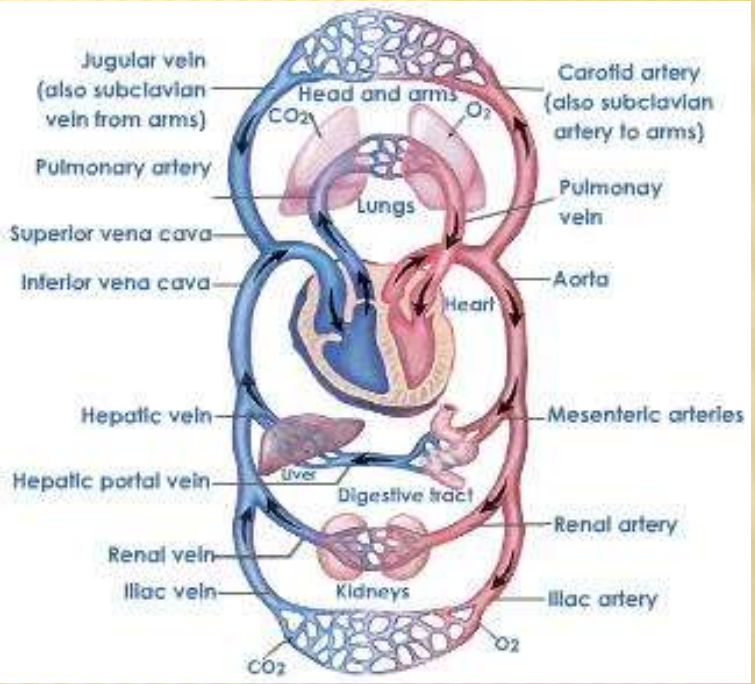
HYPERTENSION

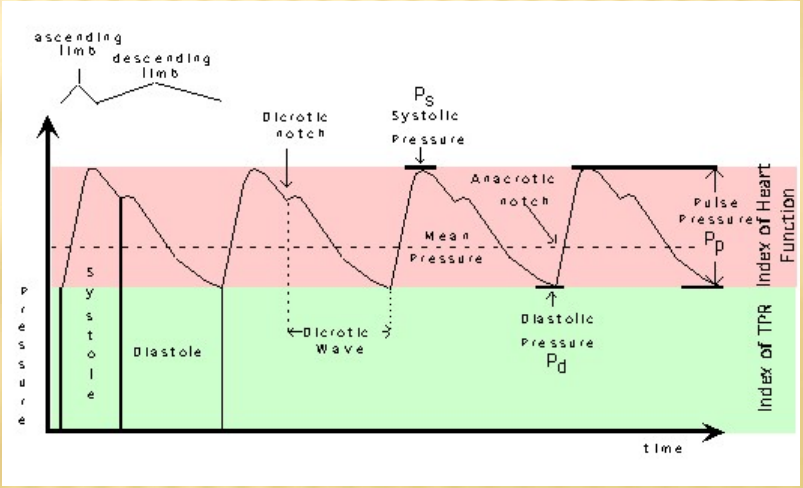
CIRCULATORY SYSTEM

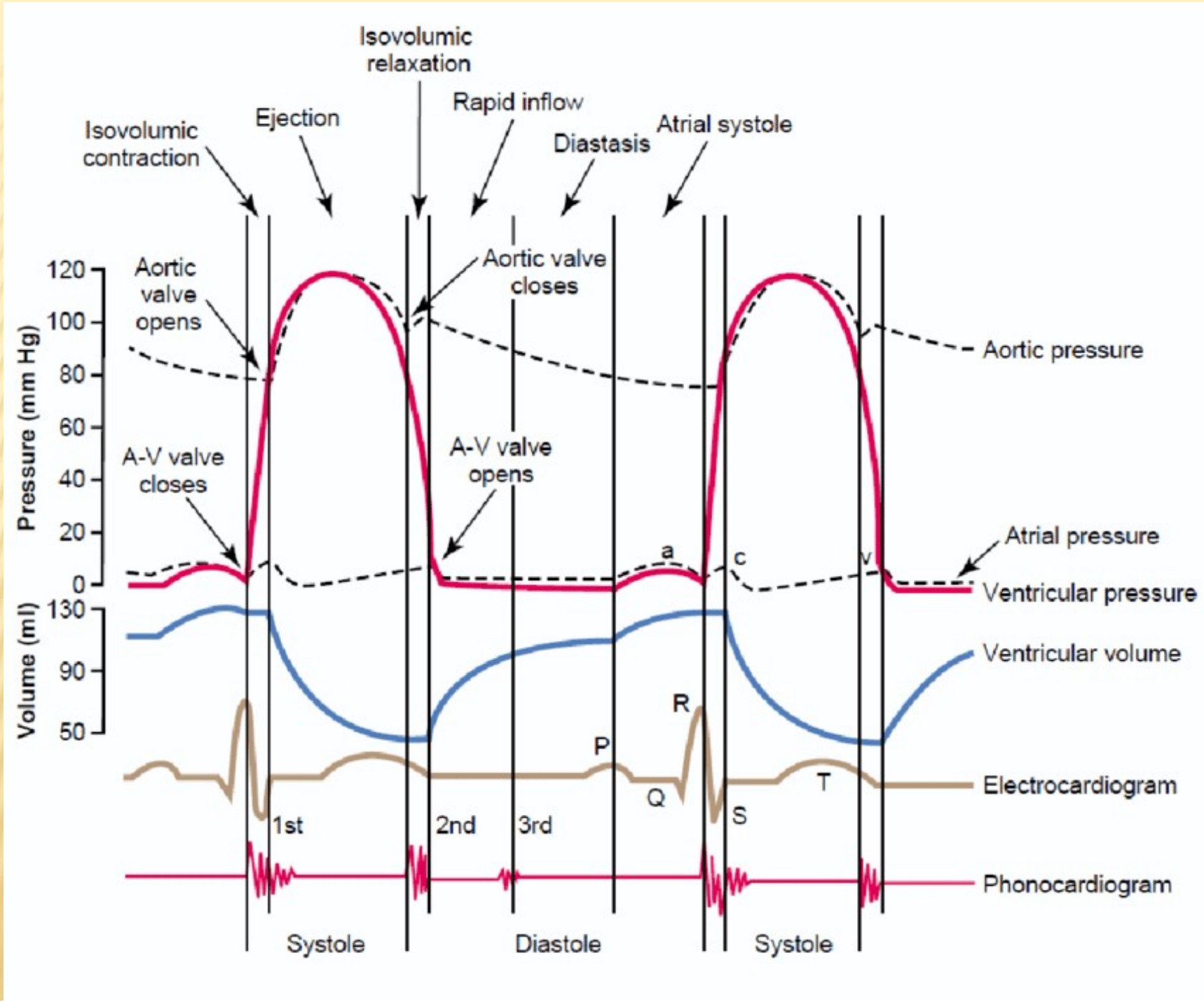
- Left atrium, left ventricle
- Arteries, arterioles
- Systemic capillaries
- Portal circulation
- Venules, venes
- Right atrium, right ventricle
- Pulmonary arteries
- Pulmonary capillaries
- Pulmonary venes
- Lymphatic vessels



ARTERIAL BLOOD PRESSURE - DEFINITION

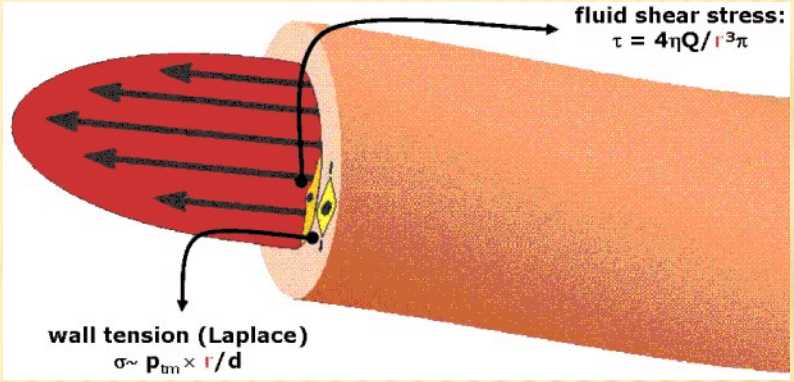
- $P = Q \times R$
- Analogous to Ohm‘s law defining voltage
- Tensor in moving viscous fluid
- Vessel wall is challenged by its radial member (i.e. pointing towards the endothelium)
  - Systolic – on the top of the pulse curve
  - Diastolic – on the bottom of the pulse curve
  - Pulse – pulse curve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



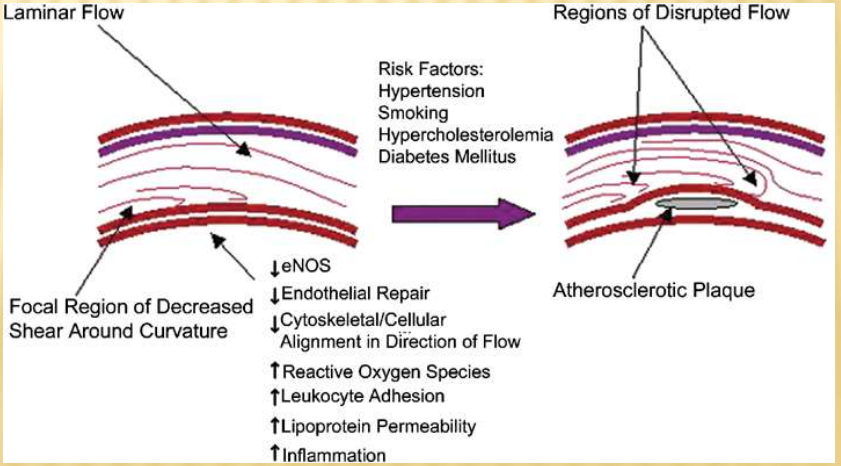

Isovolumic relaxation
Isovolumic contraction
Ejection
Rapid inflow
Diastasis
Atrial systole
Aortic valve opens
Aortic valve closes
A-V valve closes
A-V valve opens
Pressure (mm Hg)
120
100
80
60
40
20
0
Volume (ml)
130
90
50
Aortic pressure
Atrial pressure
Ventricular pressure
Ventricular volume
Electrocardiogram
Phonocardiogram
a
c
v
P
Q
R
S
T
1st
2nd
3rd
Systole
Diastole
Systole

SHEAR STRESS

- Dimension: $N.m^{-2}$ (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



CARDIAC OUTPUT

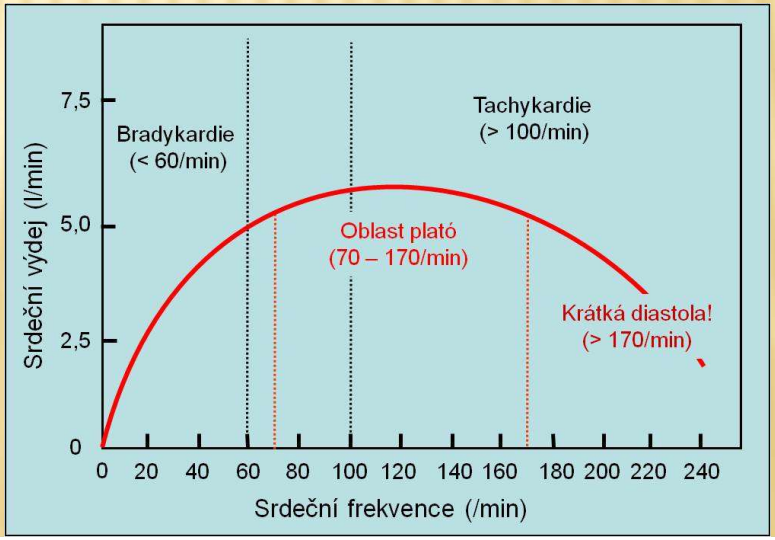
- Q: is equal to cardiac output (CO) – anatomic shunts

  CO = SV (stroke volume) × f

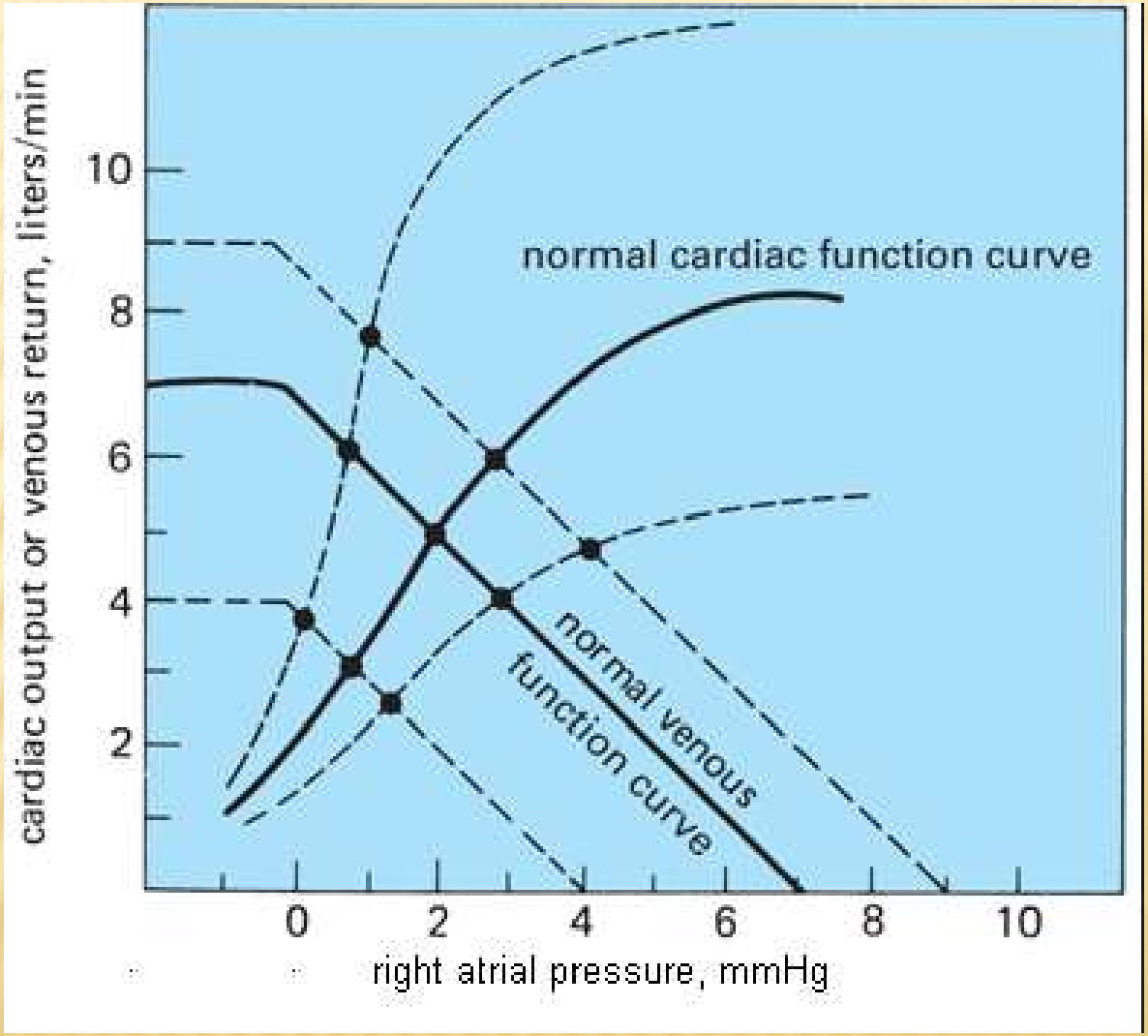
  SV = EDV (enddiastolic volume) – ESV (endsystolic volume)

  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 efectively)

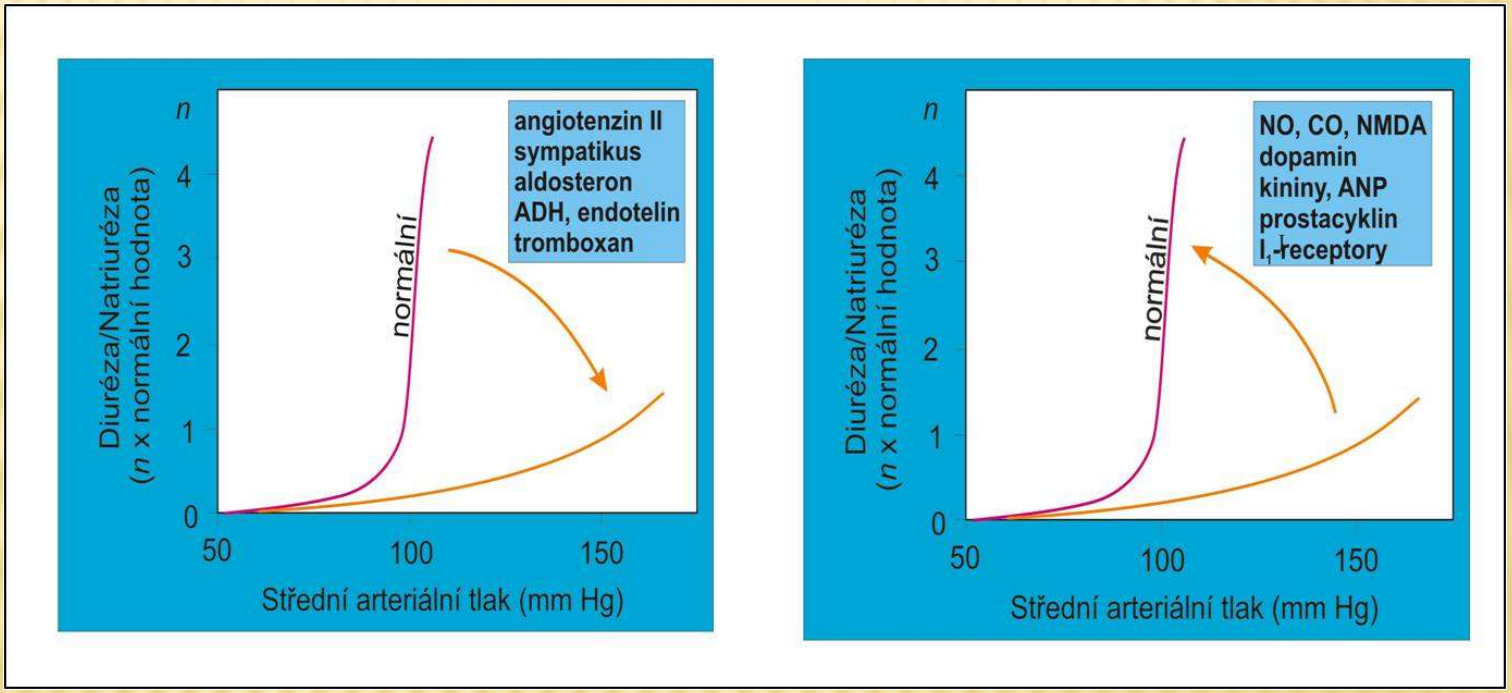


CARDIAC AND VENOUS FUNCTION CURVE



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

CIRCULATING VOLUME

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

RESISTANCE

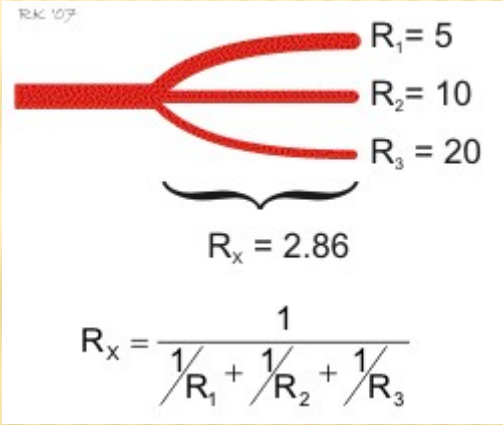
- R [$kg.s^{-1}.m^{-4}$]: can be obtained from Hagen-Poiseuill law:

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

η = viscosity

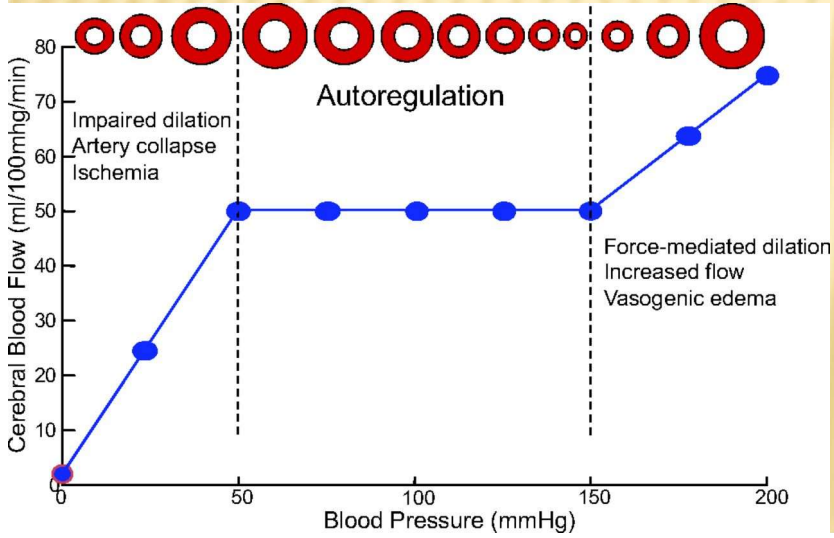
d = lenght of the segment

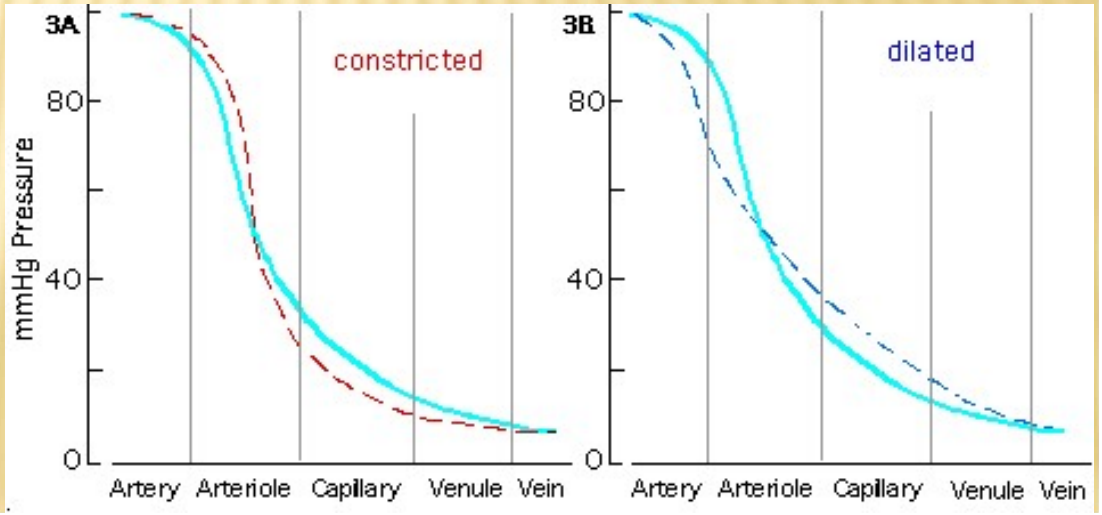
r = radius



PERIPHERAL RESISTANCE

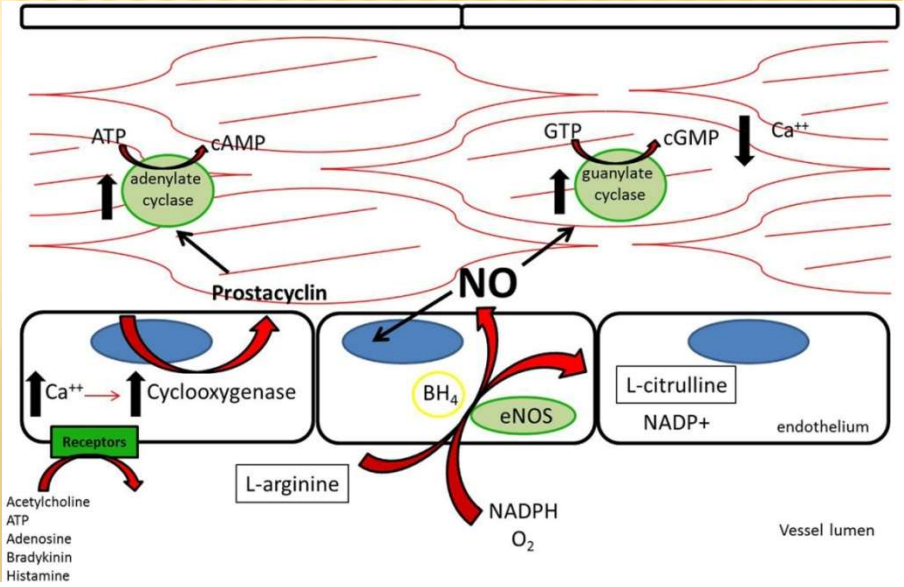
- The resistance increases inversely to the radius at the power of 4
- The decrease in radius is most evident in arterioles
- The smooth muscle tone in the wall of arterioles changes depending on many factors – this controls peripheral resistance („peripheral arterioles“)



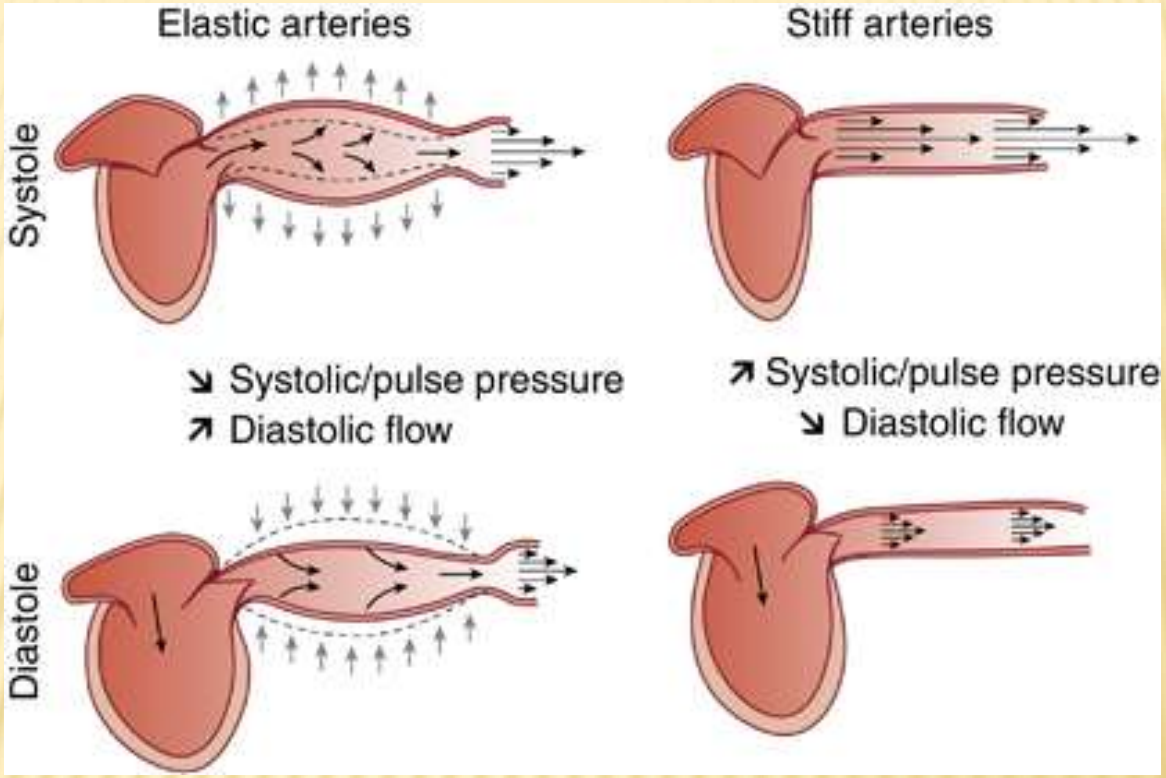


VASCULAR SMOOTH MUSCLE TONE

- Vasodilatation
  - NO – produced in the endothelium by constitutive (eNOS) and inducible (iNOS) synthase
  - prostacyclins
  - histamine
  - bradykinin
  - pO_2, pCO_2 ,pH
  - adenosine
  - catecholamines
  - cGMP, cAMP
- Vasoconstriction
  - endothelin
  - ATII
  - ADH
  - catecholamines
  - Ca^{2+}



ARTERIAL WALL ELASTICITY (ELASTIC ARTERIES)



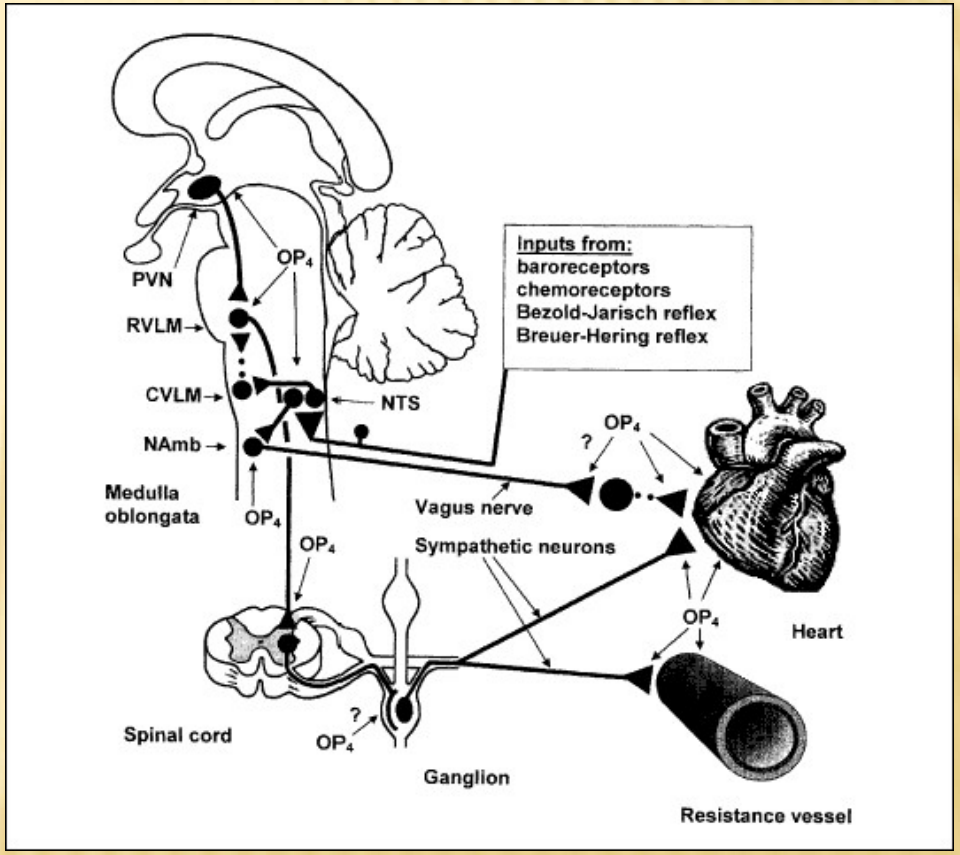
- Worsens with age
- Loss of elasticity (arterial stiffness) leads to isolated systolic hypertension

BLOOD PRESSURE REGULATION

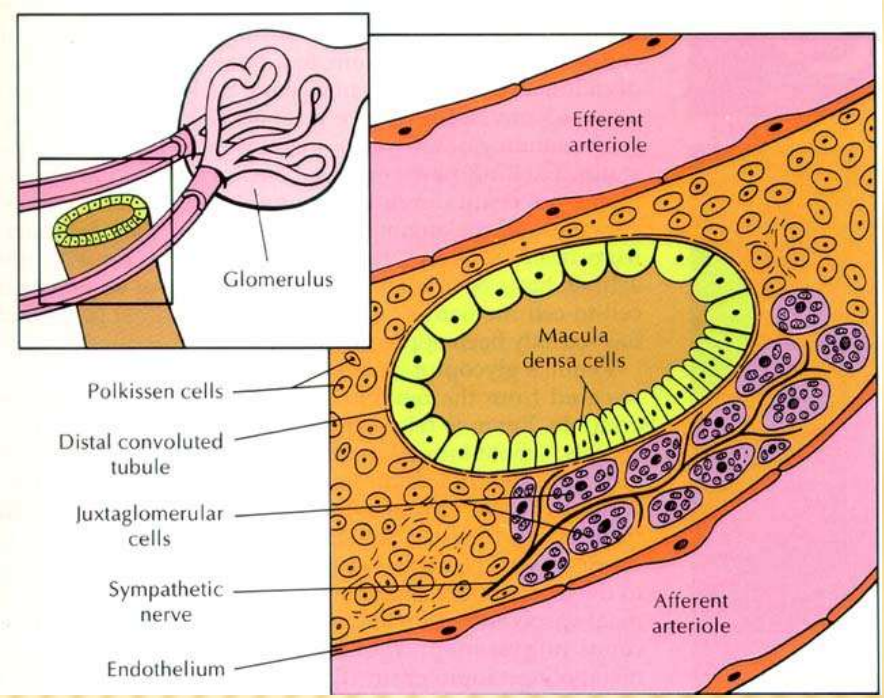
- Several interconnected systems
- Regulation of:
  - heart rate
  - cardiac contractility
  - peripheral resistance
  - circulating volume

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. β1 and M2 receptors), vessels (esp. α1 receptors), kidney (α1, α2, β1)
- Circulating catecholamines



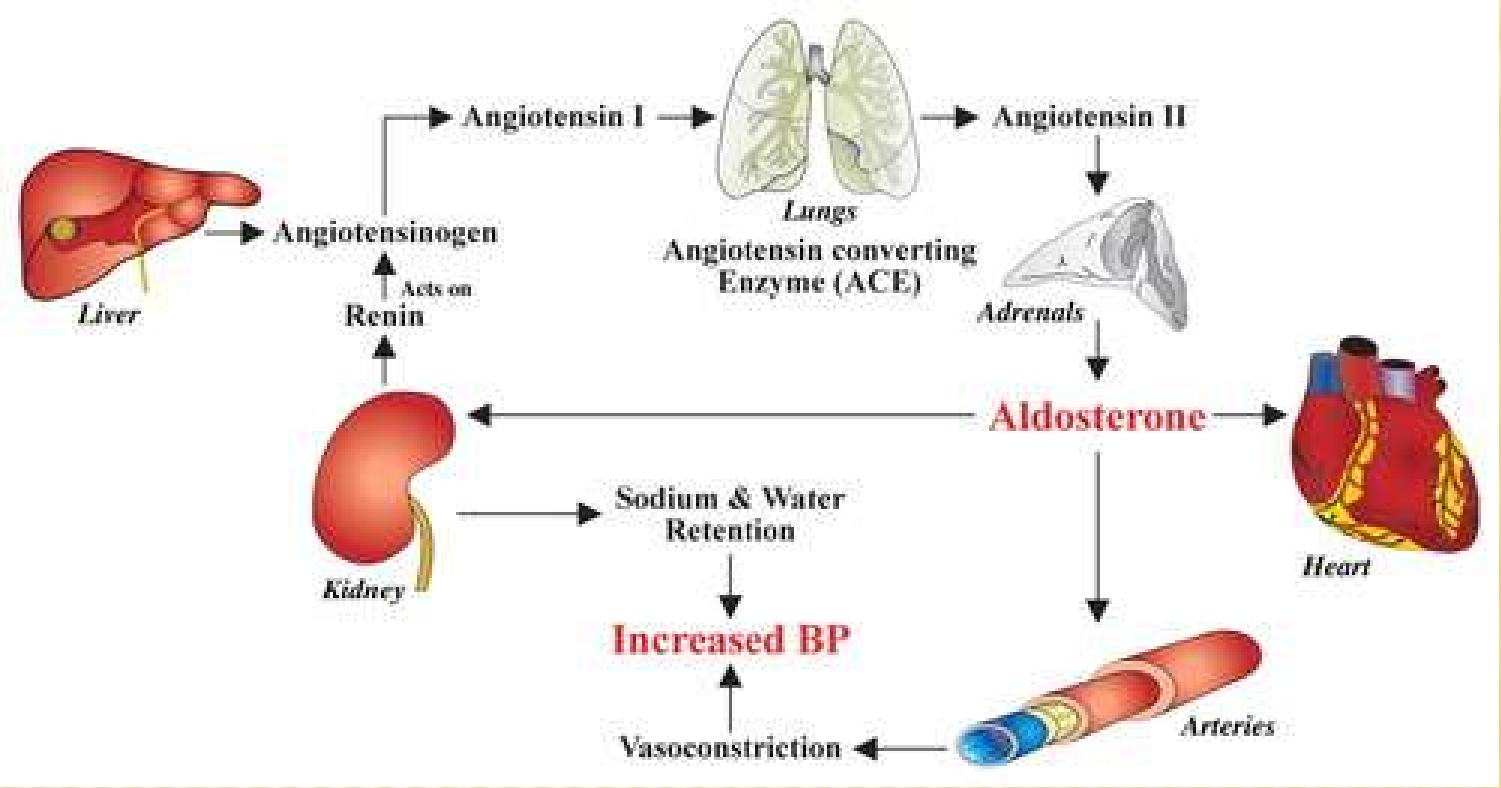
JUXTAGLOMERULAR APPARATUS



Three inputs:

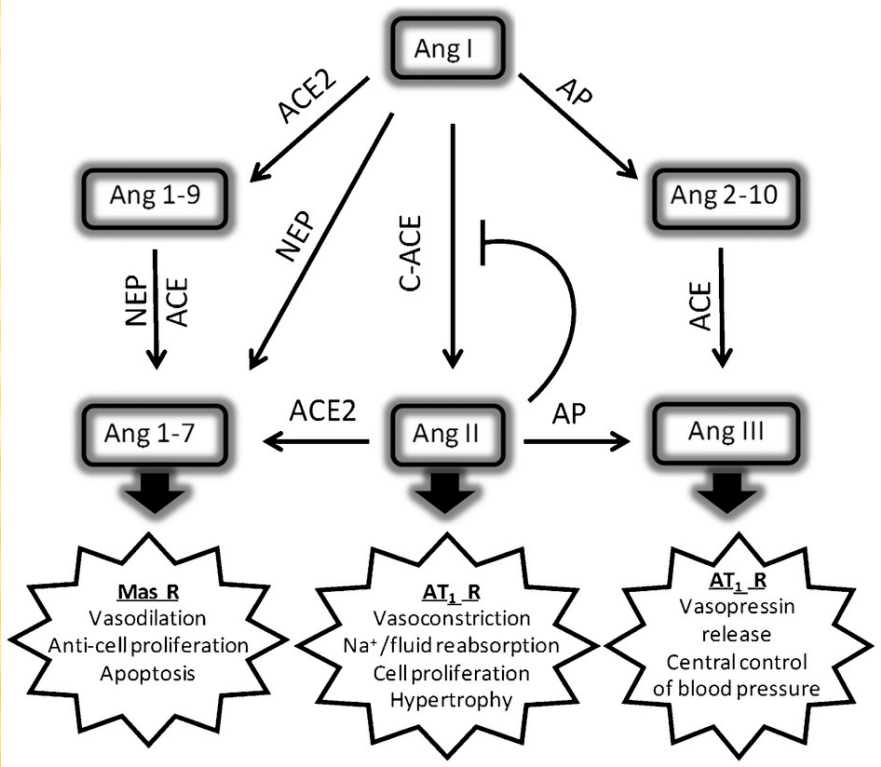
- NaCl in distal tubule
- Stretching of afferent artery
- Sympathetic nervous system

RENIN-ANGIOTENSIN-ALDOSTERONE



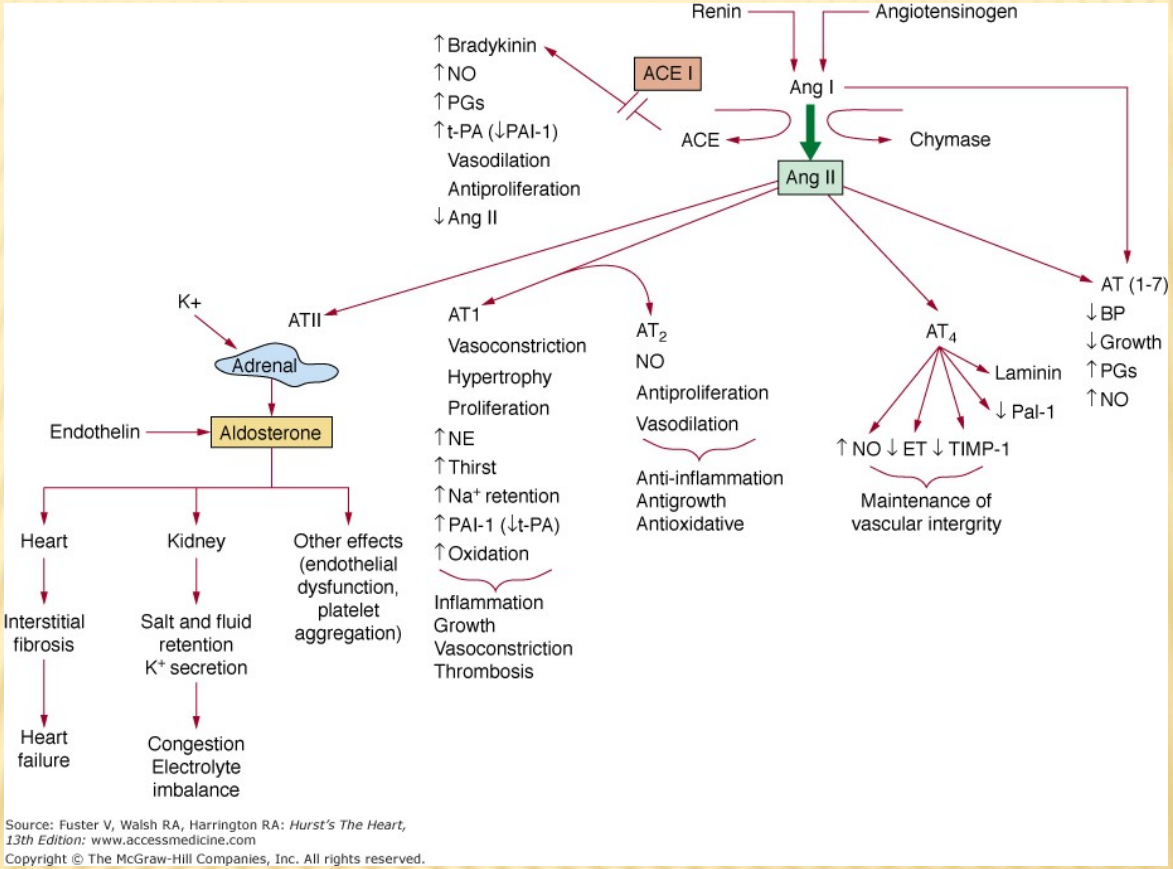
- Renin (and prorenin) binds the (pro)renin receptor (PRR)
- The binding increases the enzymatic activity of renin and leads to receptor activation (involved in central BP regulation)
- Renin also cleaves angiotensin I (dekapetide) from angiotensinogen

ACE AND ACE 2



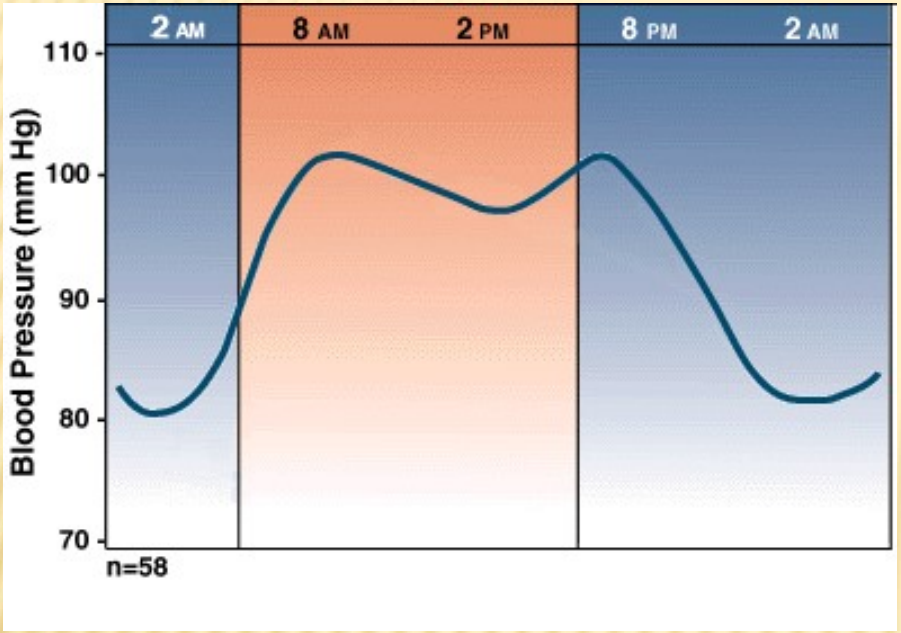
- Angiotensin I (Ang I) can be then transformed into several products
- Through ACE action, Ang II and Ang III with vasoconstriction effects are formed
- ACE also degrades bradykinin (pharmacologic inhibition of ACE leads to angioedema)
- Through the action of ACE 2, angiotensin 1-7 is formed, having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

ANGIOTENSIN II RECEPTORS AND SYSTEMIC EFFECTS OF ALDOSTERONE



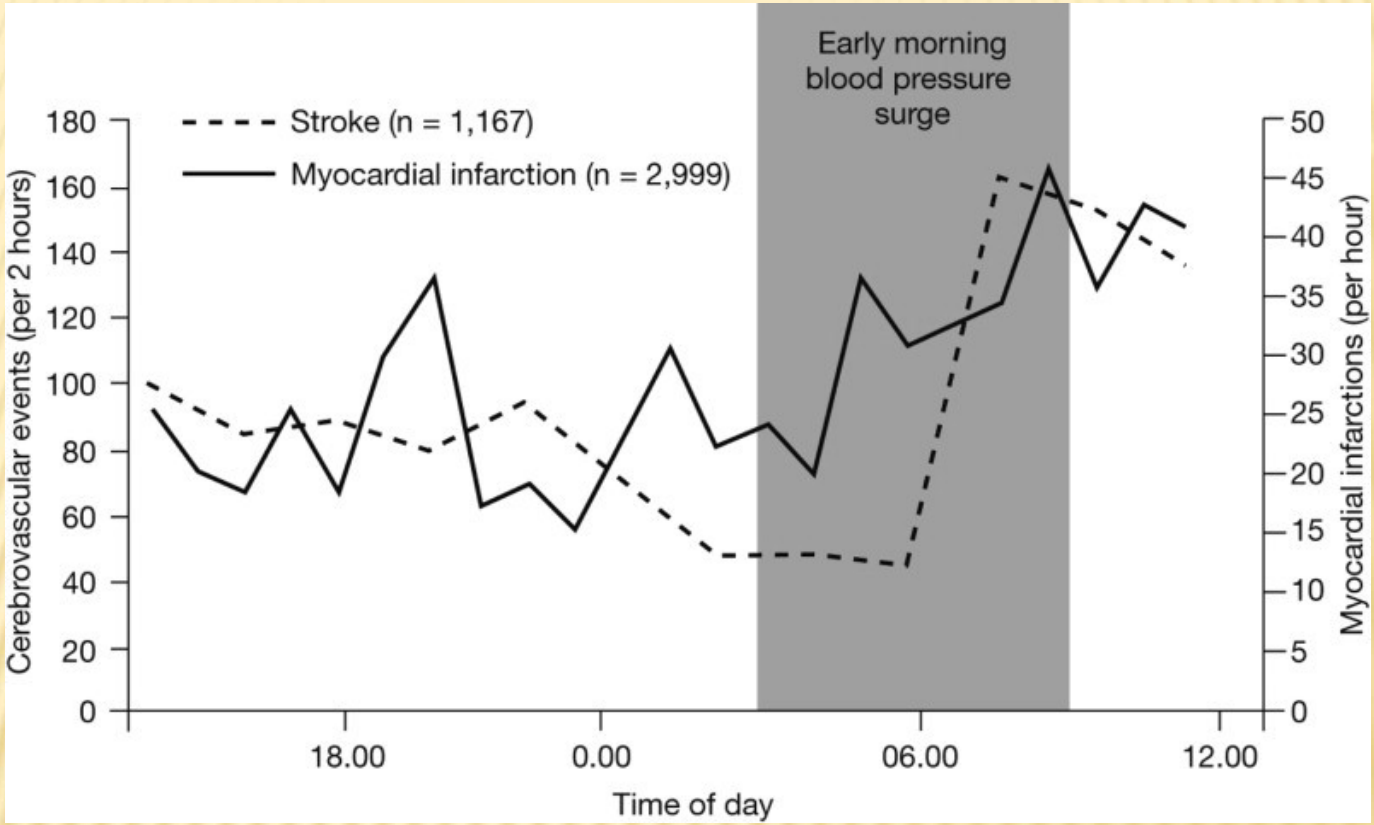
- AT 2 receptors are mostly involved in fetal development
- Ang III is mostly involved in aldosterone secretion and in the CNS

CIRCADIAN RHYTHMICITY OF THE BP



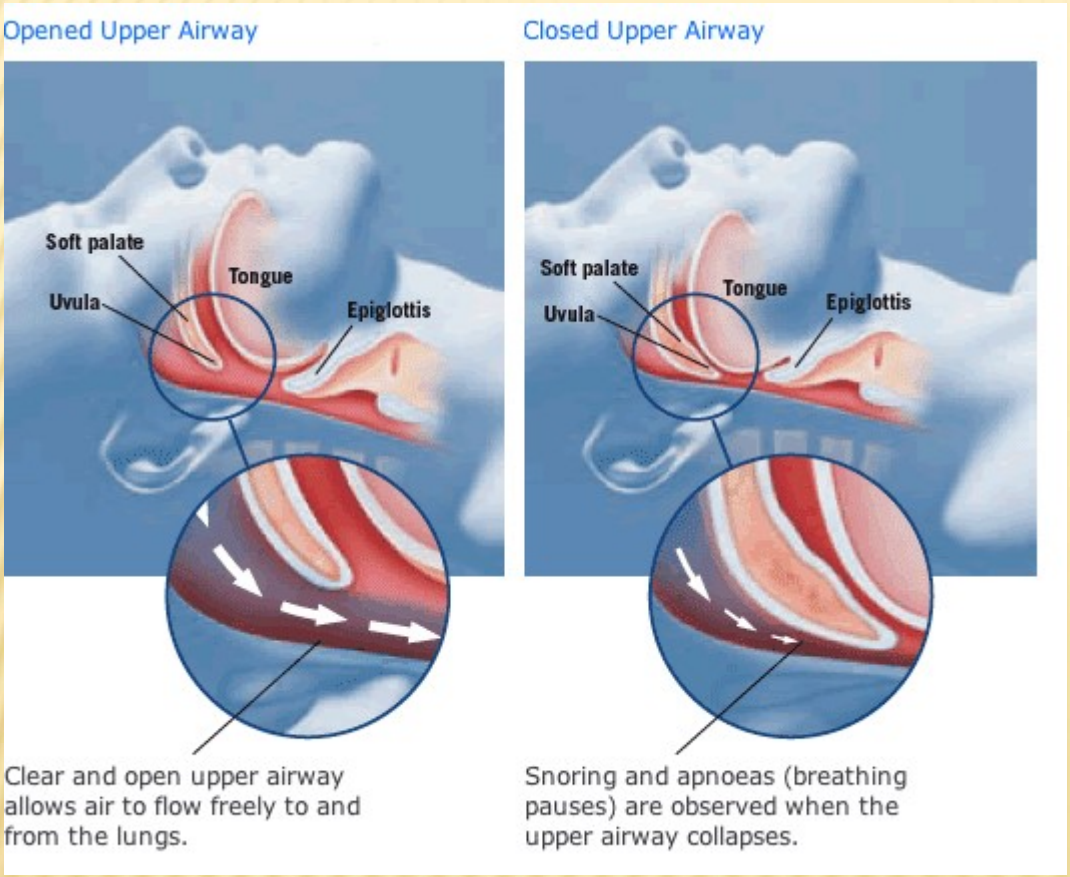
- BP drops by ~10-20% at night („dipping“)
- Hypertonics „non-dippers“ have approx. 2,5x higher odds of cardiovascular events than „dippers“
- In some „non-dippers“ there may be disturbed melatonin secretion (shift work...), often, the absence of the drop results from obstructive sleep apnea

CARDIOVASCULAR EVENTS DURING 24-H CYCLE



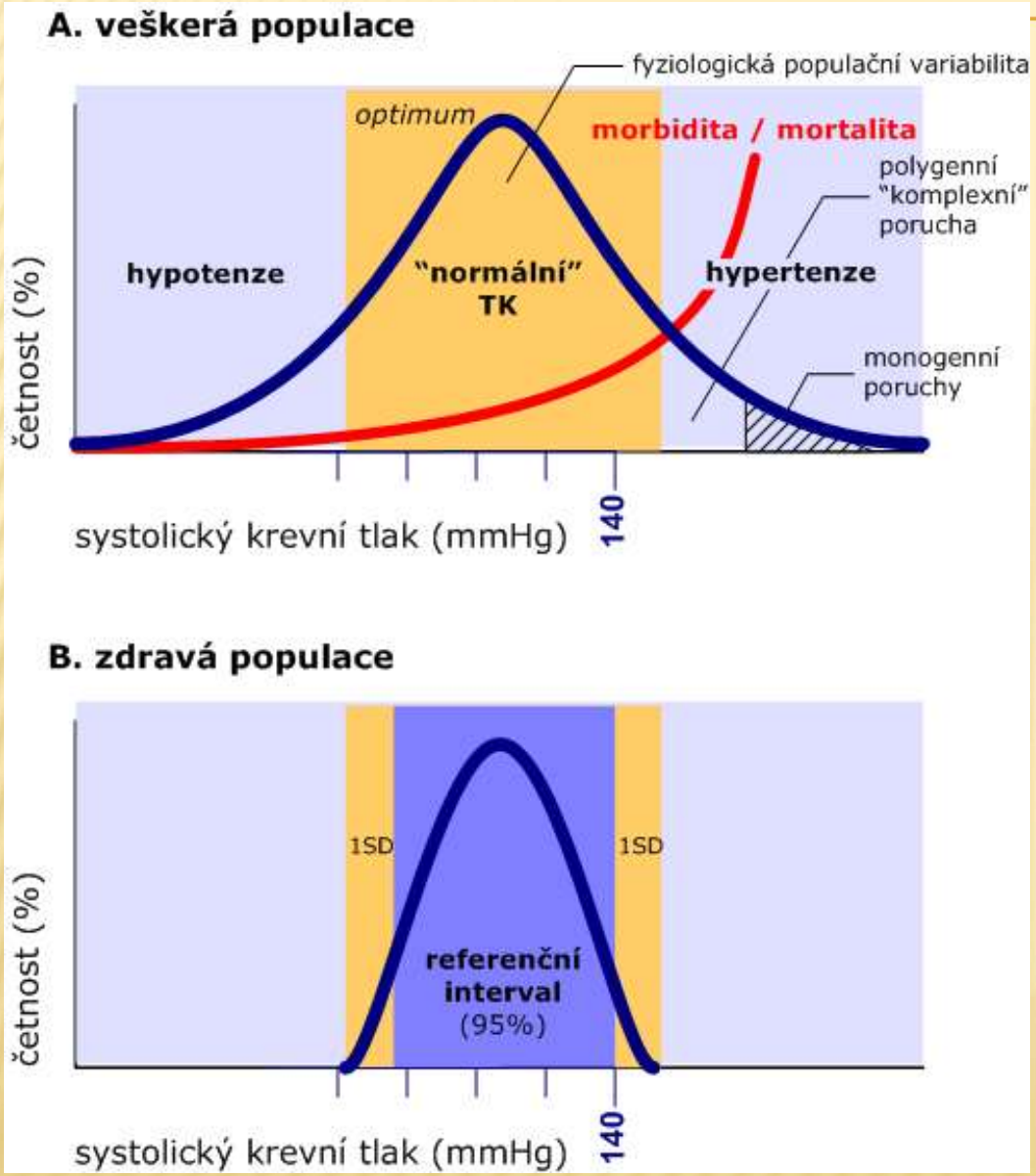
- The incidence of myocardial infarctions and cerebral strokes peaks before noon
- The patients with sleep apnea make an exception

OBSTRUCTIVE SLEEP APNEA



- 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



- 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 ± 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

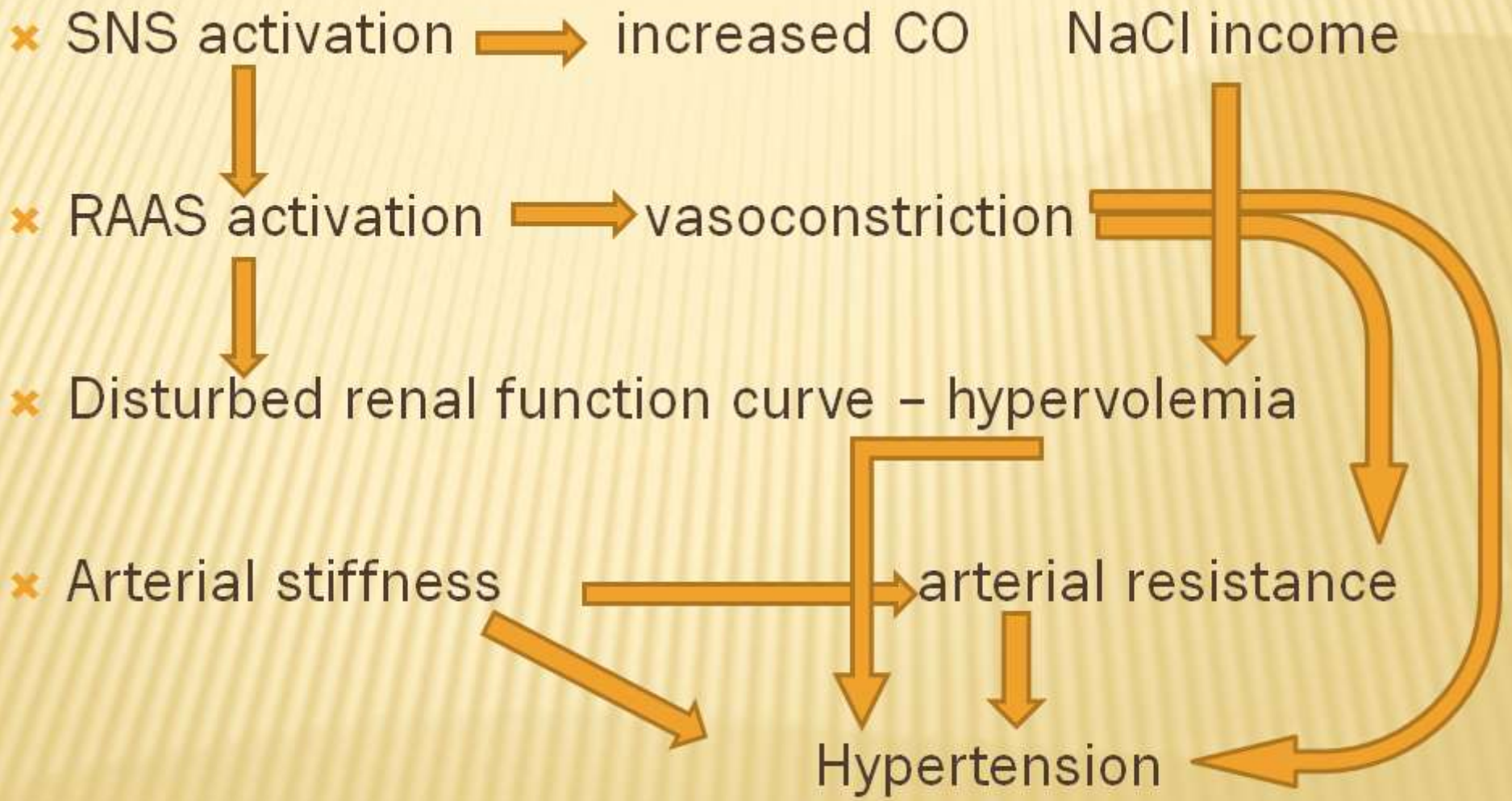
- BP ≥ **140/90 mmHg** (during day) in an adult **regardless the age** after >10min of rest repeatedly min. 2× out of 3 measurements in several days
  - In diabetes and in chronic renal failure, the BP should be <130/80mmHg
  - Ideal BP in an adult – SBP<120 and DBP<80mmHg
- stage of hypertension
  - mild 140 – 179/90 – 104
  - moderate 180 – 199/105 - 114
  - high ≥ 200/115
  - isolated systolic hypertension SBP >160 with DBP <90 mmHg
  - resistant ≥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%
  - Concommitant 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

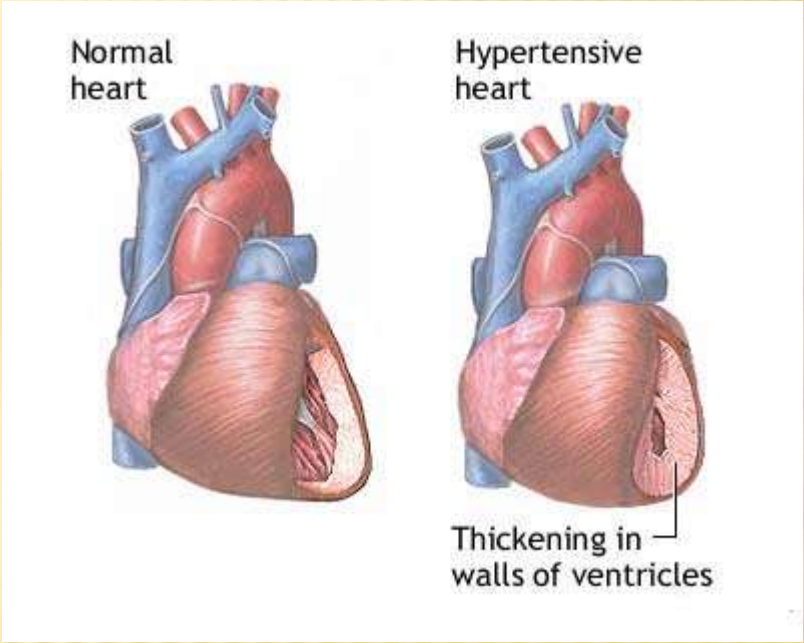


HEART AND VESSEL REMODELATION

- 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

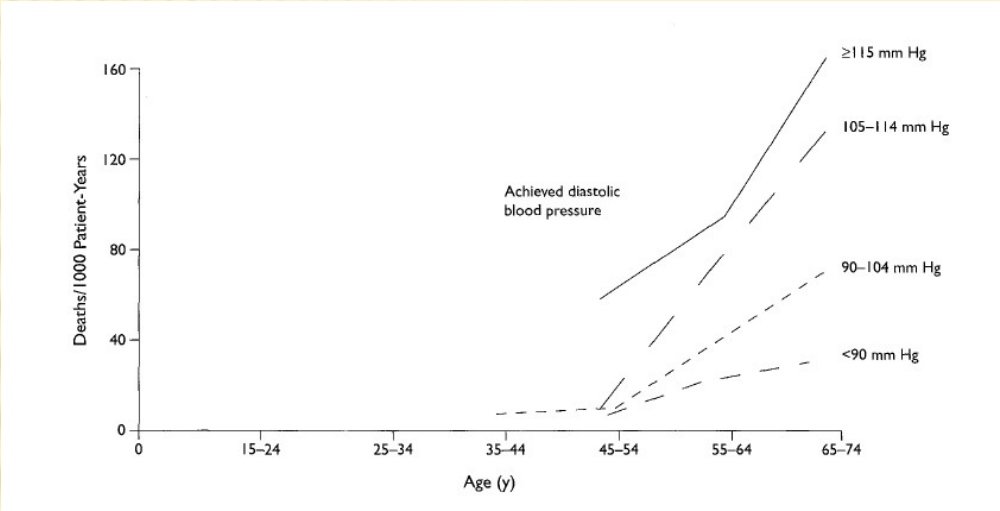
- Heart
  - hypertrophy
- Kidney
  - nephrosclerosis
- Brain
  - encephalopathy
  - dementia
  - hemorrhagic stroke
- Vessel wall
  - atherosclerosis (esp. of heart and brain)

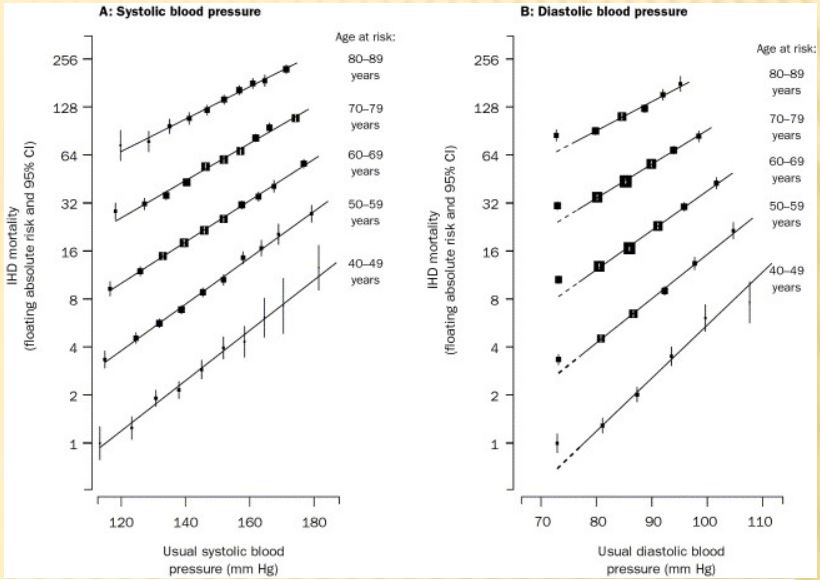


METABOLIC SYNDROME

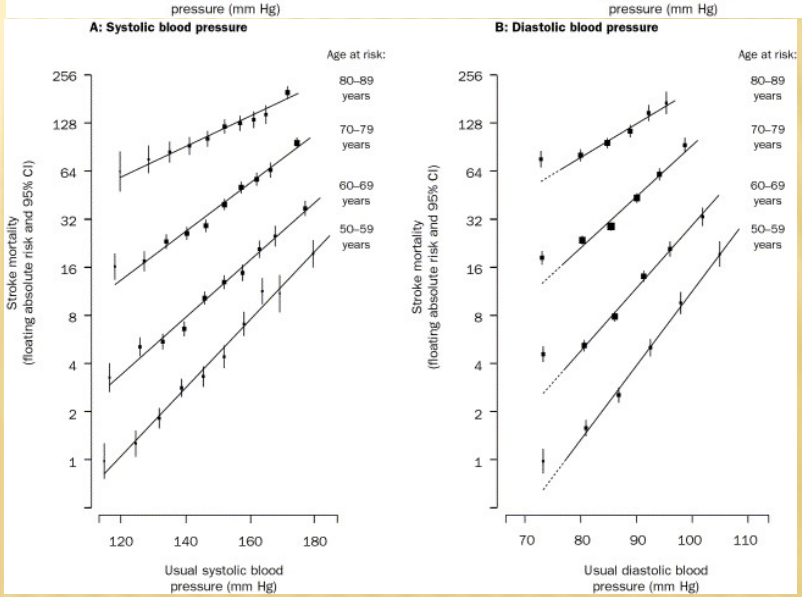
- Hypertension
- Dyslipidemia
- Insulin resistance
- Central obesity
  - Often accompanied by:
    - hyperuricemia
    - long-term increase of HR
    - ↑ fibrinogen
    - long-term ↑ CRP
    - ↑ oestrogens

BP AND MORTALITY – TOTAL, IHD AND STROKES





- linear correlation in SBP, exponential in DBP

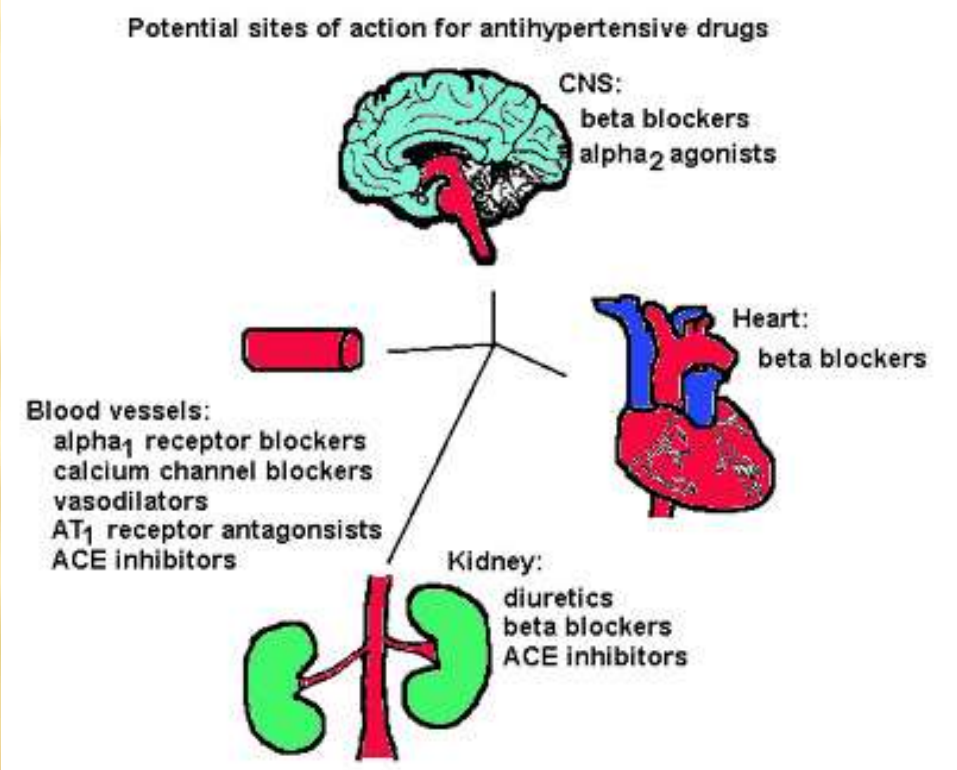


GENETICS OF ESSENTIAL HYPERTENSION

- 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: SNS
    RAAS
    sodium transport mechanisms
    vasodilatory mechanism
  - Most of total heritability is unidentified (“missing heritability“)
  - Rare monogenic forms (mineralocorticoid overproduction, Liddle syndrome)

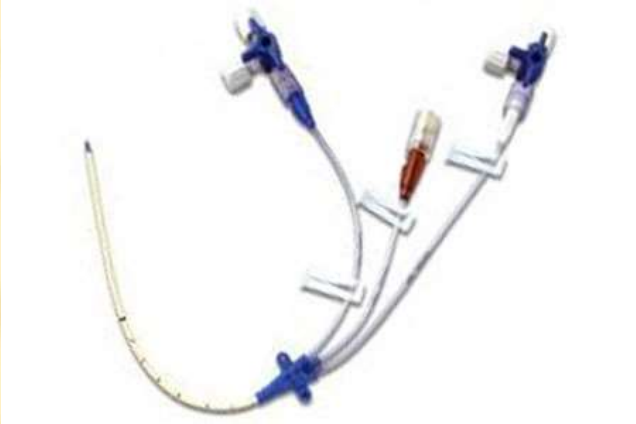
THERAPEUTIC STRATEGIES

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



MEASURING THE BP - METHODS

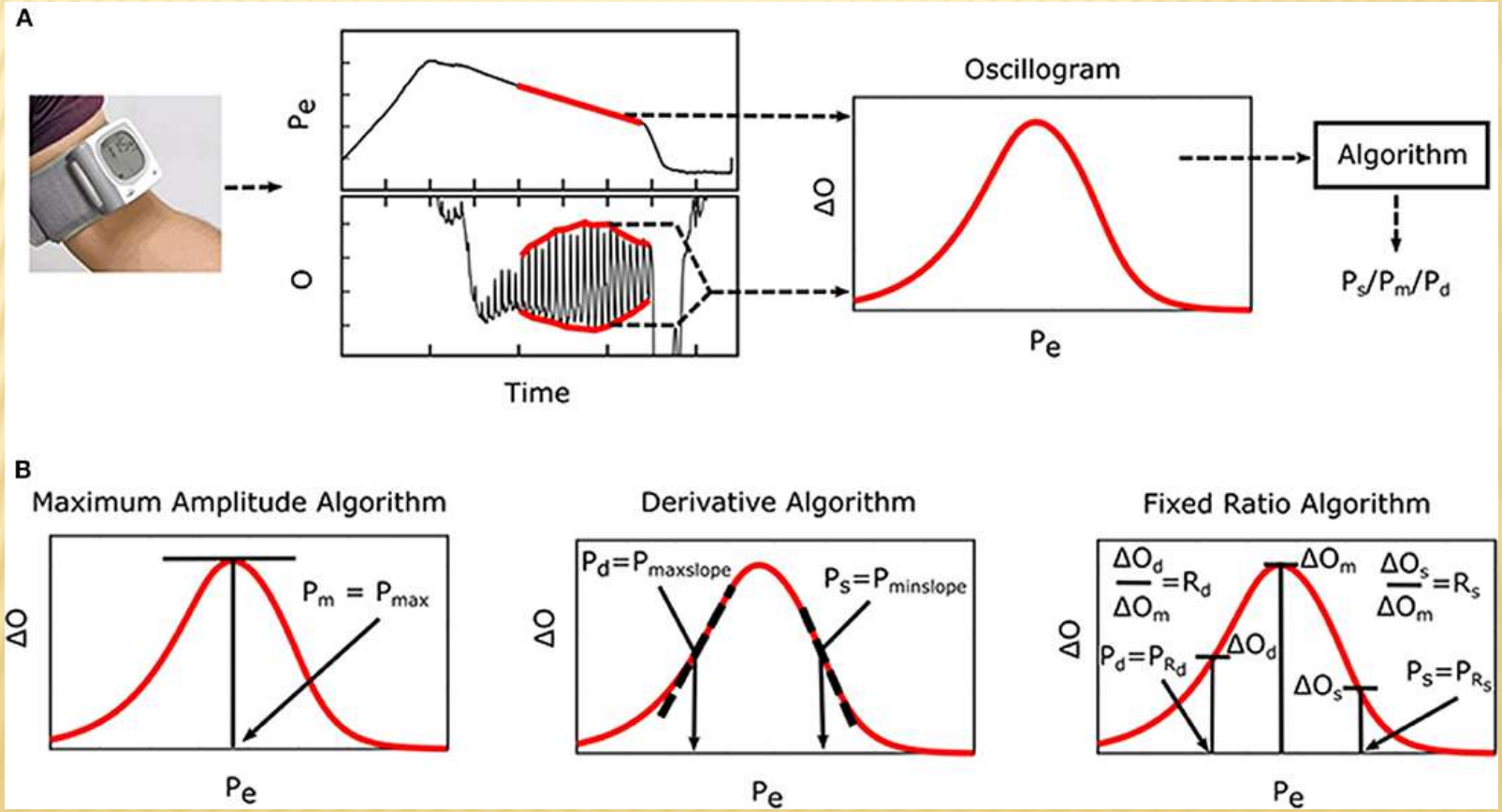
- Invasive (veins, pulmonary circulation, heart chambers)
  - Catheter with a fluid



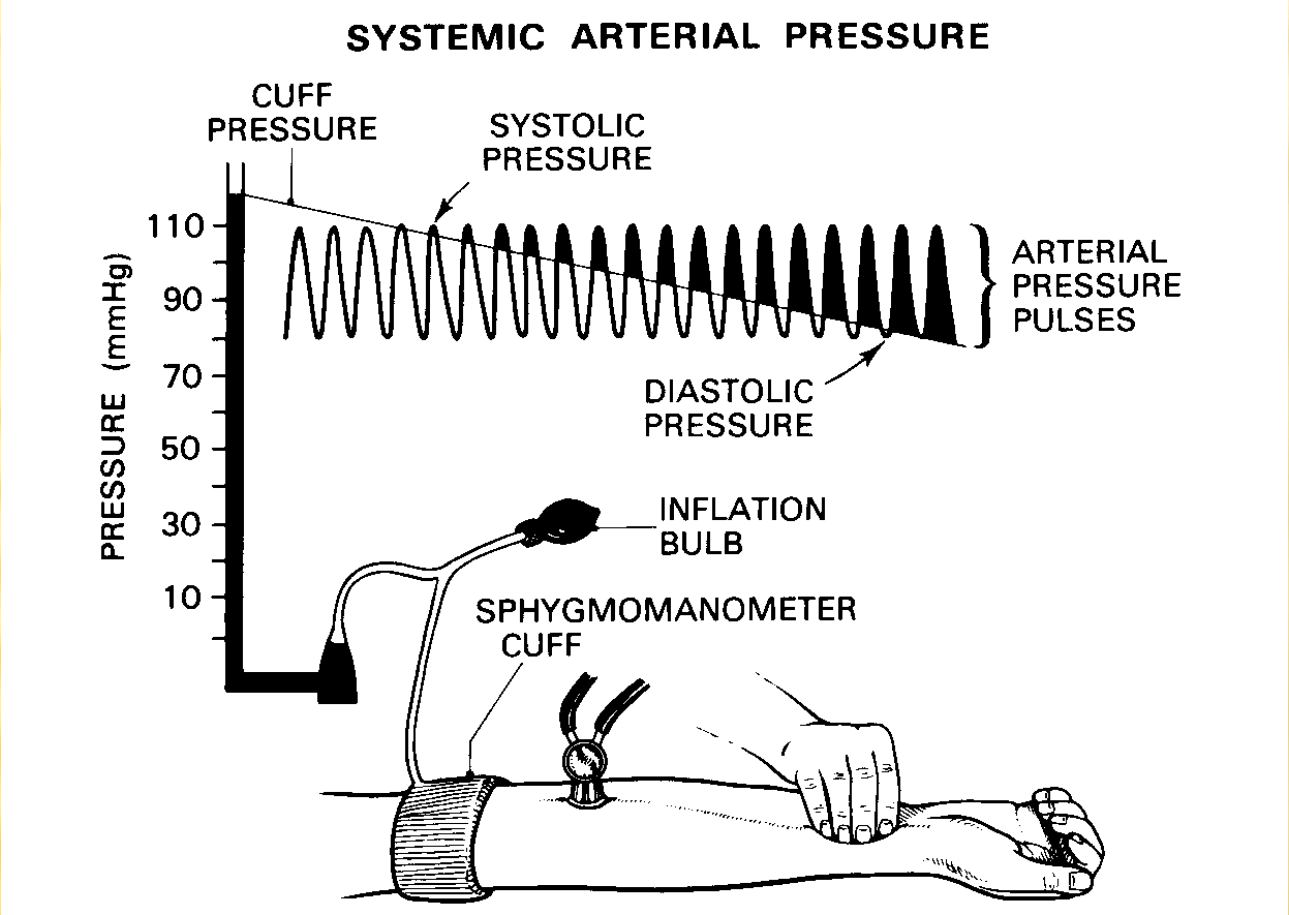
- Non-invasive
  - Occasional
  - Ambulatory
  - Continual (digital fotoplethysmography)

BLOOD PRESSURE - OSCILLOMETRIC METHOD

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



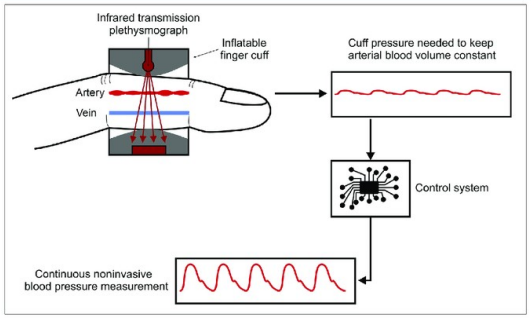
BLOOD PRESSURE – RIVA-ROCCI METHOD



- 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 (Peňáz 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