Regulation of Blood Flow

Assoc. Prof. MUDr. Markéta Bébarová, Ph.D.

Dept. of Physiology, Faculty of Medicine, Masaryk University

This presentation includes only the most important terms and facts. Its content by itself is not a sufficient source of information required to pass the Physiology exam.

Definition of Blood Flow

mathematical formulation – analogy with the electric current

Ohm´s law

$I = U / R \longrightarrow$ $Q = \Delta P / R$

Q	blood flow
ΔP	difference of pressure at the beginning and at the end of a vessel
R	resistance of the vessel (peripheral resistance)

Definition of Blood Flow

$Q = \Delta P / R$

$R = 8\eta l / \pi r^4$

Hagen - Poiseuille formula

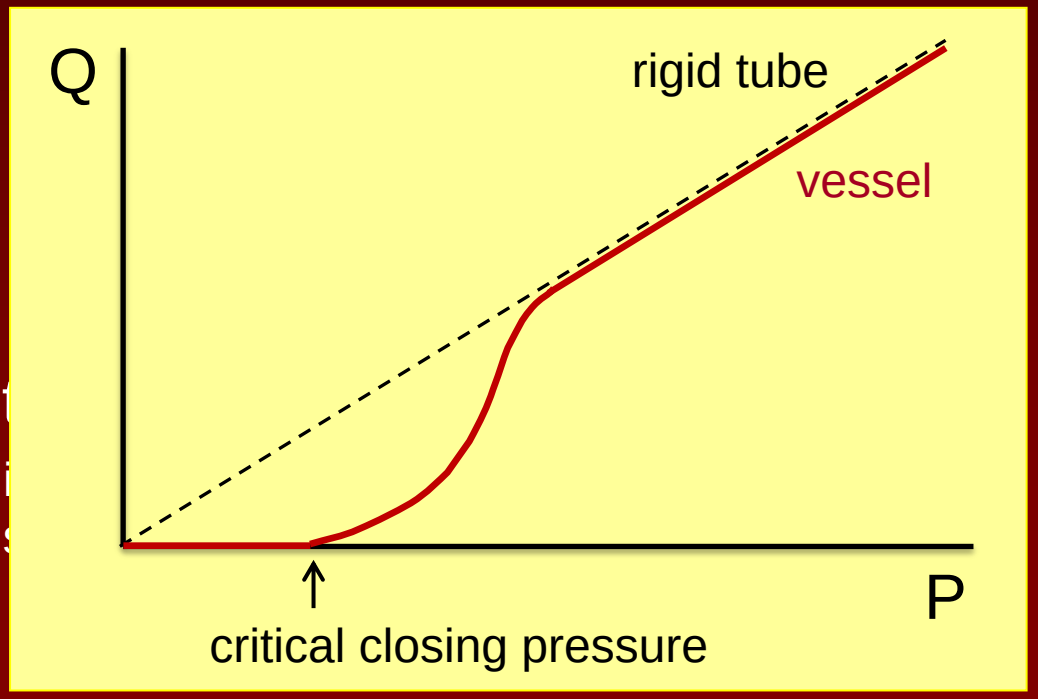
$Q = \Delta P \cdot \pi r^4 / 8\eta l$

r	radius of the vessel
η	viscosity of the blood
l	length of the vessel

This formula applies to the st

Viscosity of the blood is not constant, i
velocity of blood flow. The blood flow is
in the middle (*plasma skimming*). The

Elasticity of vessels.



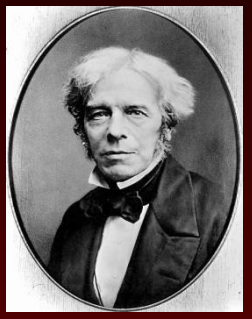
Methods for Measuring Blood Flow

A. with a cannula inserted into a vessel

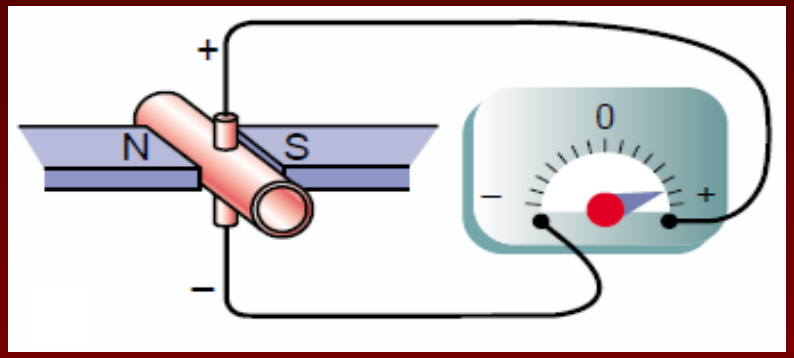
B. without direct contact with the blood flow
   1. Electrical Induction Principle
   2. Doppler Effect
   3. Plethysmography
   4. Fick Principle

Methods for Measuring Blood Flow

1. Electrical Induction Principle (Faraday, 1791-1867)



- the electromagnetic flowmeter
- an electromotive force is generated in the blood (as a conductor) when it moves through a magnetic field

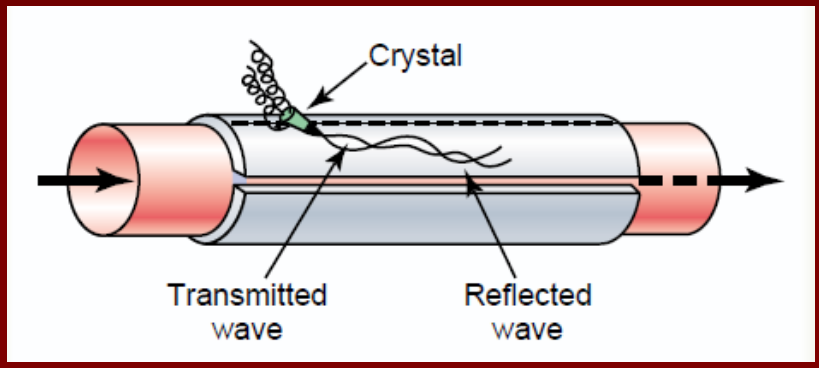


- this electromotive force (measured with an electrode placed on the vessel surface) is proportional to the velocity of blood flow
- can detect changes in the velocity <0.01 s → recording of both steady blood flow and its pulsatile changes

Methods for Measuring Blood Flow

2. Doppler Effect (Christian Doppler, Praque 1842)

- ❖ the ultrasonic Doppler flowmeter; most common
  - ultrasonic waves of a known wave length (frequency) are sent into a vessel diagonally along the blood stream from a subtle piezoelectric crystal
  - waves reflect from the red and white blood cells → a change (↑) of the wave length (↓ frequency)
  - reflected waves are picked up by a sensor
- ❖ change of the wave length (frequency) is proportinal to the velocity of blood flow

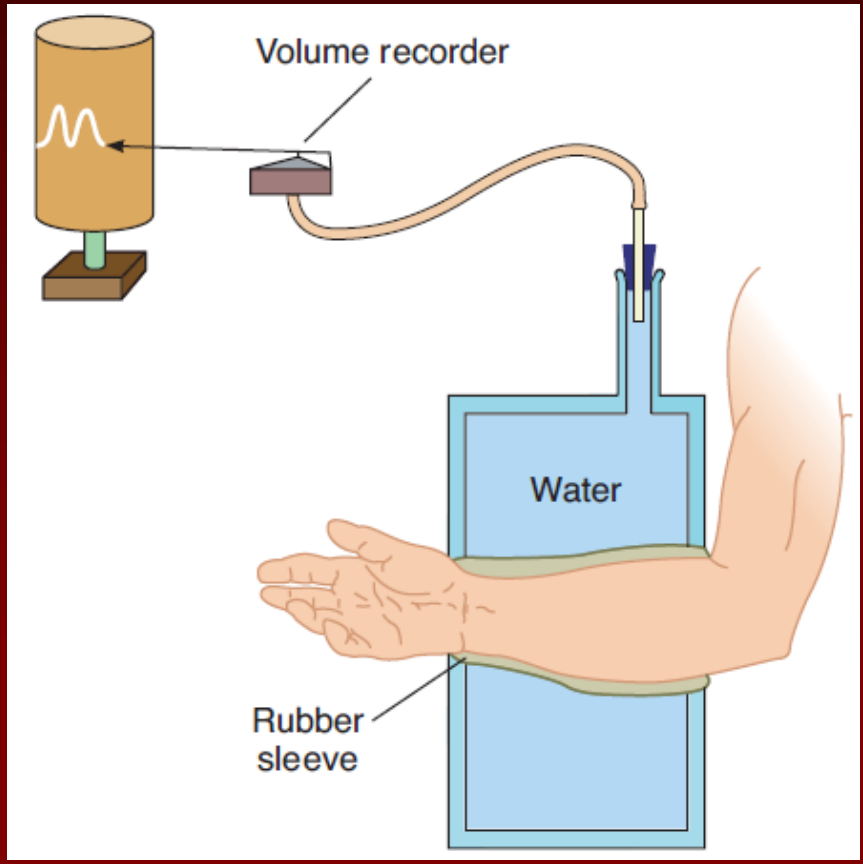


- ❖ both steady blood flow and its pulsatile changes can be measured

Methods for Measuring Blood Flow

3. Plethysmography

- ❖ usually as the venous occlusion plethysmography
- ❖ can be used on limbs



- venous drainage of the limb is stopped (e.g. with an arm cuff)
- increasing volume of the limb (expelling water from closed chamber, measured as a change of its volume) is lineary proportional to the arterial inflow of blood

Methods for Measuring Blood Flow

3. Plethysmography

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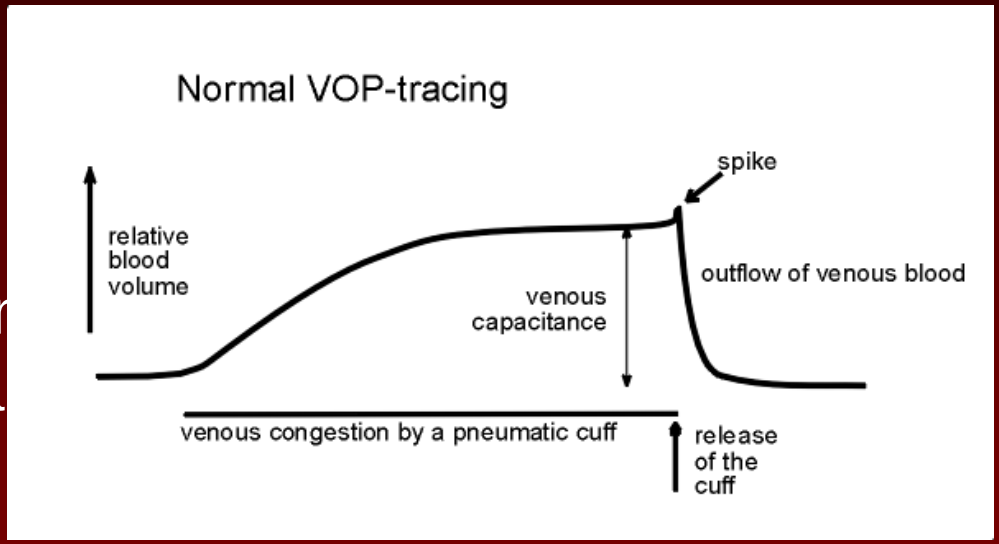

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  (expelling water from closed chamber, measured as a change of its volume)
  is lineary proportional to the arterial inflow of blood

Methods for Measuring Blood Flow

4. Fick Principle - Direct Fick Method

$$Q = \frac{A / time}{AV\ diff}$$

- blood flowing from the right heart to the lungs – about 150 ml O_2 / 1 l
  (a sample of the mixed venous blood bleeded from the pulmonary artery with a catheter inserted to the brachial vene)
- blood flowing from the lungs to the left heart – about 200 ml O_2 / 1 l
  (a sample of the arterial blood from any artery, arterial O_2 content is uniform)

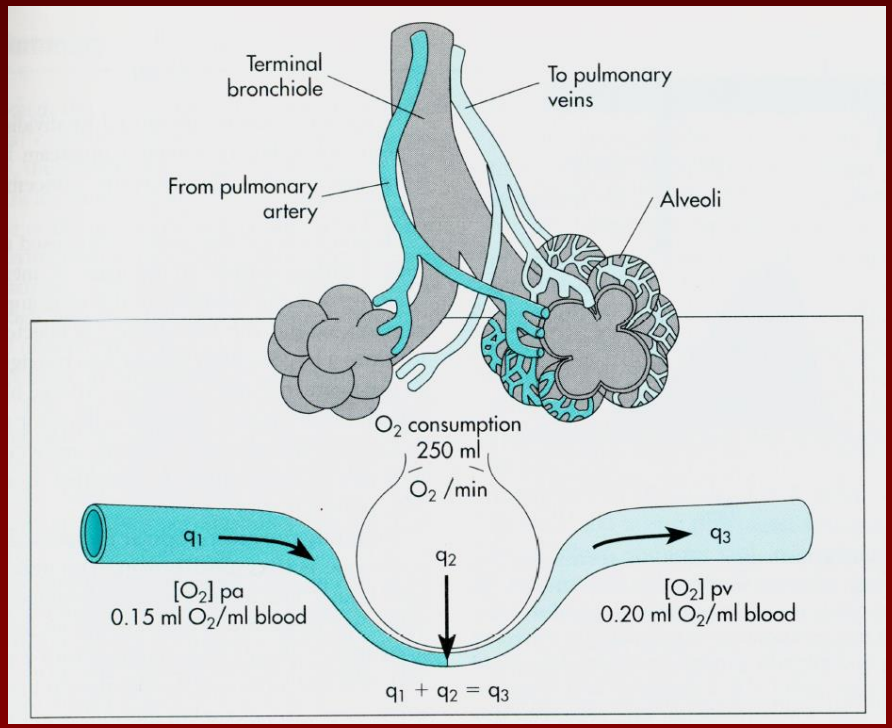
↓

The blood catches 50 ml O_2 / 1 l during passage through the lungs.

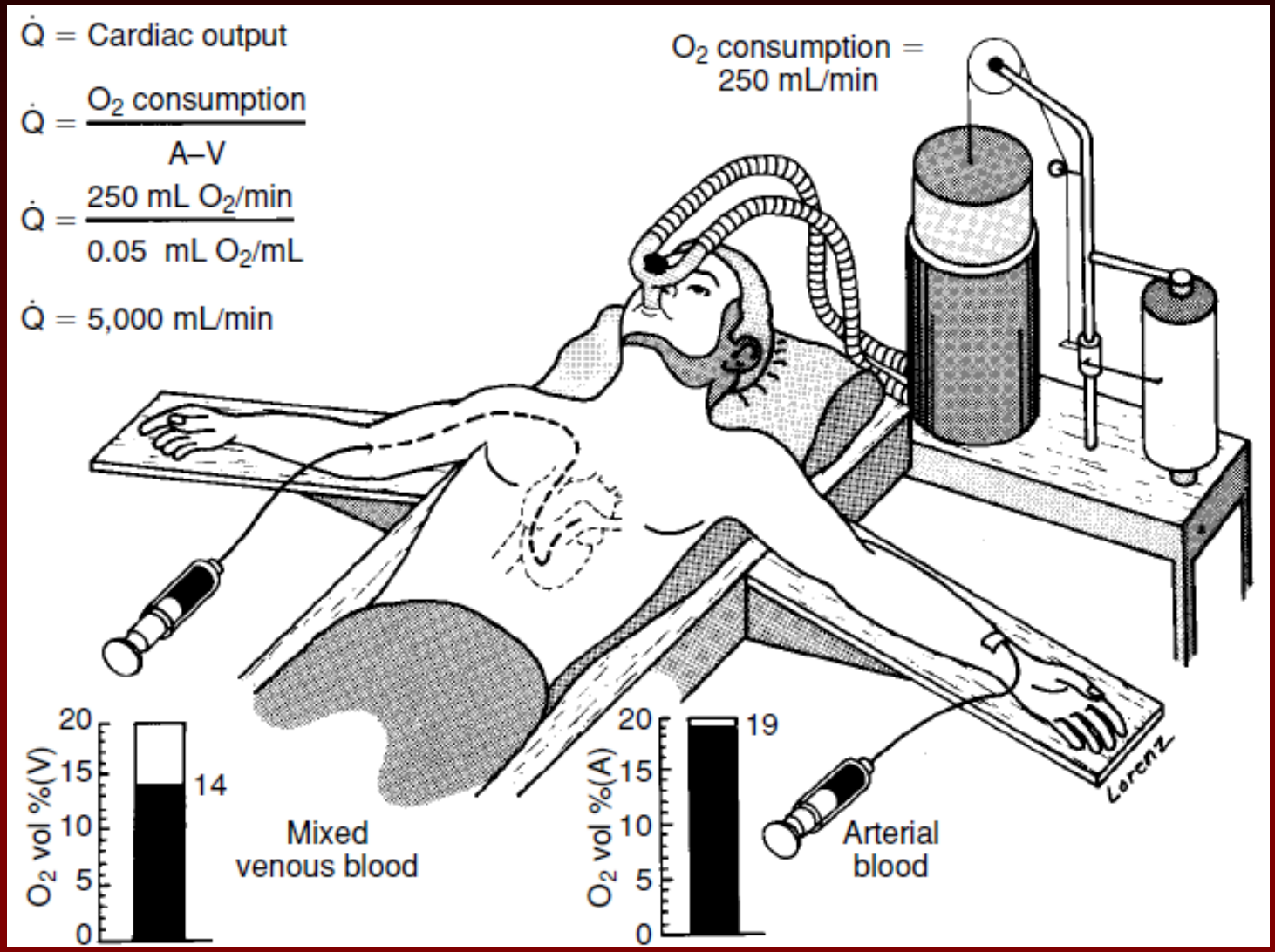
- The total O_2 consumption is 250 ml / 1 min.
  (O_2 decay in the expired air compared to the inspired air, oximeter)

↓

$$CO = \frac{250\ ml\ O_2 / min}{50\ ml\ O_2 / l} = 5\ l / min$$



Methods for Measuring Blood Flow



Methods for Measuring Blood Flow

4. Fick Principle – Method of Indicatory Gas

- to determine the instantaneous blood flow through a specific tissue
- for example the cerebral or coronary blood flow using inhaled nitrous oxide N_2O – Kety method

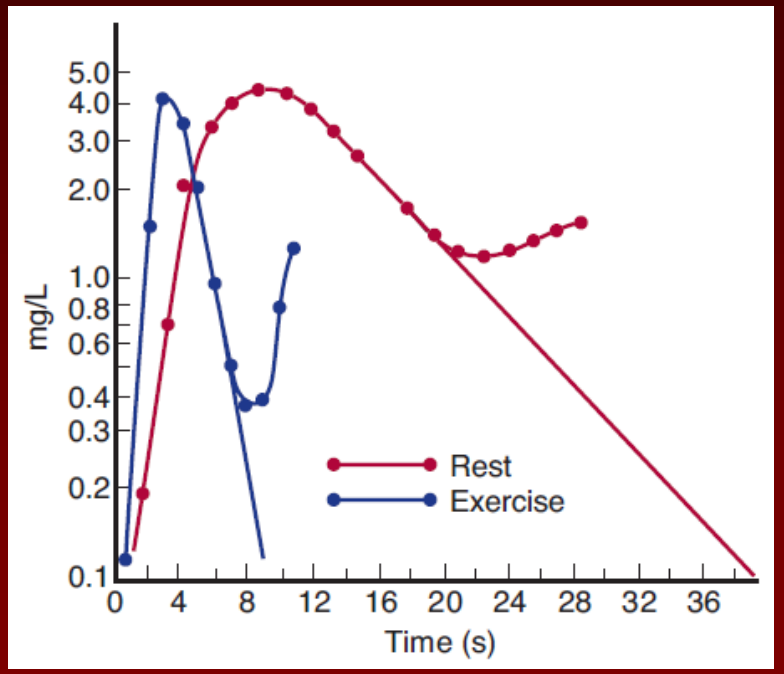
$$\text{cerebral blood flow} = \frac{N_2O \text{ removed from blood by brain / time}}{\text{averaged arteriovenous difference of } N_2O}$$

(N_2O concentration in the venous blood)

Methods for Measuring Blood Flow

4. Fick Principle - Indicator Dilution Technique

- known amount of an indicator (dye or radioactive isotope) is injected into a peripheral (an arm) vein (A, [mg])
- concentration of the indicator in serial samples of the arterial blood is determined
- estimation of the averaged concentration of the indicator in the arterial blood after a single circulation (C, [mg/ml])



$$CO = \frac{A}{C\,(t_2 - t_1)} \quad \frac{[mg]}{[mg.ml^{-1}.s]}$$

Methods for Measuring Blood Flow

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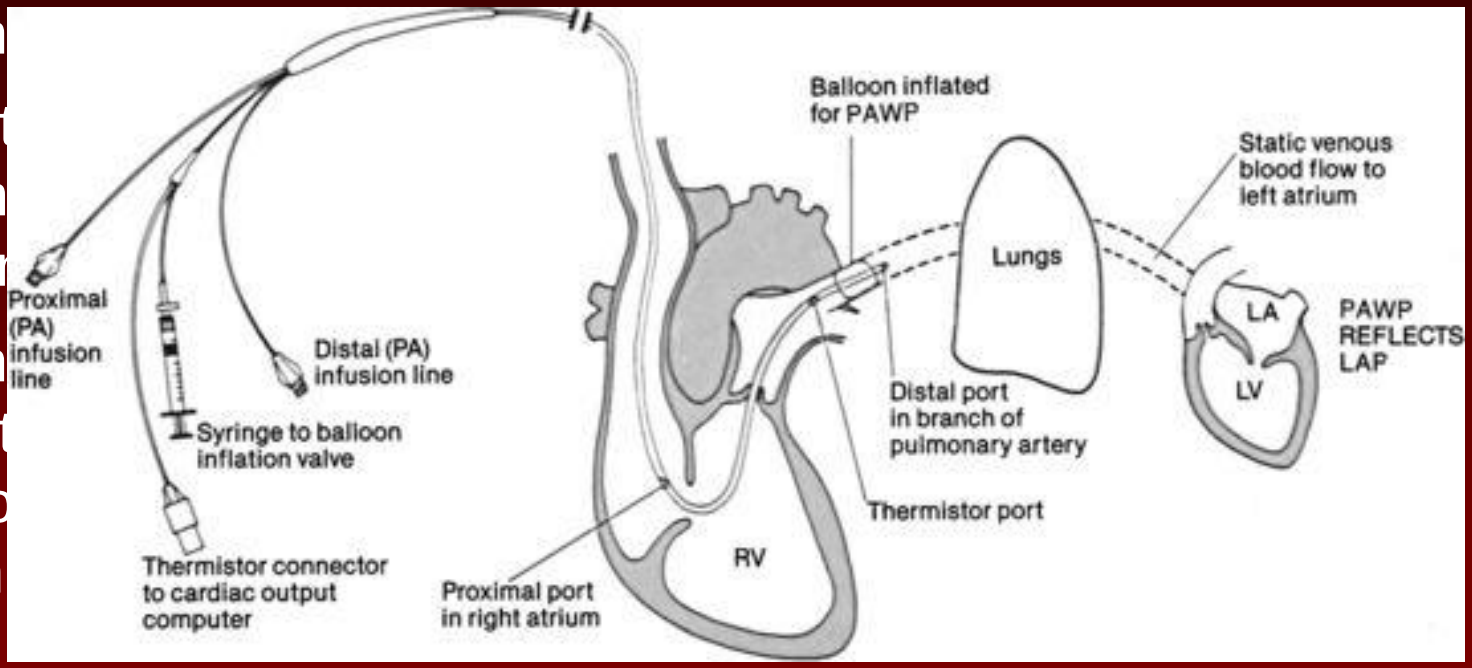


❖ thermodilution

a cold saline (indicator) is injected into the right atrium through a double lumen catheter; the change of blood temperature (inversely proportinal to the blood flow) is recorded in the pulmonary artery using a thermistor in the other side of the catheter

Regulation of Blood Flow

$$Q = \Delta P \cdot \pi r^4 / 8\eta l$$

Resting Tone (intermediary vascular muscle tone at rest)

- due to tonic activity of vasocontrictive sympathetic fibres
- a role might play also: myogenic response of vessels to the blood pressure (later), high concentration of O_2 in the arterial blood, Ca^{2+}

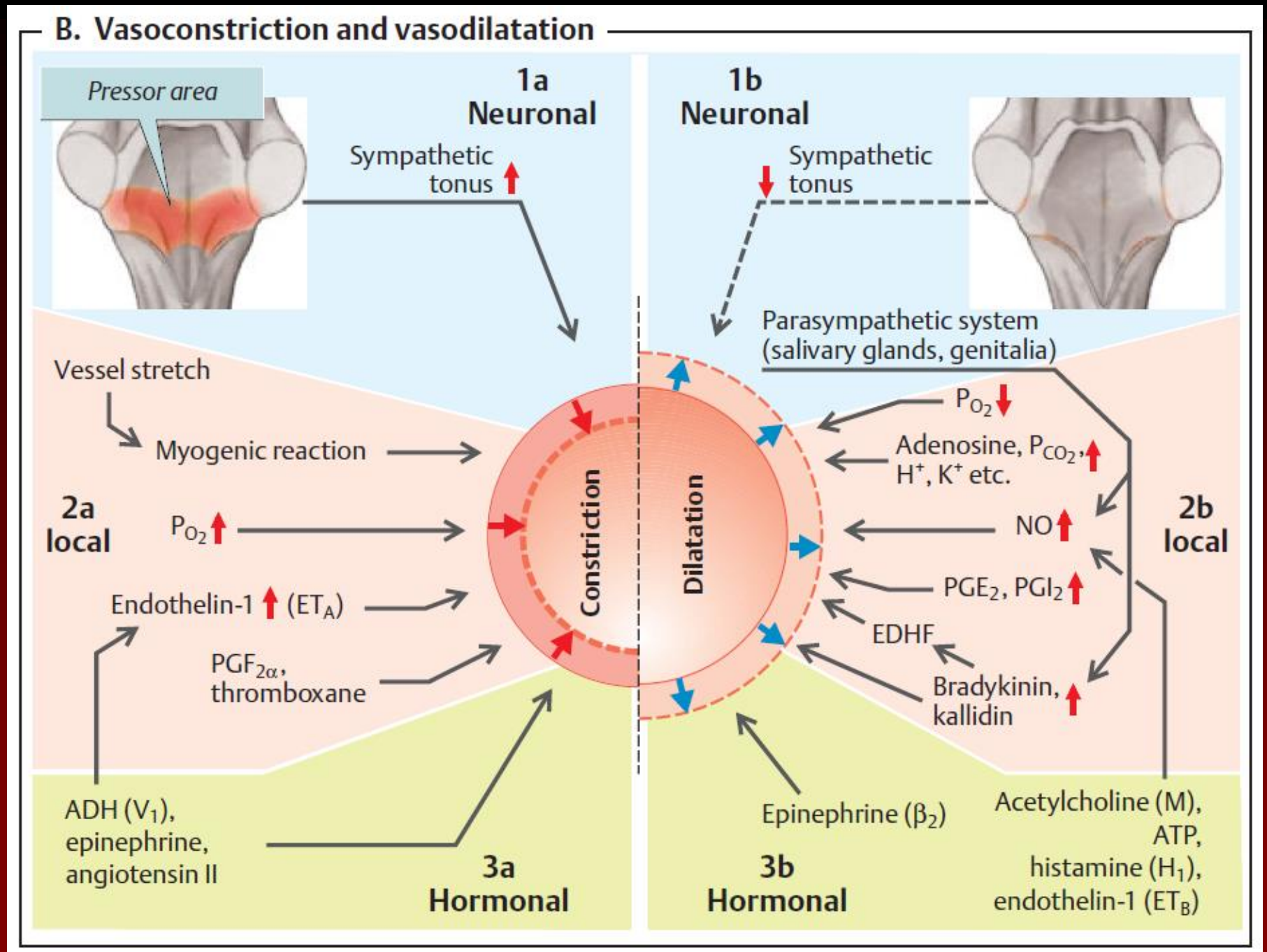
Basal Tone

- in response to denervation; due to spontaneous depolarizations of the vascular smooth muscles

Regulation

Local

Systemic



Regulation of Blood Flow - Local

A. Acute

seconds to minutes, but incomplete (about ¾ of the desired effect)

1. Metabolic Autoregulation
2. Myogenic Autoregulation
3. Regulation Mediated by Local Substances

B. Chronic

hours, days to weeks , even months

Regulation of Blood Flow - Local

Metabolic Autoregulation

insufficient blood flow < ↑ metabolic demands of a tissue
↓ or stopped blood supply

→ ↑ concentration of metabolites (CO_2, lactic acid, adenosine, K^+, phoshate), ↓ pH, ↑ osmolarity in the interstitium, ↑ tissue temperature (the metabolic heat); ↓ pO_2 (the second theory based on the lack of O_2 and nutrients)

→ vasodilatation

Preferred to the systemic regulation in case of hypoxia (to preserve the adequate tissue perfusion).

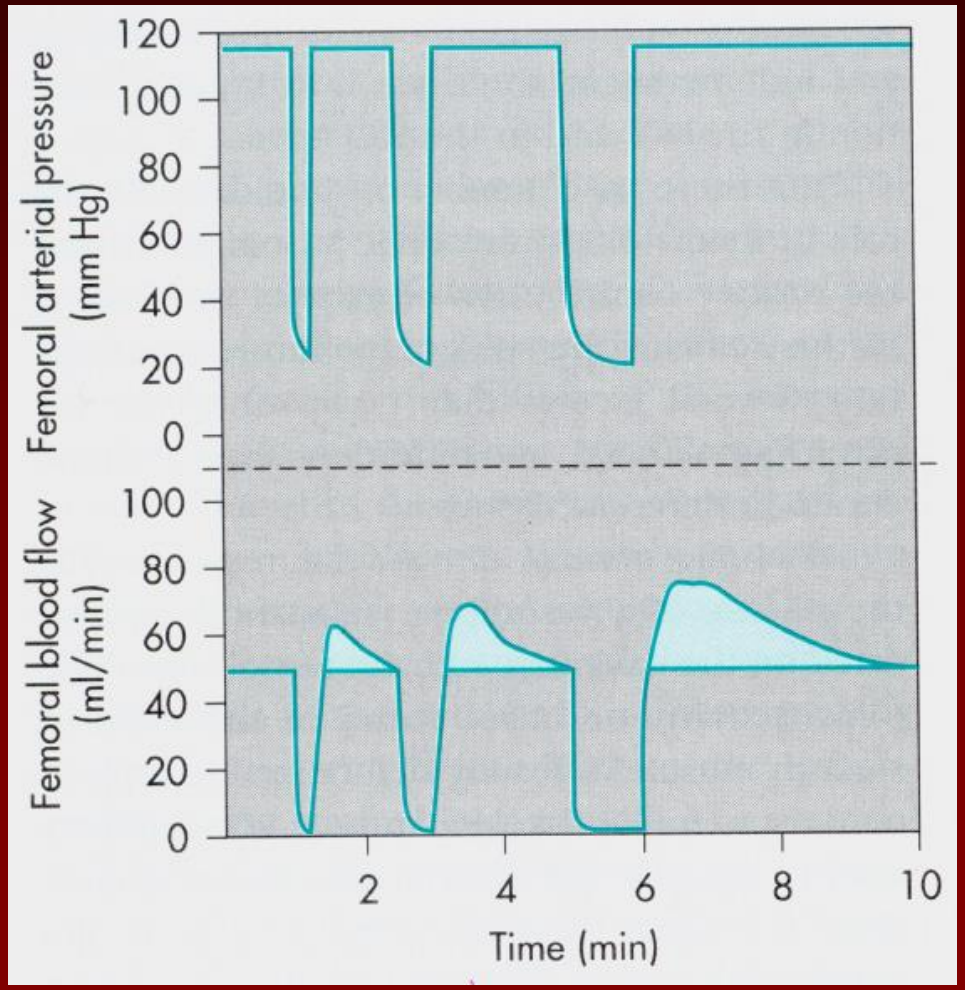
It plays the key role in e.g. brain, heart and skeletal muscles.

Regulation of Blood Flow - Local

Metabolic Autoregulation

active hyperemia
(increase of the blood flow induced by an increased metabolic activity of the tissue)

reactive hyperemia
(transient increase of the blood flow exceeding its common level after release of an occlusion; it gradually returns to the control level)



(15-, 30- and 60-s occlusions of the femoral artery in a dog)

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Regulation of Blood Flow - Local

Myogenic Autoregulation (Bayliss effect)

↑ blood pressure

⟶ ↑ blood flow and ↑ tension in the vascular wall

$Q = \Delta P / R$

Law of Laplace

$T = P \cdot r$

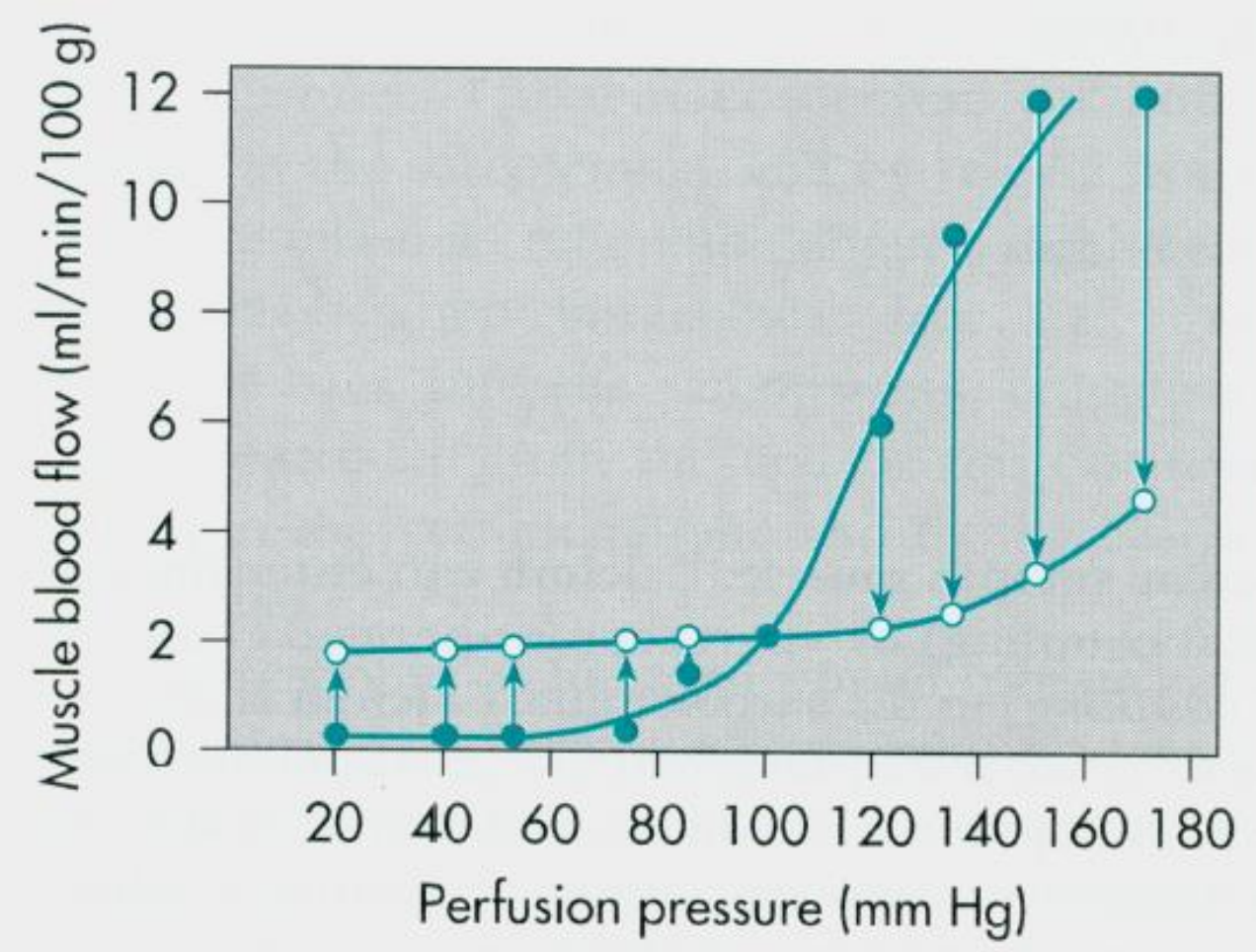
⟶ mechanical stimulation, depolarization and subsequent contraction of the smooth muscle cells in the vascular wall → vasoconstriction

⟶ return of the blood flow back on the original level

It plays an important role in the brain and kidneys.

Regulation of Blood Flow - Local

Myogenic Autoregulation



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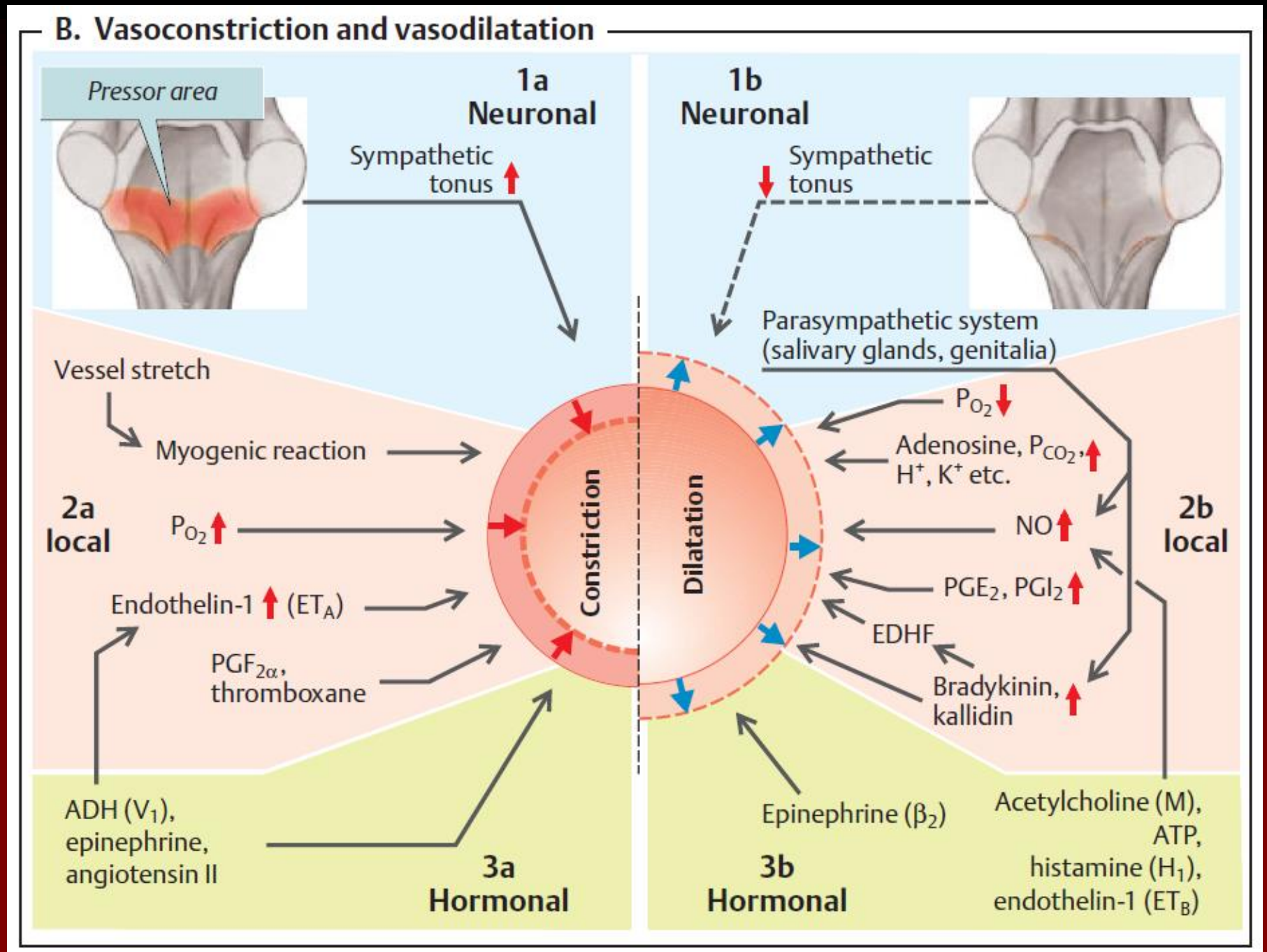
Regulation of Blood Flow - Local

Regulation Mediated by Local Substances

endothelial-derived relaxing factor (EDRF) – NO (half-life in the blood only 6 s) → vasodilatation

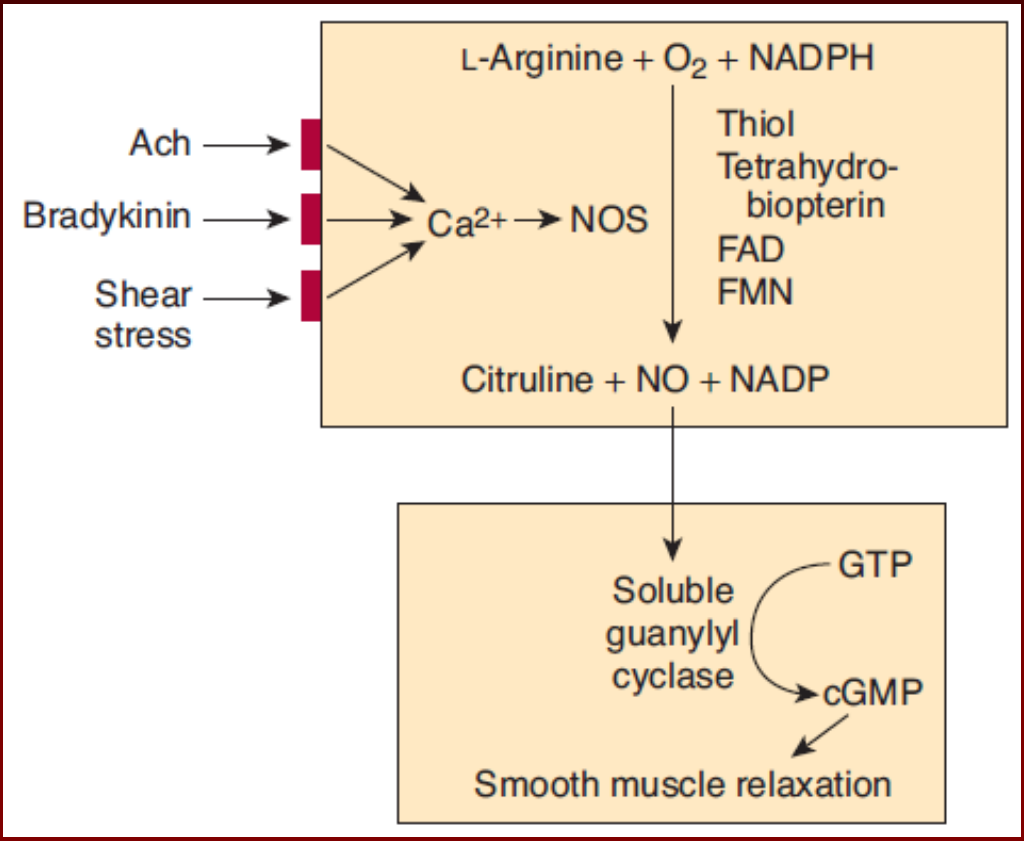
- important in the intermediate and larger arteries back upstream where the metabolic tissue changes causing dilatation of the microvessels cannot directly reach
- synthesized in the endothelial cells of arteriols and small arteries due to the shear stress induced by the flowing blood (deforms the endothelial cells in the direction of flow)
- its synthesis stimulated by the products of thrombocyte aggregation (to keep vessels with intact endothelium permeable) and also by many primary vasoconstrictive substances



Regulation of Blood Flow - Local

Regulation Mediated by Local Substances

endothelial-derived relaxing factor (EDRF) – NO



Regulation of Blood Flow - Local

Regulation Mediated by Local Substances

prostacyclin

- synthesized in the endothelial cells from the arachidonic acid
- inhibition of thrombocyte aggregation and vasodilation

thromboxane A_2

- synthesized from the arachidonic acid by thrombocytes
- support of thrombocyte aggregation and vasoconstriction

A balance between them is crucial for formation of the localized clot and preservation of the blood flow. (aspirin)

Regulation of Blood Flow - Local

Regulation Mediated by Local Substances

endothelins

- several similar polypeptides synthesized by the endothelial cells (ET-1, ET-2, ET-3)
- 2 endothelin receptors:

  ET_A – specific for ET-1, in many tissue vessels, → vasoconstriction

  ET_B – ET-1 to ET-3, unknown function (maybe vasodilatation – *through increased synthesis of NO* - and developmental effects)

- ET-1 – one of the most potent vasoconstrictive substances
- the exact physiological role not known
- released from the endothelial cells in the damaged tissue → vasoconstriction → restricts bleeding
- play a role in closing *ductus arteriosus* at birth

Regulation of Blood Flow - Local

Serotonin (5-OH tryptamine)

- vasoconstrictive effect
  - in a damaged tissue
  - direct local effect
  - released from thrombocytes
- vasodilatory effect
  - in an undamaged tissue
  - through increased activity of NO synthase

Regulation of Blood Flow - Local

Other, specific mechanisms

- local vasoconstriction of damaged arteries and arteriols
  (due to release of serotonin and thromboxane A2 from thrombocytes and endothelin-1 from the endothelial cells)
- vasoconstriction (vasodilatation) induced by a decrease (increase) of the tissue temperature
- specialized tissues (kidneys, brain, etc.)

Regulation of Blood Flow - Local

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seconds to minutes, but incomplete (about ¾ of the desired effect)

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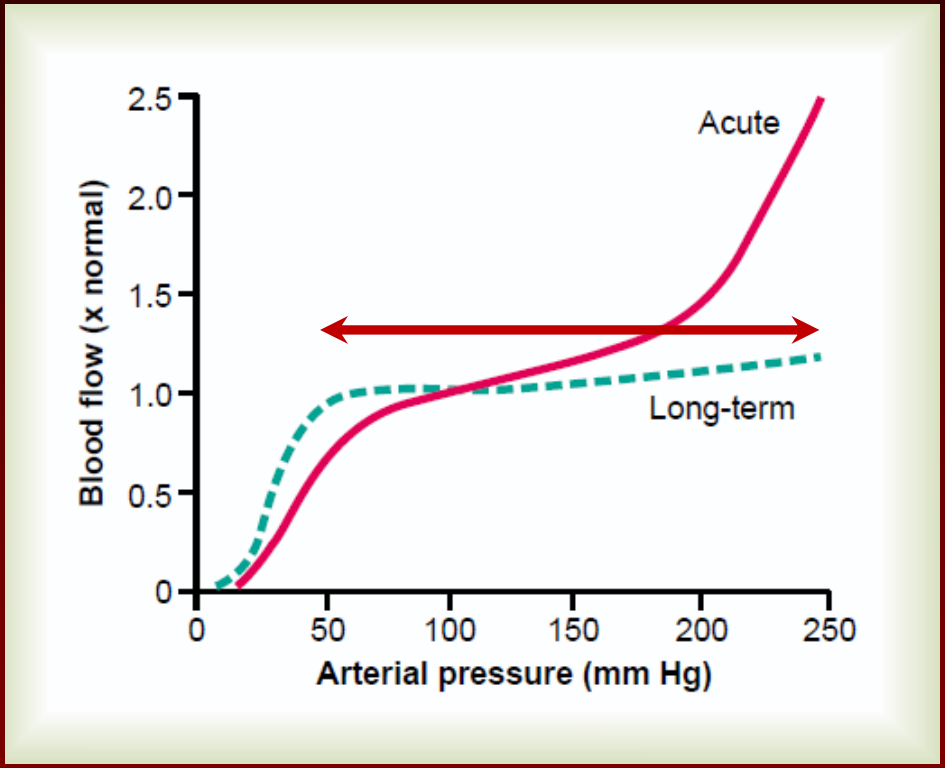
hours, days to weeks , even months

Regulation of Blood Flow - Local

Chronic regulation



It is especially important in case of the long-term change of metabolic demands of a tissue - to provide sufficient blood flow without circulation overload.

Regulation of Blood Flow - Local

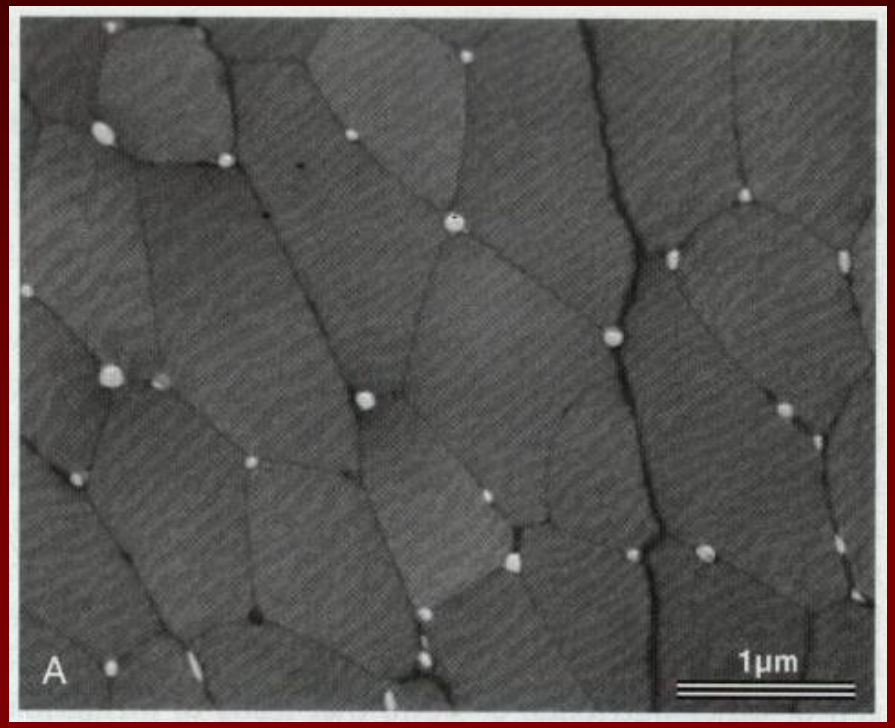
Chronic regulation

- mediated by changes of the tissue vascularity
- the key role – lack of O_2 (higher altitude, retrolental fibroplasia in premature newborns after the curative stay in the oxygen tent) and also nutrients
- identified number of factors increasing grow of new vessels - angiogenic or vascular growth factors - small peptides, best characterized: vascular endothelial growth factor (VEGF), fibroblast growth factor, and angiogenin
- proceeds fast (within days) in the young individuals and in newly formed tissue (new scar, tumor tissue) *vs.* within even months in the elderly and differentiated tissues

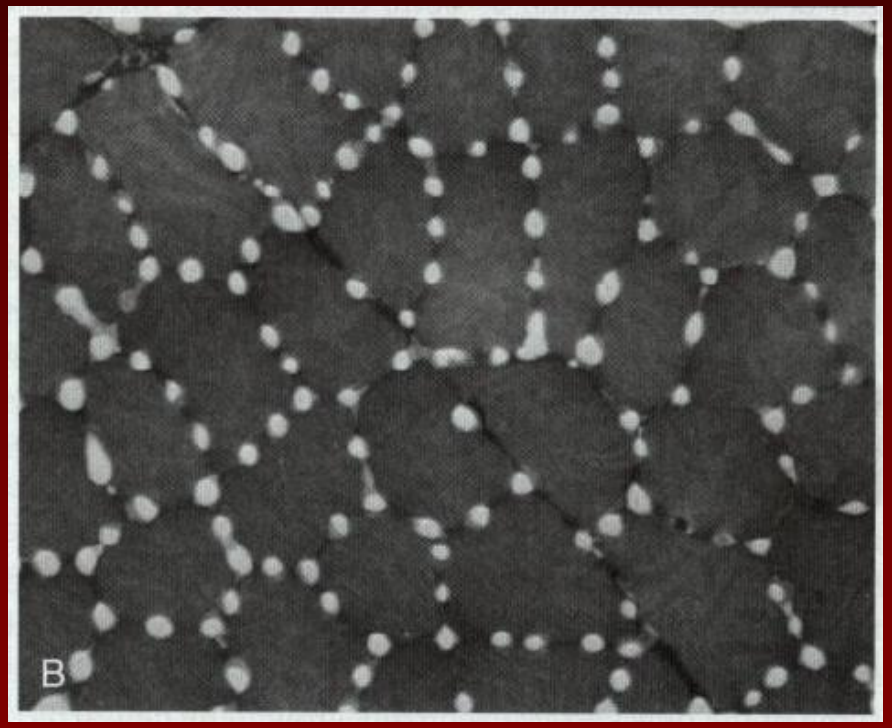
Regulation of Blood Flow - Local

Chronic regulation

unstimulated muscle



regularly stimulated muscle



Guyton and Hall - Textbook of Medical Physiology (12th edition)

Regulation of Blood Flow

Local

Systemic

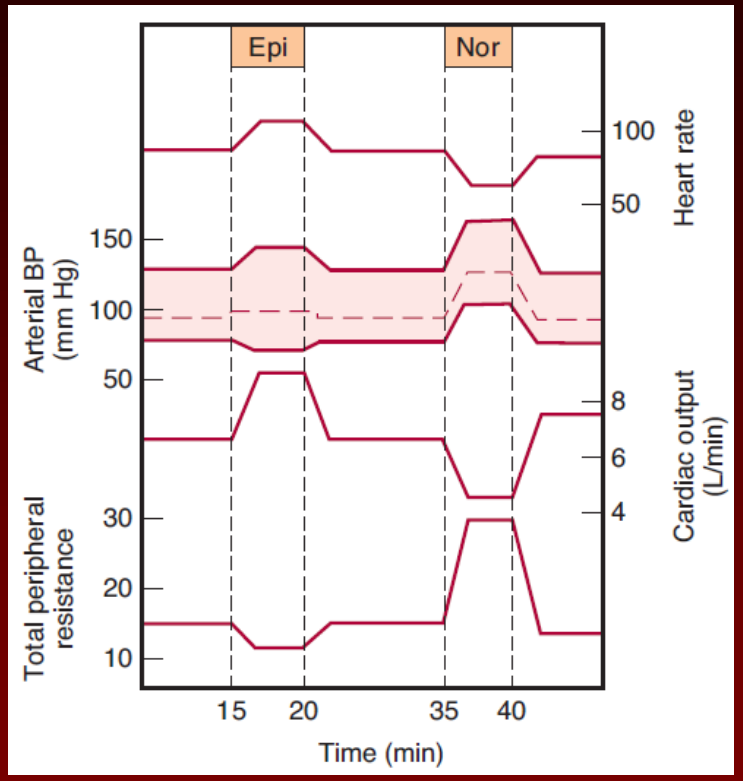
A. Neural
B. Humoral

Regulation of Blood Flow - Systemic

Humoral regulation

Vasoconstrictive substances

- **norepinephrine**
  → generalized vasoconstriction (α_1-rec.)
  (↑ BP → reflex bradycardia, ↓ CO)
- **epinephrine (high levels)**
  → vasodilatation in the skeletal muscles, liver and coronary arteries (β_2-rec.)
  → vasoconstriction in other tissues



- **angiotensin II**
  ↓ BP → ↑ sekretion of renin → formation of angiotensin II
  → generalized vasoconstriction (+ ↑ water intake and ↑ aldosterone)
- **vasopressin (antidiuretic hormone)**
  → generalized vasoconstriction (+ ↑ reabsorption of water in the kidneys)

Regulation of Blood Flow - Systemic

Humoral regulation

Vasodilatory substances

- ❖ atrial natriuretic peptide (ANP)

  → ↓ reactivity of the vascular smooth muscles on vasoconstrictive stimulation (+ ↑ natriuresis – relaxation of the measangial cells and, thus, ↑ glomerular filtration rate, + inhibition of vasopressine secretion, + ↓ aldosterone)

- ❖ VIP (vasoactive intestinal peptide)

  → vasodilatation (+ many other effects in GIT, namely relaxation of the intestinal smooth muscles including sphincters)

- ❖ histamine
  - released in tissues (from the mast cells), or from basophiles in the blood, during tissue damage or inflammation (also allergic)

  → vasodilatation of arteriols + ↑ permeability of capillaries (edemas; anaphylactic shock)

through EDRF (vasoconstrictor by itself)

Regulation of Blood Flow - Systemic

Humoral regulation

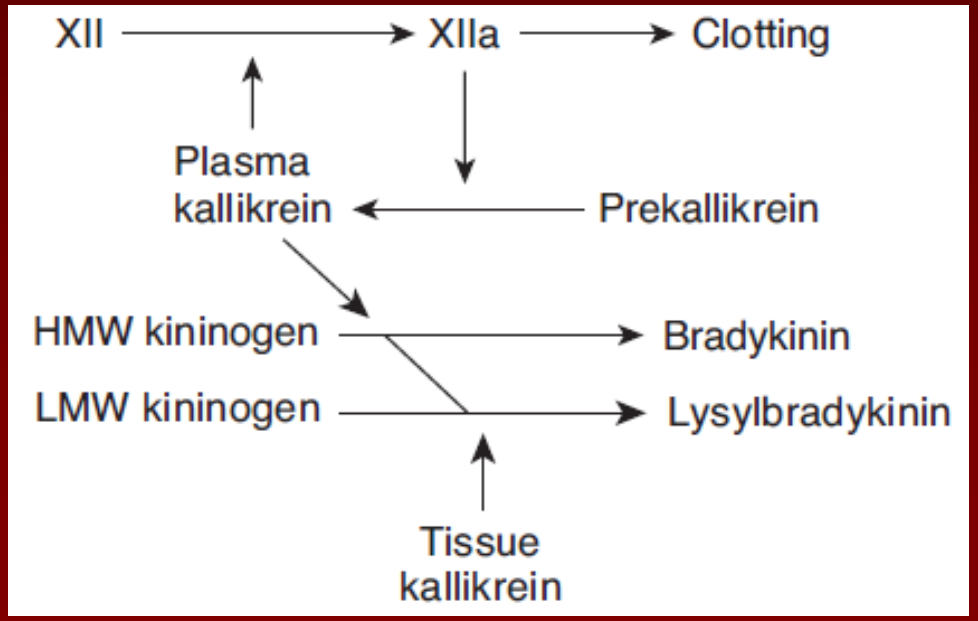
Vasodilatory substances

❖ kinins - bradykinin and lysylbradykinin (kallidin)

- small polypeptides, half-life - several minutes

→ vasodilatation of arteriols + ↑ permeability of capillaries
(similar to histamine)

regulation of the blood flow and leak of fluids from capillaries in the inflamed tissue
+
regulation of the blood flow in the skin, salivary and GIT glands in common conditions



Regulation of Blood Flow - Systemic

Humoral regulation

Other factors

- ions

vasoconstriction: ↑ Ca^{2+}, slightly ↓ H^{+}

vasodilatation: ↑ K^{+}, ↑ Mg^{2+}; ↑ H^{+}, notably ↓ H^{+}

acetate, citrate (anions) – only mild effect