Physiological Aspects of Major Cardiovascular Pathologies:

Arterial Hypertension
Ischemic Heart Disease

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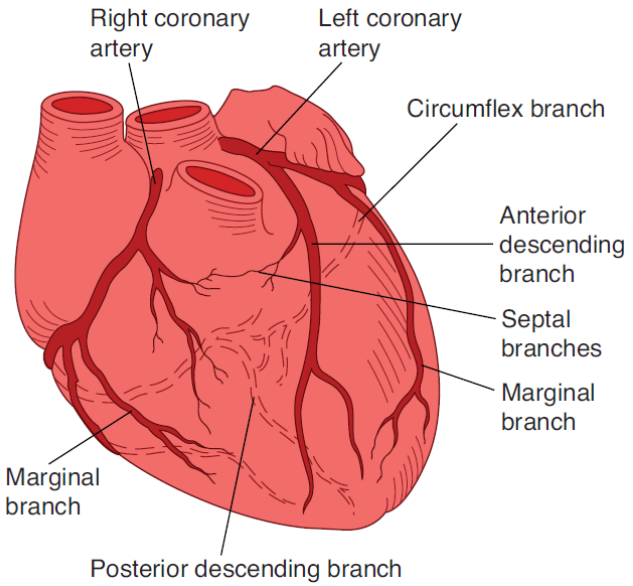
Ischemic Heart Disease

Coronary Circulation

- *a. cor. sinistra* (85%)
- *a. cor. dextra*



- epicardial coronary arteries
- intramuscular arteries
- plexus of subendocardial arteries

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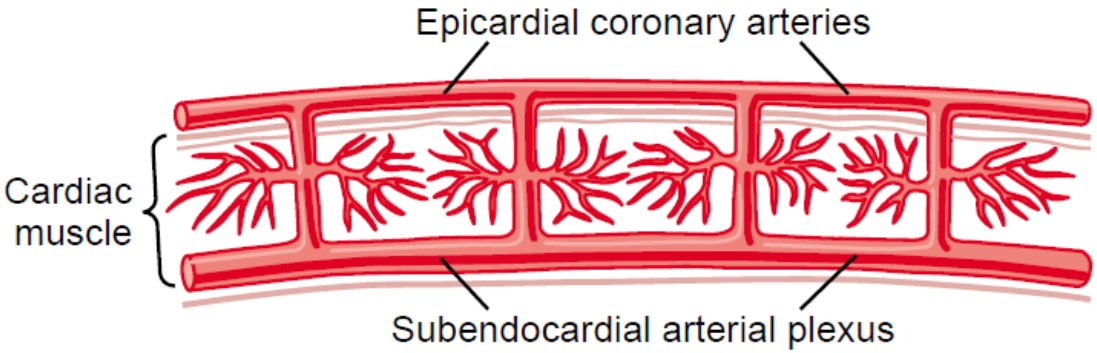


Guyton and Hall. Textbook of Medical Physiology, 11th edition

Coronary Circulation

- **the resting blood flow:** 225 ml/min (4-5% of CO)
- **increases at physical exertion, mental stress, …**

- O_2 extraction is almost maximal already at rest, capillaries are open

↓

- The only possibility how to increase O_2 supply is the coronary vasodilation!
- **metabolic vasodilation**, sympathicus/parasympathicus

Coronary Reserve

- ability of coronary vessels to adapt blood flow to the actual cardiac work (**ergometry**)
- **the maximal blood flow / the resting blood flow**
- reduction of the coronary reserve:
  - relative coronary insufficiency
    (too high resting demands, high resting blood flow cannot be sufficiently increased)
  - absolute coronary insufficiency (~ ischemic heart disease)
    (the stenotic arteriosclerotic process)

Reduced coronary reserve is a limiting factor of the cardiac output, thus, also of the effort of organism!

Ischemic Heart Disease

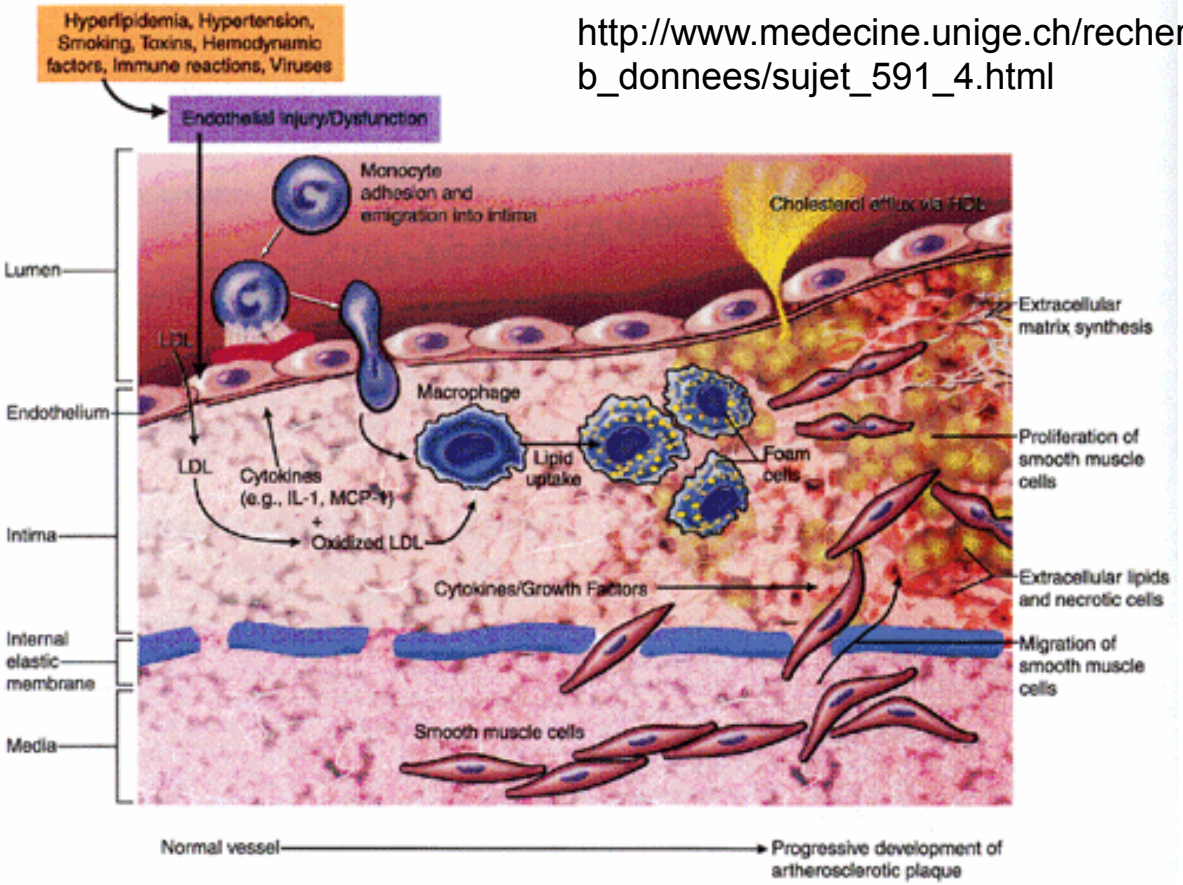
= ischemic heart disease, coronary artery disease

- the most often cardiac disease in Western culture
- about 1/3 of all deaths
- *vs.* myocardial ischemia (a more general term; anaemia, hypotension, myocardial hypertrophy, thyreotoxicosis)
- causes of death:
  - acute coronary occlusion
  - ventricular fibrillation
  - slow, progressive weekening of contractility due to slowly increasing myocardial ischemia
    (the most often cause of the congestive heart failure)

Ischemic Heart Disease

- pathogenesis: atherosclerotic process of one or more branches of the coronary circulation

http://www.medecine.unige.ch/recherche/groupes/b_donnees/sujet_591_4.html



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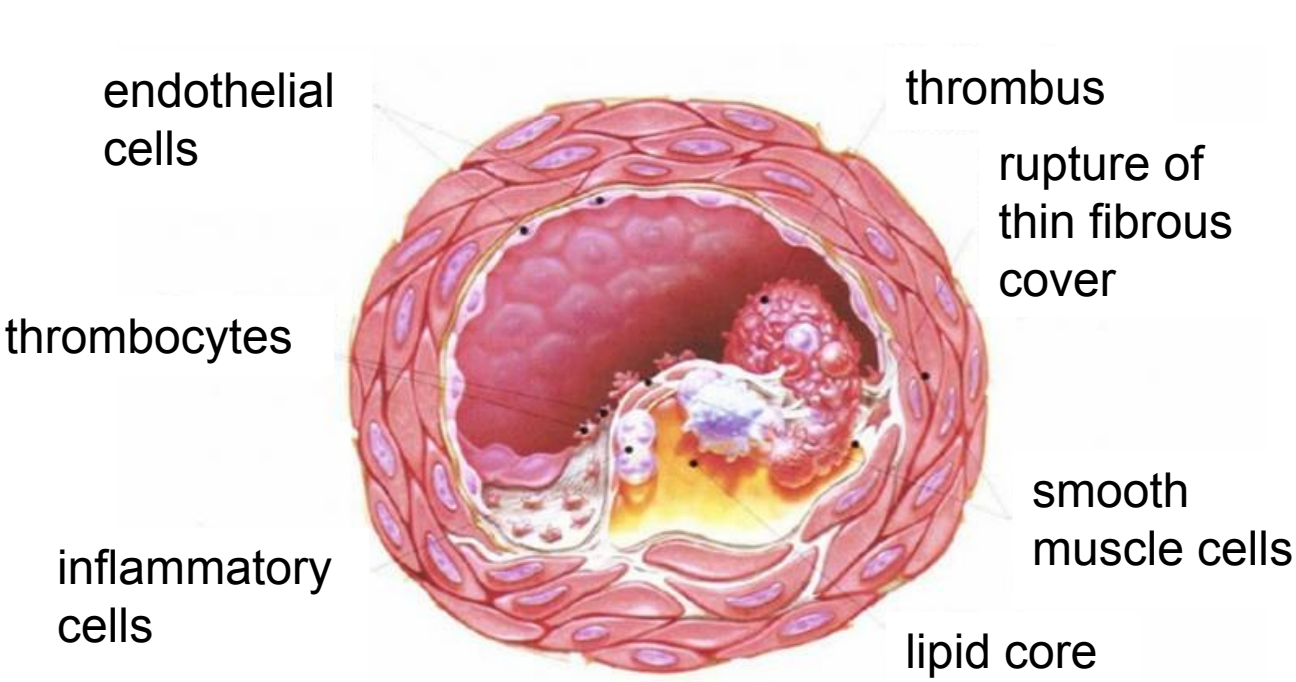
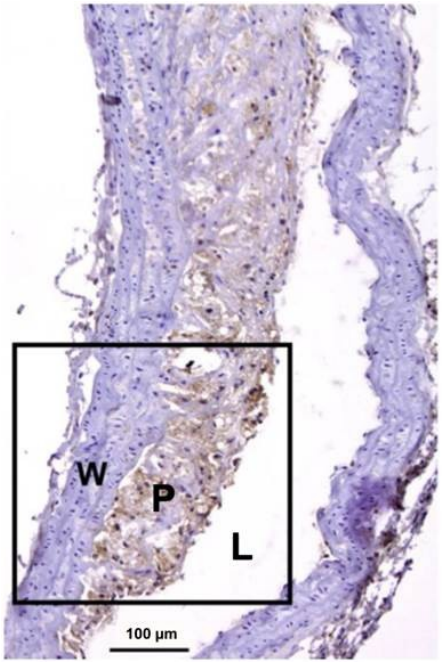




http://www.thno.org/v03p0894.htm

http://int2.lf1.cuni.cz/pruvodce-pro-pacienty-pred-katetrizacnim-vysetrenim-srdce

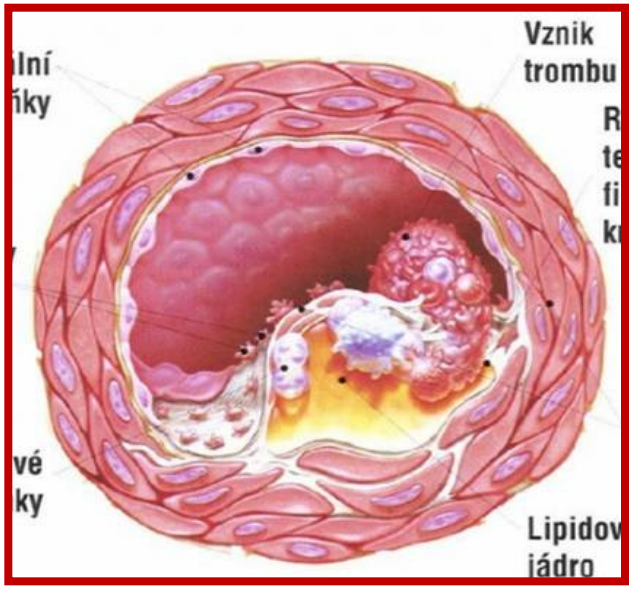
Ischemic Heart Disease

- pathogenesis: atherosclerotic process of one or more branches of the coronary circulation
- symptoms
  (always when blood inflow demands exceed the capacity of stenotic artery):
  - pain behind the sternum (*angina pectoris*)
  - changes of ST segment and T wave on ECG due to sooner repolarization in the ischemic myocardial region, usually in the subendocardium

Symptoms are usually provoked by physical exertion, cold, rapid increase of the blood pressure, etc.

Ischemic Heart Disease

- pathogenesis: atherosclerotic process of one or more branches of the coronary circulation
- **acute coronary occlusion** due to:
  - thrombus (rupture of the plaque)
  - embolus
  - local muscular spasm



Ischemic Heart Disease

- pathogenesis: atherosclerotic process of one or more branches of the coronary circulation
- **acute coronary occlusion** due to:
  - thrombus (rupture of the plaque)
  - embolus
  - local muscular spasm

The degree of damage of the heart muscle is determined to a great extent by the degree of collateral circulation!

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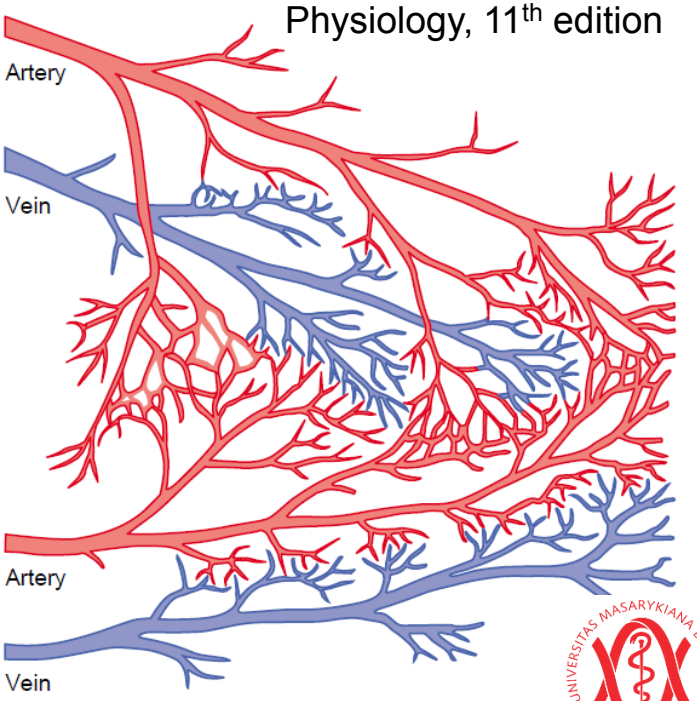
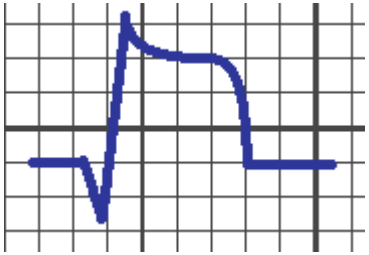


Ischemic Heart Disease

- **Myocardial infarction**

  = sudden closure of a coronary branch, usually by a thrombus originating on the strength of a rupture of the atherosclerotic plate, changes are irreversible

  - <u>symptoms</u>:
    - severe unremitting pain behind sternum
    - heart failure (in the case of a bigger extent)
    - on ECG: ST elevation followed by T wave without any decrease to the isoelectric line (the Pardee s sign)

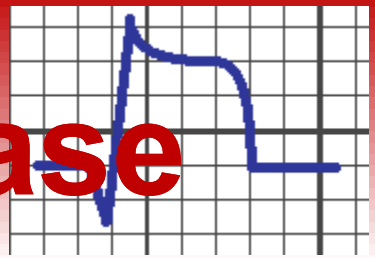


http://www.wikiskripta.eu/index.php/Popis_EKG

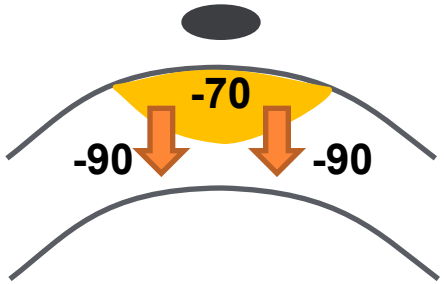
  - healing by a scar

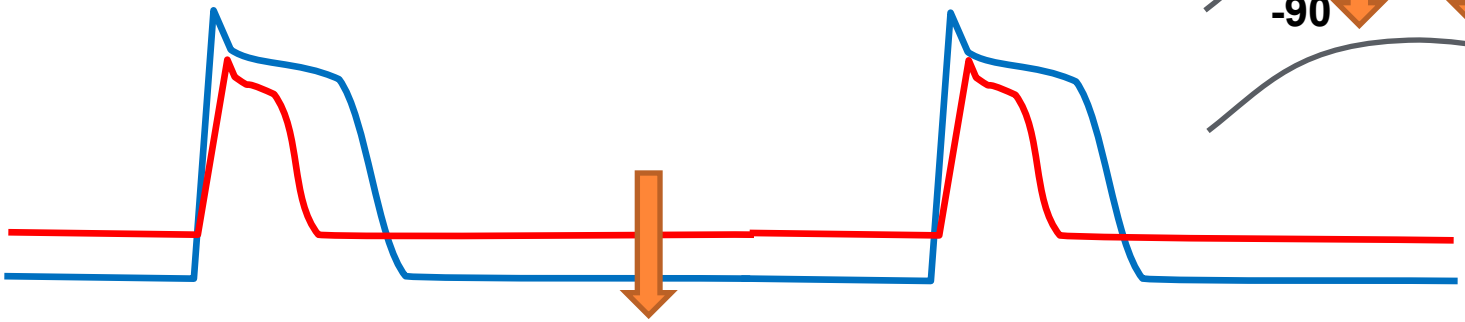
    (a sign of non-conductive tissue remains on ECG – a deep Q wave)

Ischemic Heart Disease

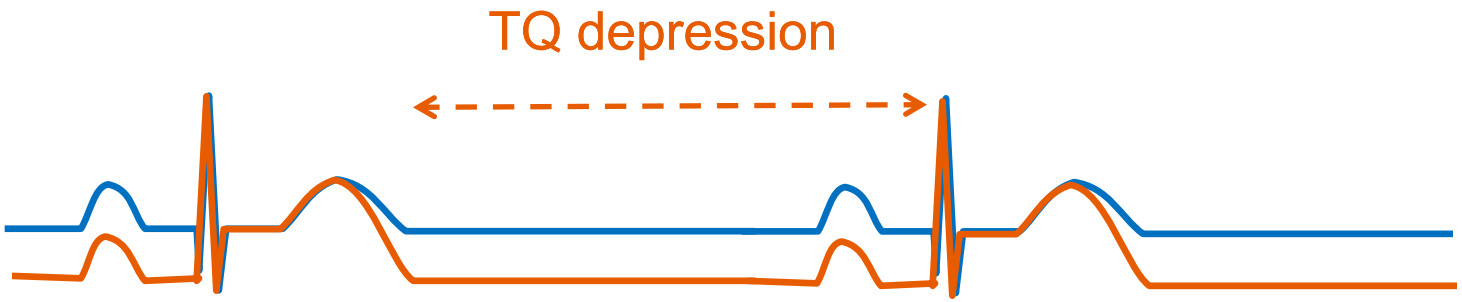


- **Myocardial infarction**





- TQ depression due to depolarization of RMP (accumulation of K^+ in ECT)



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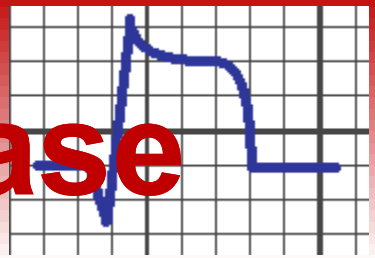
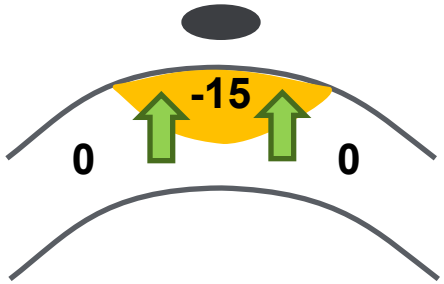
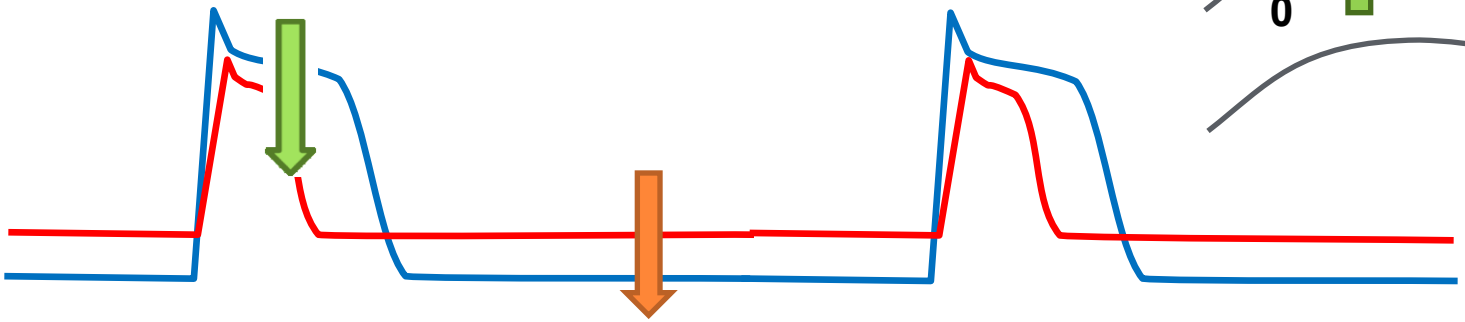
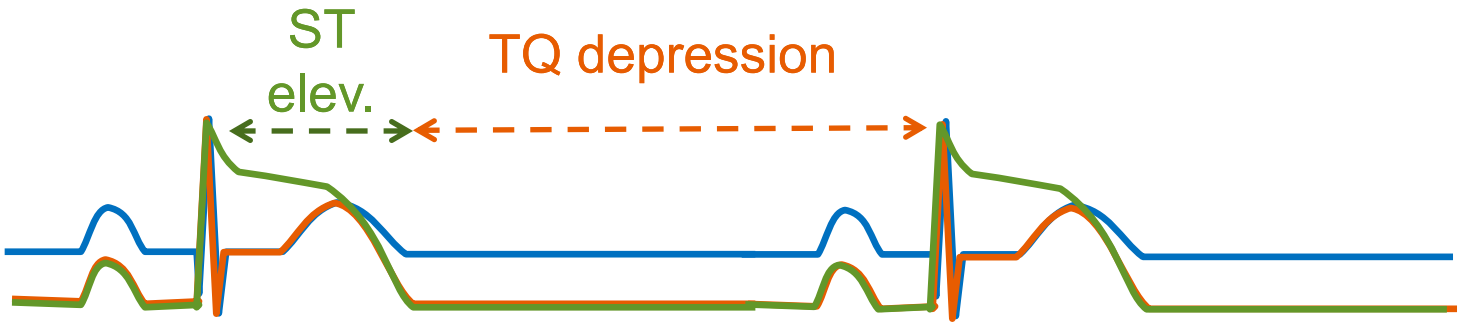


- **Myocardial infarction**





- TQ depression due to depolarization of RMP (accumulation of K^+ in ECT)
- ST elevation due to shortening of AP and delayed depolarization



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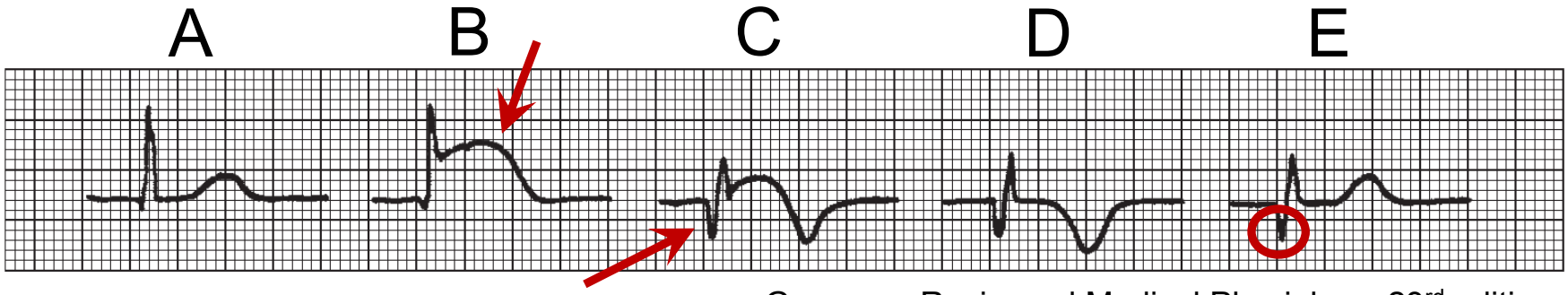

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A. Physiological tracing in lead I
B. Myocardial infarction – acute phase – hours from infarction.
C. Many hours till days from infarction.
D. Late pattern - many days till weeks from infarction.
E. Very late pattern – months till years from infarction.

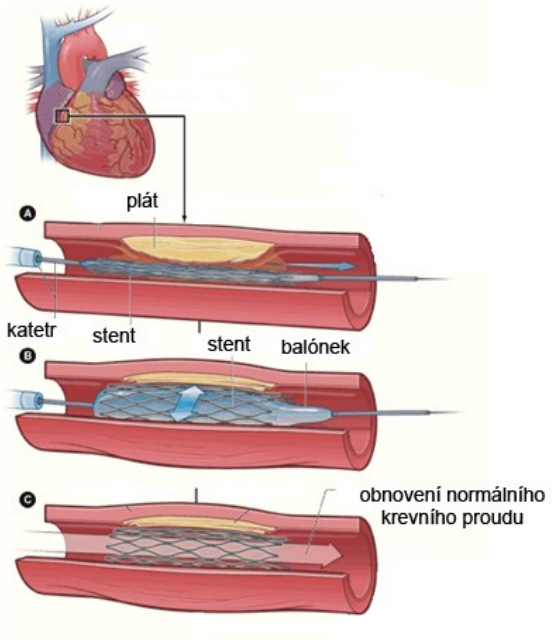
Ischemic Heart Disease

- **Treatment with drugs**
  - Vasodilatory drugs (nitroglycerine, other nitrate drugs)
  - Beta-blockers (propranolol)

Ischemic Heart Disease

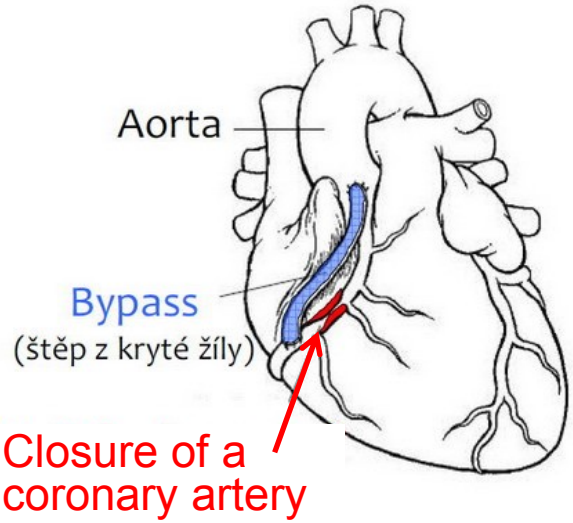
- **Surgical treatment**

Coronary Angioplasty

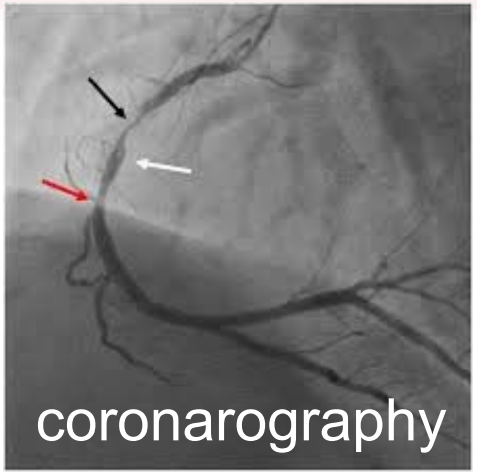


http://www.ikem.cz/www?docid=1005912

Aortic-Coronary Bypass



http://www.sedmstatecnych.cz/clanek/opravene-srdce-po-trech-letech/



Arterial Hypertension

Definition and Consequences

Arterial hypertension - chronic increase of the systemic blood pressure.

Symptoms indistinctive and nonspecific in the first stages of hypertension most 50% of the hypertensive patients do not know about their hypertension!

If not diagnosed in time and adequately treated, arterial hypertension results in:

- overload of the left ventricle (hypertrophy, heart failure)
- arteriosclerosis
  - increased risk of the myocardial infarction
  - increased risk of the stroke
  - the renal failure, etc.

Hypertension significantly shortens the life span.

Definition and Consequences

Arterial hypertension - chronic increase of the systemic blood pressure.

Table 1 Definitions and classification of blood pressure (BP) levels (mmHg)

Category	Systolic		Diastolic
Optimal	<120	and	<80
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Grade 1 hypertension	140–159	and/or	90–99
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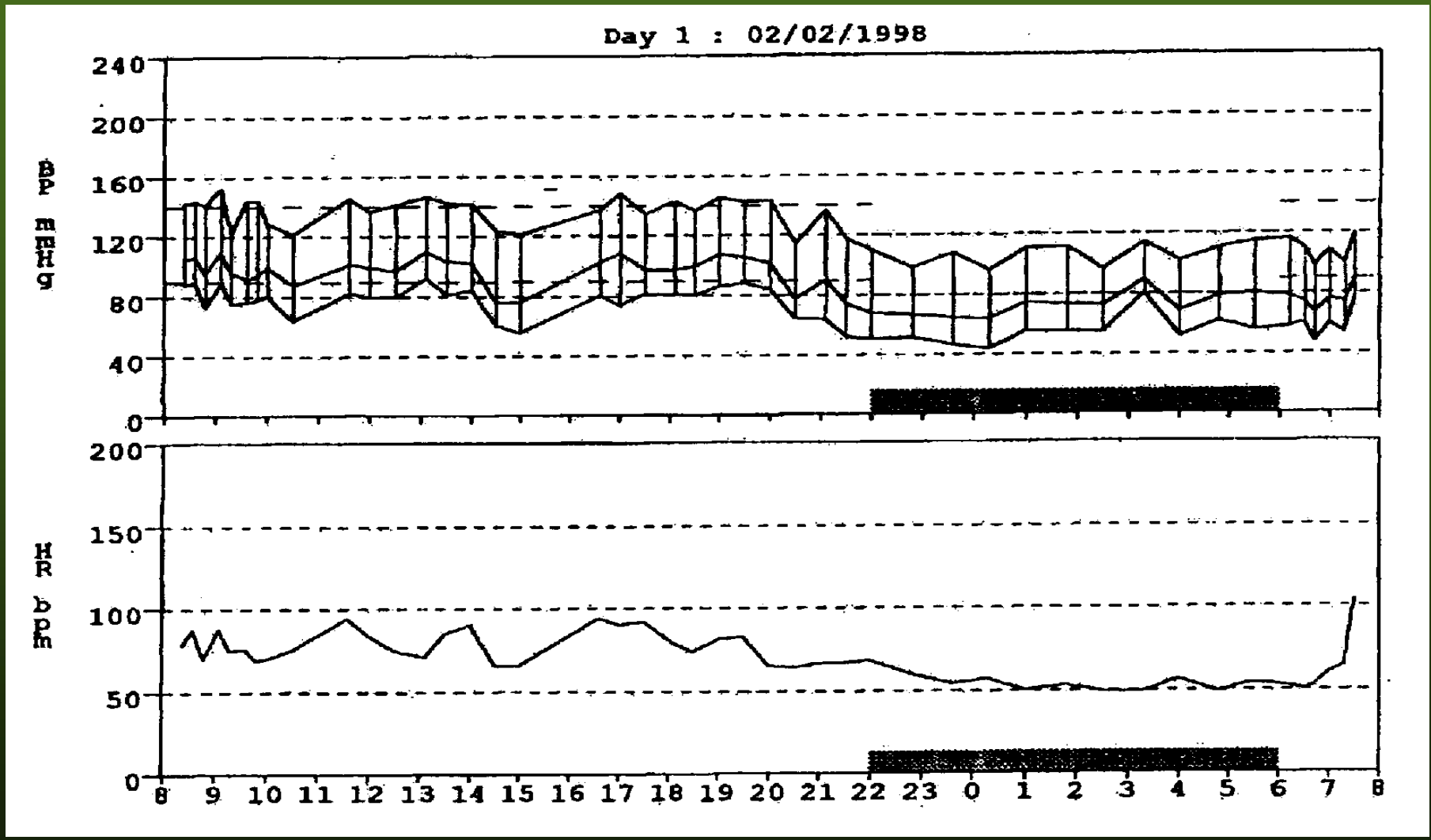
Grade 3 hypertension	≥180	and/or	≥110
Isolated systolic hypertension	≥140	and	<90

Guidelines for the management of arterial hypertension. Eur Heart J 2007;28:1462-1536.

24-hours Monitoring of Blood Pressure



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prehypertension

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Definition and Consequences

Stratification of cardiovascular risk

Other risk factors, OD or Disease	Blood pressure (mmHg)				
	Normal SBP 120–129 or DBP 80–84	High normal SBP 130–139 or DBP 85–89	Grade 1 HT SBP 140–159 or DBP 90–99	Grade 2 HT SBP 160–179 or DBP 100–109	Grade 3 HT SBP ≥180 or DBP ≥110
No other risk factors	Average risk	Average risk	Low added risk	Moderate added risk	High added risk
1–2 risk factors	Low added risk	Low added risk	Moderate added risk	Moderate added risk	Very high added risk
3 or more risk factors, MS, OD or Diabetes	Moderate added risk	High added risk	High added risk	High added risk	Very high added risk
Established CV or renal disease	Very high added risk	Very high added risk	Very high added risk	Very high added risk	Very high added risk

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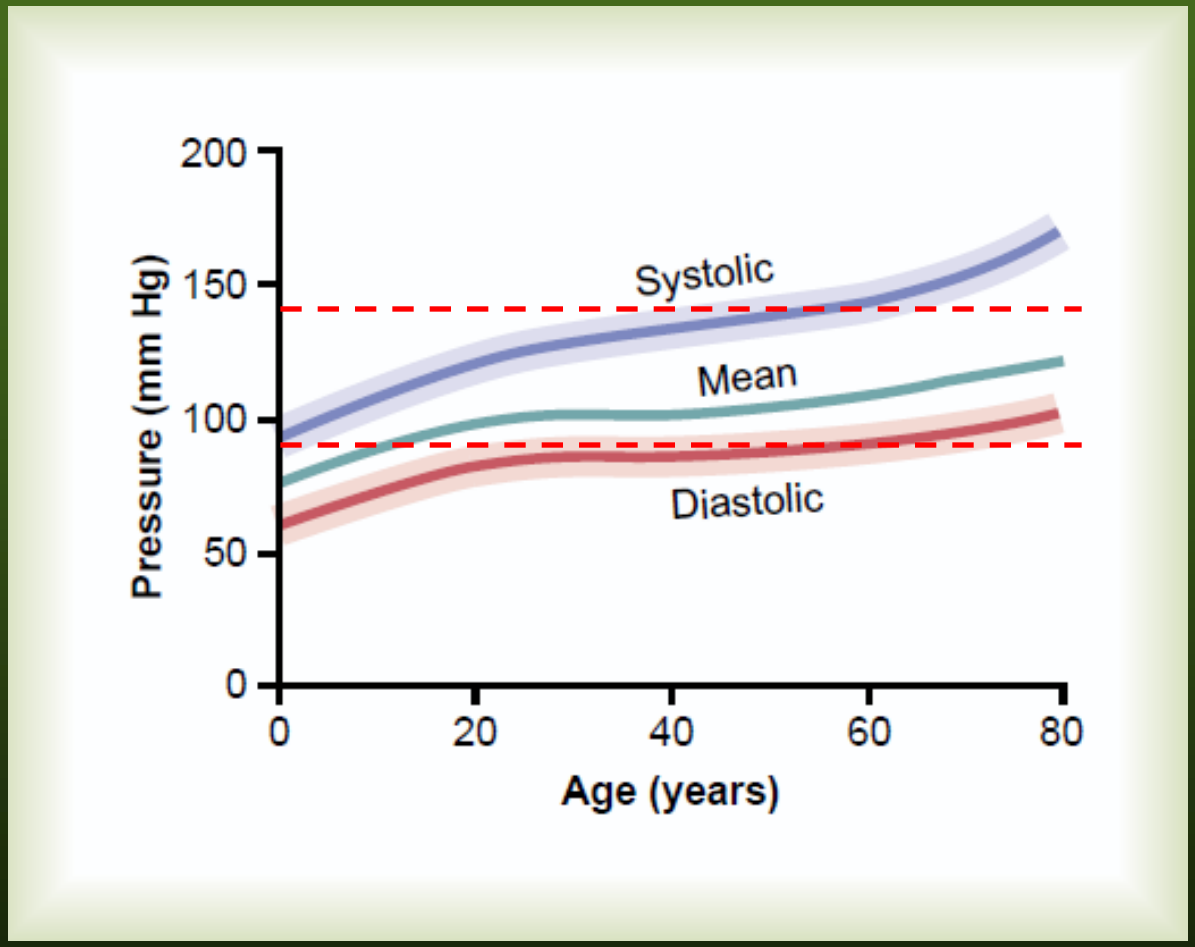
Definition and Consequences



in children and adolescents – special percentile tables

Factors Determining Blood Pressure

Ohm´s law

$U = I \cdot R \longrightarrow$ **$P = CO \cdot TPR$**

P	arterial pressure
CO	cardiac output
TPR	total peripheral resistance

- ↑ cardiac output (usually due to ↑ extracellular fluid)
  → volume-loading (hyperdynamic) hypertension
- ↑ total peripheral resistance
  → resistance hypertension

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- ↑ total peripheral resistance
  → resistance hypertension
- ↓ compliance → isolated systolic hypertension

$C = \Delta V / \Delta P$

heart

CO = SV . HR

HR is guided by sympathetic and parasympathetic system

SV depends on:

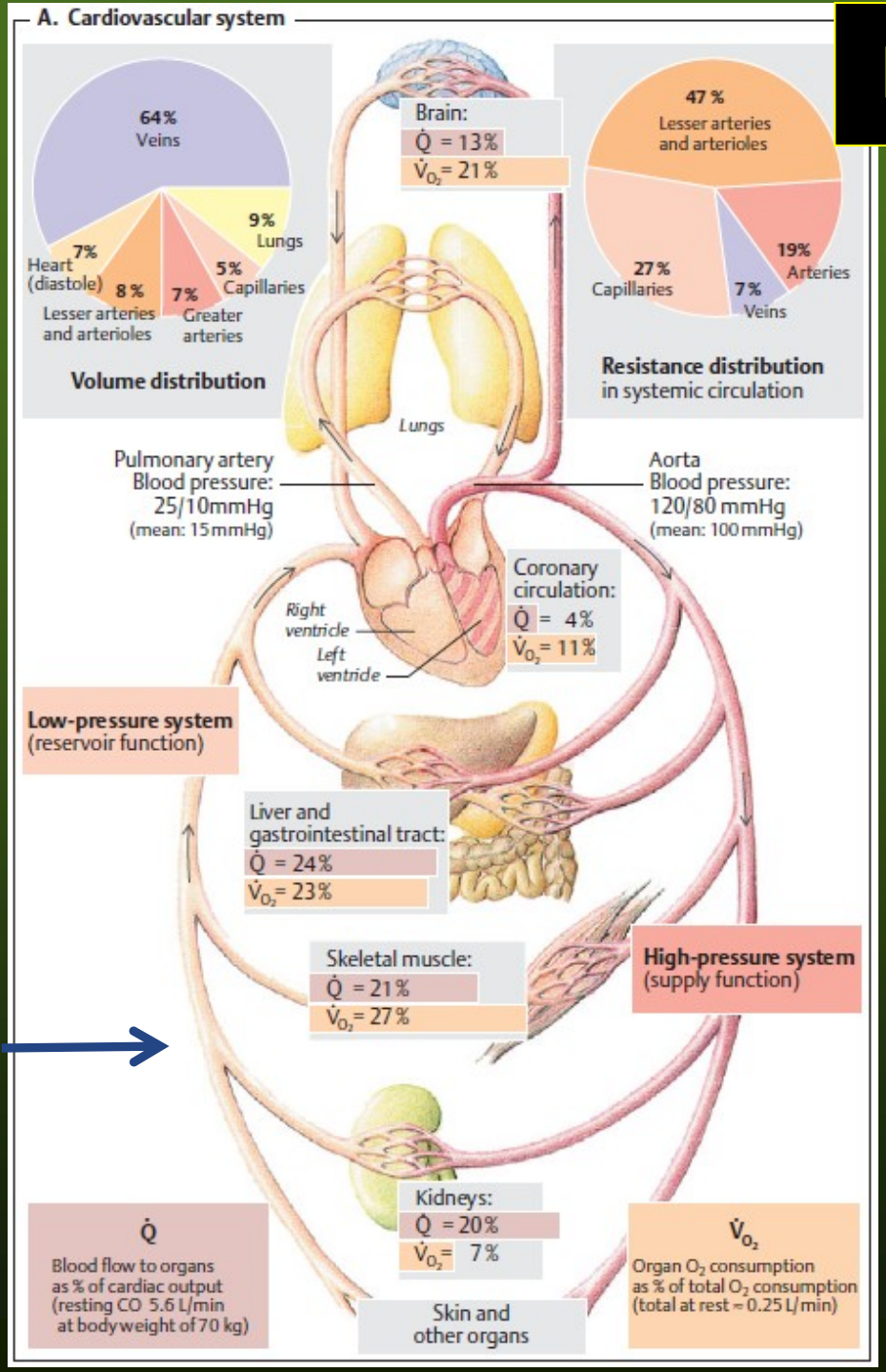
1.venous return (blood volume, tonus of veins)

2.contractility

3.peripheral pressure

veins

blood reservoire



P = CO . TPR

kidneys

regulation of blood volume

heart

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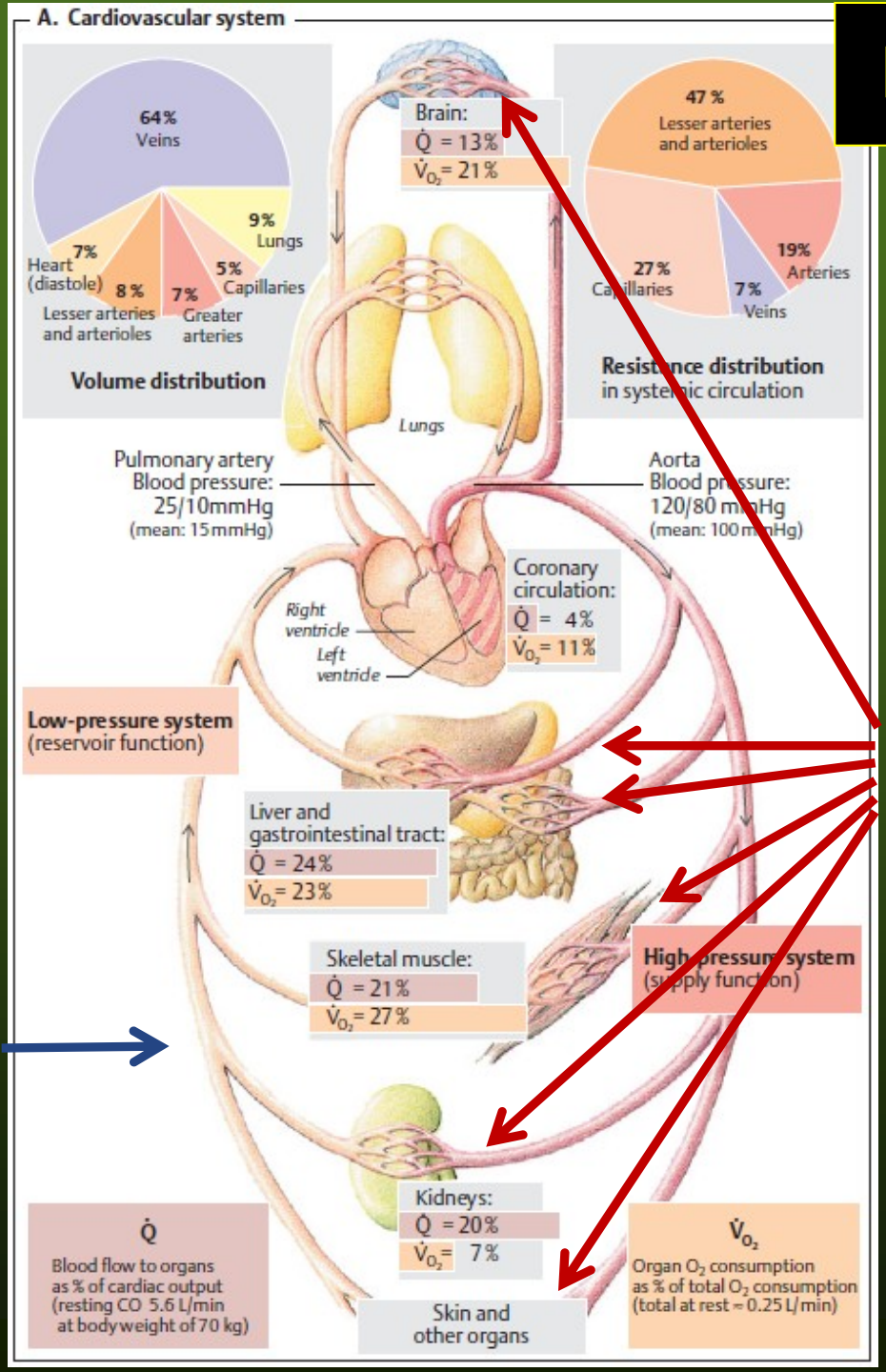


P = CO . TPR

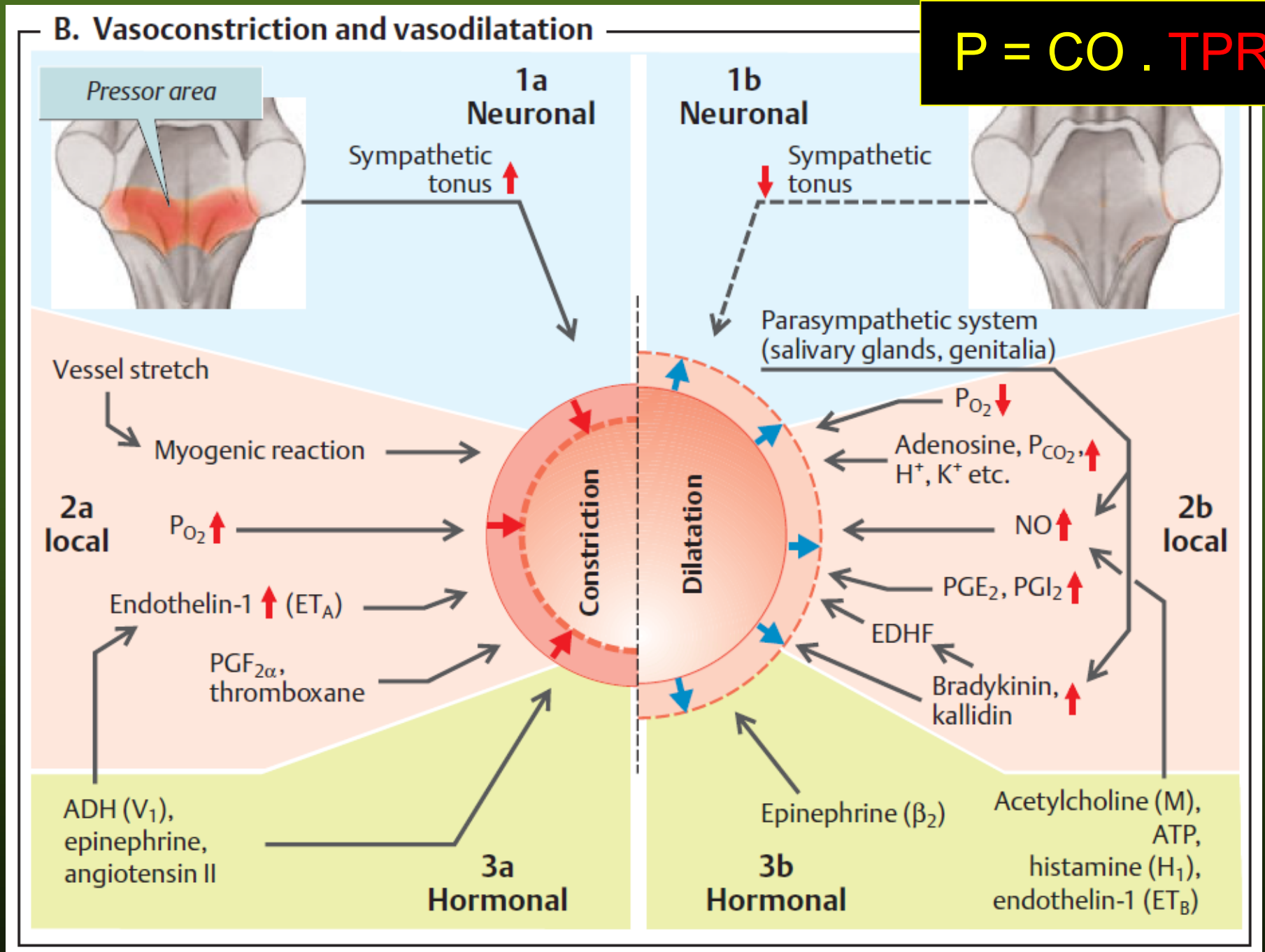
arterioles

regulation of TPR

kidneys

regulation of blood volume

also TPR (RAS)



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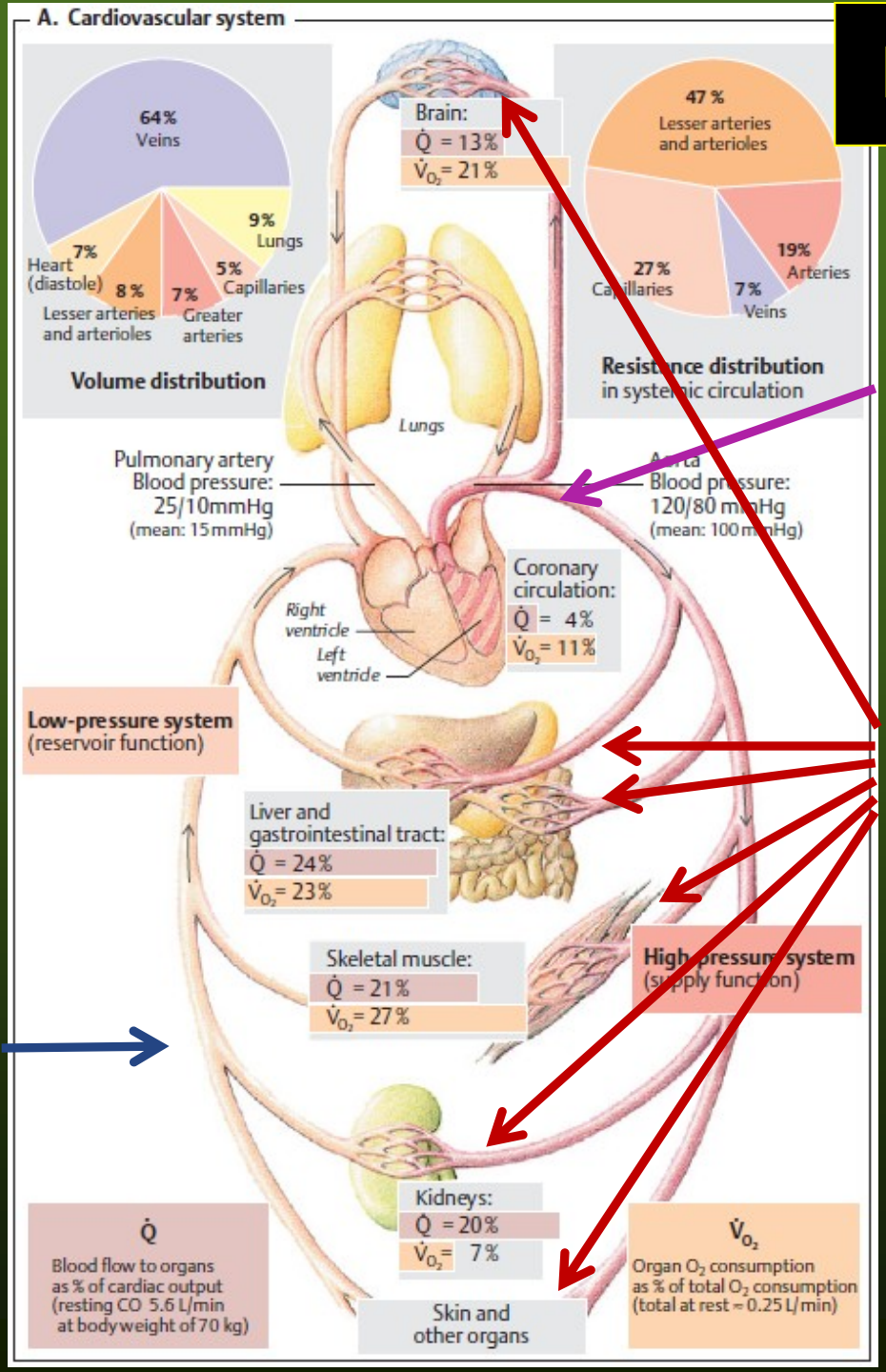


P = CO . TPR

aorta and big elastic arteries

compliance

arterioles

regulation of TPR

kidneys

regulation of blood volume, also TPR (RAS)

heart

CO = SV . HR

HR is guided by sympathetic and parasympathetic

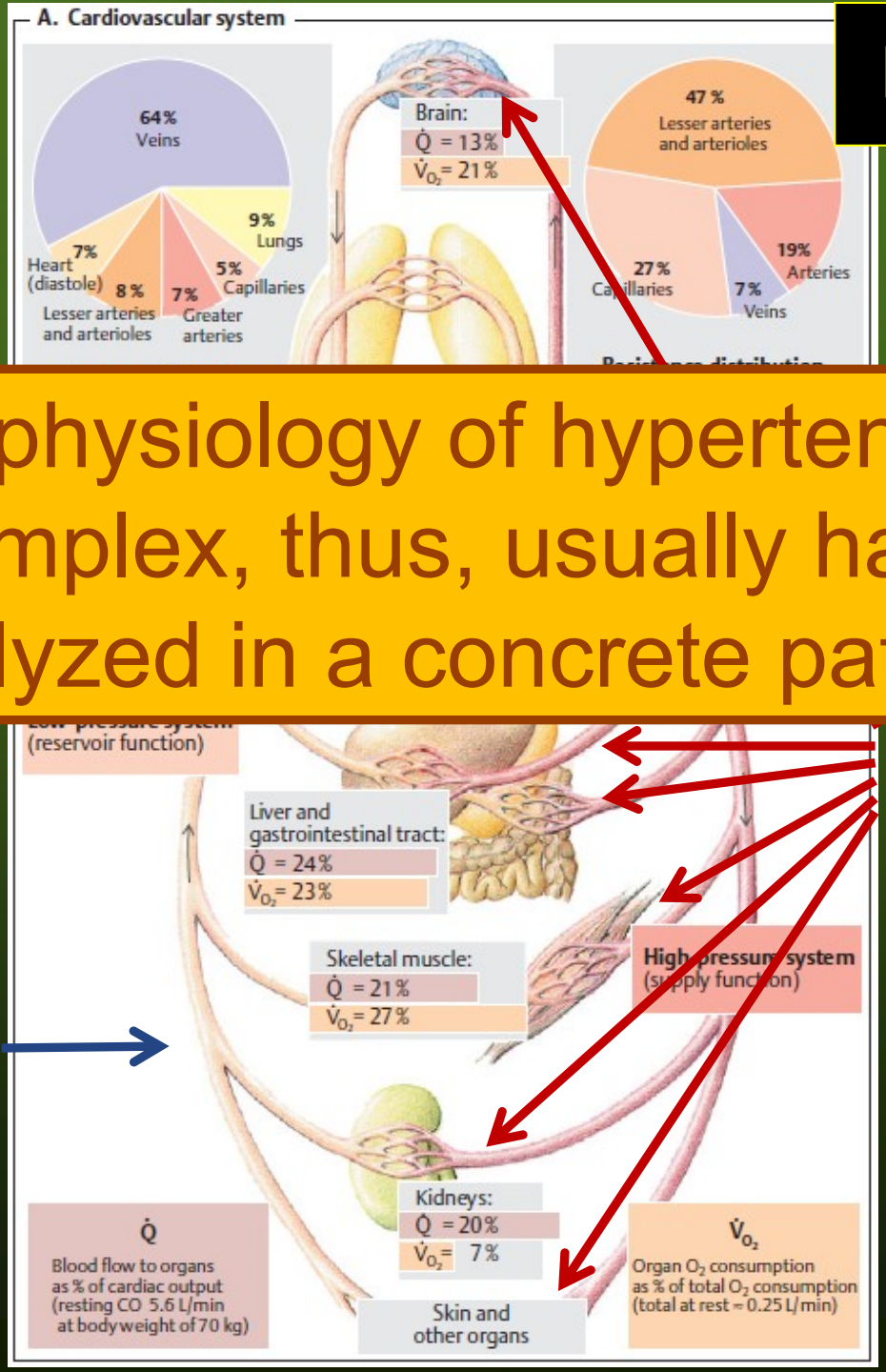
SV

2.contractility

3.peripheral pressure

veins

blood reservoire



P = CO . TPR

aorta and big

s

arterioles

regulation of TPR

regulation of blood volume:

- kidneys
- thirst
- ADH

Pathophysiology of hypertension is very complex, thus, usually hard to be analyzed in a concrete patient!

Classification

A. Essential (primary) hypertension

- „hypertension of an unknown origin“
- 90 – 95%

B. Secondary (symptomatic) hypertension

- symptom of another primary disease with identifiable cause

Essential Hypertension

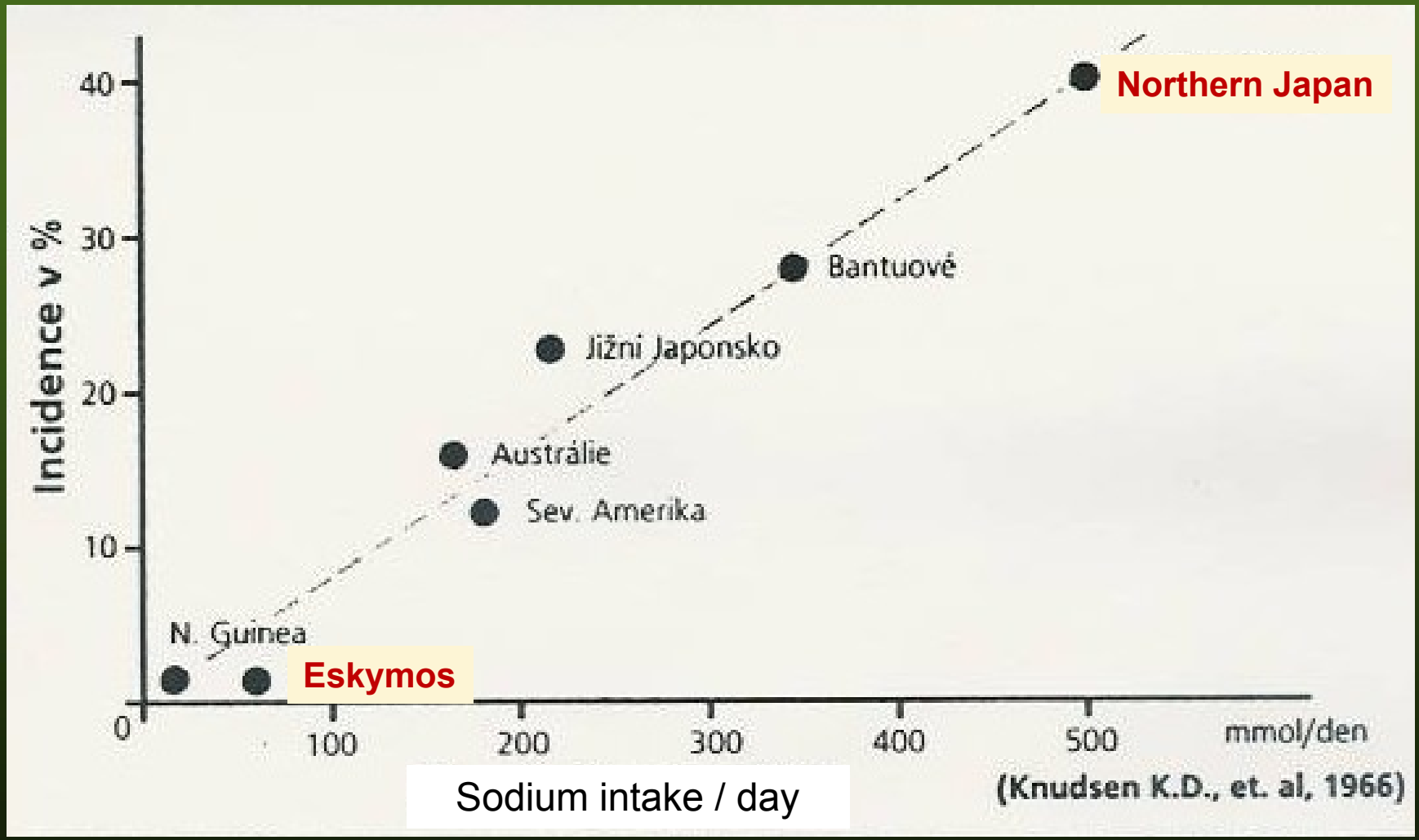
- strong hereditary tendency in some patients
  (polygenic ground – genetic defects, often polymorphisms, causing abnormality/ies in a factor regulating the blood pressure)

- provoking factors:
  - excess weight gain, obesity – account for about 65-70% of the risk for developing of essential hypertension
  - sedentary lifestyle

  New clinical guidelines recommend increased physical activity and weight loss as the first step in treating most patients with the essential hypertension.

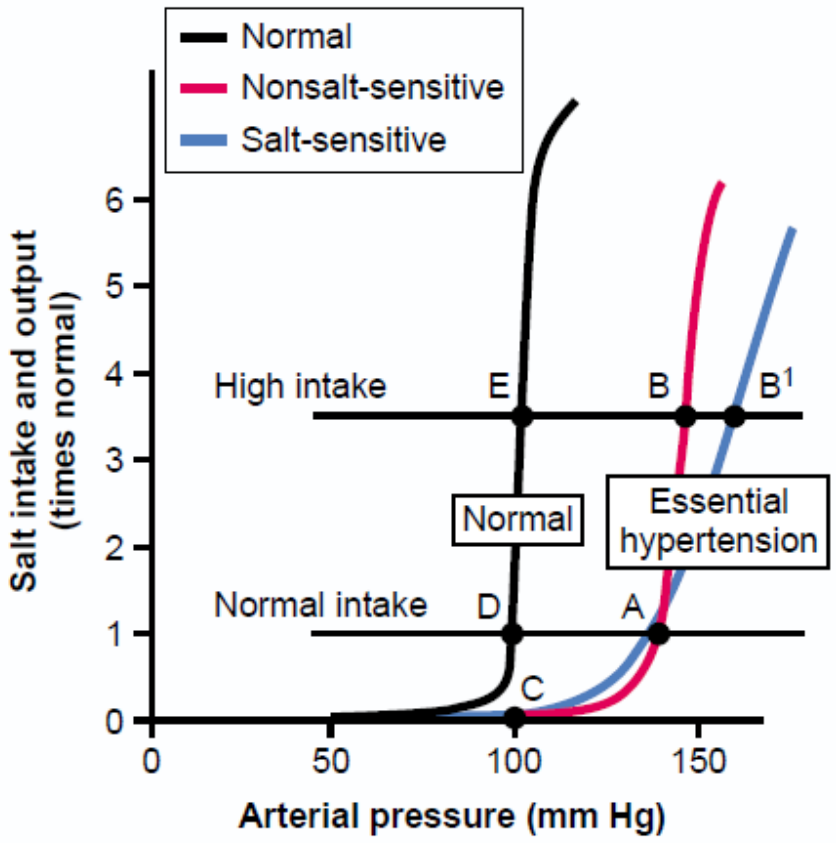
  - stress (namely mental)
  - excessive sodium intake (interpopulation studies – Eskimos *vs.* people living in the North Japan)

Essential Hypertension



Essential Hypertension

Sodium-loading renal function curves



Increased salt intake

↓

Increased extracellular volume

↓

Increased arterial pressure

↓

Decreased renin and angiotensin

↓

Decreased renal retention of salt and water

↓

Return of extracellular volume almost to normal

↓

Return of arterial pressure almost to normal

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Essential Hypertension

Isolated Systolic Hypertension

- ↑ systolic and pulse pressure
- in the elderly
- due to:
  - age-dependent remodelling of the wall of elastic arteries (less elastic and more collagen fibres)

    → ↑ stiffness, ~↓ compliance:

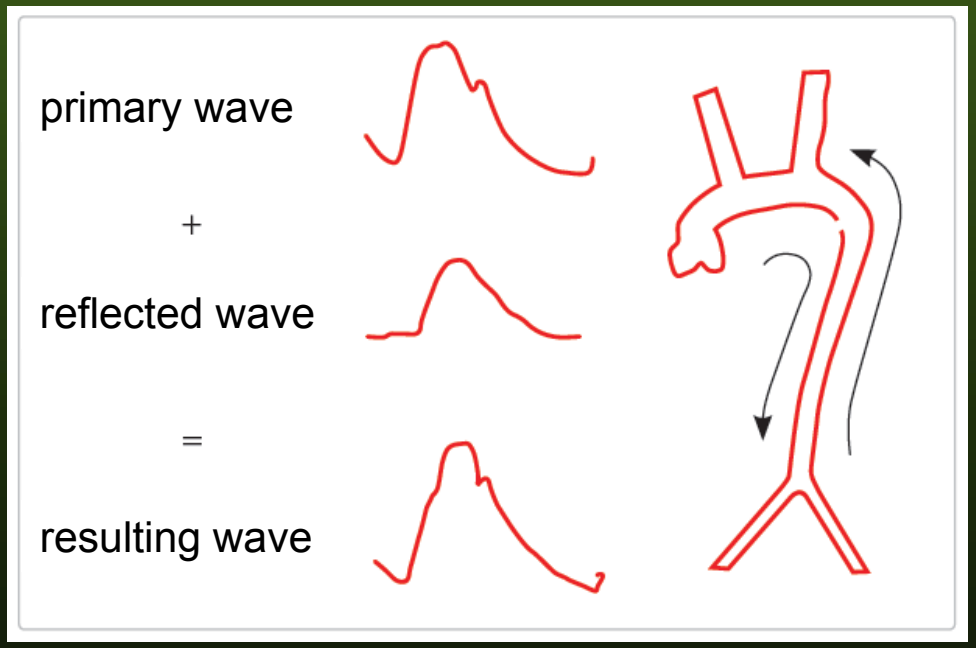
    1. → ↓ distension of elastic arteries during the systole (physiologically accommodating the expansion of the volume after ejection of blood from the heart) eeply ↑ arterial systolic pressure + ↓ blood volume (and also pressure) in arteries during the diastole

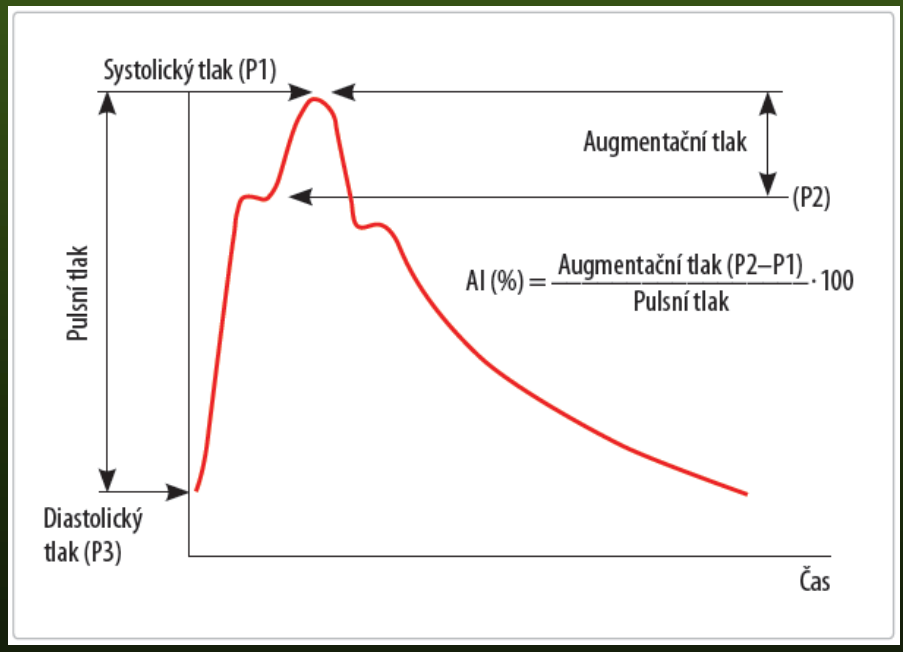
    2. → ↑ pulse wave velocity

Essential Hypertension

Isolated Systolic Hypertension

↑ pulse wave velocity [redacted]e secondary, reflected pulse wave comes back to the aorta and elastic arteries sooner and, thus, superimposes on the primary pulse wave still during the systolic phase [redacted] systolic pressure and may even ↓ diastolic pressure





Rosa J, Widimský J jr. **Charakteristika velkých tepen u arteriální hypertenze.** *Cor Vasa 2011;53:418–422.*

Essential Hypertension

Isolated Systolic Hypertension

- ↑ systolic and pulse pressure
- in the elderly
- due to:
  - age-dependent remodelling of the wall of elastic arteries
    (less elastic and more collagen fibres)
  - endothelial dysfunction
    (↑ reactivity on vasoconstrictive mediators, namely the local ones as endothelins, thromboxane A2, …)

Essential Hypertension

Treatment

New clinical guidelines recommend increased physical activity and weight loss as the first step in treating most patients with EH.

Decrease of sodium and increase of potassium intake, relaxation ...

$P = CO \cdot TPR$

- ❖ vasodilatory drugs
  - ↓ TPR, some of them ↑ renal blood flow as well (ACEI)
  a. by inhibiting sympathetic nervous system (sympatolytics)
  b. by directly paralyzing the smooth muscle of the renal vasculature (vasodilatory agents or calcium channel blockers)
  c. by blocking action of the renin-angiotensin system on the renal blood vessels or tubules (inhibitors of angiotensin I-converting enzyme, ACEI)
- ❖ natriuretic (diuretic) drugs
  - ↓ renal tubular reabsorption of salt and water ↓ CO
  (by blocking the active transport of sodium through the tubular wall)

Classification

A. Essential (primary) hypertension
   - „hypertension of an unknown origin“
   - 90 – 95%

B. Secondary (symptomatic) hypertension
   - symptom of another primary disease with identifiable cause

Secondary Hypertension

1. Renal hypertension
   - Prerenal causes - Renovascular hypertension
   - Acute and chronic diseases of the renal parenchyma
   - Postrenal causes (renal vein trombosis, urinary tract obstruction)
   - Renin-producing renal tumor
2. Endocrine hypertension
   - Adrenocortical hyperfunction (Cushing´s, Conn´s, adrenogenital sy)
   - Sympatoadrenal hyperfunction (pheochromocytoma)
   - Exogenic hormones (gluko-, mineralocorticoids, sympatomimetics)
   - Hyperthyroidism
   - Acromegaly
3. Coarctation of the aorta
4. Hypertension in preeklampsia
5. Neurogenic hypertension

Secondary hypertension

Renal hypertension

- *circulus vitiosus* in some cases (renal disease can cause hypertension and hypertension can again cause injury to the glomeruli and renal blood vessels)
- hypertensive kidney diseases
  a. lesions ↓ GFR (due to ↑ renal vascular resistance – renovascular hypertension - or ↓ glomerular capillary filtration coefficient – e.g. chronic glomerulonephritis causing thickening of the membranes)
  b. lesions ↑ tubular reabsorption of sodium (hyperaldosteronism)
  c. patchy renal damage causing local ischemia (e.g. local arteriosclerosis; changes similar to „two-kidney“ Goldblatt hypertension)

Once hypertension develops, GFR and urinary excretion rate return to the physiological values (pressure natriuresis and diuresis).

- non-hypertensive kidney diseases (loss of whole nephrons)

Secondary hypertension

Renovascular hypertension

- experimental „two-kidneys“ Goldblatt hypertension (arteficial constriction of one renal artery, the second kidney preserved)

  (in clinics – e.g. stenosis of one renal artery due to atherosclerosis in the elderly or fibromuscular dysplasia in younger patients)

↓ blood pressure in the kidney on the side of constriction

1. → ↓ GFR → retention of salt and water in the ischemic kidney
2. → ↑ secretion of renin in the ischemic kidney angiotensin II vasoconstriction + retention of salt and water also in the second, healthy kidney

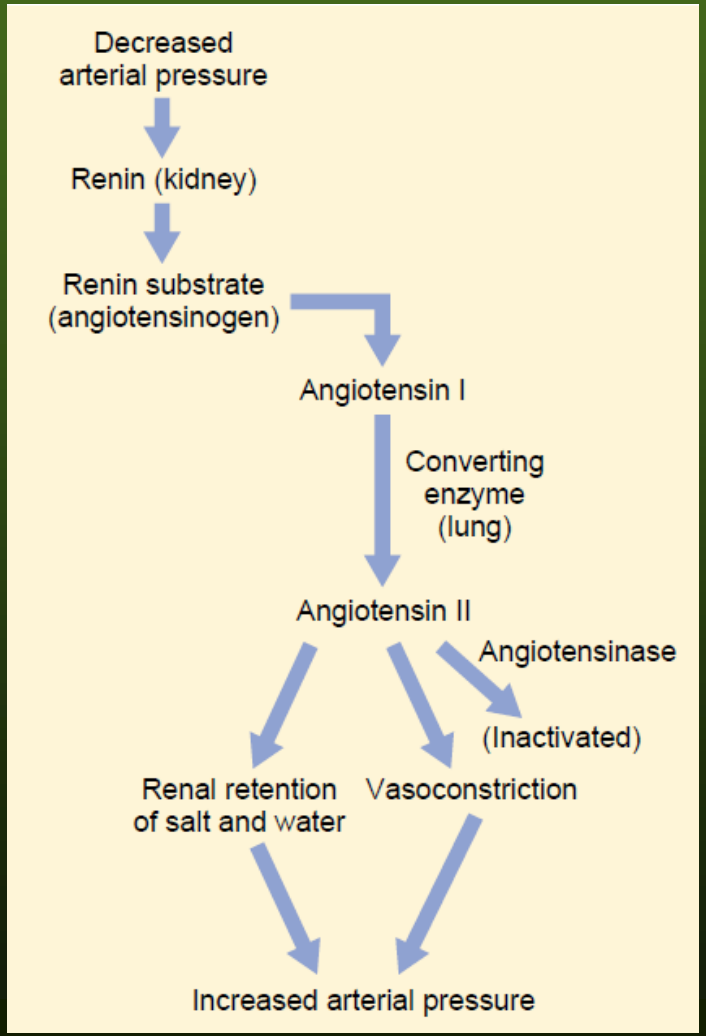
Secondary hypertension

Renin-producing renal tumor (primary hyperreninism)

- benign tumor
  from the juxtaglomerular cells
- severe hypertension

↑ secretion of renin → ↑ angiotensin II →

1. vasoconstriction (seconds) → ↑ TPR
2. retention of salt and water (days) → ↑ CO



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Secondary hypertension

Adrenocortical hyperfunction (Cushing´s, Conn´s, adrenogenital sy)

Conn´s syndrome
(primary hyperaldosteronism)

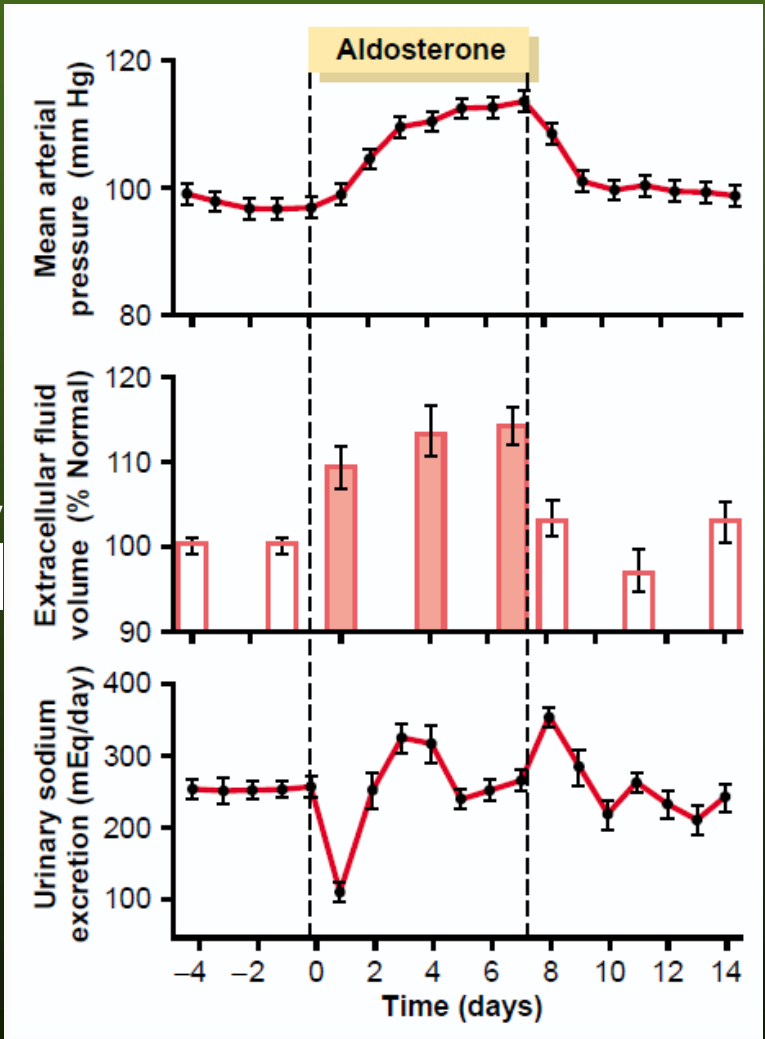
- unilateral aldosterone-producing adenoma (less often carcinoma)
- bilateral hyperplasia of *zona glomerulosa*

→ ↑ absorption of sodium

→ osmotic absorption of water (eventually ↑ water intake) → extracellular fluid → CO → hypertension → pressure natriuresis/diuresis + ↓ renin

→ ↑ secretion of potassium and H^+

→ hypokalemic alkalosis (causing periods of muscle weekness/paralysis, nephropathy)



Secondary hypertension

Hyperthyroidism

- stimulation of the thyroid tissue by autoantibodies (thyroid-stimulating immunoglobulin) - same receptors as TSH
- thyroid adenoma

❖ mean pressure remains physiological but ↑ pulse pressure (systolic blood pressure - ↑ by 10 to 15 mmHg, diastolic blood pressure - ↓)

→ ↑ tissue metabolism → metabolic vasodilatation + vasodilatation in the skin (↑ heat elimination) → ↑ blood flow → ↑ CO (including ↑ HR)

→ ↑ amount and affinity of cardiac (also other) β-receptors → ↑ sensitivity to their chrono- and inotropic effects

→ ↑ expression of α-isoform of MHC (higher ATPase activity than β-isoform) → ↑ heart strength

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Hypertension in preeklampsia (toxemia of pregnancy)

- one of the manifestations of the syndrome called preeklampsia which may develop in the last trimester
- causes not fully known

  thickening of the kidney glomerular membranes (autoimmune process?) → ↓ glomerular filtration rate → ↑ long-term level of the arterial pressure to preserve the physiological level of formation of urine
- salt-sensitive
- the most serious type of hypertension during pregnancy considering prognosis for both mother and the fetus
- other types of hypertension during pregnancy:
  - hypertension which began before pregnancy
  - hypertension which starts in the first months of the pregnancy