleep apnea syndrome, high altitude (3000 m), etc.
 - **OBSTRUCTIVE HYPERTENSION** - idiopathic primary pulmonary hypertension - cell proliferation in the vessel wall, mostly a congenital mutation of the morphogenic protein gene, progression, right heart failure
 - **PARENCHYMA REDUCTION** - emphysema (extinction of interalveolar septa in which pulmonary capillaries take place), pulmonary fibrosis, conditions after lung resection
 - **PULMONARY EMBOLISM** - a precapillary type of increased lung resistance; thrombus embolization (most often from the veins of the lower limbs or pelvic plexuses), air embolism (air penetration into the veins), fat embolism (fat droplets in multiple fractures)
- Massive embolism leads to acute pulmonary hypertension and acute right heart failure. Repeated minor embolizations cause chronic overloading of the right heart with its hypertrophy and later with possible decompensation (dilation and failure). The right ventricle without hypertrophy cannot compensate for the large increase of resistance in the pulmonary circulation. Simultaneously, output into the systemic circulation is decreasing.

HYPOTENSION

The line between norm and hypotension cannot be positively determined.

Systemic arterial hypotension - 100/65 mmHg and below - is usually reported; constitutively low blood pressure is not considered a disease and is not a problem if the individual tolerates it well.

Types and causes of hypotension:

- **Idiopathic (= primary) arterial hypotension** - these are transient conditions with reduced cerebral perfusion, sometimes leading to syncope (syncope = short-term unconsciousness, "faintness")
- **Orthostatic hypotension** - a physiological but more pronounced reaction to a change in body position (temporary reduction of venous return, output decreases by about 20%, compensation through baroreceptors, sympathetic activation, parasympathetic depression - if this compensation is not sufficient or fast enough, there is a temporary decrease in pressure with hypoperfusion of the brain with impaired consciousness - known faintness after sudden standing after prolonged lying). In case of ANS failure, this reaction is changed, it can be tested. Also with hypovolemia (e.g. dehydration) orthostatic hypotension easily appears.
- **Secondary hypotension:** dehydration (diarrhea, vomiting, sweating, diuretics; Addison's disease), mitral or aortic valve stenosis, bradycardia, heart failure
- **Long-term immobilization**

COLLAPSE OF CIRCULATION

= sudden complete interruption of circulation

Causes:

- Cardiac arrest or syncope
- Closure of the pulmonary artery (thrombus)
- Generalized vasodilation

The dominant symptom is impaired consciousness from limited cerebral perfusion resulting to hypoxia of the brain with its energy limits (aerobic capacity for about 10 - 20 seconds, then anaerobic glycolysis - 4 - 5 minutes, irreversible changes followed (the most sensitive is the neocortex and reticular formation of brain stem).

SYNCOPE

= short-term loss of consciousness due to brain hypoperfusion.

- Neurogenic - sudden bradycardia + vasodilation; cause - increased parasympathetic activity (sometimes prodromes: nausea, hypersalivation, intense peristalsis)

Emotional stress - fear of death, injury

Pain

Ortostasis (long standing in heat and humidity)

- Cardiac syncope - arrhythmia (3rd degree AV block, asystole - Adams-Stokes syndrome - loss of consciousness, convulsions, approx. 30 s)

Strong stimulation of the vagus nerve (sinocarotic reflex - pressure on the sinus, oculocardial reflex - pressure on the bulbs)

Hit on the solar plexus, chin

Elderly people with carotid atherosclerosis - baroreceptor hypersensitivity - external pressure stimulation (tight collar, shaving, head rotation)

HEART FAILURE = HEART INSUFFICIENCY

It is a state of reduced ability of the heart to perform the function of a pump. Basic characteristics:

- Decreased cardiac output (MAP decrease)
- Increased venous pressure (accumulation of blood in front of the left or right ventricle)

Etiology:

- Ischemic heart disease (40%), cardiomyopathies (30%), valve defects, hypertension, congenital heart defects, chronic cardiac arrhythmias, etc.

Symptoms of heart failure vary depending on whether the left side of the heart, which pumps blood to the whole body (the large bloodstream), or the right part of the heart, which pushes blood into the pulmonary circulation, is affected. Some causes affect the heart as a whole, then the symptoms combine. Even in more advanced failure, there is often a combination of manifestations from both halves of the heart.

Left heart failure

The blood stagnates in front of the affected section, which is not able to pump it further (i.e. in the pulmonary circulation). Gradually, fluid accumulates in the lungs - in the spaces between the capillaries and the alveoli, eventually the alveoli themselves are flooded. A life-threatening condition develops = edema of the lungs. The main symptom is dyspnea = cardiac asthma; first with more exertion, later with deterioration, shortness of breath develops (typically lying down at night). ↓ cardiac output → ↓ blood pressure and ↓ organ perfusion, which

manifests itself in weakness, inefficiency, sometimes a tendency to collapse. Decreased renal perfusion activates the renin-angiotensin-aldosterone system, leading to fluid retention and increased blood volume, which worsens congestion in the lungs and thus pulmonary edema. In acute left heart failure, the development of dyspnea is rapid - more extensive myocardial infarction or complications (tearing of the papillary muscle or tendon, rupture of the interventricular septum), myocarditis, infectious endocarditis, decompensation of hypertension, cardiac arrhythmias, but also general diseases such as sepsis, increased thyroid function, kidney failure.

Right heart failure

Blood stagnates in front of the right half of the heart. Due to the large capacity of bloodstream in the whole body, at first only the body weight increases, then the formation of edemas, first in the parts of the body which are located at the lowest and where the hydrostatic pressure is therefore highest. Typically, these are edema of the lower limbs (perimalleolar), gradually going up, then edema of the lower abdomen (inqual), in the extreme case there is edema of the whole body (anasarca). Congestion of the liver and GIT leads to anorexia and pain in the right lower jaw.

Failure is usually accelerated in patients with chronic lung disease (e.g. chronic obstructive pulmonary disease, pulmonary fibrosis, pulmonary embolism). Pulmonary hypertension of various origins (see above) is a major cause of right heart failure (both acute and chronic). Through postcapillary pulmonary hypertension, it can also lead to right heart failure also initially left heart failure. The right ventricle is forced to pump blood into the overfilled pulmonary vessels under higher pressure, so it is overloaded and eventually begins to fail; this phenomenon is referred to as *cor dextrum translatum*.

Compensatory mechanisms (muscle hypertrophy, dilation of the heart) can be applied during the gradual development only and to some extent and temporarily maintain the condition at a level compatible with life. However, decompensation may occur later. In the case of sudden right heart failure, hypertrophy cannot be developed.

SHOCK

General definition = hypoperfusion of most tissues and organs leading to insufficient supply of oxygen and nutrients on the one hand together with the accumulation of metabolites on the other hand.

General characteristics:

- Disturbance at the level of microcirculation
- Imbalance between nutritional function (= ability of vasodilation) and circulatory (= vasoconstriction)
- Positive feedbacks and the origin of "*circulus vitiosus*"
- Multiorgan failure

BASIC CLASSIFICATION

- Hypovolemic
- Cardiogenic
- Distribution

Phases of shock

Compensation phase

- Activation of the sympathoadrenal system due to hypotension

- Release of catecholamines
- Blood volume moves to vital tissues, arterial pressure is normal or increased at this stage, faster breathing, increased heart rate and the strength of myocardial contraction

Decompensation phase

- Vasodilation occurs in hypoperfused (i.e. poorly perfused) tissues
- Extravascular fluid penetration → deepening of hypovolemia
- Reduction of fluid volume in the “centralized circulation” → deepening of hypotension
- Release of metabolites and enzymes from damaged cells
- DIC - due to the released tissue factor from damaged cells

Irreversible phase

- Changes are uncompensated and uncomensable, leading to permanent damage of organs and death

HYPOVOLEMIC SHOCK

Etiology:

- External and internal bleeding
- Fluid sequestration (ascites, fluidothorax)
- Large fluid losses (burns, dehydration, polyuria)
- Capillary leakage syndrome - generalized increased capillary permeability (= Starling balance disorder), part of the systemic inflammatory response (septic shock); resistant to therapy

Pathogeny and symptoms:

- Loss below 10% of blood volume - cardiac index is not changed, without significant arterial hypotension, redistribution of cardiac output, interstitial fluid intake, tachycardia, oliguria
 - approximately 20% of blood volume - ↓ MOS, later ↓ BP, tachycardia + hypotension, cold acral parts of the body, oliguria to anuria and acidosis (lactic, possibly also respiratory), in case of plasma loss and dehydration ↑ hematocrit, ↓ central venous pressure

CARDIOGENIC SHOCK

Etiology:

- Acute myocardial infarction - cardiogenic shock occurs in necrosis of more than about 40% of the myocardium, complications of myocardial infarction (rupture of the papillary muscle or tendon, rupture of the ventricular wall, etc.)
- Pulmonary embolism (closure of 50% of pulmonary circulation)
- Acute myocarditis, endocarditis
- Acute mitral or aortic regurgitation
- Cardiomyopathy (dilated, restrictive, ischemic)
- Ventricular tachyarrhythmias
- Acute worsening of chronic heart failure
- Heart tamponade

Pathogeny and symptoms:

- Heart failure as a pump with consequent insufficient cardiac output
- Vicious circle - increased heart rate → widening of the ischemia zone → decreased cardiac output

- ↓ BP (systole below 90 torr), ↑ central venous pressure (x hypovolemic shock)
- *Pulsus alternans* and gallop
- Pulmonary edema (stagnation of blood in the small circulation), central cyanosis

DISTRIBUTION SHOCK

This type of shock begins directly with changes in the peripheral circulation, which lead to a reduction in peripheral resistance in much of the circulation, resulting in arterial hypotension. Unlike collapse or syncope, this is a permanent condition.

The main clinical condition is **septic shock**:

- Main pathogenetic mechanism - generalized vasodilation
- Regardless of nutritional need and thermoregulation
- Induction of vasodilators in the microcirculation - overproduction of NO, proinflammatory cytokines (TNF α , IL1) and endotoxins

Systemic inflammatory response syndrome (SIRS)

Other pathogenetic mechanisms and complications:

- decreased myocardial contractility (myocardial depression) → decreased cardiac output, hypotension
- DIC
- Microthrombi in the pulmonary circulation, ARDS (acute respiratory distress syndrome)
- MODS = multiple organ dysfunction syndrome (typically kidney, myocardium - does not respond to catecholamines)

Anaphylactic shock - is caused by a generalized allergic reaction, usually when a large amount of allergen enters the blood rapidly (injection of a drug such as penicillin, sting, etc.). Histamine release plays a role in the pathogeny, which induces vasodilation and increases vascular wall permeability. If this happens in much of the circulation, peripheral resistance drops significantly and fluid leakage from the blood vessels into the interstitium causes hypovolemia. Both of them lead to hypotension and develop a circulatory failure with another course common to all types of circulatory shock.

Neurogenic shock - CNS lesions (injury, bleeding) - circulatory dysregulation

ATHEROSCLEROSIS

- Pathological process in the wall of blood vessels (arteries) causes a change in their mechanical properties.
- Possibility of expansion, rupture, partial closure of the lumen
- The decisive importance of the so-called endothelial dysfunction

Basic development:

1. Accumulation of lipoproteins in the intercellular mass of the intima (LDL, VLDL)
2. Structural modeling (participation of overproduction of free oxygen radicals)
3. Influence of gene expression in myocytes and endothelium → production of cytokines and adhesion molecules
4. Capture of monocytes → penetrate the endothelium into the intima → change in macrophages phagocytic lipoproteins = foam cells
5. Change of myocyte properties (phenotype) from "contractile" to "synthetic" - cytokines, special proteins (collagen, elastin, etc.)
6. Formation of the so-called lipid strip - above the deposit

7. Endothelial disturbance → platelet adhesion and aggregation, growth factor synthesis (PDGF) → further proliferation of smooth muscle cells
8. Foam cells are subject to apoptosis or necrosis (hypoxia, malnutrition) - evidence of new vessel formation from the *vasa vasorum*; influence of radicals
9. The breakdown of the atheroma and bleeding into the plaque leads to the thrombus formation

Risk factors

Confirmed:

- Hypercholesterolemia (especially LDL x low HDL)
- Hypertension
- Diabetes mellitus
- Positive familial occurrence (coronary arteries)
- Gender (men)

Probable: hyperhomocysteinemia, obesity, physical inactivity, infections (Chlamydia pneumoniae, Escherichia coli, Helicobacter pylori, Coxsackie virus, Cytomegalovirus), tobacco smoking, menopause in women

ISCHEMIC HEART DISEASE (IHD)

A group of disease states arising from the pathology of the coronary arteries (etiologically it is an atherosclerotic process), the result is myocardial ischemia (of varying extent, reversible or irreversible). This is the most common cause of death in the Czech Republic.

Classification usually according to clinical characteristics:

acute forms

- acute myocardial infarction - STEMI (usually develops pathological Q = Q-infarction, often a transmural lesion), NSTEMI (pathological Q does not develop = non-Q infarction, often a non-transmural lesion)
- Unstable angina pectoris
- Arrhythmic form of ischemic heart disease
- Sudden death

chronic forms

- Stable angina pectoris
- Post-infarction condition (after 6 weeks)
- Other (vasospastic - Prinzmetal's angina pectoris, silent ischemia, etc.)

Stable angina pectoris is caused by a stable atherosclerotic plaque, which narrows the lumen of the coronary arteries, resp. their branches; however, the progression of narrowing is gradual.

Unstable angina pectoris is caused by an unstable atherosclerotic plaque, on which, for example, a thrombus sits, rapidly enlarging the occlusion of the lumen of the vessel. Thus, angina pectoris worsens in a very short time. This condition is associated with a high risk of progression to myocardial infarction. The second possibility is the stabilization of the plaque, the organization of part of the thrombus into the connective tissue and the transition to stable angina pectoris, but more difficult, with a tolerance of less load than before.

Myocardial infarction (MI) is one of the consequences and forms of ischemic heart disease. It is an ischemic focal death (ischemic necrosis) of a part of the heart muscle, which occurs during occlusion or significant narrowing in the supply area of the left or right coronary artery. In most cases, it is a occlusion caused by a blood clot (thrombus) at the site of the narrowed coronary artery (i.e. a thrombus attached to the atherosclerotic plaque). Rarely, this condition can be caused by inflammation of the artery, embolus or spasm. The size of the dead heart muscle varies according to the location and size of the occluded coronary artery. The current oxygen demand of the myocardium also plays a role. This is mainly due to the activity of the heart, i.e. heart rate. Physical work that increases the heart rate worsens the imbalance between myocardial needs and the supply of oxygen limited by narrowing of the artery and increases the extent of the necrotic lesion. Therefore, physical rest is essential when myocardial infarction occurs. Hypoxia is most severe in the middle of an ischemic lesion, where necrosis develops. At its edge, where oxygen enters the environment, there is a zone of damage and, around, a zone of ischemia with only functional changes. Reducing oxygen consumption by reducing cardiac work or, conversely, maintaining it at a higher level of physical activity can significantly affect the location of the boundary between these zones, and thus the degree of probability of survival of myocardial infarction and the extent of its permanent consequences.

The development of ischemic changes also has a time course (see below) and eventual timely resumption of blood flow may also affect the resulting extent of damage. Other associated factors may also play a role, such as various forms of general hypoxia in respiratory disorders or anemia, which reduce the supply of oxygen to the tissues, including the myocardium.

Myocardial infarction usually affects the left ventricle (rarely the right ventricle or atria). The left ventricle works against the higher resistance of systemic circulation, has a larger myocardial mass, and therefore greater demands on oxygen. The higher pressure exerted by the left ventricle also restricts blood flow through its coronary artery (left ventricular myocardial perfusion occurs in diastole, when the pressure in its wall drops below the pressure maintained in the aorta from which the coronary arteries depart, by its elastic function). The right ventricle and atria of the heart have less muscle mass and the pressure conditions are more beneficial for perfusion. Therefore, right ventricular or atrial infarction is rare and occurs under special conditions, such as coronary artery developmental anomalies.

Dynamics of changes due to occlusion of a coronary artery branch:

- Most often STEMI (sometimes NSTEMI); in myocardial wall (left ventricle) a infarction (necrosis) gradually develops
- Time intervals are individual for each patient
- Myocardial viability depends primarily on the collateral blood stream

Ischemia (< 20min)

- Myocardium is hypoxic (\downarrow pO₂), reversible phase, high (pointed) T waves on ECG

Ischemic damage - alteration (> 20min)

- Deepening myocardial hypoxia, also reversible, on ECG development of ST elevations

Infarction - necrosis (> 2 hours)

- Already irreversible damage, on ECG development of pathological Q

THROMBEMBOLIC DISEASE

The basis is the development of a thrombus in the venous systemic circulation (most often sinuses in the lower leg and thigh, pelvic plexuses); detachment (tearing) of the thrombus and its embolization then closes the pulmonary arteries. A thrombus can also form in the atria of the heart during atrial fibrillation. Embolization from the right atrium is to the pulmonary arteries, from the left atrium to the systemic circulation.

Clinically, this includes 1. Phlebothrombosis and 2. Pulmonary embolism

Etiology:

- Hypercoagulable state (congenital and acquired thrombophilic conditions, e.g. Leiden mutation, major surgical procedures, hormonal contraception, etc.)
- Venostasis (immobilization, travel thrombosis, varices of lower limbs, obesity, etc.); Remember that any slowing of blood flow means an increased risk of thrombus formation.
- Endothelial dysfunction

Pulmonary embolism

= the third most common cause of death among cardiovascular diseases (after acute myocardial infarction and brain stroke); in contrast, more often without symptoms (= clinically silent!).

Etiology - mostly deep vein thrombosis, rarely embolization of fat (polytrauma), air (even iatrogenic), amniotic fluid, tumor tissue.

Pathogeny - anatomical obstruction and increase in pulmonary vascular resistance → ↑ pulmonary arterial pressure, dilation of right ventricle (RV) and ↓ heart rate → ↑ stretching of RV myocytes, neurohumoral stimulation, ↑ demand for oxygen in the myocardium, prolongation of RV contraction time → right-left ventricular asynchrony + ↓ coronary perfusion in RV → failure of RV, further worsening in the situation of hypotension and low oxygen saturation.

The result is ↑ ventilation / perfusion ratio → arterial desaturation → ↓ pAO₂ → arrhythmias and / or shock.

Symptoms - dyspnea (sudden onset - resting or worsening of chronic dyspnea), chest pain (such as infarction), cough (sometimes hemoptysis), hypotension, sometimes visible edema of the limb (from thrombosis of veins), tachypnea, tachycardia, cyanosis – view of *cor pulmonale acutum*.

COMPARTMENT SYNDROME

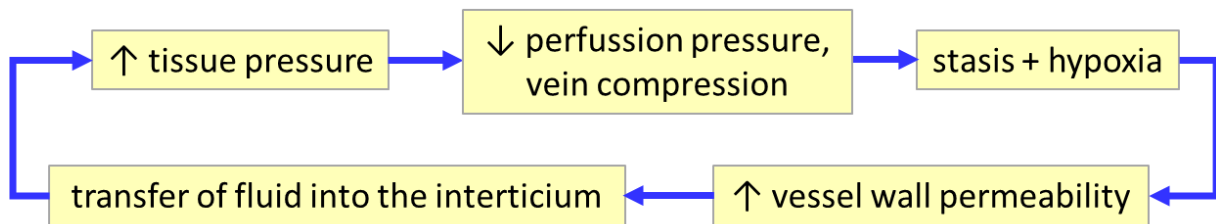
= a set of symptoms arising from an increase in pressure in a closed anatomical space (compartment), leading to vascular occlusions causing local ischemia; compartment - space defined by the skeleton and fascial muscle cover or intermuscular septa.

Etiology:

1. Increased pressure inside the intrafascial space (bleeding, inflammation, burns, venous obstruction, etc.)
2. Compression of the intrafascial space from the outside (tight bandage, incorrect plaster fixation, scarring of the skin)
3. Reduction of the volume of the intrafascial space (closure of the fascial defect, excessive pull on the limb). In active young athletes, chronic compartment syndrome can occur (increased muscle volume after exercise and increased hydrostatic pressure in the capillaries with the transfer of intravascular fluid to the interstitium)

Pathogeny:

In a compartment with increased intrafascial pressure, venous pressure first increases. The venous walls have low resistance and collapse, the arterio-venous pressure gradient decreases. It gradually decreases until the perfusion of the tissue stops and therefore its functions are impaired (up to necrosis). With the stagnation of the blood and the disorder of the permeability of the blood vessels, the fluid is transferred from the blood vessels to the interstitium (intrafascial space), where the pressure gradually increases - a circulus vitiosus is formed. Irreversible changes occur in nerve hypoxia in about 2 hours, muscle in 6 hours, skin in 8-12 hours.



HEART DEFECTS

- Congenital developmental and acquired changes in cardiac morphology
- Influence the heart's function as a pump

Functional consequences:

- left - right circulatory shunt - the amount of circulating blood in the pulmonary circulation is increased, cyanosis does not occur
- right - left circulatory shunt - admixture of mixed venous blood to arterial blood (increase in volume in the systemic circulation), typical cyanosis (oxygenated blood is mixed to the oxygenated blood in the left part of the heart, the resulting saturation of this mixed blood with oxygen is lower, higher concentration of reduced hemoglobin may reach the limit of 50 g/l at which cyanosis occurs)
- Stenosis - change in the resulting systolic volume, congestion in front of barrier
- Insufficiency - blood regurgitation (opposite flow direction)

CONGENITAL DEFECTS OF THE HEART

Defects without cyanosis

- Atrial septal defect - volume overload of right atrium and ventricle, pulmonary hypertension, right ventricle failure
- Ventricular septal defect - volume overload of right and left ventricle, pulmonary hypertension
- Ductus arteriosus (Botalli) patens - predisposition in perinatal hypoxia (immature and premature newborns with respiratory insufficiency)
- Pulmonary stenosis – right ventricle pressure overload, dilatation, failure
- Aortic coarctation - at the site of ligamentum arteriosum, collaterals - intercostal, subclavian (higher BP on upper limbs and head, hypertension - epistaxis, headache)
- Aortic stenosis - at the site of the aortic valve, often a long-term process, pressure overload of the left ventricle (angina pectoris, syncope during physical exertion)

Septal defects (ventricles or atria) can be described as late-cyanotic defects. The pressure in the left heart, which works against the resistance of the systemic circulation, is higher than in the right heart, which pumps blood into the low-pressure pulmonary circulation; therefore, it is a left - right shunt. Only blood that has passed through the lungs and is properly saturated with oxygen flows from the left heart into the great circulation; therefore, cyanosis does not occur. However, part of the blood flows through the lungs repeatedly. The flow through the pulmonary circulation is therefore higher and the right heart is overloaded. The result is a gradual increase of pressure in the right heart, which can later lead to a reversal of shunt to the right – left and the development of cyanosis. Whether this happens and after what time depends on the size of the septal defect (its hemodynamic significance).

Defects with cyanosis

- Fallot's tetralogy: ventricular septal defect, aorta to the defect, pulmonary stenosis and right ventricle hypertrophy (permanent cyanosis, worsening during exercise, secondary polycythemia, higher hematocrit, higher blood viscosity, clubbed fingers)
- Transposition of large arteries (without a septal defect it is incompatible with life, because the small and large circulation are completely separated)
- Eisenmenger's complex: ventricular septal defect, attached aorta, dilation of pulmonary artery

ACQUIRED HEART DEFECTS

- Higher incidence before the ATB era, causes: rheumatic fever, endocarditis, degenerative changes
- Basic division: estuary stenosis and valve insufficiency

Mitral stenosis

- Rheumatic disease - a complication of streptococcal infection
- LS pressure overload → LS dilatation → transmitted to the pulmonary veins, venules, capillaries
- Development of pulmonary hypertension, transudation into the alveoli → hemoptysis
- Predisposition to atrial fibrillation → thrombi in the atria → embolization (see above)

Mitral insufficiency

- Infectious endocarditis, degenerative changes, papillary muscles disorder, large left ventricle dilation
- Volume overload of left ventricle and atrium (here also pressure)
- Developing acutely (pulmonary edema) or slowly (atrial dilation, fibrillation)
- Mitral valve prolapse (in healthy people, high gradient between left atrium and ventricle; Marfan's syndrome)

Aortic stenosis

- Degeneration and calcification (reduction of lumen from 3 cm² to approx. 1/3)
- High gradient between left ventricle and aorta during systole), pressure overload → concentric left ventricle hypertrophy
- Left atrium hypertrophy due to increased diastolic pressure in the ventricle, functional significance for ventricle filling

- Left ventricle ejection fraction is lower, pressure amplitude decreases (*pulsus parvus et tardus*)

Aortic insufficiency

- Infectious endocarditis, rheumatism, degeneration, Marfan's syndrome, syphilis
- During diastole regurgitation from the aorta to the left ventricle → volume overload
- Heart rate increasing leads to an increase of systolic pressure → pressure overload
- Low aortic pressure during diastole → decreased coronary perfusion
- Acute condition - rapid destruction of the valve, propagation of increased pressure through the mitral valve during diastole to the left atrium and pulmonary circulation – dyspnea, pulmonary edema; chronic – left ventricle dilatation
- Changes in blood pressure - pressure amplitude increased (systolic pressure is increased - increase of systolic volume, diastolic pressure is decreased - part of the blood from the aorta returns to the ventricle, vasodilation in the periphery (*pulsus magnus, celer et altus*))

Tricuspid valve stenosis

- Rheumatism, uncommon
- Increase of pressure in right atrium, hypertrophy development

Insufficiency of the tricuspid valve

- Dilation of the right heart
- Propagation of pressure from right ventricle to atrium and large veins, pulsation of jugular veins, liver

Pulmonary valve stenosis

- Usually an inborn defect
- Right ventricle pressure overload

Pulmonary valve insufficiency - in pulmonary hypertension

HEART REACTION TO INCREASED LOAD

See also educational material:

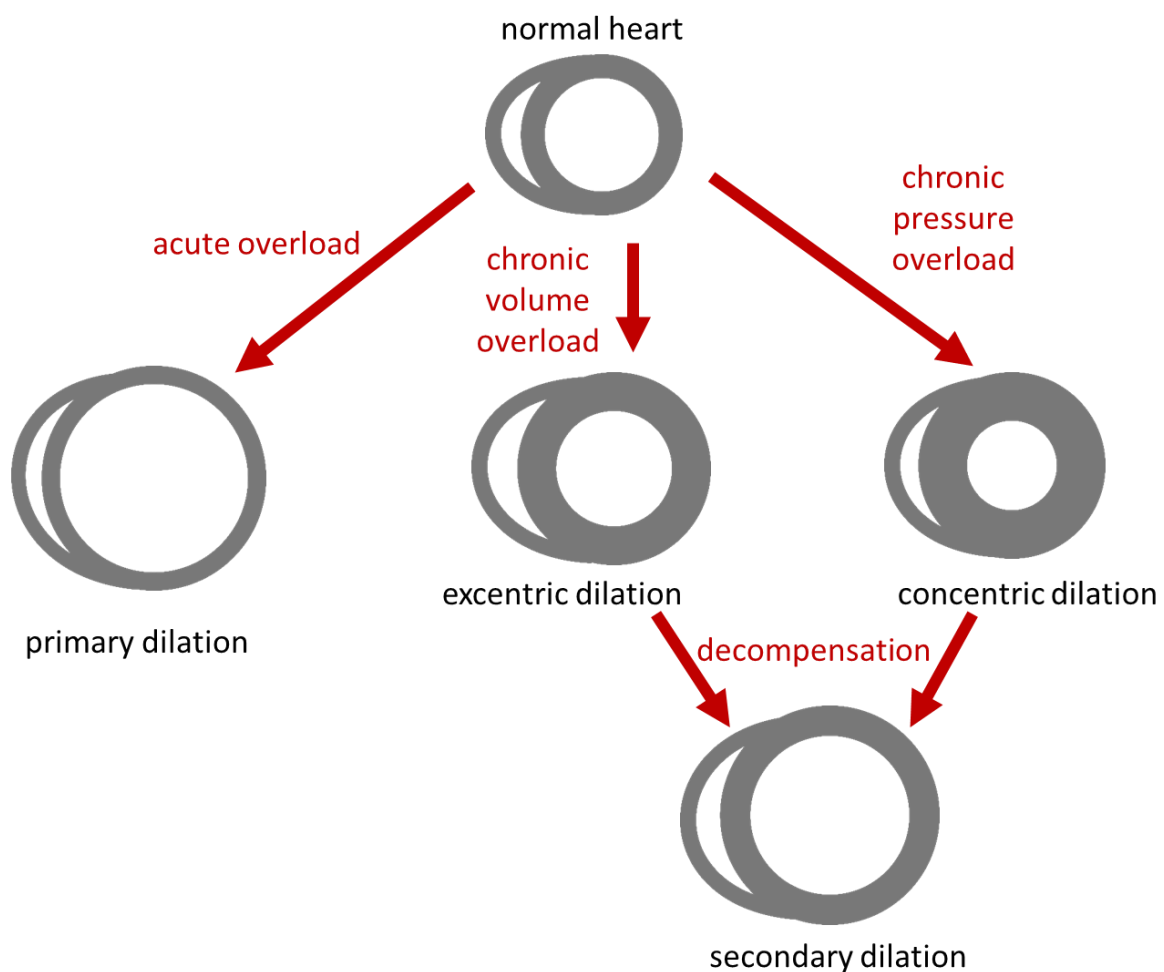
<http://patofyziologie.lfp.cuni.cz/wp-content/uploads/2019/03/Step-test-Letunov.pdf>

Cardiac compartments can be overloaded with the increased volume of filling blood (volume overload), increased resistance against which they pump of blood, and they must develop higher pressure (pressure overload). Of course, the pressure in the heart cavity rises even with volume overload. In the case of a sudden overload, compensation in the form of hypertrophy cannot develop. In the case of a gradual development of congestion, the heart responds by the hypertrophy. The volume overload tends to dilate the relevant cardiac compartment.

Also a sporting activity has increased load on the heart. A suitable sport based on static-dynamic load (running, cycling, rowing) combines the load of the heart by volume and pressure in a reasonable way. The result is a proportional increase in the diameter and length of cardiomyocytes. The sports heart therefore has greater contraction strength and a larger cavity volume. Both contribute to its higher efficiency and increase in heart rate. Therefore,

the athlete's heart reaches the required cardiac output with lower heart rate than in an untrained individual.

Sports activity with the pressure load (e.g. weightlifting) promotes cardiac muscle hypertrophy without increasing volume. It is therefore an effect similar to some pathological overload of the heart working against increased resistance. The resulting concentric hypertrophy may even reduce the volume of the ventricular cavity. In the hypertrophic myocardium, the conditions for the supply of oxygen to cardiomyocytes are more unfavorable (greater demands on the heavier myocardium, greater capillary distance, a bad pressure conditions limiting perfusion) and there is also an imbalance of signaling cascades controlling apoptosis. Thus, regressive myocardial changes may finally lead to the dilation and failure.



EVALUATION OF CARDIAC EFFICIENCY

See also educational material:

<http://patofyziologie.lfp.cuni.cz/wp-content/uploads/2019/03/Step-test-Letunov.pdf>

Ejection fraction = portion of ventricle content ejected during systole

$$EF = (EDV - ESV) / EDV \times 100$$

where

EF = ejection fraction (in %)

EDV = end-diastolic volume
ESV = end-systolic volume
Normal value: 55 – 80%

Systolic volume = the volume of blood ejected by one systole

Decreased systolic volume can be compensated temporarily by increased heart rate (to maintain cardiac output). In this way, the body may respond to decreased myocardial contractility, hypovolemia or decreased peripheral resistance (see shock). As an indicator of the development of this state the shock index is used:

Shock index: heart rate/systolic BP

Normal value: < 1

During the shock development, the index increases (blood pressure decreases, heart rate rises as the compensation); however, an increase in heart rate has significant adverse effects:

- 1) It increases the oxygen demand of the myocardium and thus potentiates myocardial hypoxia.
- 2) It shortens diastole, resulting in:
 - A) Impaired filling of the coronary arteries with blood, especially deterioration of the left ventricular myocardial perfusion, which occurs during diastole; it also promotes myocardial hypoxia;
 - B) Shortening the ventricular filling time - this reduces the end-diastolic volume and consequently the systolic volume; - therefore at high heart rates the cardiac output does not increase linearly with heart rate and at very high rates (supraventricular or ventricular tachycardia, etc.) it actually decreases.

SYSTOLIC AND DIASTOLIC HEART DYSFUNCTION

The heart performs systolic function (= blood ejection from the heart cavity during contraction) and diastolic function (= filling the heart cavity during relaxation). Both processes are necessary for the proper functioning of the heart as a pump, and in both cases their disorders result in a reduction of cardiac output and a reduction of tissue perfusion of the relevant circulation (systemic or pulmonary) and blood accumulation in front of a failing heart section.

Systolic dysfunction = reduced ability to contract

Causes: ischemia, myocarditis, cardiomyopathy

Diastolic dysfunction = impaired blood filling of the heart

Causes: reduced compliance of the ventricular wall and decreased volume in concentric hypertrophy, pericarditis (thickening of the pericardium and pericardial effusion limiting ventricular dilation), cardiac tamponade (= fluid, pericardial blood).