Regulation of Blood Flow

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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

$$Q = \Delta P / R$$

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

Poiseuille – Hagen 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 steady laminar flow in a rigid tube!

Blood viscosity is not constant, *plasma skimming*, turbulent flow, elastic vessels!

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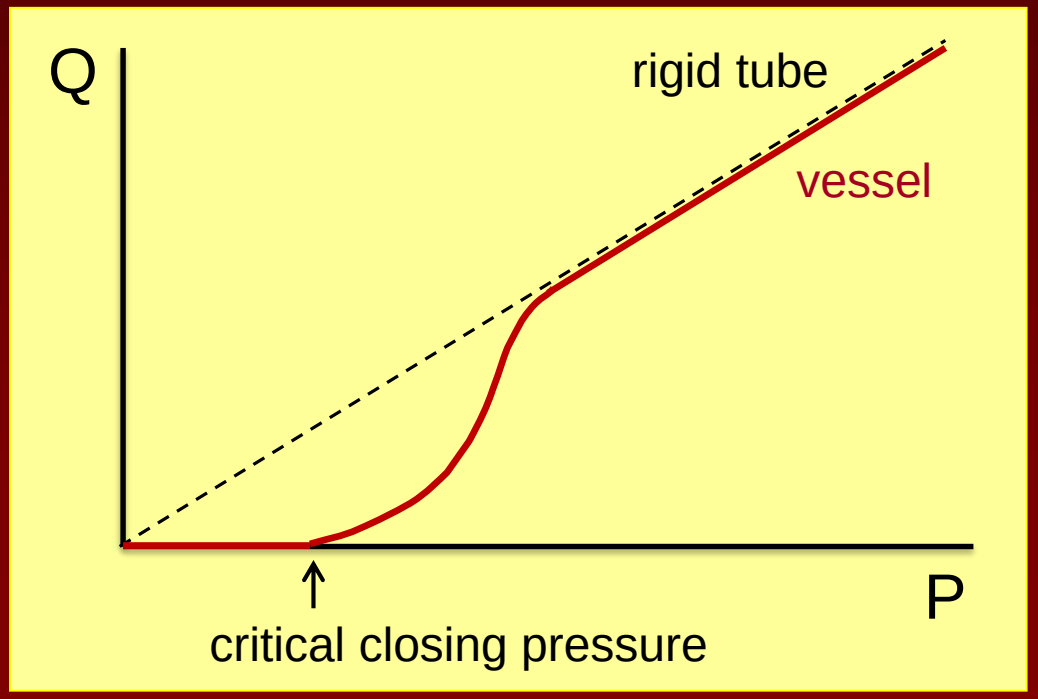


Methods for Measuring Blood Flow

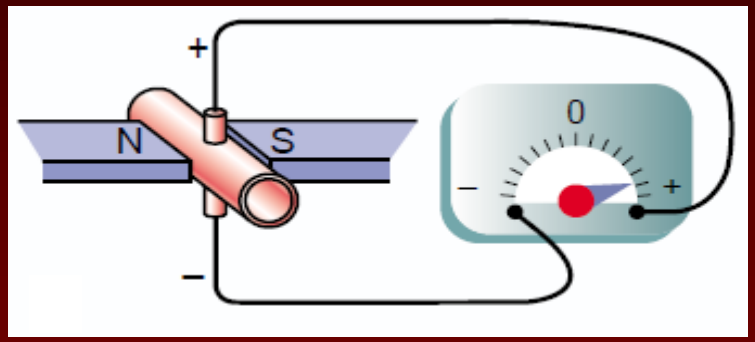
A. with a cannula inserted into a vessel

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

- the electromagnetic flowmeter



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- the generated electromotive force 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

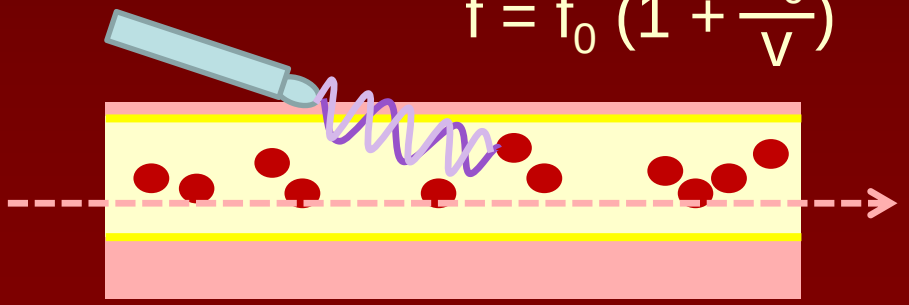
Methods for Measuring Blood Flow

2. Doppler Effect

- the ultrasonic Doppler flowmeter; most common
  - ultrasonic waves of a known wave length (frequency)
  - 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

$$f = f_0 \left(1 + \frac{v_0}{v}\right)$$



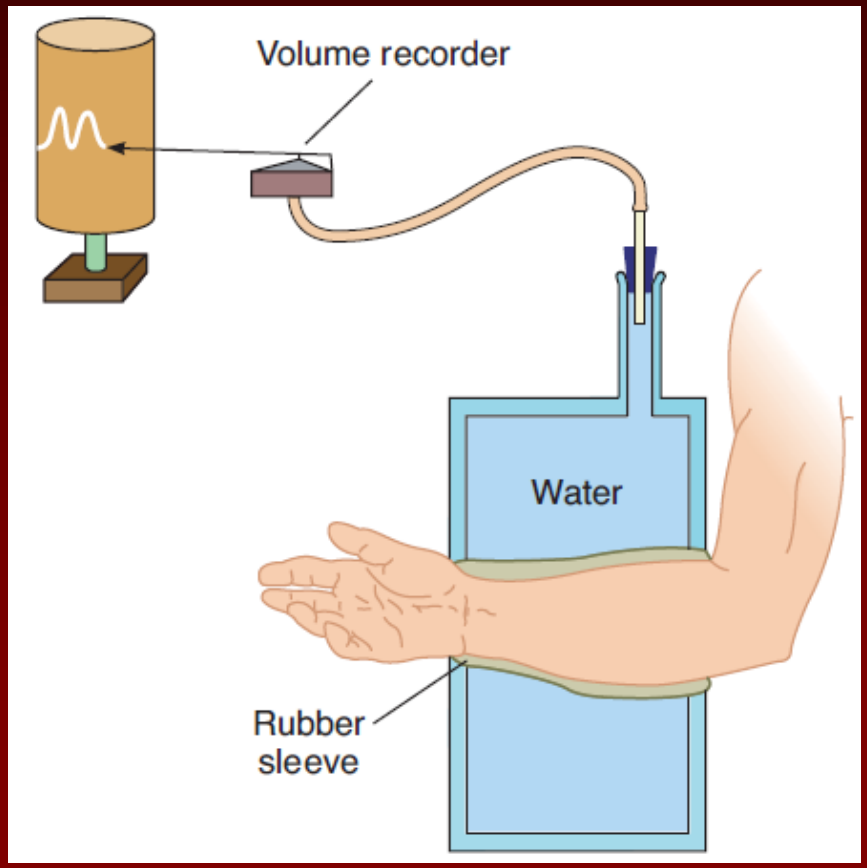
- both steady blood flow and its pulsatile changes can be measured

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 is lineary proportional to the arterial inflow of blood



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Methods for Measuring Blood Flow

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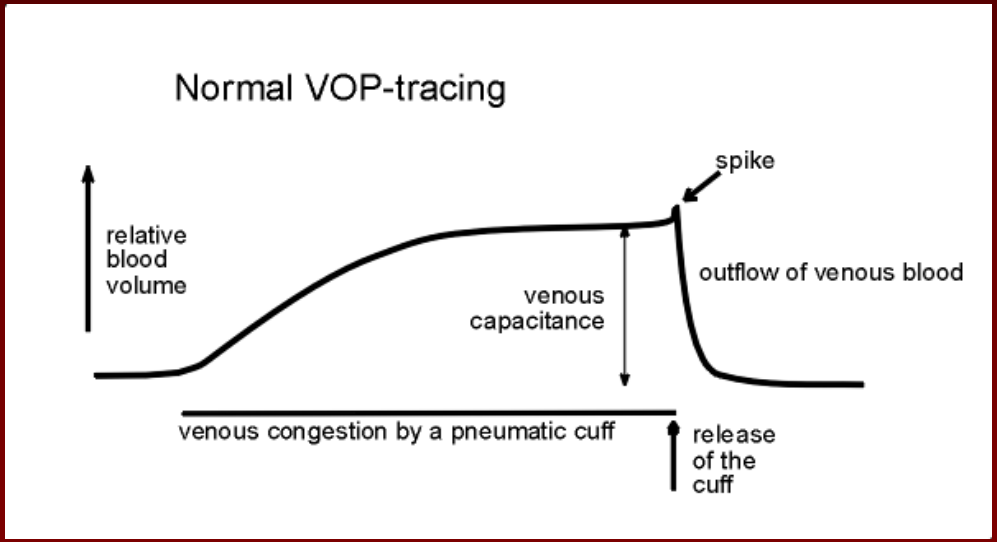

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Methods for Measuring Blood Flow

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
- blood flowing from the lungs to the left heart – about 200 ml O_2 / 1 l

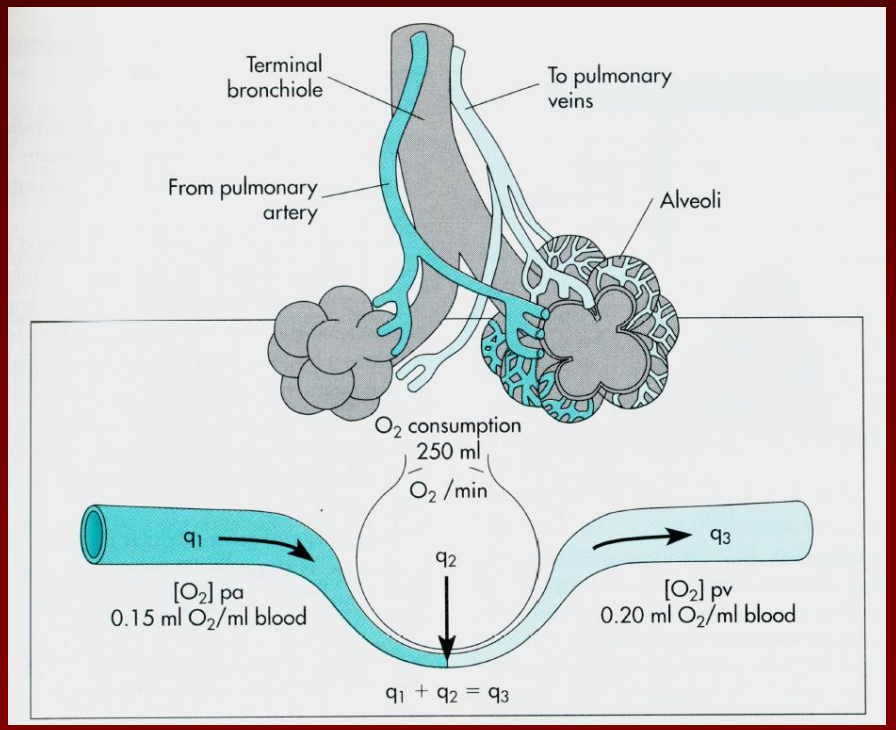
↓

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

- The total O_2 consumption is 250 ml / 1 min.

↓

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



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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)

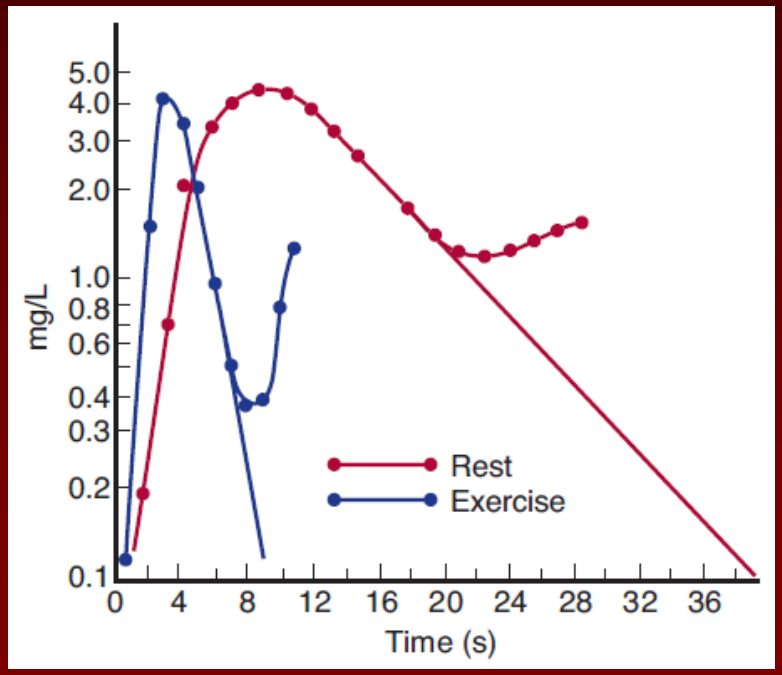
Methods for Measuring Blood Flow

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])

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

❖ thermodilution



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Regulation of Blood Flow

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

Resting Tone

- 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+}

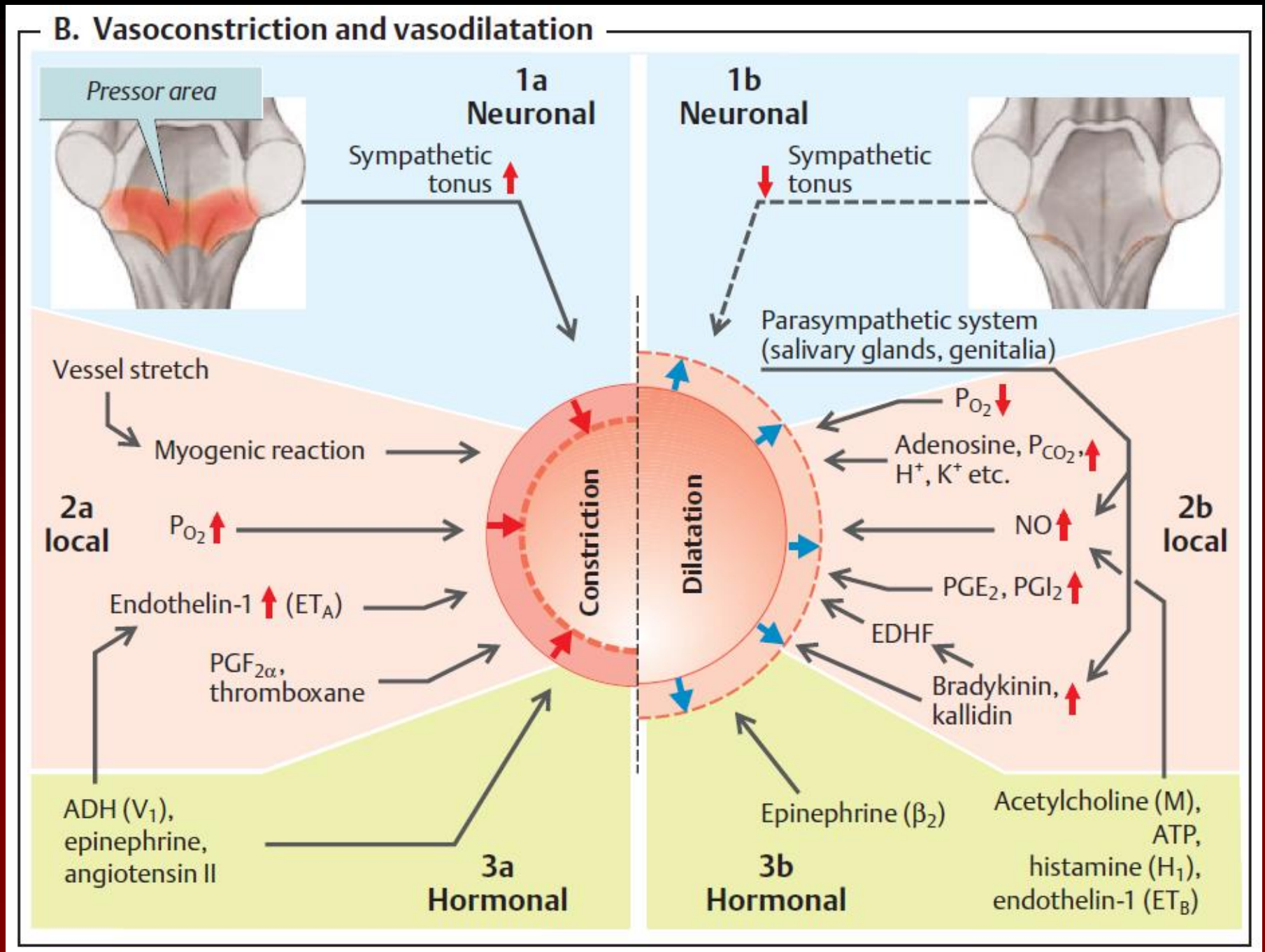
Basal Tone

- 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 Endothelium

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, ↓ pH, ↑ osmolarity in the interstitium, ↑ tissue temperature; ↓ pO_2, 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

reactive hyperemia

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.

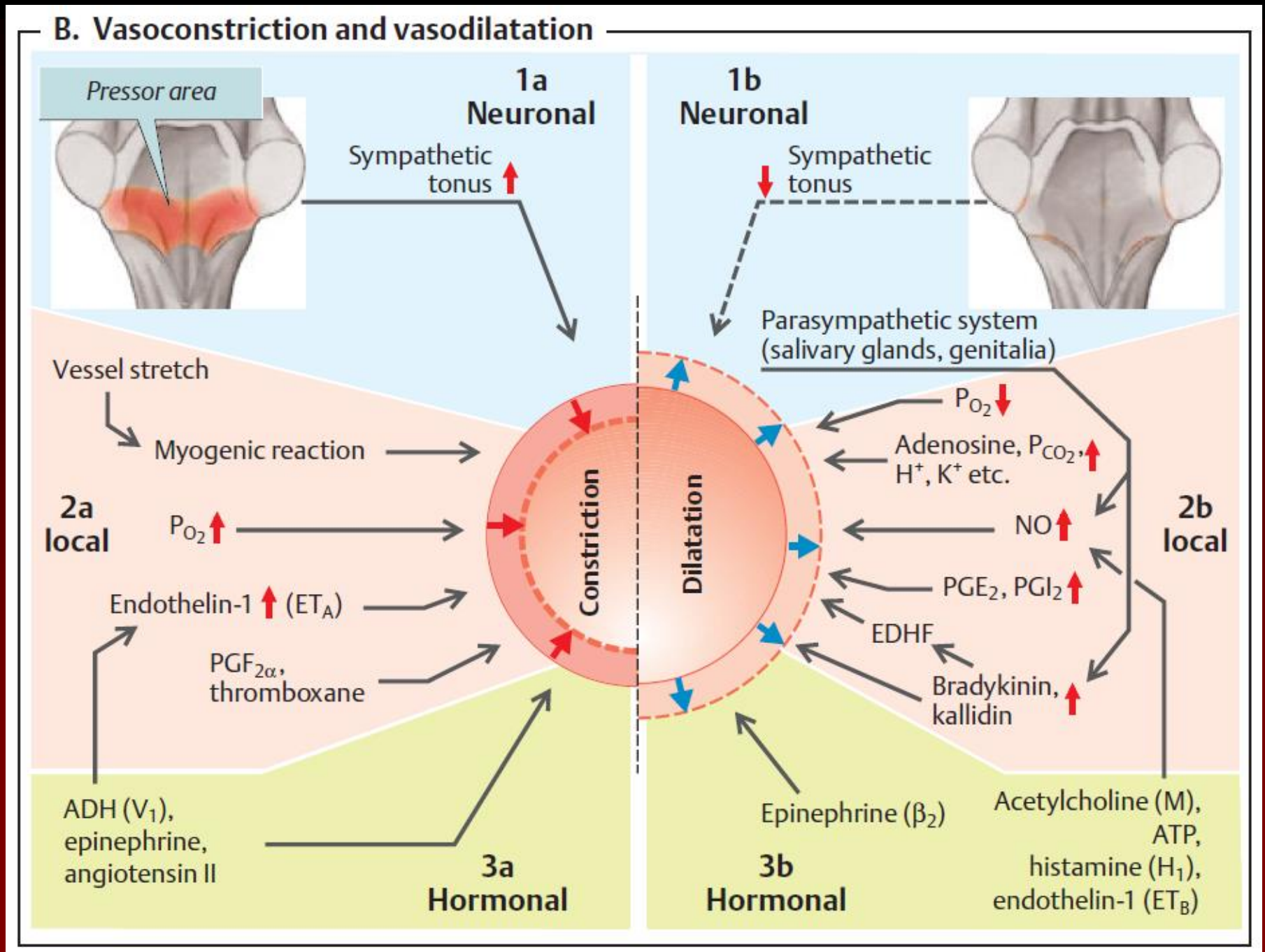
Regulation of Blood Flow - Local

Regulation Mediated by Endothelium

endothelial-derived relaxing factor (EDRF) – NO

→ vasodilatation

- synthesized in the endothelial cells of arteriols and small arteries due to the shear stress induced by the flowing blood
- synthesis stimulated by the products of thrombocyte aggregation and also by many primary vasoconstrictive substances



Regulation of Blood Flow - Local

Regulation Mediated by Endothelium

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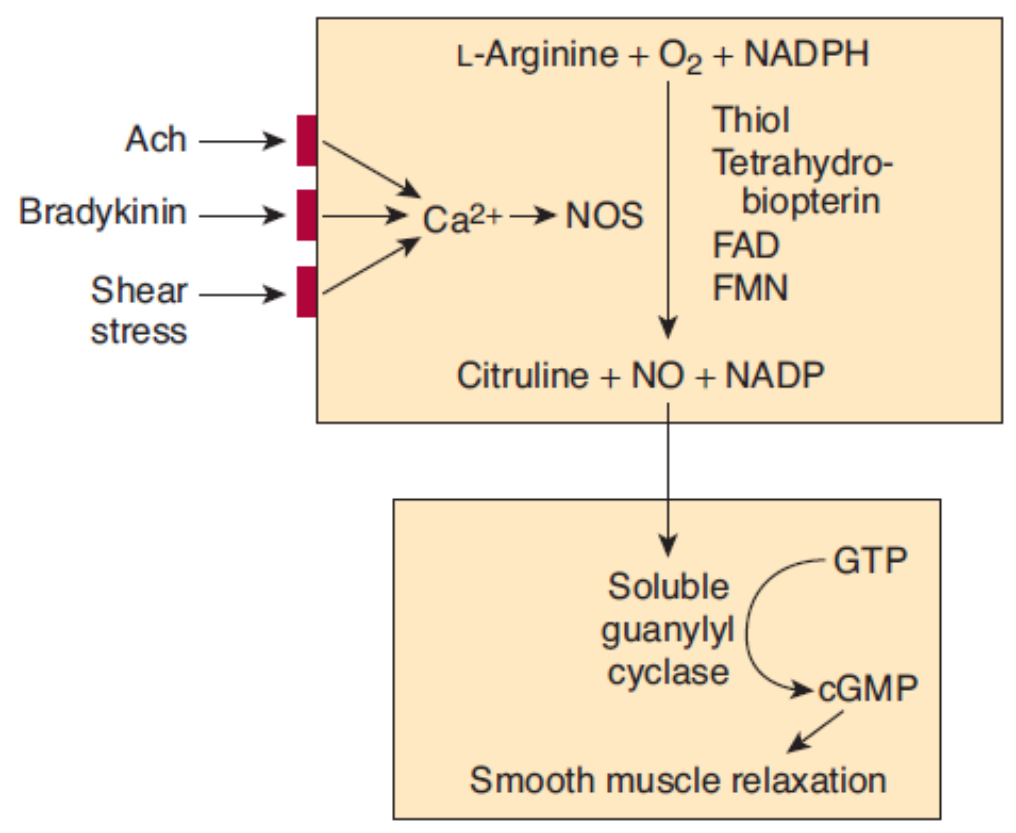

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Regulation of Blood Flow - Local

Regulation Mediated by Endothelium

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.

Regulation of Blood Flow - Local

Regulation Mediated by Endothelium

endothelins

- polypeptides synthesized by 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, function?

- ET-1 – one of the most potent vasoconstrictive substances
- the exact physiological role not known
- 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 mechanisms

- temperature, …
- damaged vessels
- specialized tissues (kidneys, brain, etc.)

Regulation of Blood Flow - Local

A. Acute

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

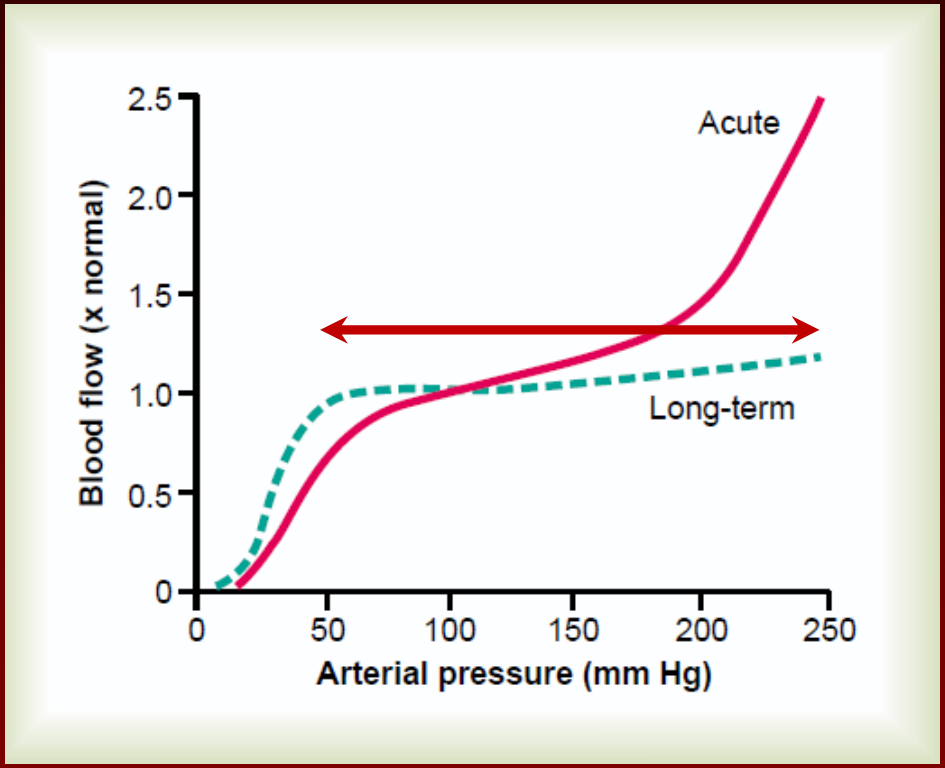
1. Metabolic Autoregulation
2. Myogenic Autoregulation
3. Regulation Mediated by Endothelium

B. Chronic

hours, days to weeks , even months

Regulation of Blood Flow - Local

Chronic regulation



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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

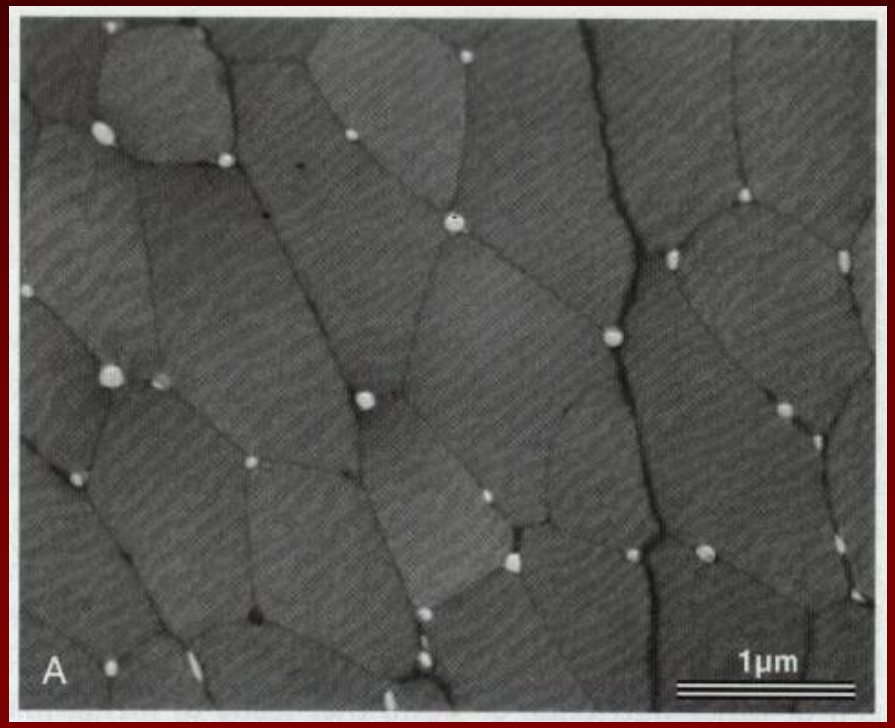
Chronic regulation

- mediated by changes of the tissue vascularity
- the key role – lack of O_2, also nutrients
- angiogenic or vascular growth factors - small peptides, best characterized: vascular endothelial growth factor (VEGF), fibroblast growth factor, and angiogenin
- fast in young individuals and in newly formed tissue

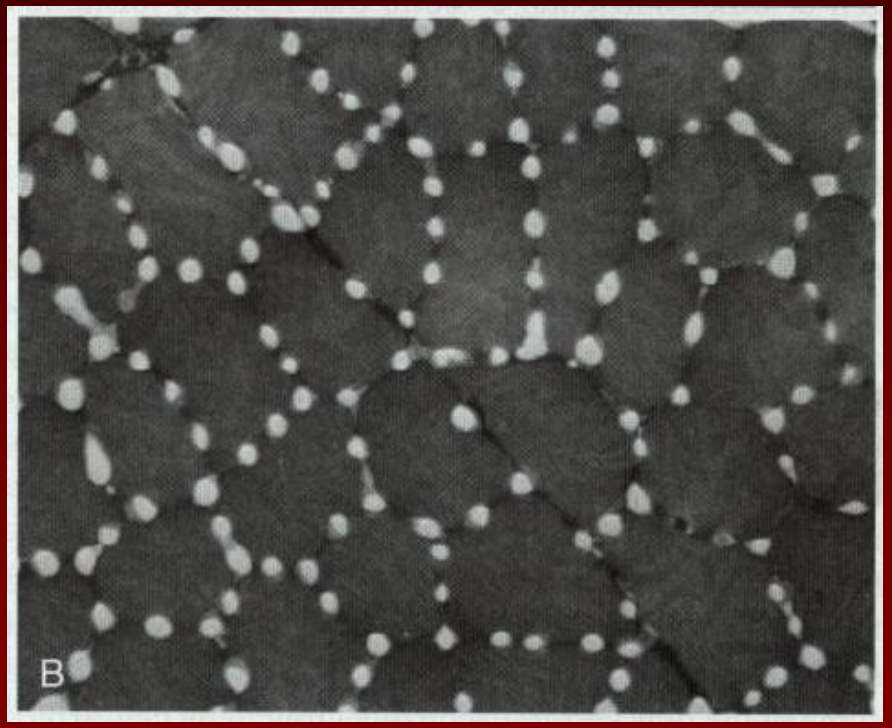
Regulation of Blood Flow - Local

Chronic regulation

unstimulated muscle



regularly stimulated muscle



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Regulation of Blood Flow

Local

Systemic

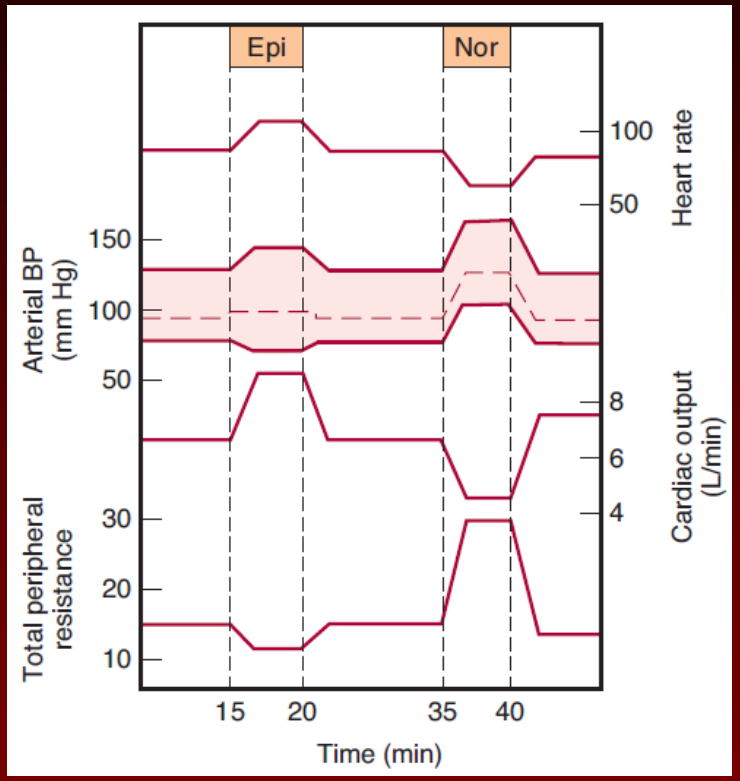
A. Neural
B. Humoral

Regulation of Blood Flow - Systemic

Humoral regulation

Vasoconstrictive substances

- ❖ norepinephrine
  → generalized vasoconstriction (α_1-rec.)
- ❖ epinephrine (high levels)
  → vasodilatation in the skeletal muscles, liver and coronary arteries (β_2-rec.)
  → vasoconstriction in other tissues



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- ❖ 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 - mechanisms)

- ❖ 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

Regulation of Blood Flow - Systemic

Humoral regulation

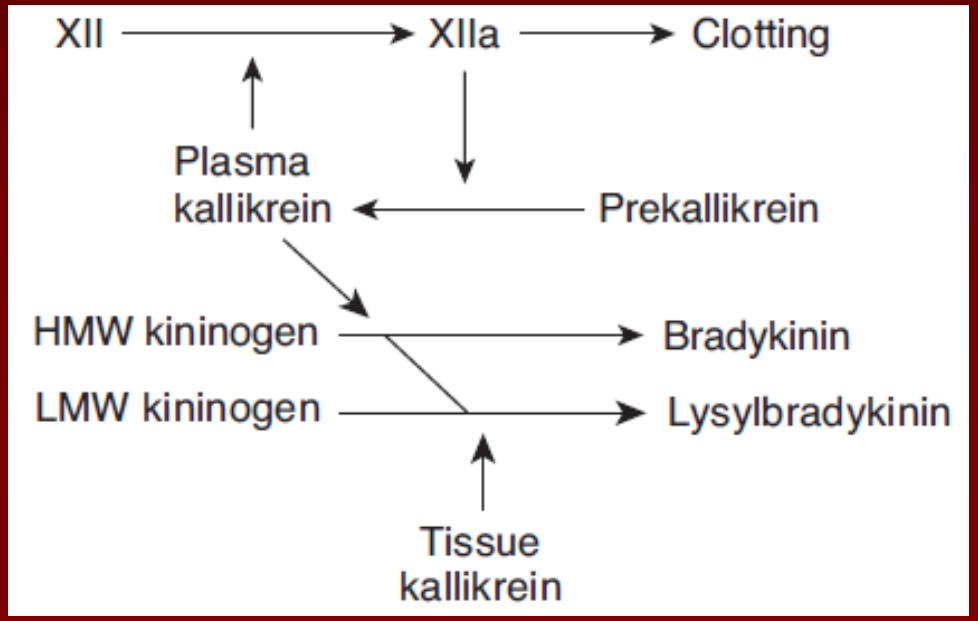
Vasodilatory substances

❖ kinins - bradykinin and lysylbradykinin (kallidin)

- small polypeptides, half-life - several minutes

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

inflamed tissue
+
skin, salivary and GIT glands (in common conditions)



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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