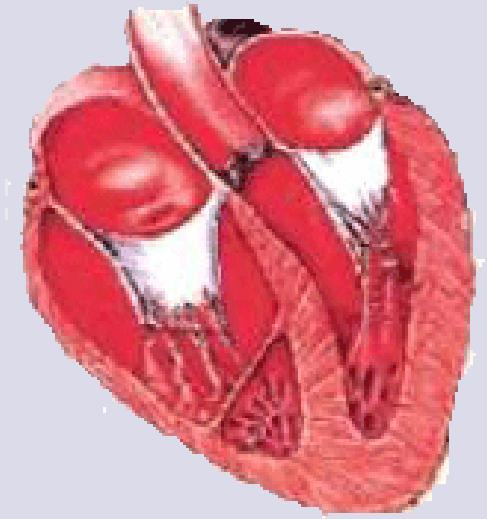

Coronary heart disease (CHD)

Institute of Pathological Physiology

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Winter Semester

CORONARY CIRCULATION AND MYOCARDIAL METABOLISM

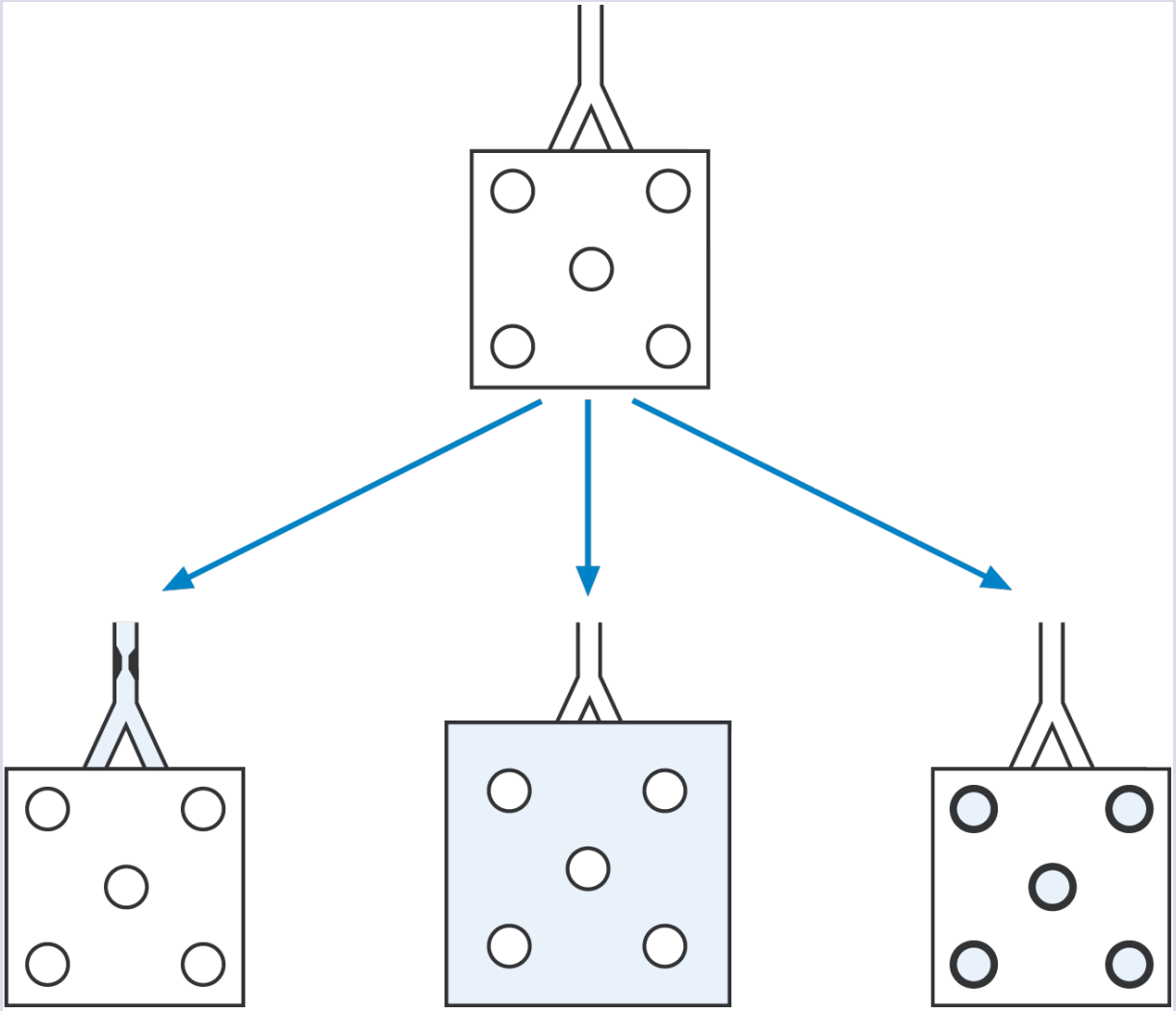
Blood flow:

resting: 250 ml/min

Main components:

- coronary arteries in epicardial part
- small coronary vessels
- myocardium

Perfusion pressure x resistance



Zátěžová echokardiografie, Maxdorf

Perfusion

extravascular pressure ↑

- high in systole
- higher in subendocardium
- myocardium diseases

↓

perfusion pressure

↑

diastolic BP

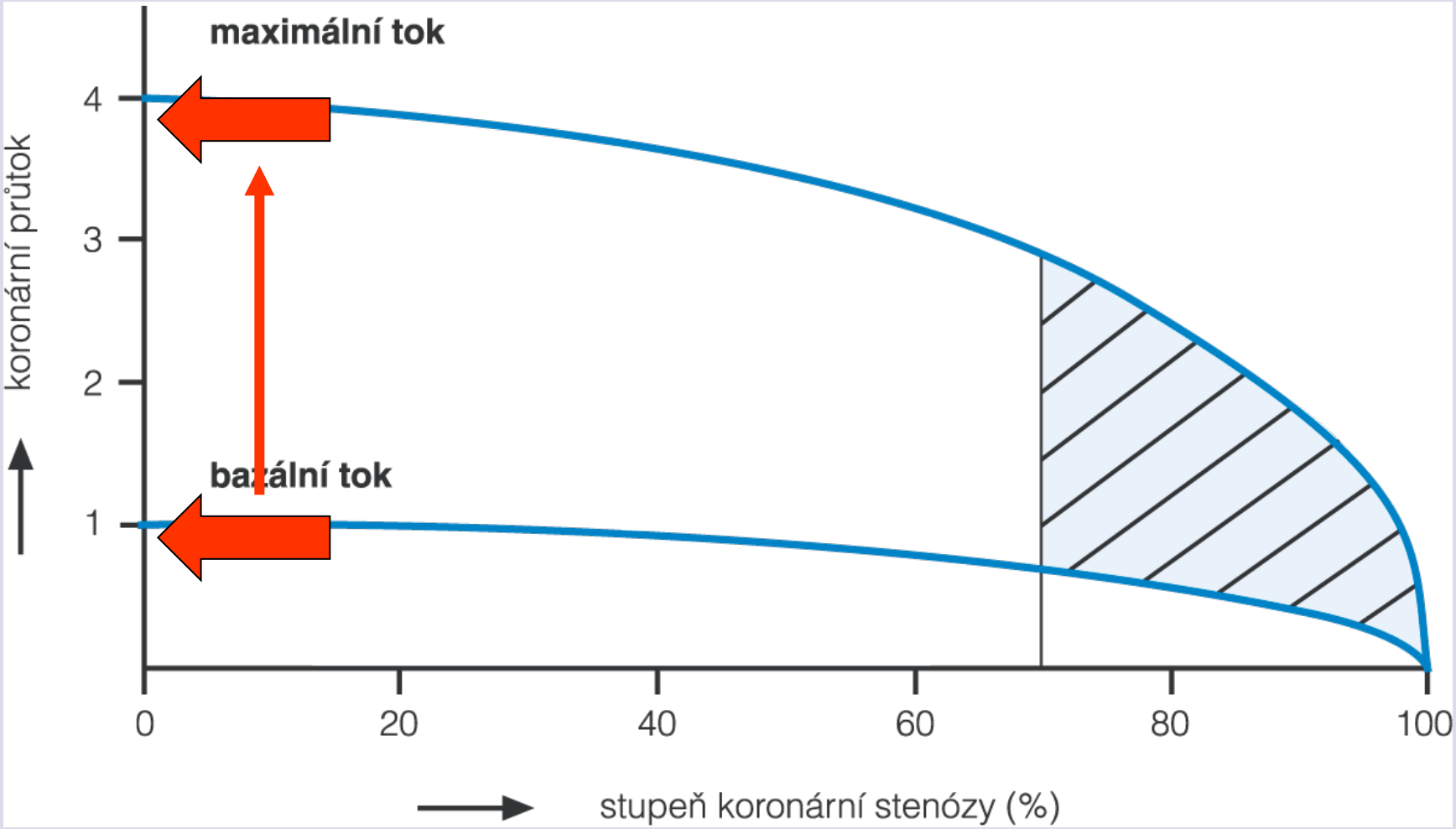
vascular resistance ↕

- dilatation of larger epicard. arteries
  - VNS
  - $\beta_2 \times \alpha$
- **arteriolar dilatation**
  - main mechanism of increasing the blood flow
  - metabolic influence
  - autoregulation
- endothelium

Perfusion pressure:
pressure difference between the beginning of coronary arteries and estuary of coronary sinus

Coronary reserve:
maximal increase of blood flow through myocardium – cca 4×
vasodiatation of small vessels

Differences in perfusion:
impaired perfusion of subendocardial parts

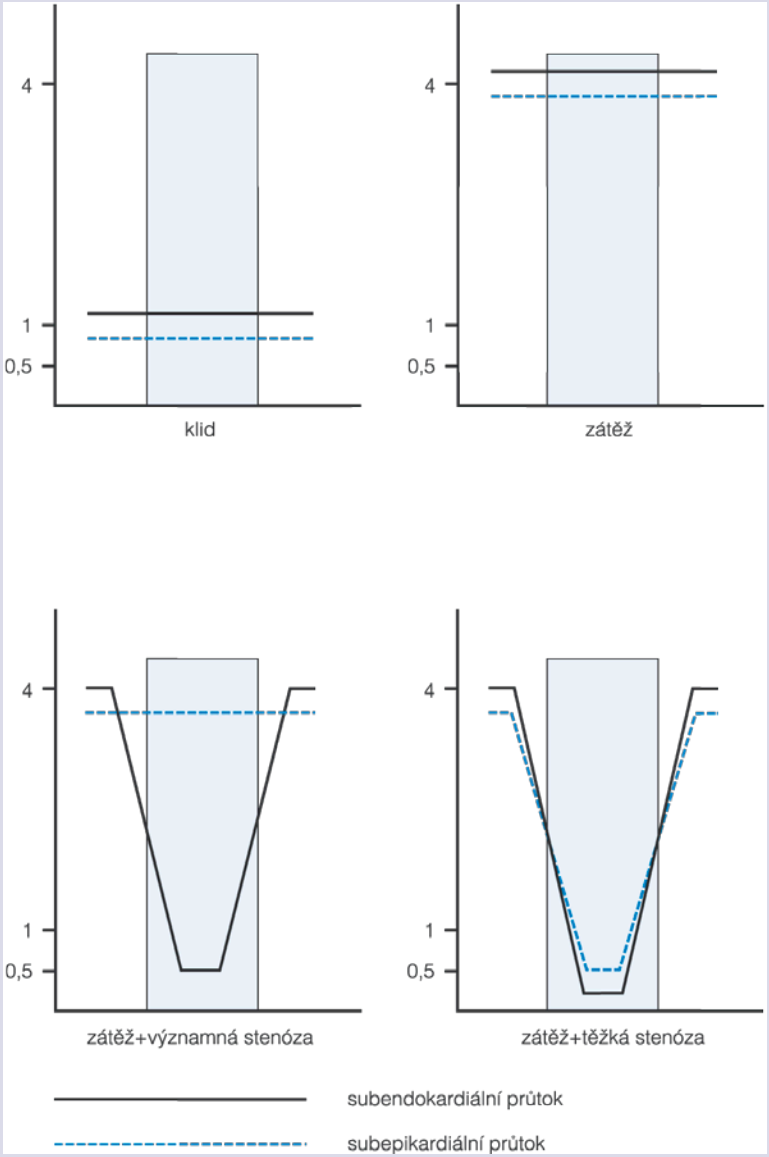


Zátěžová echokardiografie, Maxdorf

Blood flow through the **subendocardial** vessels
is less during systole
than in the outer coronary vessels.
To compensate, *the subendocardial vessels are far more extensive* than the outermost arteries, allowing a disproportionate increase in subendocardial flow during diastole.

Because blood flow mainly occurs during diastole, there is a risk for subendocardial ischemia

* diastolic pressure is low
* elevation in diastolic intraventricular pressure sufficient to compress the vessels in the subendocardial plexus
* rapid heart rates, the time spent in diastole is greatly reduced.



Zátěžová echokardiografie, Maxdorf

Oxygen extraction: almost maximal (as in intensively working skeletal muscles)

AV difference: 140–160 ml O_2/L blood

Oxygen consumption (AV difference × flow):
rest – 140 × 0,25 = 35 ml
exercise – 160 × 1,00 = 160 ml
Mainly achieved by increase of flow – vessel parameters are crucial for oxygen delivery to the myocardium during exercise

Energy consumption:

- 90 % mechanical activity (contraction, relaxation)
- 9,5 % proteosynthesis
- 0,5 % electrical activity

- tension in the wall of LV ~ blood pressure
- inotropy
- heart rate

Energy sources in the myocardium:

rest – FFA, glucose, lactate
exercise – increase of lactate up to 2/3

Factors infuencing oxygen consumption:

- heart work
- contractility
- **heart rate**
- myocardium properties: wall tension (dilatation, afterload – **blood pressure**), hypertrophy
- adrenergic stimulation

Factors infuencing oxygen delivery to the myocardium:

- parcial tension of oxygen in the environment
- respiratory functions
- hemoglobin
- blood flow through myocardium

ISCHEMIA

Ischemia

insufficient delivery of oxygen and nutrients and insufficient outflow of metabolites from the tissues due to the impaired perfusion

Imbalance between metabolic requirements and perfusion:

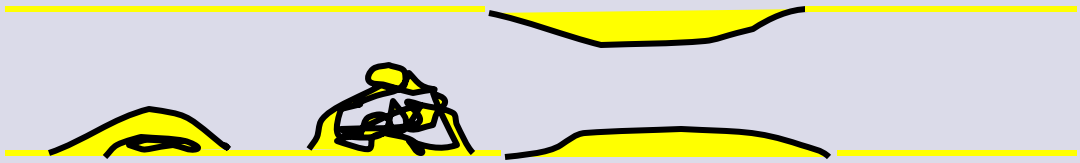
1. **increased requirements– *simulation by***
e exercise tests
2. **impaired perfusion**
3. **combination**

Vessel narrowing

- organic
- functional
- combined

- fixed
- dynamic

plaque + thrombus + spasmus



atherom. plaque **thrombus** **spasmus**

localisation
- concentric
- excentric

stability
- fibrotisation
- lipids
- inflammation

platelets:
vasoconstr. factors
growth factors

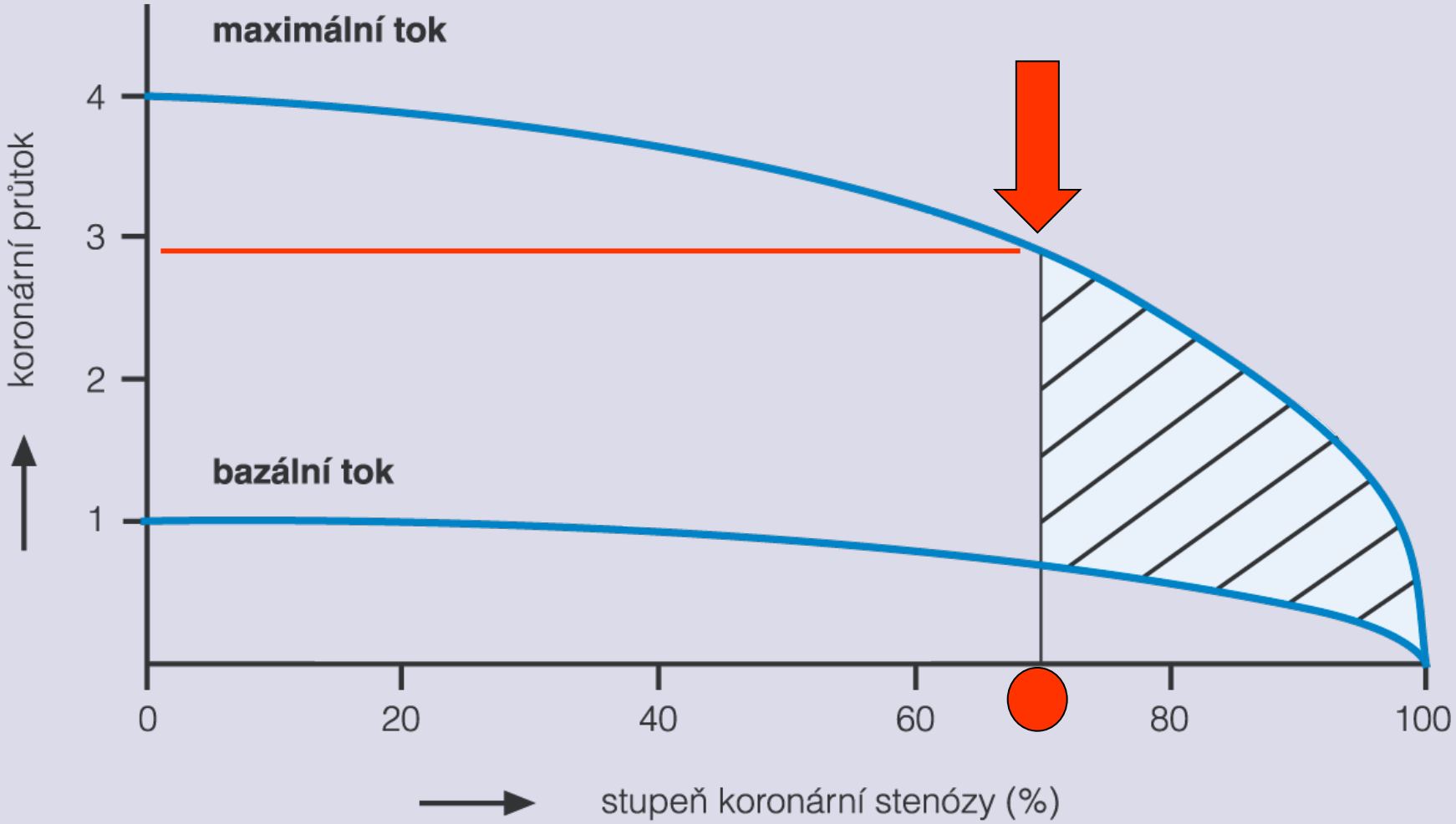
diurnal rhytm (morning!)
cold
smoking
psychic influences

Impact of the size of stenosis on hemodynamics of coronary blood flow:

- do 40 % – without influence
- 40–70 % – ischemia not apparent in physiological exercise
- **70**–90 % – ischemia not in resting, distinct in exercise
- over 90 % – ischemia even in rest

Hemodynamically unimportant atherosclerotic plaque can be the cause of life-threatening myocardial infarction:

rupture ⇒ thrombus + spasmus ⇒ necrosis ⇒
arrhytmia (ventricular fibrillation) ⇒ death



Zátěžová echokardiografie, Maxdorf

Consequences of ischemia:

- metabolic changes: ATP depletion, lokal acidosis, increased inflow of *calcium* to the cells
- impaired contractility (*decrease of stroke volume*):
- impaired relaxation (*diastolic dysfunction*)
- impaired electrical events (*arrhytmias, ECG*)
- morphological changes (*myocytes, necrosis, fibrotisation, steatosis etc.*)
- clinical symptoms (*pain, arrhytmia, heart failure*)

Postischemic changes

- ischemia duration
- reperfusion

Stunned myocardium

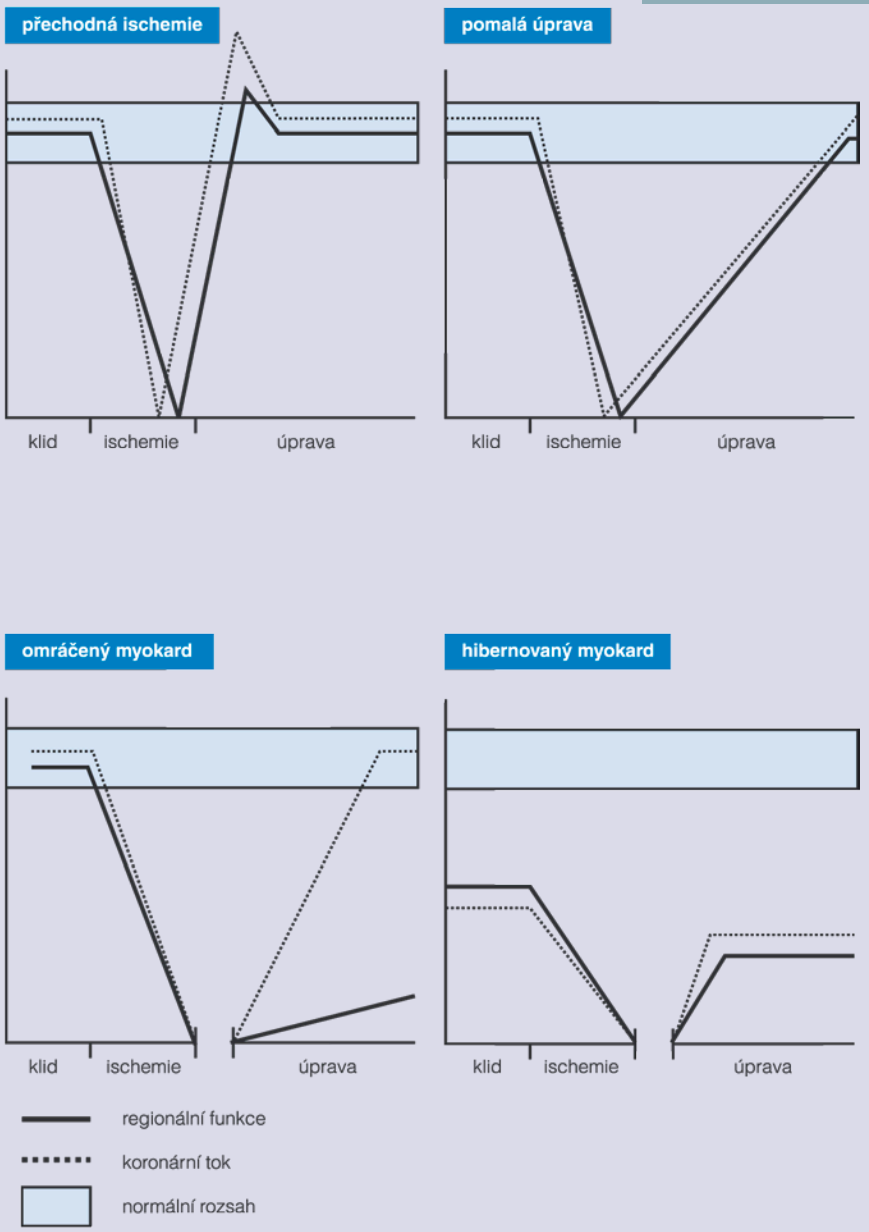
perfused but not functioning

reversible continuous dysfunction of myocardium after reperfusion without apparent changes

Hibernating myocardium

chronically hypoperfused and functionally impaired
situation with continuously decreased blood flow
accompanied by impaired contractility

adaptation of cells to decreased energy delivery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ischemie
úprava
hibernovaný myokard
klid
ischemie
úprava
regionální funkce
koronární tok
normální rozsah

Ischemic preconditioning

increased resistence of myocardium against damage due to ischemia

caused by preceding ischemia and reperfusion

Reperfusion

Collaterals

Angiogenesis
VEGF (vascular endothelial growth factor)
FGF (fibroblast growth factor)
Angiopoetin
and others...

Therapeutical angiogenesis
gene therapy: direct intramyocardial aplicatioon of plasmid or use of vector (adenovirus) VEGF or FGF

Revascularization by invasive treatment
- PTCA (percutanneous transluminal coronary angioplastic)
- stents
- bypass

Reperfusion damage

- oxygen radical species: source in mitochondria, or leukocytes,xanthinoxidase (less important in myocardium)
- increased amount of intracellular calcium
- neutrophils: radical formation, mechanical plugging of capillaries, proteolytic enzymes

clinically - ***arrhytmias***

CLINICAL FORMS OF CHD

- ***Angina pectoris (AP)***

- ***stable***: fixed stenosis

- atherosclerotic plaque decreases coronary reserve, increased oxygen requirements of myocardium (tachycardia) ... subendocardial ischemia

- *Other contributing factors*: anemia, increased blood viscosity, diastolic hypotension, hypertrophy of myocardium

- ***vasospastic*** (Prinzmetal):
spasmus of epicardial artery,
transmural ischemic changes;
in rest (frequently nocturnally),
reperfusion may be accompanied
by arrythmia

Mechanisms (?):

- hyperactive sympathetic nervous system
- defect in the handling of calcium in vascular smooth muscle
- imbalance between endothelium-derived relaxing and contracting factors, incl. NO

Acute coronary syndromes

unstable AP + acute MI

Unstable AP: unstable stenosis
rupture, thrombosis, spasmus,
uncomplete obturation + shorter time of ischemia without necrosis

Plaque rupture

- spontaneously
- triggered by hemodynamic factors
  - blood flow characteristics
  - vessel tension.

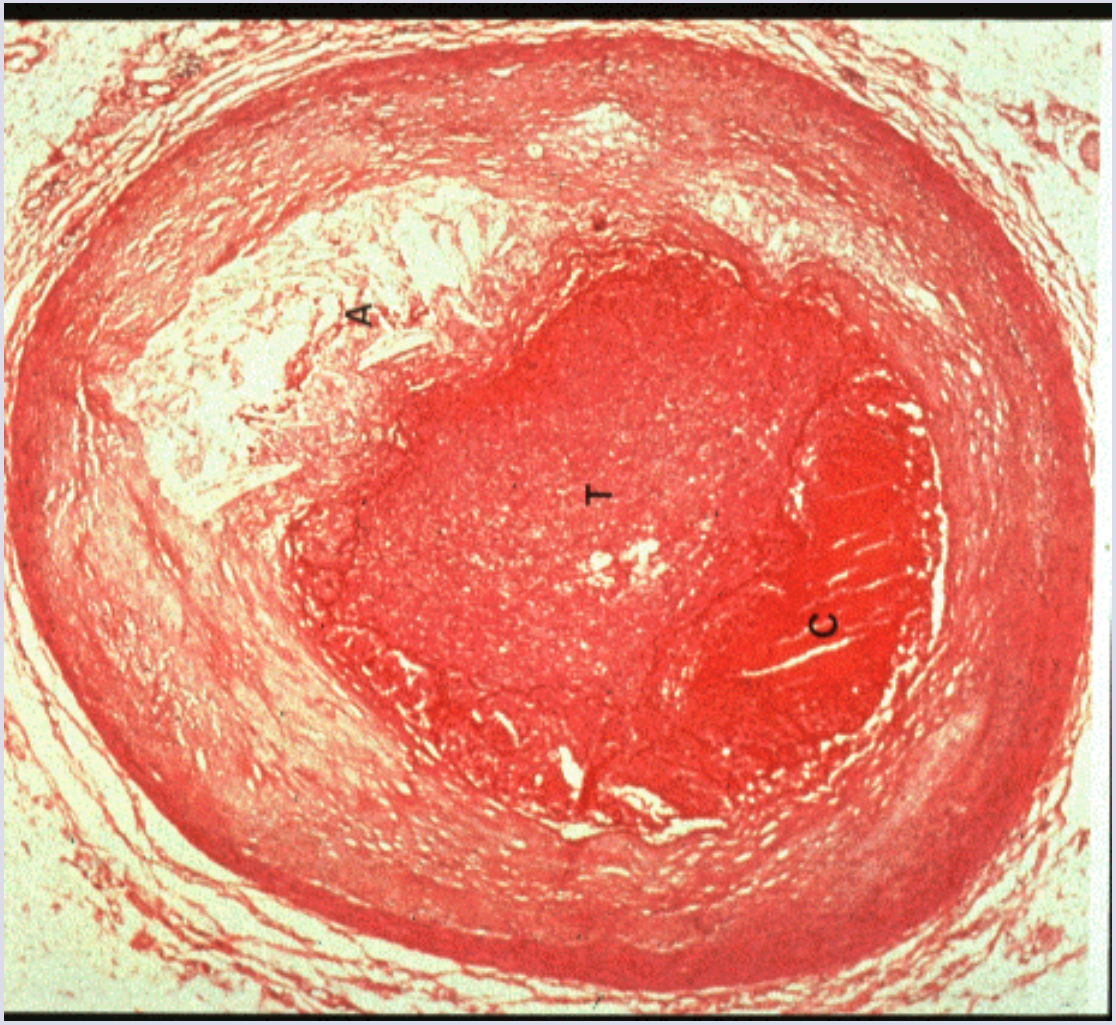
Sudden surge of **sympathetic activity:** an increase in blood pressure, heart rate, force of cardiac contraction, and coronary blood flow

Plaque rupture also has a **diurnal variation**, occurring most frequently during the first hour of arising.
It has been suggested that the sympathetic nervous system is activated on arising, resulting in changes in platelet aggregation and fibrinolytic activity that tend to favor thrombosis. This diurnal variation in plaque rupture can be minimized by β-adrenergic blockers and aspirin

Acute myocardial infarction (AMI)

thrombosis leading to the ***necrosis*** of myocardium

transmural *(Q)*
nontransmural *(nonQ)*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Symptoms

- pain
- vegetative nerves activation (anxiety, sweating, tachycardia)
- atypical (without important pain, abdominal symptoms)
- arrhytmias
- heart failure

Basic diagnostics

Necrosis

- enzymes: CK-MB, AST, LD
- structural proteins: myoglobin, troponin
- reaction to the necrosis: leucocytosis, RBC sedimentation rate

Electrical changes

- ECG: development of the curve
  localisation + infarction extent
- arrhytmias

Size of the necrosis

- extent of the blood flow
- collaterals
- myocardial needs of oxygen (heart rate, wall tension - afterload / systolic BP)
- ischemic preconditioning

Sequelae of the necrosis

- ***hemodynamic*** (disturbances of contractility, decrease of ejection fraction) – large necrosis or repeated infarction - heart failure, if about 40% of myocardium destroyed, *cardiogenic* shock can develop

- ***electrical instability*** – arrhytmias, ventricular fibrillation, sudden death

- ***remodelation*** of the ventricle – scarring, aneurysma (dyskinesis, thrombosis with embolism), dilatation – importance for prognosis

- ***rupture*** of the wall, aneurysma (pericardial tamponade), septum, papillary muscle

Localisation of the necrosis

- ***layer of the wall***: transmurale, subendocardial, intramural

- ***part of the heart***: according to the coronary artery
anterior wall (RIA)
lateral wall (RC)
diaphragmatic (RIP)

Syndrome X

stable AP + normal coronarography
small vessels

CHD TREATEMENT

Primary prevention

Treatment of risk factors

Blood flow through myocardium

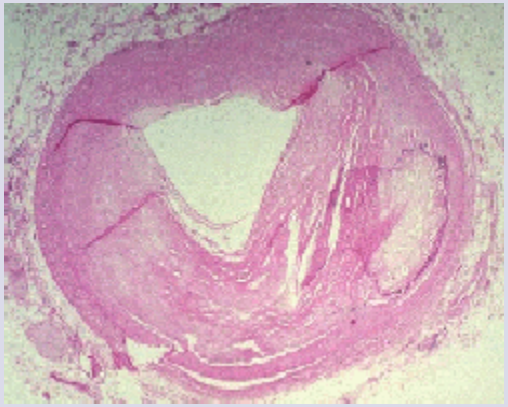
Vessels (calcium antagonists, vasodilatation)
Decrease of oxygen consumption (betalytics)
Coagulation (aspirin...)

Treatment of complications

Revascularization

Fibrinolysis
Percutaneous coronary arteries treatment – angioplastics (PTCA), stent
Bypass
Angiogenetic therapy

Stem cells



The End