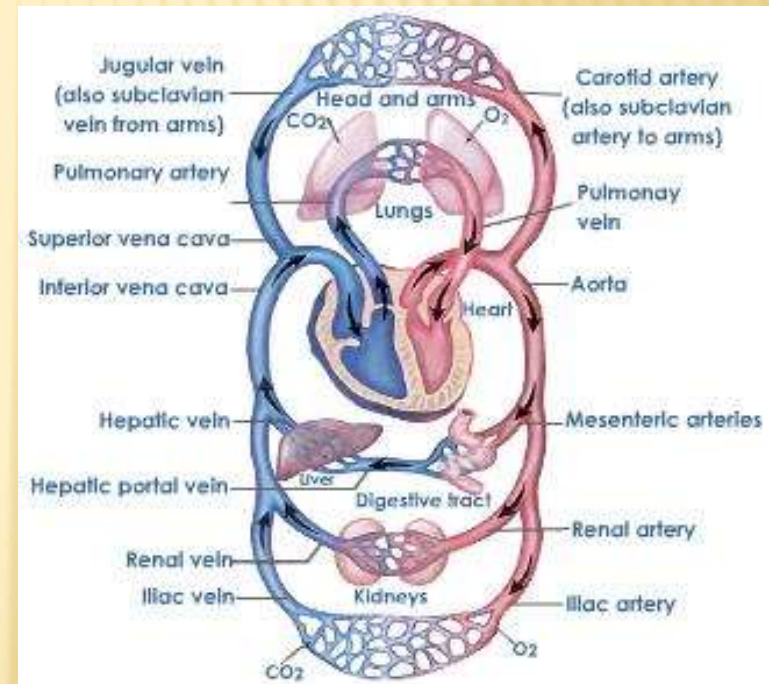


HYPERTENSION



CIRCULATORY SYSTEM

- ✘ Left atrium, left ventricle
- ✘ Arteries, arterioles
- ✘ Systemic capillaries
- ✘ Portal circulation
- ✘ Venules, venes
- ✘ Right atrium, right ventricle
- ✘ Pulmonary arteries
- ✘ Pulmonary capillaries
- ✘ Pulmonary venes
- ✘ Lymphatic vessels

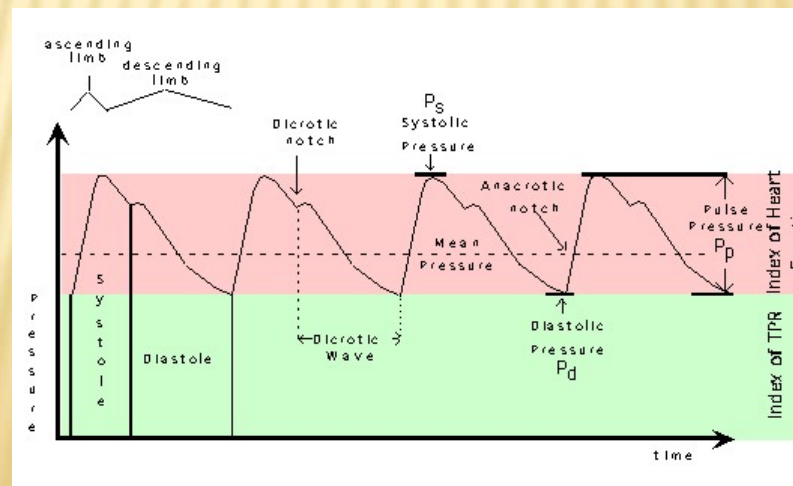


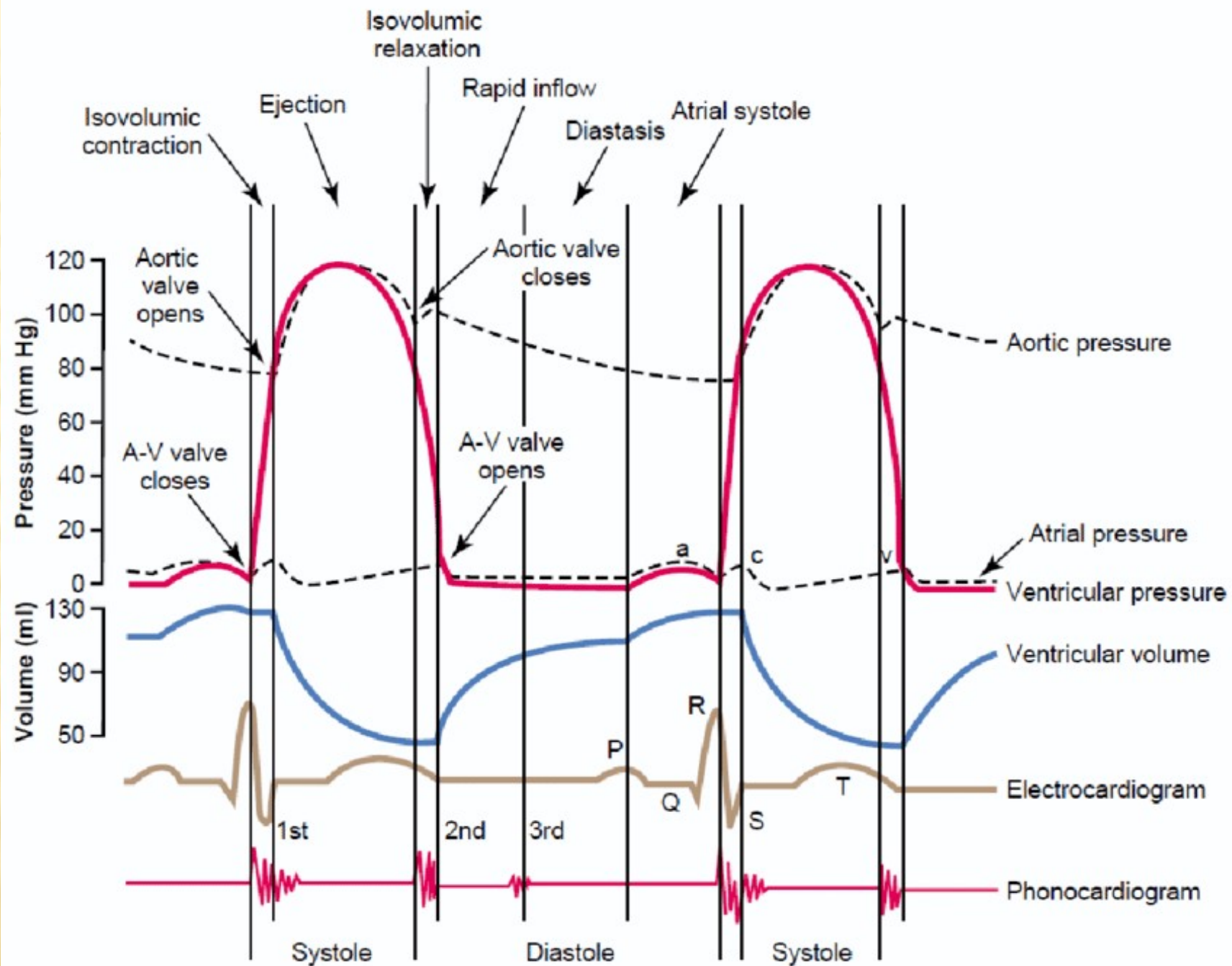
VESSEL CAPACITY AND RESISTANCE

Part of circulatory system	%	ml
Pulmonary circulation	9 %	450
Heart	7 %	350
Arteries	13 %	650
Arterioles and capillaries	7 %	350
Venules, venes and venous sinuses	64 %	3200

ARTERIAL BLOOD PRESSURE - DEFINITION

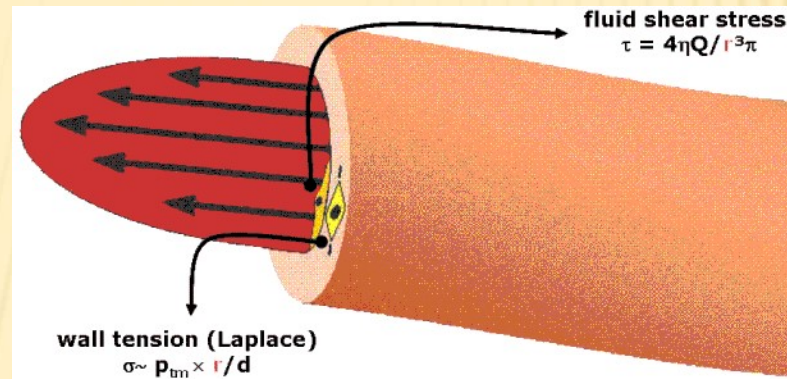
- ✗ $P = Q \times R$
- ✗ Analogous to Ohm's law defining voltage
- ✗ Tensor in moving viscous fluid
- ✗ Vessel wall is challenged by its radial member (i.e. pointing towards the endothelium)
 - + Systolic – on the top of the pulse curve
 - + Diastolic – on the bottom of the pulse curve
 - + Pulse – pulse curve amplitude
 - + Mean – average pressure during the cycle



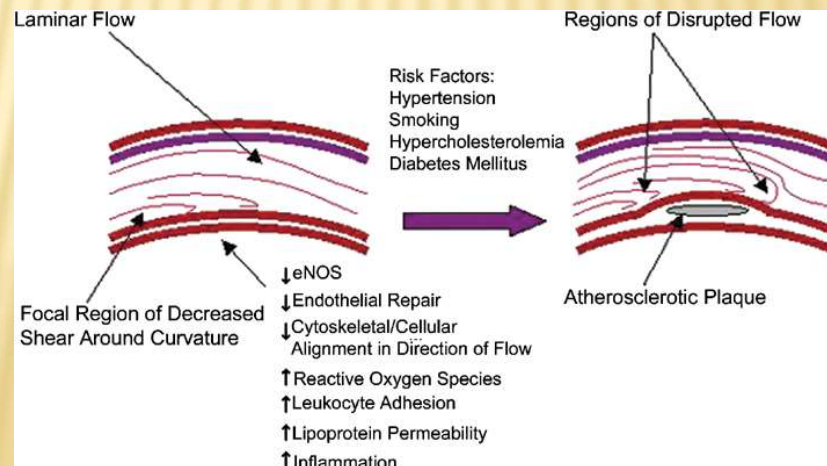


SHEAR STRESS

- ✘ Dimension: $\text{N}\cdot\text{m}^{-2}$ (Pa) – same as in blood pressure, axial vector



- ✘ Sites with low and/or variable shear stress (sharp turns, bifurcations) are especially prone to the onset of atherosclerosis



RESISTANCE

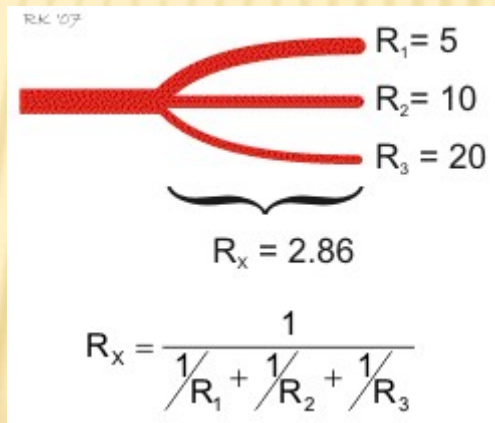
- ✗ R [kg.s⁻¹.m⁻⁴]: can be obtained from Hagen-Poiseuill law:

$$R = 8 \times \eta \times d / \pi \times r^4, \text{ where:}$$

η = viscosity

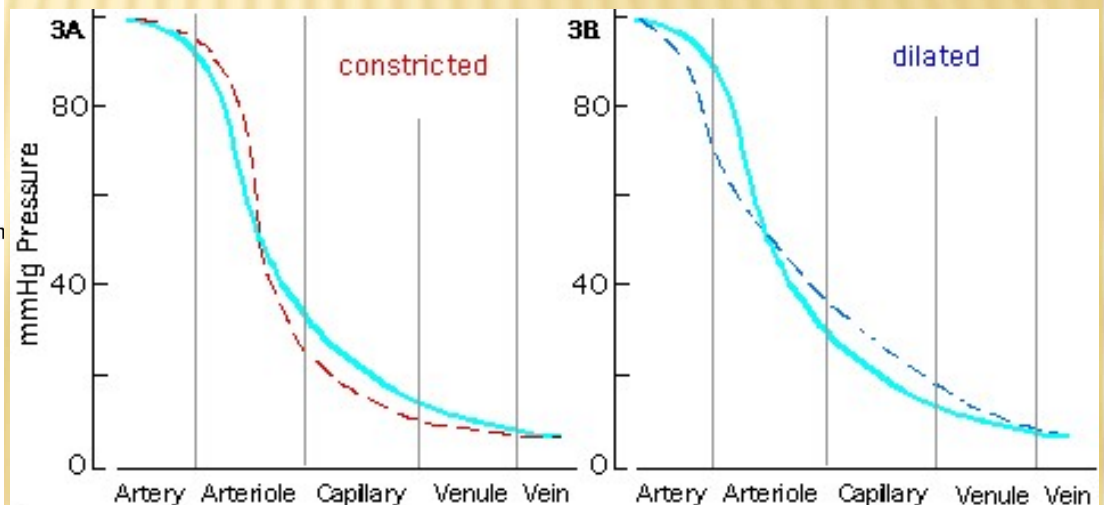
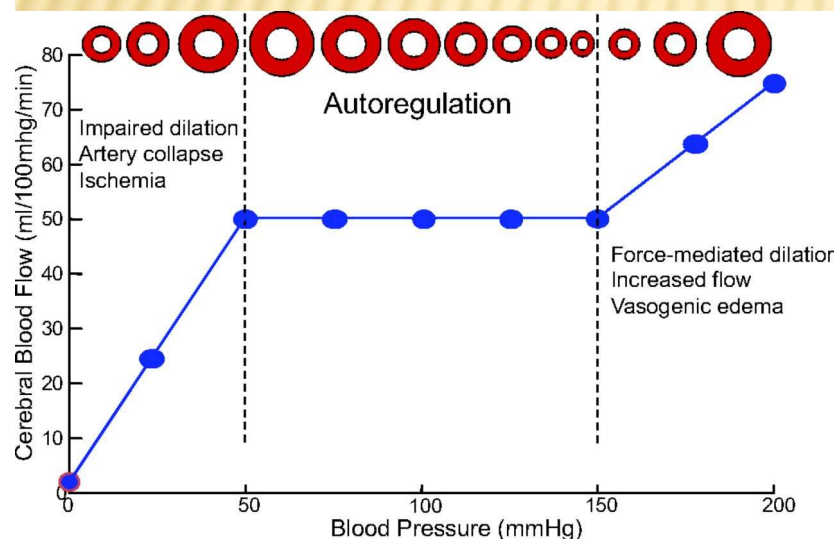
d = lenght of the segment

r = radius



PERIPHERAL RESISTANCE

- ✘ The resistance increases inversely to the radius at the power of 4
- ✘ The decrease in radius is most evident in arterioles
- ✘ The smooth muscle tone in the wall of arterioles changes depending on many factors – this controls peripheral resistance („peripheral arterioles“)



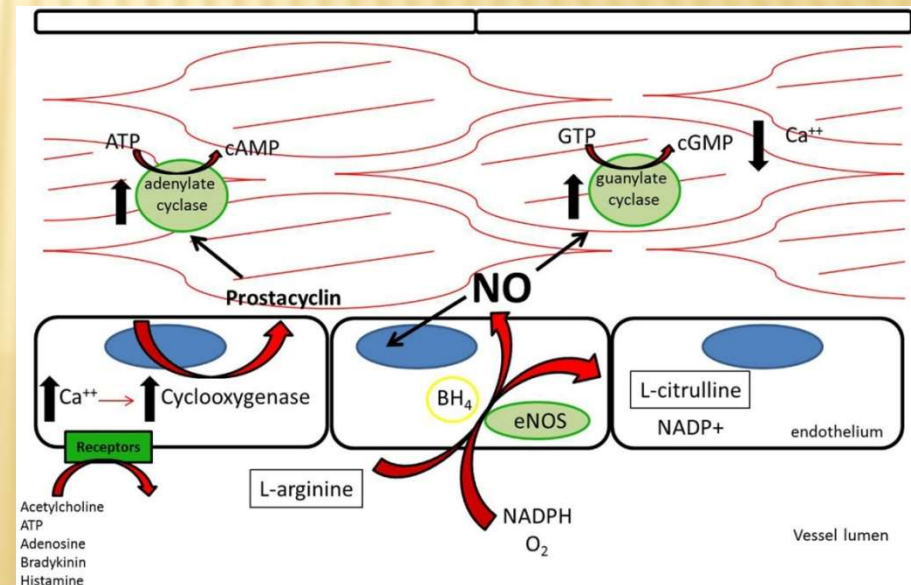
VASCULAR SMOOTH MUSCLE TONE

✘ Vasodilatation

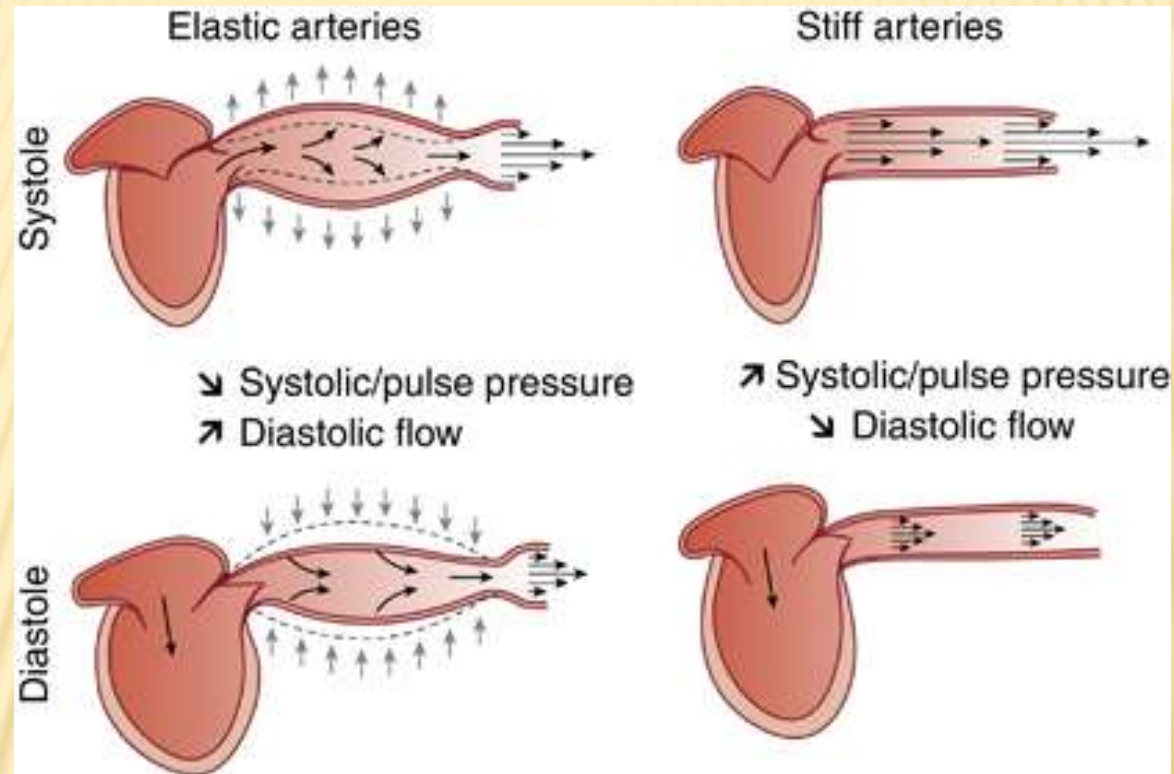
- + NO – produced in the endothelium by constitutive (eNOS) and inducible (iNOS) synthase
- + cGMP, cAMP
- + prostacyclins
- + catecholamines
- + histamine
- + bradykinin
- + pO_2 , pCO_2 , pH

✘ Vasoconstriction

- + Endothelin
- + Ca^{2+}
- + ATII
- + ADH
- + catecholamines



ARTERIAL WALL ELASTICITY (ELASTIC ARTERIES)



- ✘ Worsens with age
- ✘ Loss of elasticity (arterial stiffness) leads to isolated systolic hypertension

CARDIAC OUTPUT

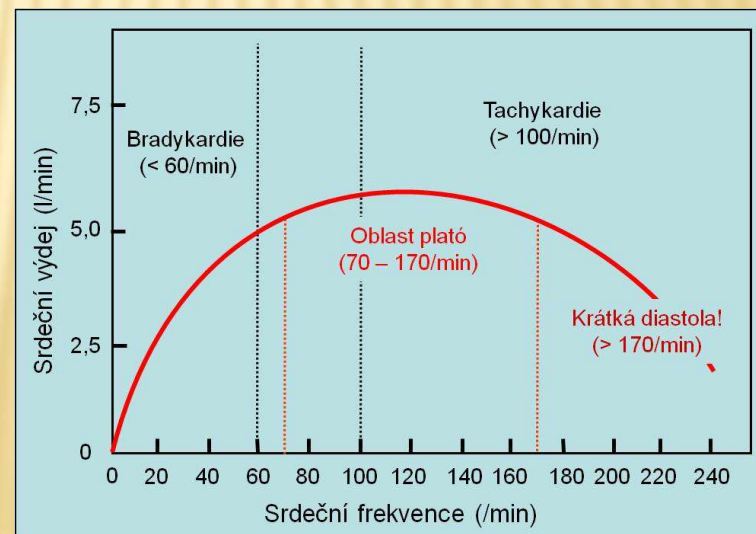
- ✘ Q: is equal to cardiac output (CO) – anatomic shunts

$$CO = SV \text{ (stroke volume)} \times f$$

$$SV = EDV \text{ (enddiastolic volume)} - ESV \text{ (endsystolic volume)}$$

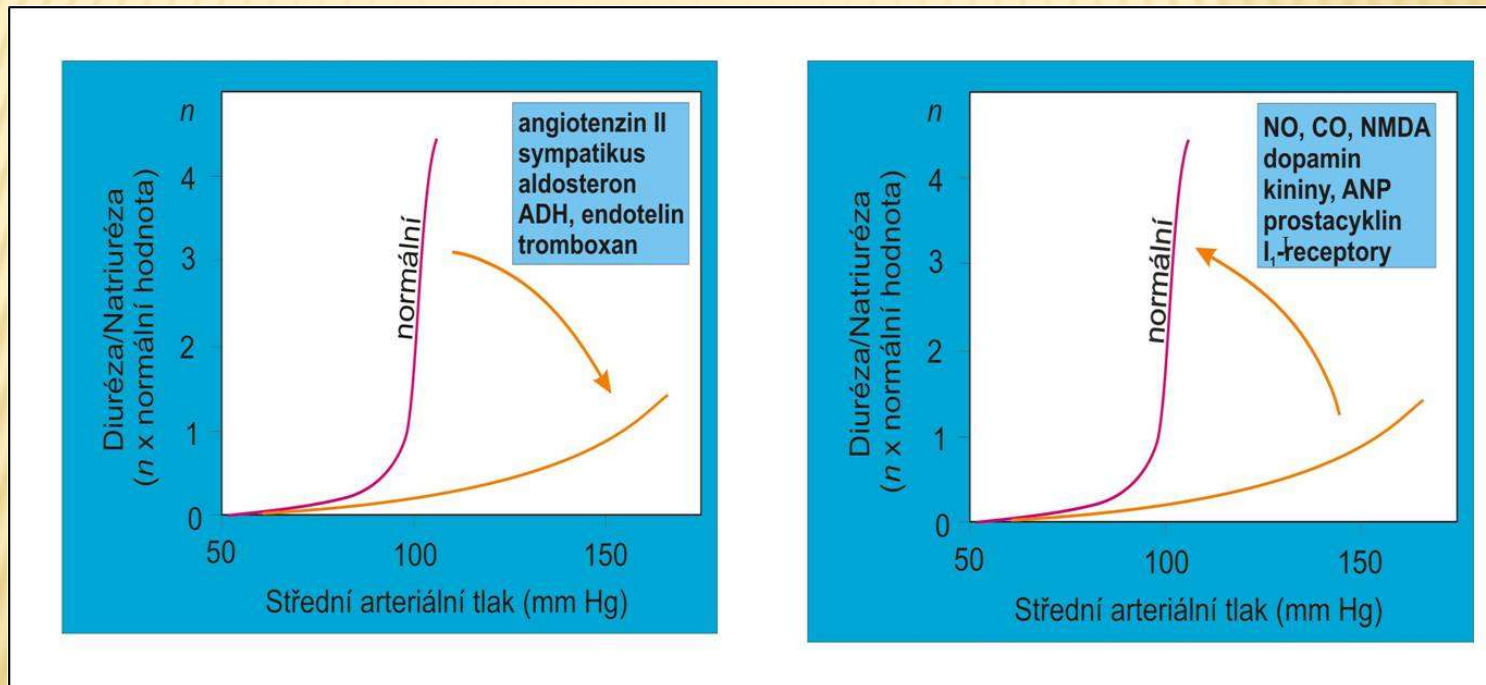
$$EF [\%] = SV/EDV$$

- CO is physiologically equal to venous return (depends on circulating volume)
- In very high HR the CO paradoxically decreases (the ventricles are not filled effectively)



RENAL FUNCTION CURVE

- ✘ Provided the renal functions are untouched, the increase in CO or resistance can be compensated by lowering of circulating volume



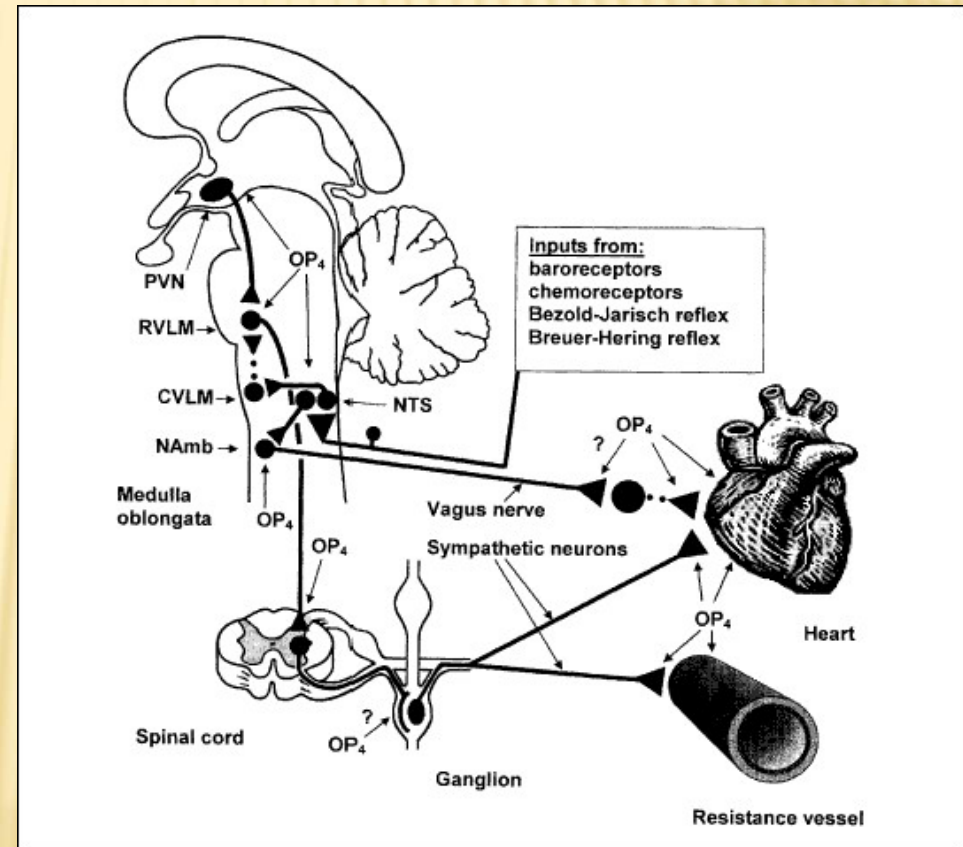
- ✘ This can be disturbed under pathological conditions - hypervolemia

BLOOD PRESSURE REGULATION

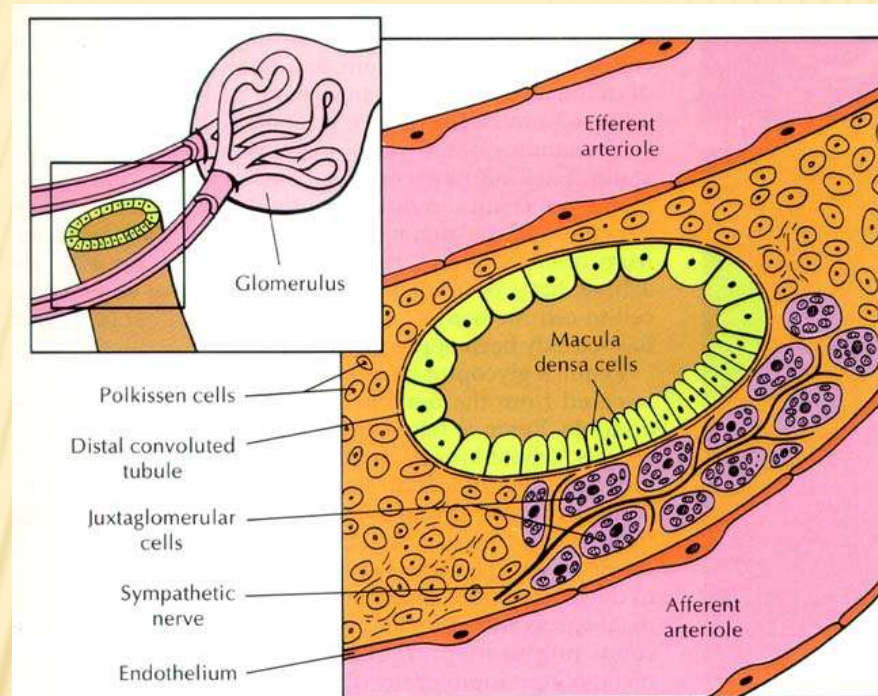
- ✘ Several interconnected systems
- ✘ Regulation of:
 - + heart rate
 - + cardiac contractility
 - + peripheral resistance
 - + circulating volume

VEGETATIVE REGULATION OF THE BLOOD PRESSURE

- ✘ fastest regulation
- ✘ afferentation – baroreceptors in glomus caroticum, arcus aortae; central and peripheral chemoreceptors
- ✘ centre – nucleus tractus solitarii (NTS), area postrema, rostral ventrolateral medulla (RVLM) with imidazolin receptors
- ✘ Efferentation – heart (esp. β_1 and M2 receptors), vessels (esp. α_1 receptors), kidney (α_1 , α_2 , β_1)
- ✘ Circulating catecholamines



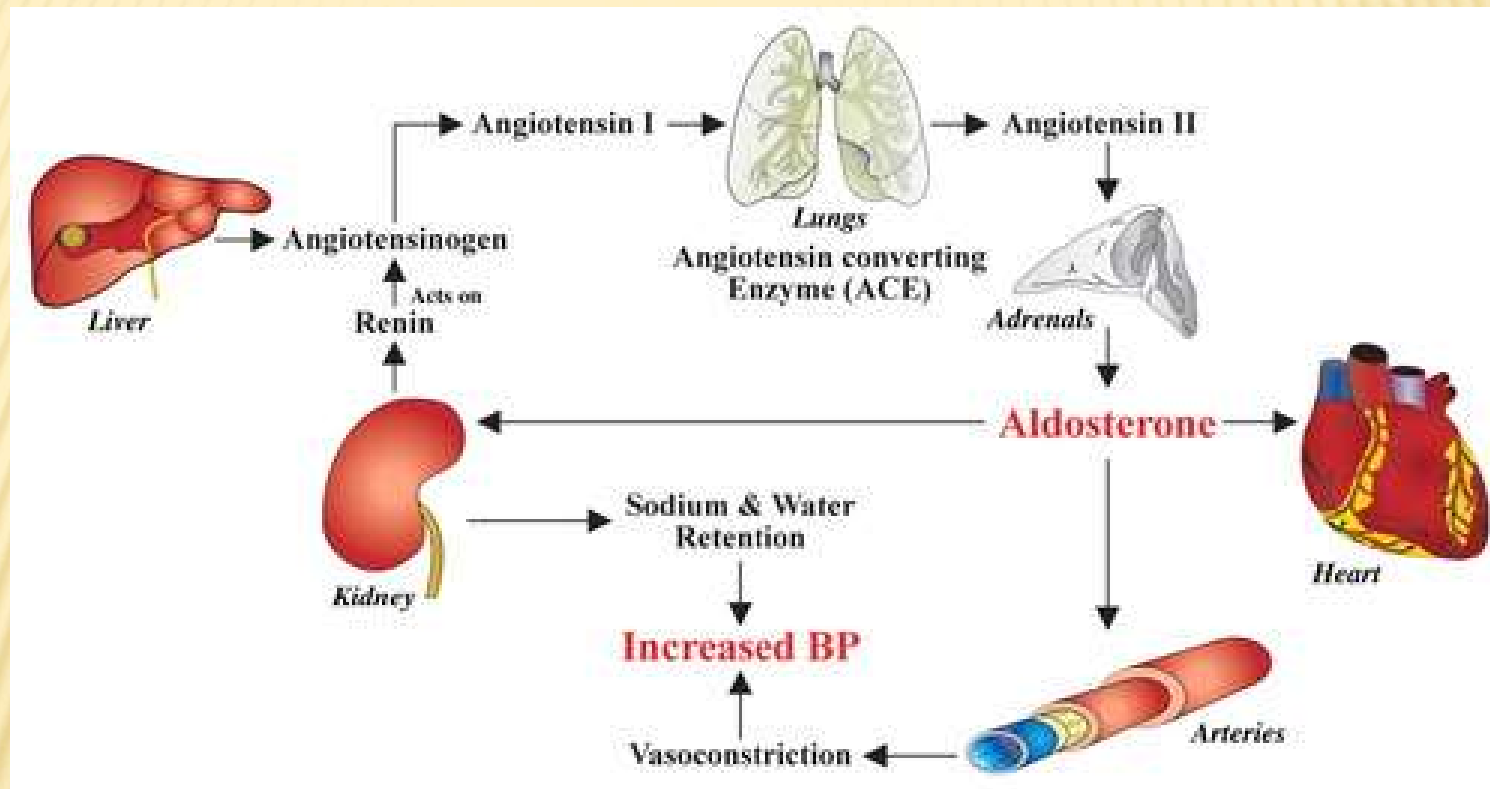
JUXTAGLOMERULAR APPARATUS



Three inputs:

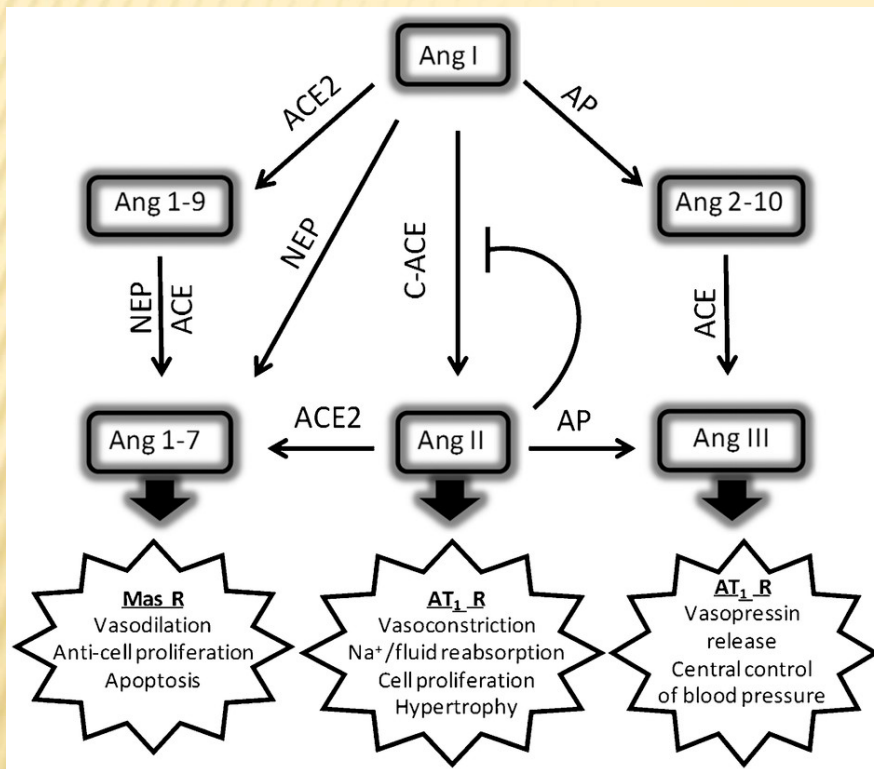
- NaCl in distal tubule
- Stretching of afferent artery
- Sympathetic nervous system

RENIN-ANGIOTENSIN-ALDOSTERONE



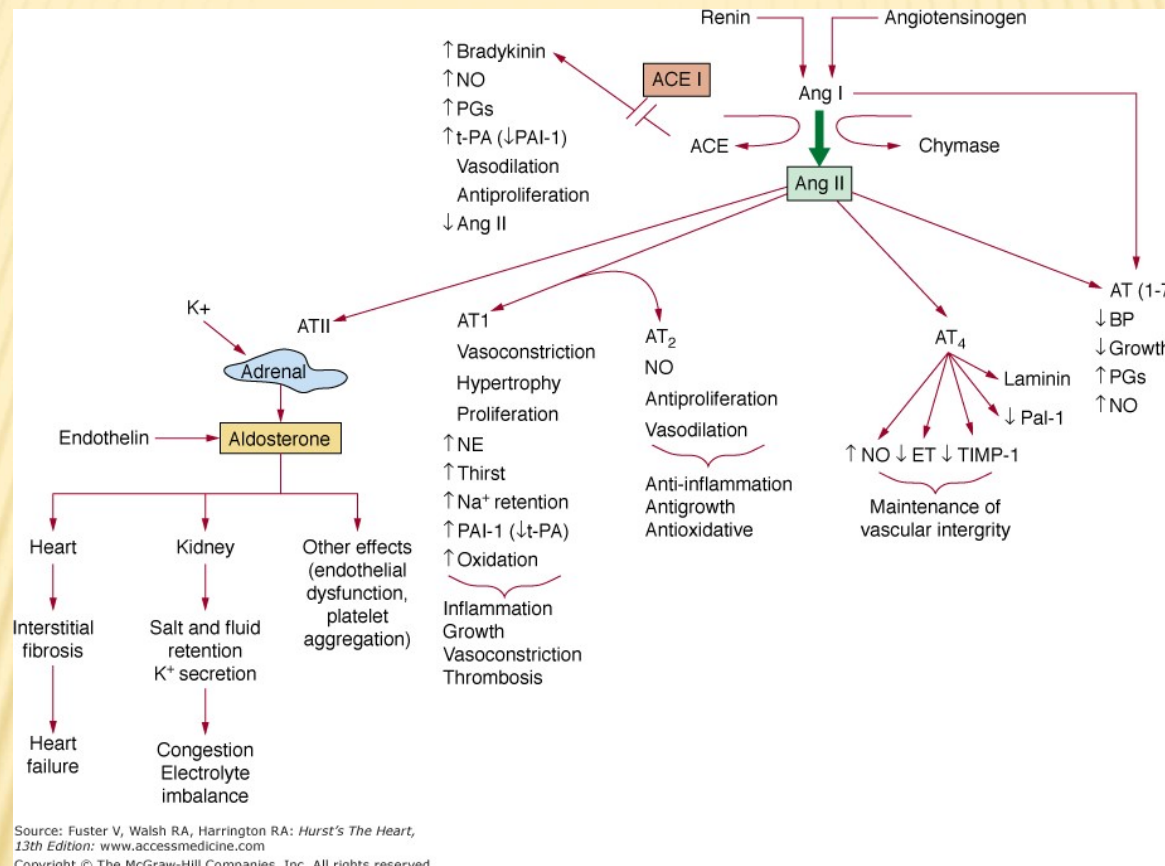
- Renin (and prorenin) binds the (pro)renin receptor (PRR)
- The binding increases the enzymatic activity of renin and leads to receptor activation (involved in central BP regulation)
- Renin also cleaves angiotensin I (dekapetide) from angiotensinogen

ACE AND ACE 2



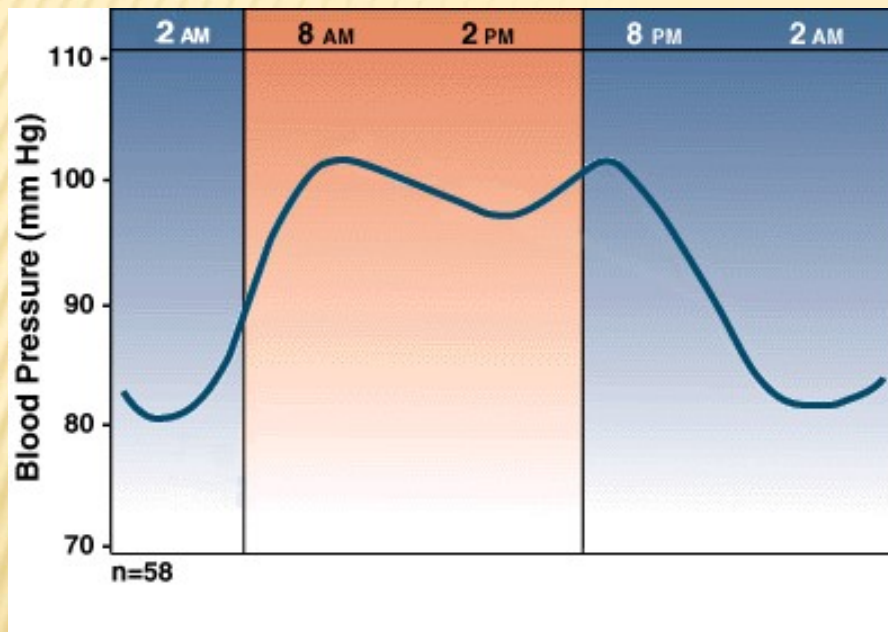
- ✘ Angiotensin I (Ang I) can be then transformed into several products
- ✘ Through ACE action, Ang II and Ang III with vasoconstriction effects are formed
- ✘ ACE also degrades bradykinin (pharmacologic inhibition of ACE leads to angioedema)
- ✘ Through the action of ACE 2, angiotensin 1-7 is formed, having vasodilatation and antiproliferation effect on vessel wall (contributing to the decrease of peripheral resistance – Mas receptors)

ANGIOTENSIN II RECEPTORS AND SYSTEMIC EFFECTS OF ALDOSTERONE



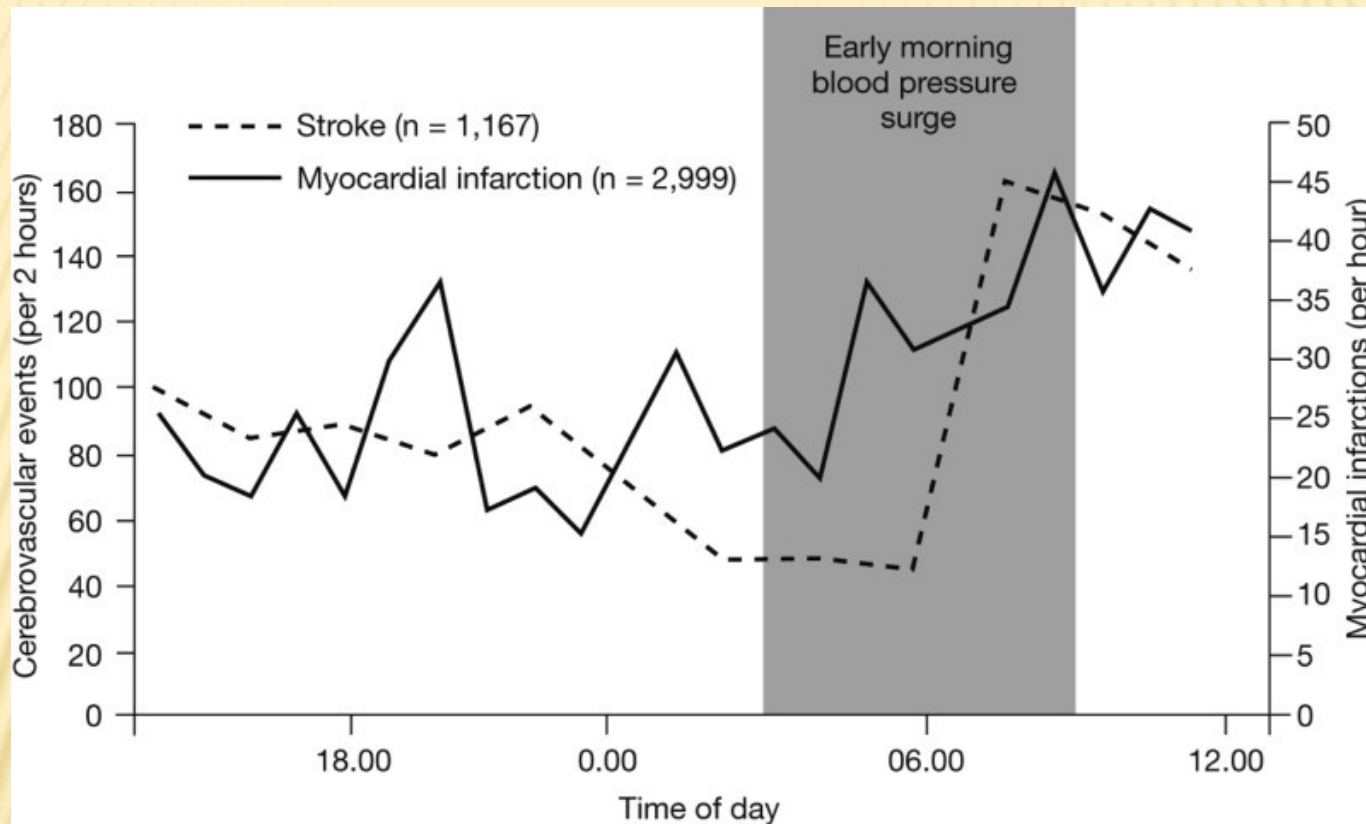
- ✘ AT 2 receptors are mostly involved in fetal development
- ✘ Ang III is mostly involved in aldosterone secretion and in the CNS

CIRCADIAN RHYTHMICITY OF THE BP



- ✘ BP drops by ~10-20% at night („dipping“)
- ✘ Hypertonics „non-dippers“ have approx. 2,5x higher odds of cardiovascular events than „dippers“
- ✘ In some „non-dippers“ there may be disturbed melatonin secretion (shift work...), often, the absence of the drop results from obstructive sleep apnea

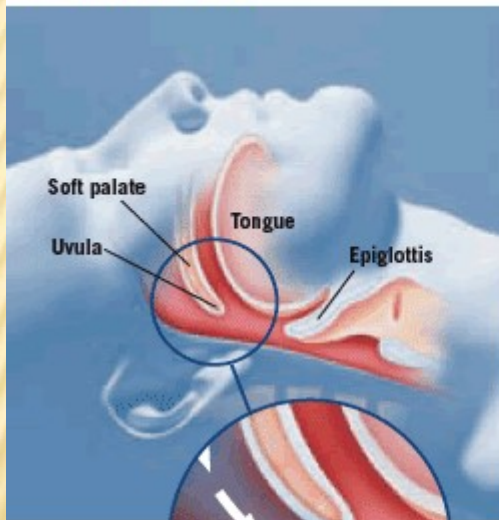
CARDIOVASCULAR EVENTS DURING 24-H CYCLE



- ✘ The incidence of myocardial infarctions and cerebral strokes peaks before noon
- ✘ The patients with sleep apnea make an exception

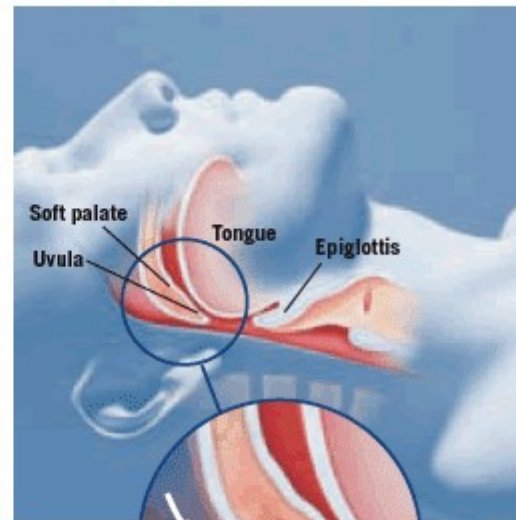
OBSTRUCTIVE SLEEP APNEA

Opened Upper Airway



Clear and open upper airway allows air to flow freely to and from the lungs.

Closed Upper Airway

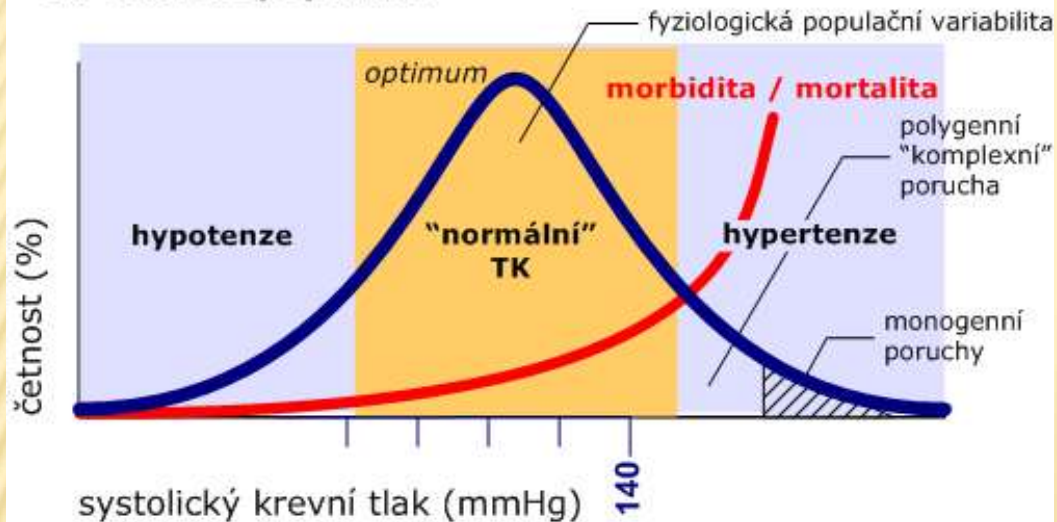


Snoring and apnoeas (breathing pauses) are observed when the upper airway collapses.

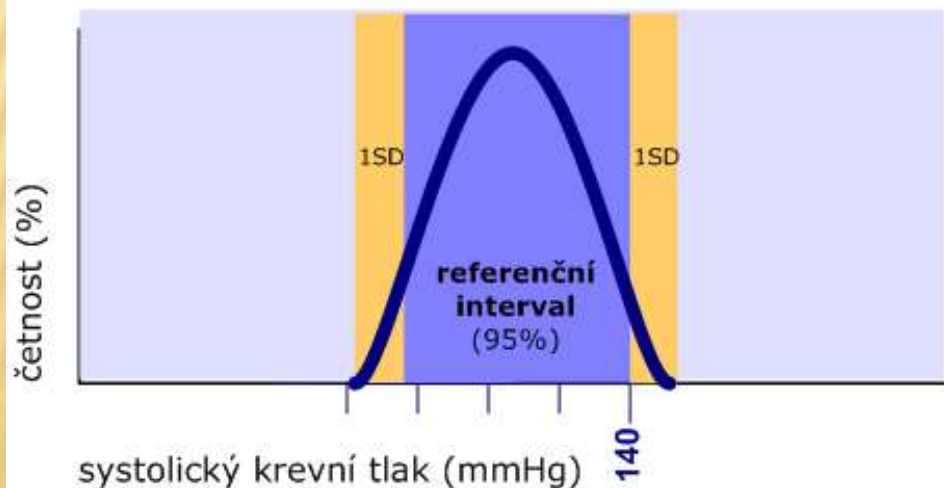
- ✘ Intermittent apnea (up to 60 s) with hypoxia leading into SNS activation at night
- ✘ Caused by the loss of muscle tone in upper airways (soft palate) – associated with snoring
- ✘ 4-30% of men (underdiagnosed), up to 9% of women
- ✘ Risk factors: obesity, high neck circumference, alcohol intake (having central myorelaxant properties)
- ✘ Effects: higher BP and risk of cardiovascular events at night, chronic stress, cognitive disorders (memory), sleepiness, headache

NORMAL BLOOD PRESSURE AND HYPERTENSION

A. veškerá populace



B. zdravá populace



- ✗ BP is continuous parameter with characteristic population distribution
- ✗ Setting the border of "normality" is always arbitrary → "reference interval" (contains 95% of healthy population, excluding outlying 5%)
 - + In parameters with normal (Gaussian) distribution mean \pm 2SD
 - + In other parameters generally median [2.5% - 97.5% quantile]
- ✗ general population does not to have optimal values of the parameter!
 - + Value-associated mortality is often taken into account
- ✗ Reference interval may be adjusted based on prospective studies

HYPERTENSION

- + BP \geq 140/90 mmHg (during day) in an adult regardless the age after >10min of rest repeatedly min. 2× out of 3 measurements in several days
 - × In diabetes and in chronic renal failure, the BP should be <130/80mmHg
 - × Ideal BP in an adult – SBP<120 and DBP<80mmHg
- + stage of hypertension
 - × mild 140 – 179/90 – 104
 - × moderate 180 – 199/105 – 114
 - × high \geq 200/115
 - × isolated systolic hypertension SBP >160 with DBP <90 mmHg
 - × resistant \geq 140/90 with the combination of 3 antihypertensives
- + stage of end-organ damage
 - × I – increased BP without affecting the end-organ
 - × II – organ involvement - LV hypertrophy, microalbumin-/proteinuria, aortic calcification
 - × III – organ failure: heart failure, renal insufficiency, cerebral stroke

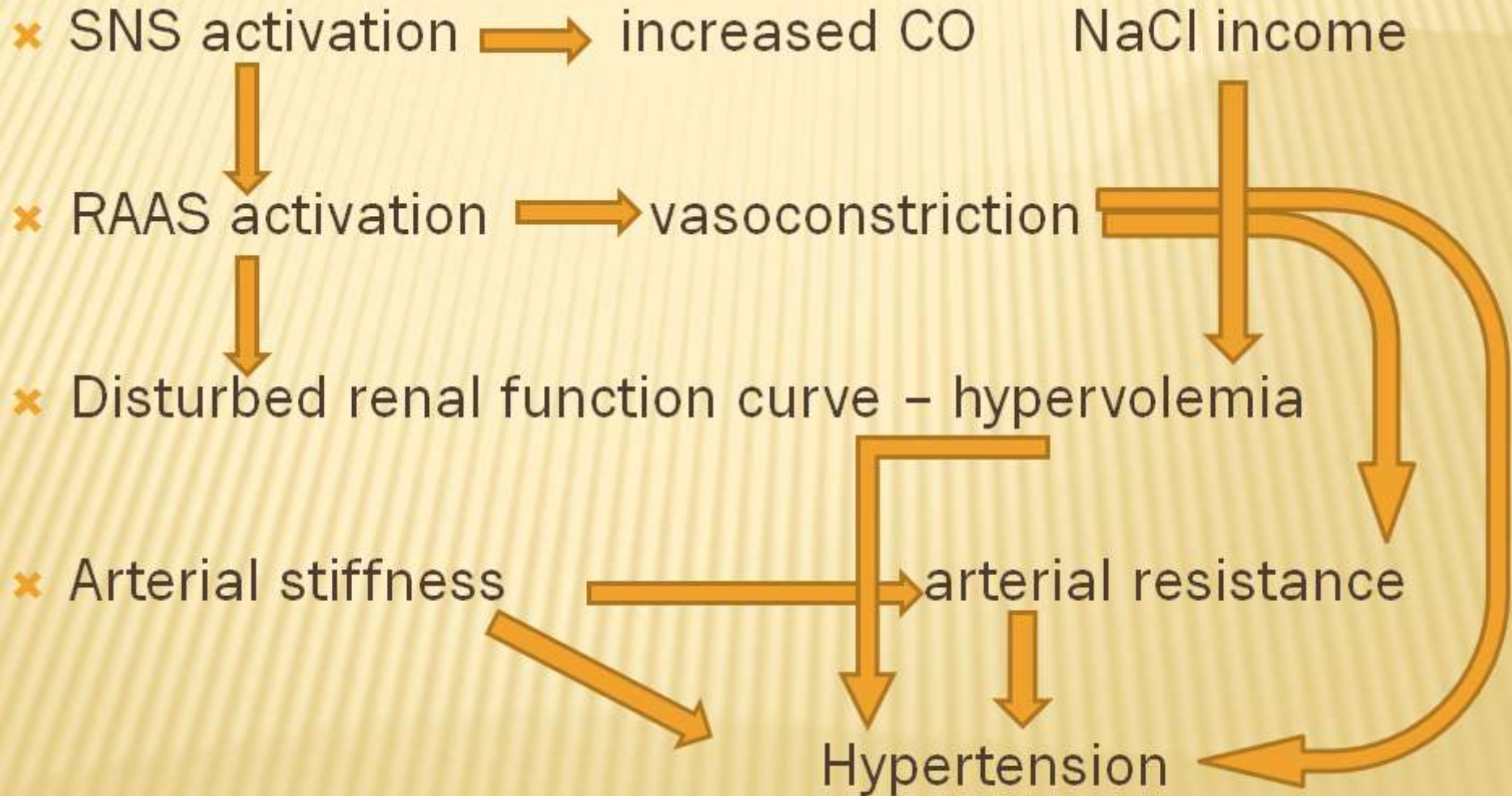
PATHOGENESIS

- ✗ essential – 90-95%
 - + Concomitant dysregulation of several mechanisms



- ✗ secondary – 5-10%
 - + renal
 - ✗ renovascular
 - ✗ renoparenchymatous
 - + endocrine
 - ✗ adrenal gland
 - * prim. hyperaldosteronism
 - * Cushing syndrome
 - * pheochromocytoma
 - ✗ others
 - * Acromegaly
 - * Hyperthyroidism
 - + Other causes
 - * Aortic coarctation

PATHOGENESIS OF ESSENTIAL HYPERTENSION

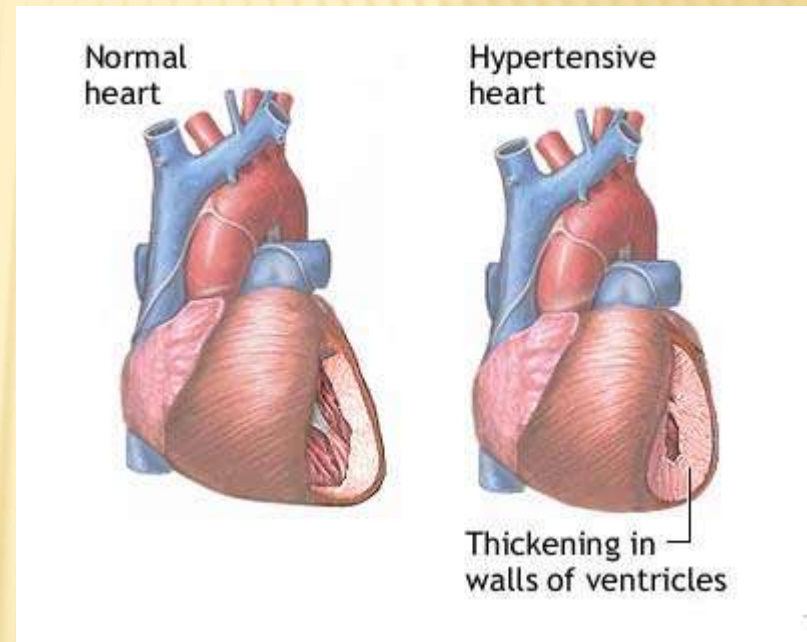


HEART AND VESSEL REMODELATION

- × Consequence of long-term hypertension
- × In fact a compensatory mechanism
 - + heart – reacts to increased preload in hypervolemia or afterload in peripheral resistance
 - + vessels – compensate higher CO, arterial stiffness and/or hypervolemia by higher resistance
- × RAAS components – (pro)renin, angiotensin, aldosterone – play an important role

CONSEQUENCES OF HYPERTENSION

- ✘ Heart
 - + hypertrophy
- ✘ Kidney
 - + nephrosclerosis
- ✘ Brain
 - + encephalopathy
 - + dementia
 - + hemorrhagic stroke
- ✘ Vessel wall
 - + atherosclerosis (esp. of heart and brain)

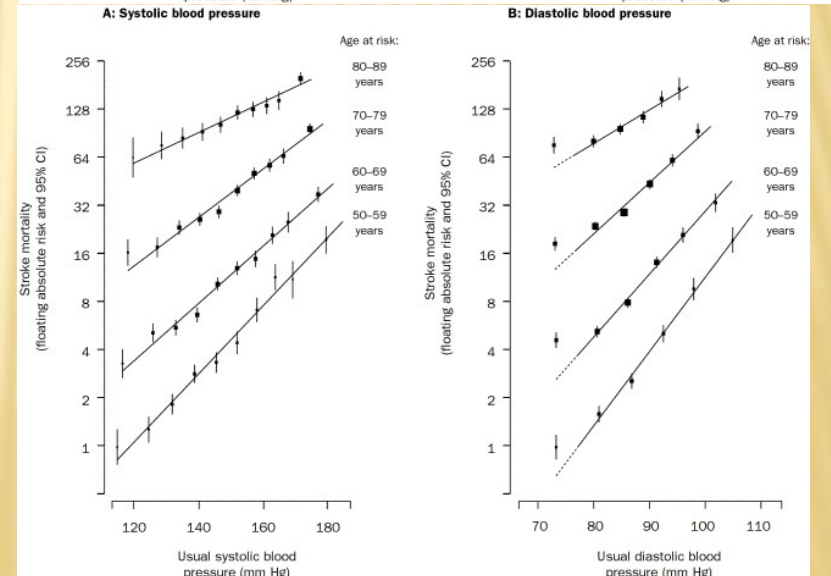
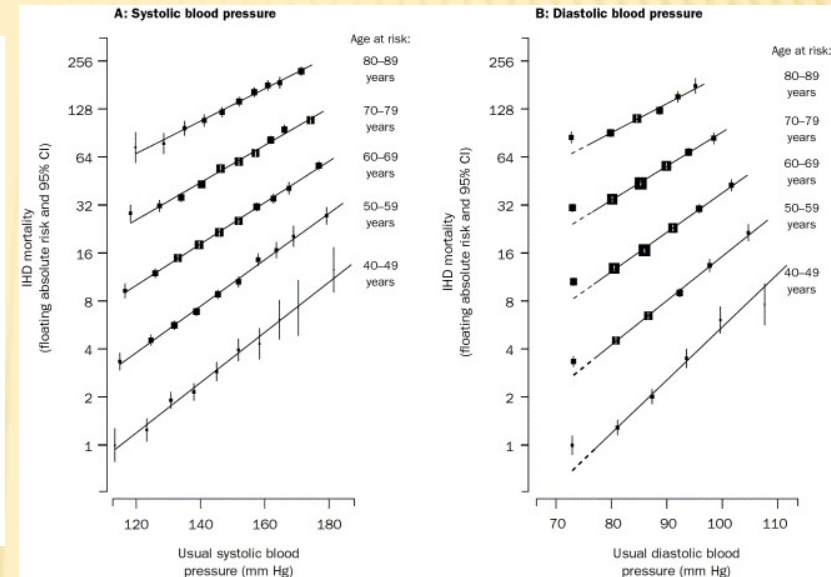
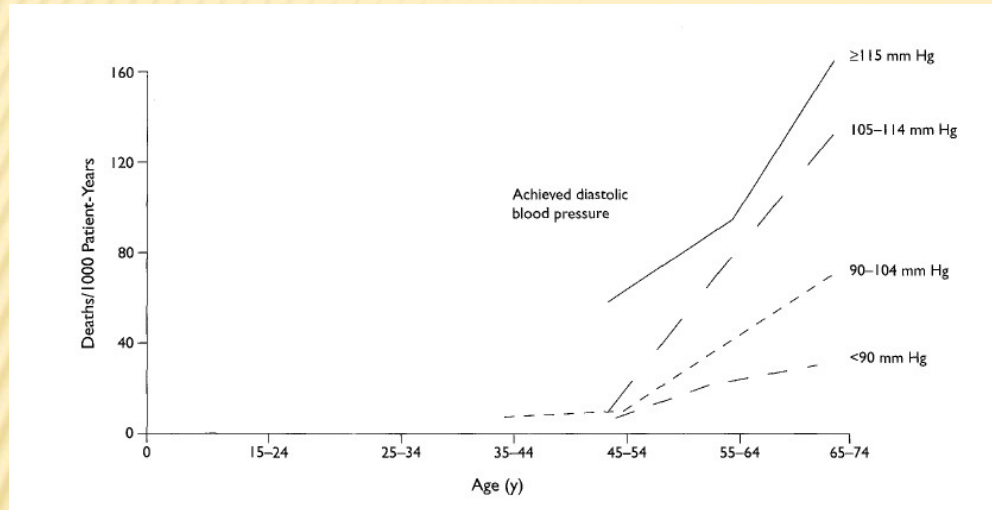


METABOLIC SYNDROME

- × Hypertension
- × Dyslipidemia
- × Insulin resistance
- × Central obesity
 - + Often accompanied by:
 - × hyperuricemia
 - × long-term increase of HR
 - × ↑ fibrinogen
 - × long-term ↑ CRP
 - × ↑ oestrogens



BP AND MORTALITY – TOTAL, IHD AND STROKES



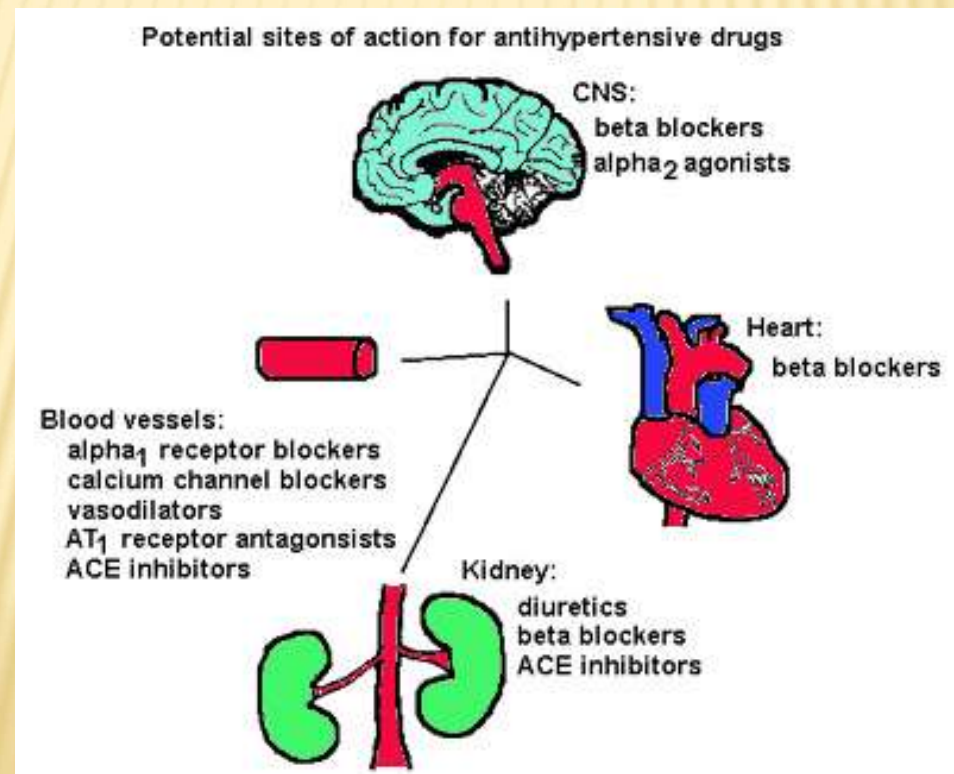
- linear correlation in SBP, exponential in DBP

GENETICS OF ESSENTIAL HYPERTENSION

- ✘ Usually polygenic
- ✘ Ratio of heritable vs. all factors in overall variability 20-70% (most studies approx. 40%)
 - + Only small proportion (several percents) is identified
 - + Usually variants in:
 - RAAS
 - sodium transport mechanisms
 - vasodilatory mechanism
 - + Most of total heritability is unidentified (“missing heritability”)
 - + Rare monogenic forms (mineralocorticoid overproduction, Liddle syndrome)

THERAPEUTIC STRATEGIES

- ✘ Lowering of SNS activity
- ✘ Lowering of CO
- ✘ Lowering of vascular resistance
- ✘ Adjustment of renal function curve



MEASURING THE BP - METHODS

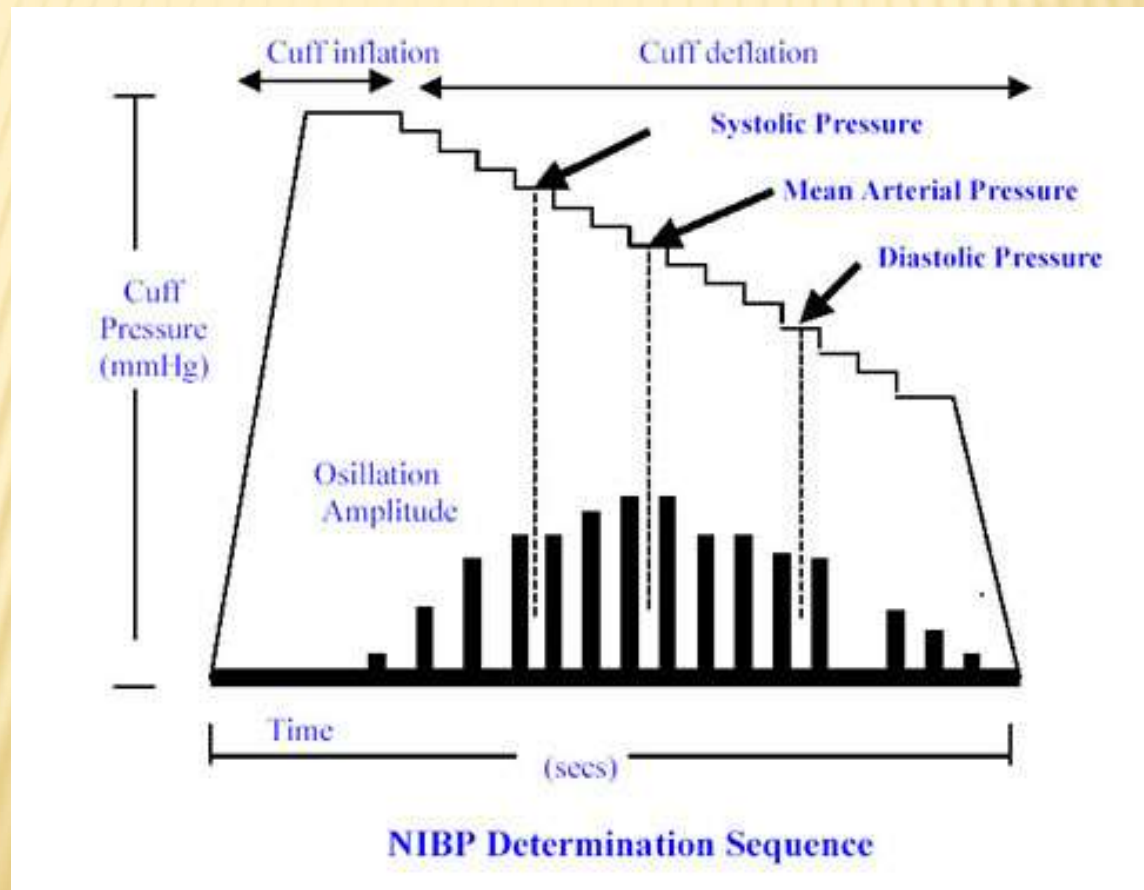
- ✗ Invasive (veins, pulmonary circulation, heart chambers)
 - + Catheter with a fluid



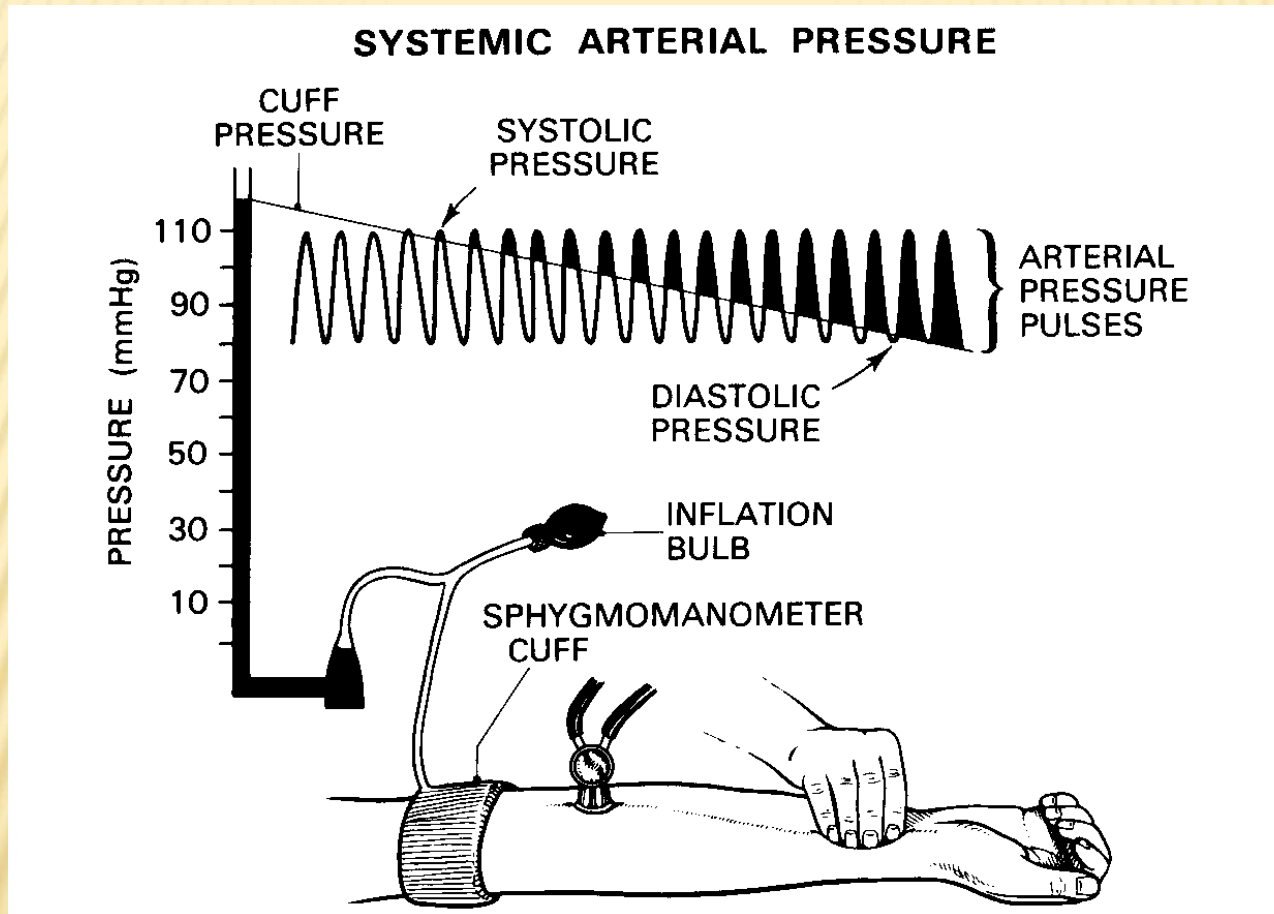
- ✗ Non-invasive
 - + Occasional
 - + Ambulatory
 - + Continual (digital fotoplethysmography)

BLOOD PRESSURE - OSCILLOMETRIC METHOD

- By oscillometry, the mean blood pressure is measured accurately, SBP and DBP are estimated



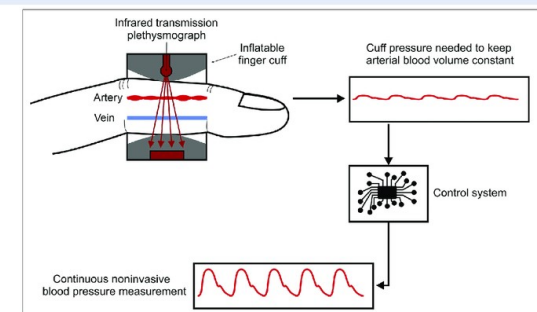
BLOOD PRESSURE – RIVA-ROCCI METHOD



- SBP and DBP are exact, mean blood pressure is estimated

AMBULATORY BLOOD PRESSURE MONITORING

- ✘ ABPM („blood pressure Holter“)
- ✘ Intermittent monitoring
- ✘ Measurements by oscillometric method in approx. 15 min interval (30-60 min at night)
- ✘ Alternative: continual BP monitoring using digital fotoplethysmography (Peñáz method)
 - + A detector measures the intensity of light passing through the finger, uses negative feedback loop
 - + A change in blood flow in digital arteries leads into the change in light intensity; change of cuff pressure needed for correction = change of blood pressure
 - + Cannot be used in peripheral vasoconstriction



ABPM INDICATIONS

- ✘ Diagnostics of collapses (together with Holter ECG)
- ✘ Pharmacoresistant hypertension
- ✘ Paroxysmal hypertension (often in pheochromocytoma)
- ✘ White coat hypertension

- values in home environment are typically lower than in clinical environment

- therefore, the limits are stricter: <135/85 during the day, <120/70 at night

- more than 40% of values above those limits point to arterial hypertension

- according to prospective studies, the ABPM has better prognostic ability to predict cardiovascular events than occasional measurement

CHANGES IN BP DURING 24 HOURS

