Regulation of blood vessel diameter

Mechanisms that regulate blood vessel diameter:

- Central:
  - Neural,
  - Hormonal,
- Peripheral:
  - Myogenic,
  - Humoral,
  - Metabolic.

Neural regulation

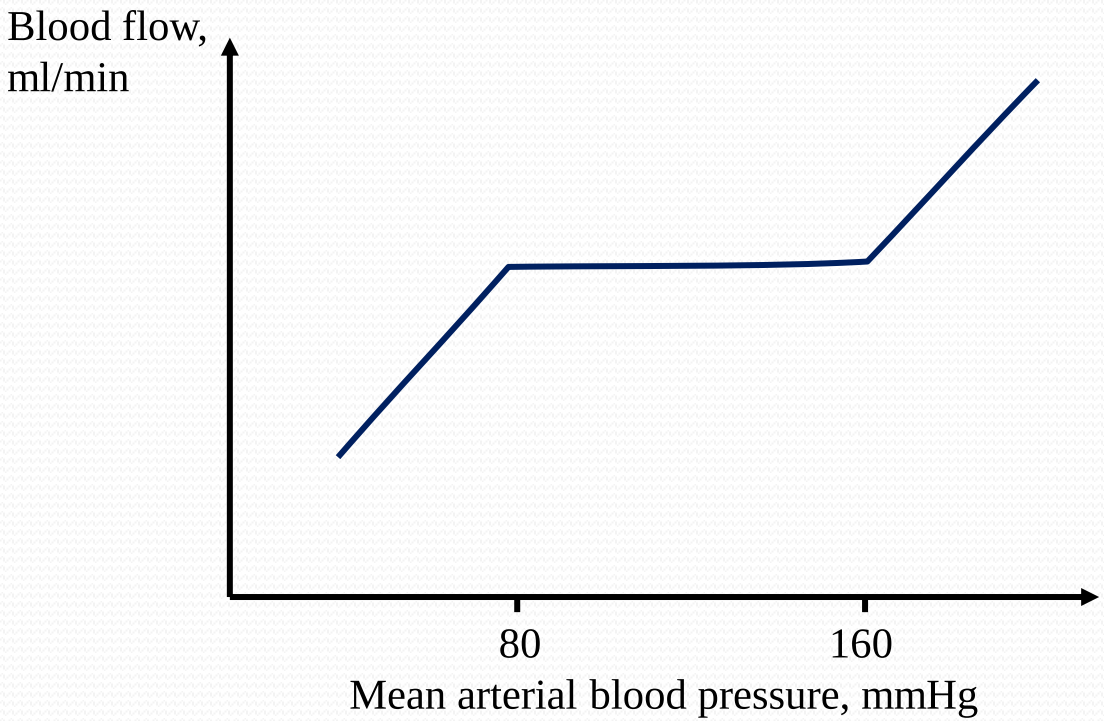
- Vasoconstrictor nerve fibers – innervate all blood vessels
  - Sympathetic fibers (T_1-L_3; norepinephrine$\rightarrow\alpha_1$ adrenoreceptors)
- Vasodilator nerve fibers:
  - Parasympathetic fibers (acetylcholine$\rightarrow M_3$ cholinoreceptors):
    - Pelvic organs (S_2-S_4)
    - Coronary circulation (n.vagus)
  - Sympathetic vasodilator fibers (T_1-L_3; acetylcholine$\rightarrow M_3$ cholinoreceptors):
    - Skeletal muscle arterioles,
    - Coronary arterioles,
    - Brain arterioles.
  - Dorsal root vasodilators – axon reflex.

Central hormonal regulation

- Vasoconstrictor hormones:
  - Epinephrine, norepinephrine (α_1),
  - Renin-angiotensin system (AT_1, AT_2),
  - Vasopressin (V_1).
- Vasodilator hormones:
  - Epinephrine (β_2),
  - ANP, BNP.

Peripheral myogenic regulation

- Stretch of blood vessel wall leads to contraction of smooth muscle cells in it.



Peripheral humoral regulation

- Vasoconstrictor substances:
  - Serotonin,
  - Tromboxan A_2,
  - Leucotrienes,
  - Endothelins.

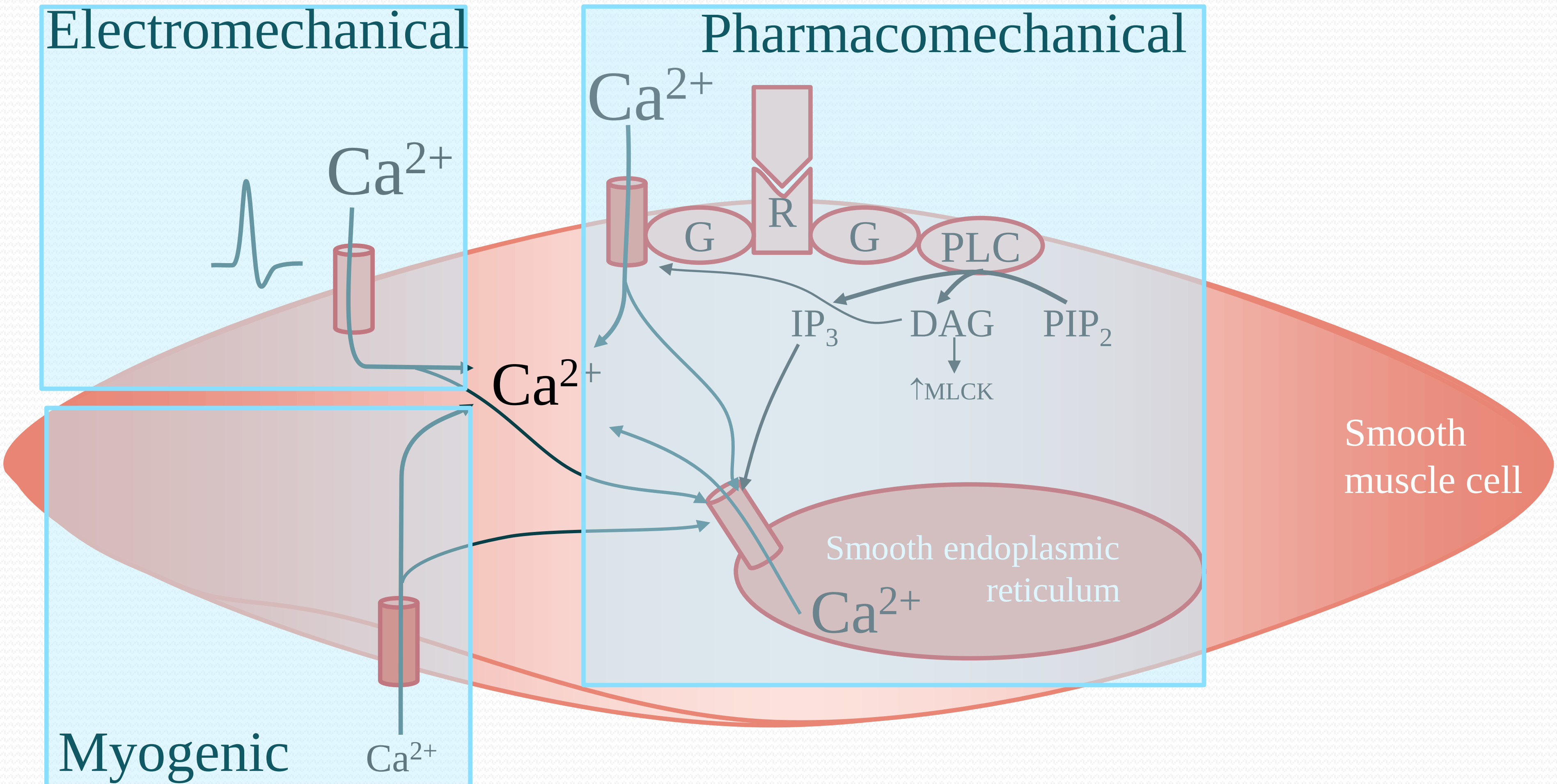
- Vasodilator substances:
  - Histamine,
  - Kinines,
  - NO (nitric oxide)
  - Prostacycline (PGI_2), PGE_2,
  - Endothelium derived hyperpolarizing factor (EDHF).

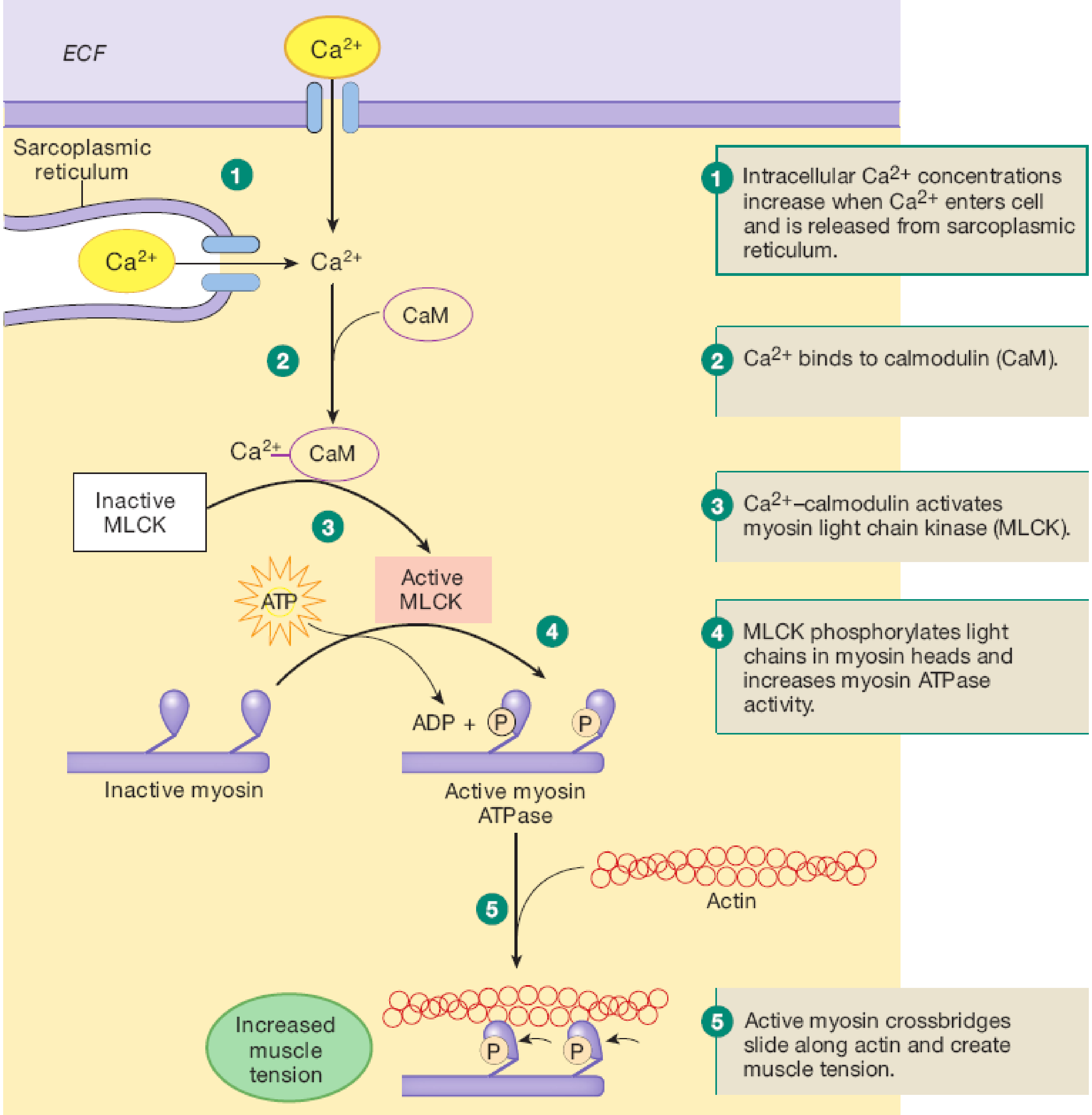
Peripheral metabolic regulation

Arterioles are dilated if:

- ↑P_{CO_2},
- ↓P_{O_2},
- ↓ pH,
- ↑adenosine,
- ↑ K^+.

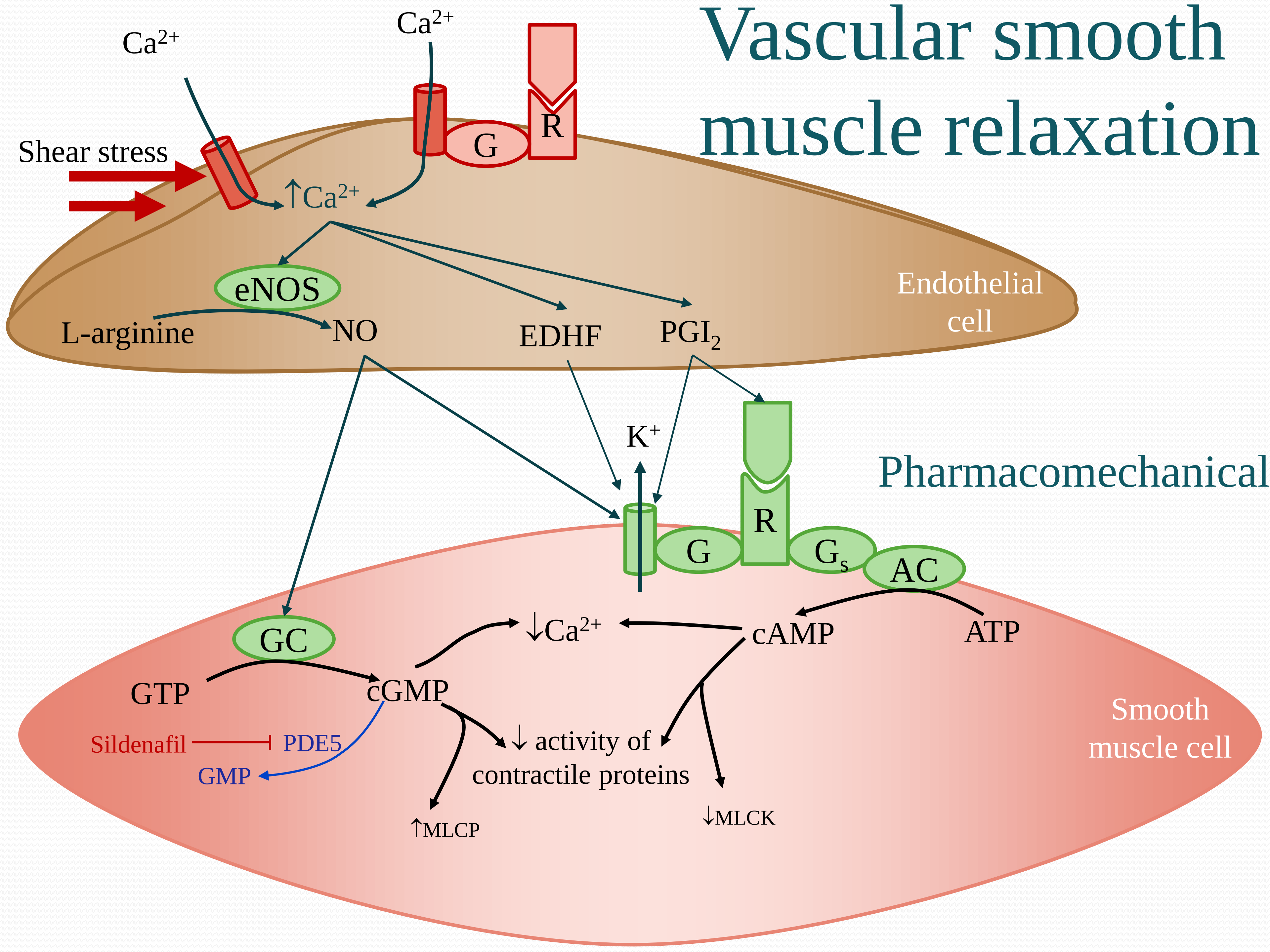
Coupling in vascular smooth muscle contraction





ECF
Ca^{2+}
Sarcoplasmic reticulum
Ca^{2+}
Ca^{2+}
CaM
Ca^{2+} CaM
Inactive MLCK
Active MLCK
ATP
ADP + P
P
Inactive myosin
Active myosin ATPase
Actin
P
P
Increased muscle tension
1 Intracellular Ca^{2+} concentrations increase when Ca^{2+} enters cell and is released from sarcoplasmic reticulum.
2 Ca^{2+} binds to calmodulin (CaM).
3 Ca^{2+}–calmodulin activates myosin light chain kinase (MLCK).
4 MLCK phosphorylates light chains in myosin heads and increases myosin ATPase activity.
5 Active myosin crossbridges slide along actin and create muscle tension.

Vascular smooth muscle relaxation

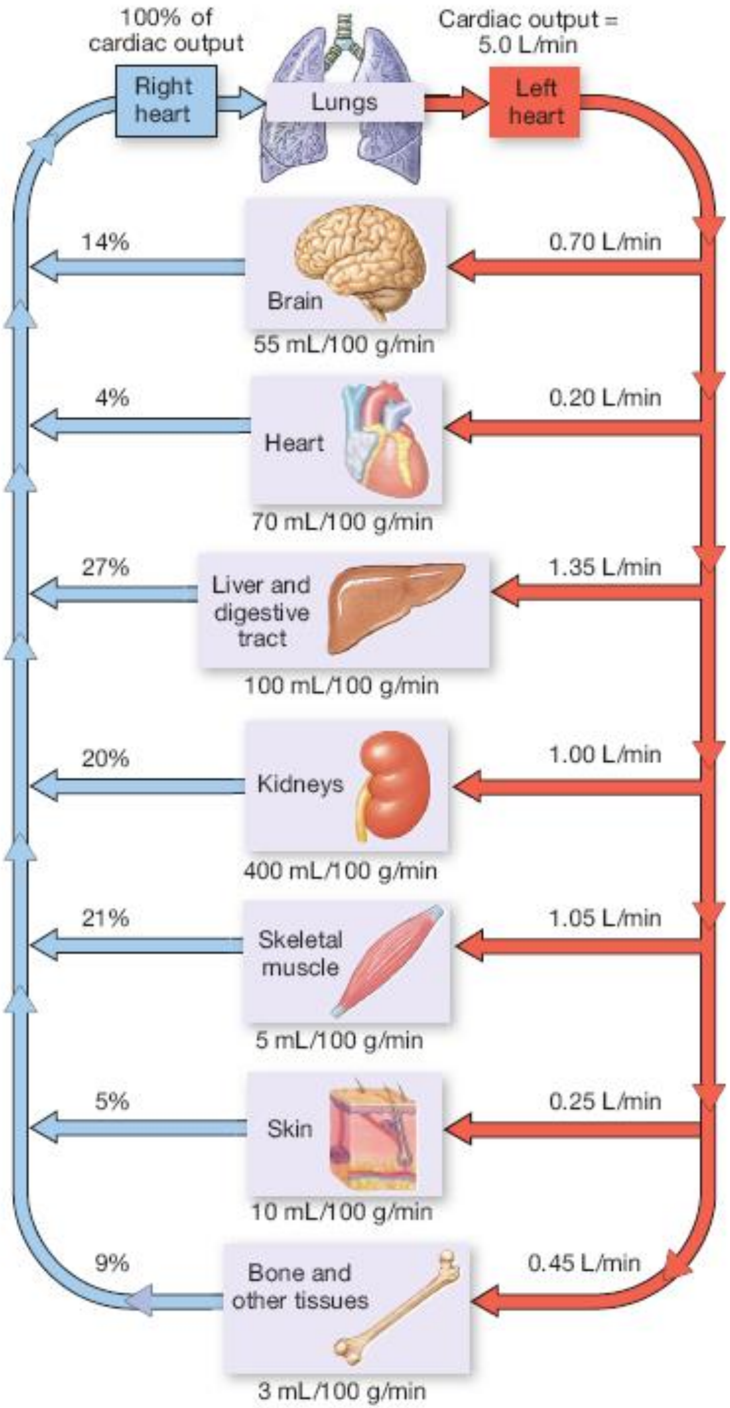


Regional blood flow

Distribution of cardiac output

- Due to metabolism of tissues
- Due to performance of specific functions

Distribution of cardiac output at rest and during physical exercise



Physical exercise
(CO=25 l/min)

3% (0.75 L/min)

4% (1 L/min)

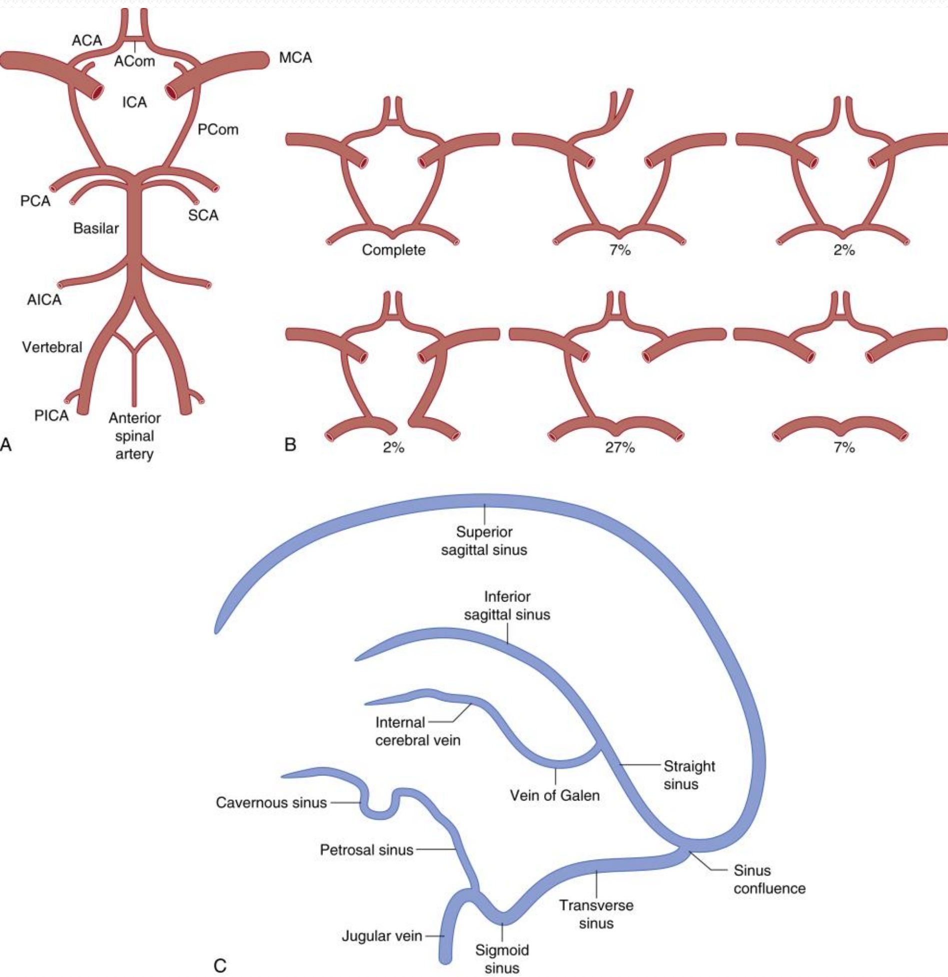
2% (0.5 L/min)

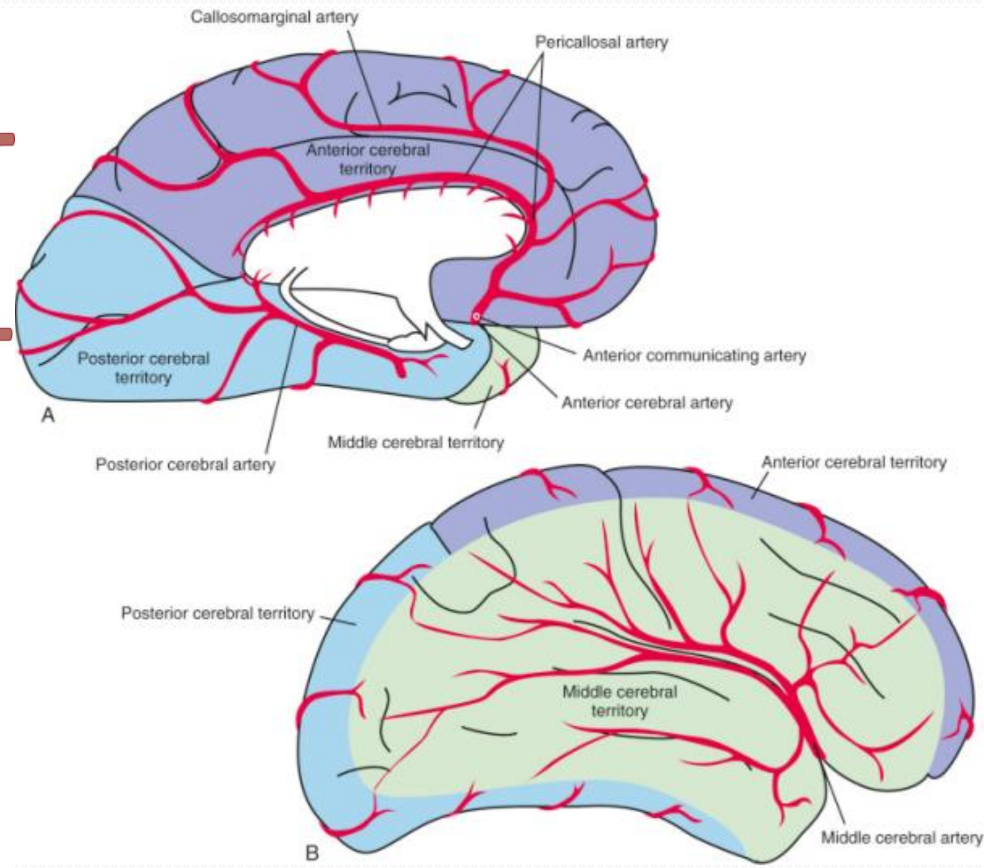
1% (0.25 L/min)

85% (21 L/min)

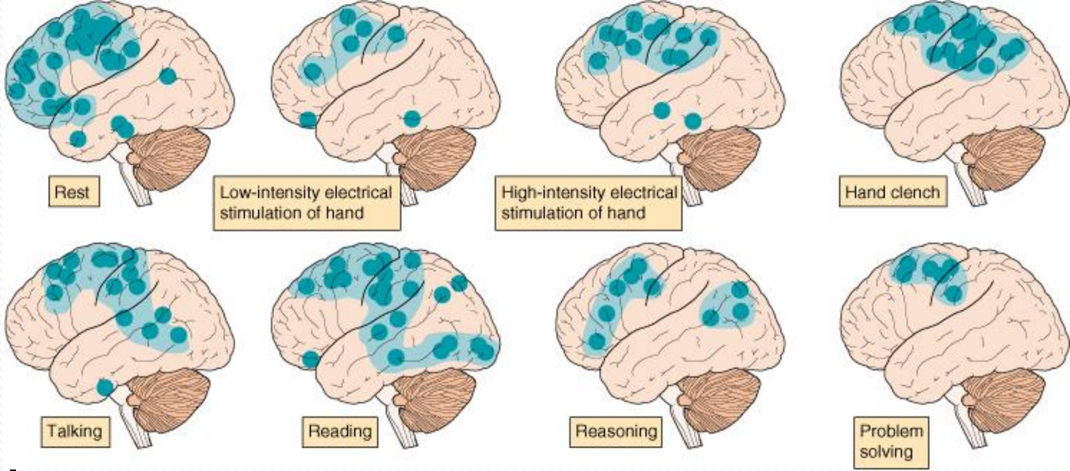
3% (0.75 L/min)

Cerebral blood flow


ACA
ACom
MCA
ICA
PCom
PCA
SCA
Basilar
AICA
Vertebral
PICA
Anterior
spinal
artery
A
B
Complete
7%
2%
2%
27%
7%
Superior
sagittal sinus
Inferior
sagittal sinus
Internal
cerebral vein
Straight
sinus
Vein of Galen
Cavernous sinus
Petrosal sinus
Sinus
confluence
Transverse
sinus
Jugular vein
Sigmoid
sinus
C


Callosomarginal artery
Pericallosal artery
Anterior cerebral
territory
Posterior cerebral
territory
Anterior communicating artery
Anterior cerebral artery
A
Middle cerebral territory
Posterior cerebral artery
Anterior cerebral territory
Posterior cerebral territory
Middle cerebral
territory
Middle cerebral artery
B

Cerebral blood flow



- ~14% from cardiac output
- ~ 700 ml/min
- 50-60 ml/min/100 g
- Grey matter (75-80 ml/min/100g) supplied better than white (10-20 ml/min/100g)
- Relatively constant
- Activity of different brain areas

Cerebral blood flow affecting factors

- Intracranial pressure
- Arterial blood pressure – decrease below 60 mmHg is critical for cerebral circulation
- Diameter of cerebral arteries

Regulation

- Peripheral:
  - Metabolic
  - Myogenic
  - Humoral
- Central:
  - Neural
  - Hormonal
  - CNS ischemic regulation – Cushing's reflex

↑P_{CO_2} !a
↓pH
↓P_{O_2}
↑adenosine
↑K^+

Absence of stretch

Histamine
Kinins
NO
PGI_2, PGE_2
EDHF

Symp NS
N.trigeminus
N. basalis
N.raphe
L.coeruleus

E (β_2)
ANP, BNP

↓P_{CO_2}
↑pH
↑P_{O_2}
↓adenosine
↓ K^+

Stretch

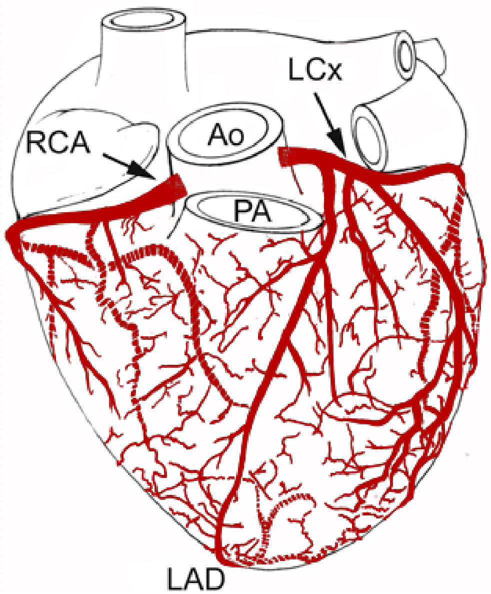
Serotonin
TxA_2
Leucotrienes
Endothelin

Symp NS

E, NE (α_1)
R-A system
Vasopressin

Coronary blood flow

Coronary blood flow

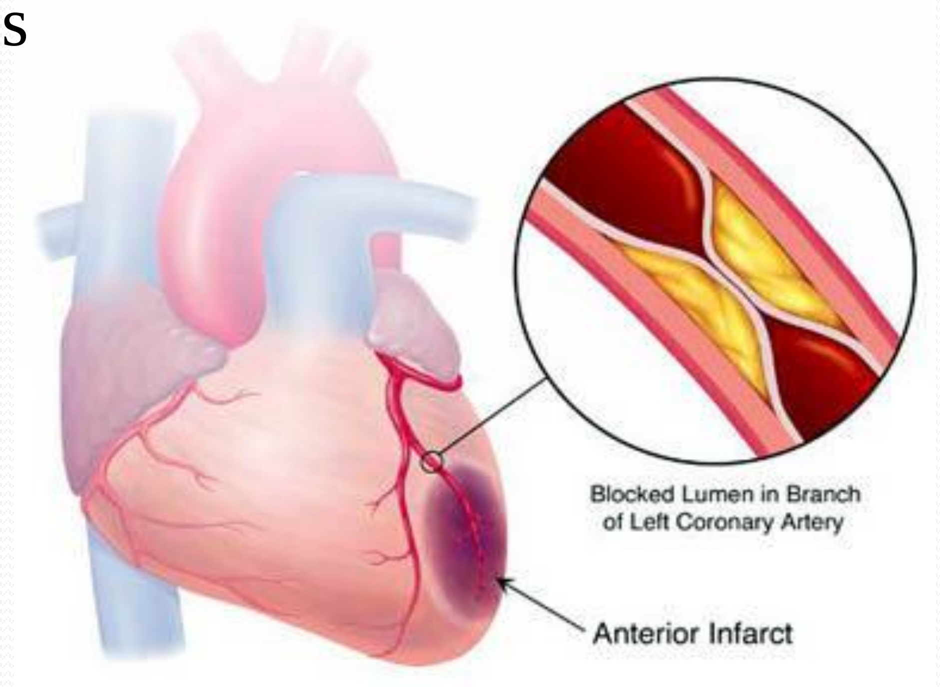


- 4 % from cardiac output,
- 200 ml/min;
- 70-100 ml/min/100g
- 250 ml/min/100g during exercise
- High arterio-venous difference (70 – 80%)
- Great capillary density (~3000/mm^2)
- High number of anastomoses

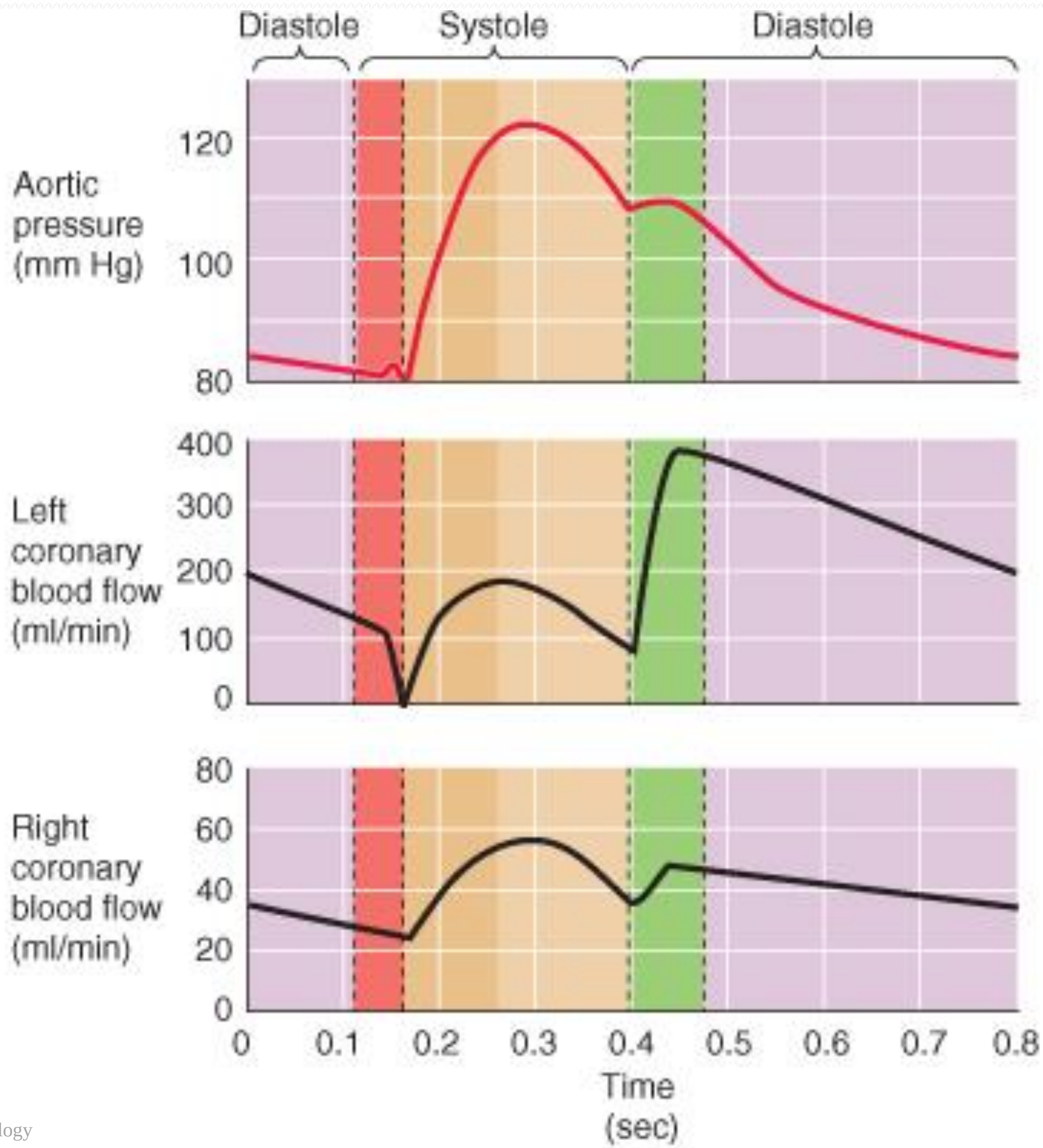

20 ml O2/100 ml
5 ml O2/100 ml

Factors that affect coronary blood flow

- Phase of cardiac cycle,
- Diastolic pressure in the aorta,
- Heart rate,
- Diameter of coronary arteries



Coronary blood flow during the cardiac cycle

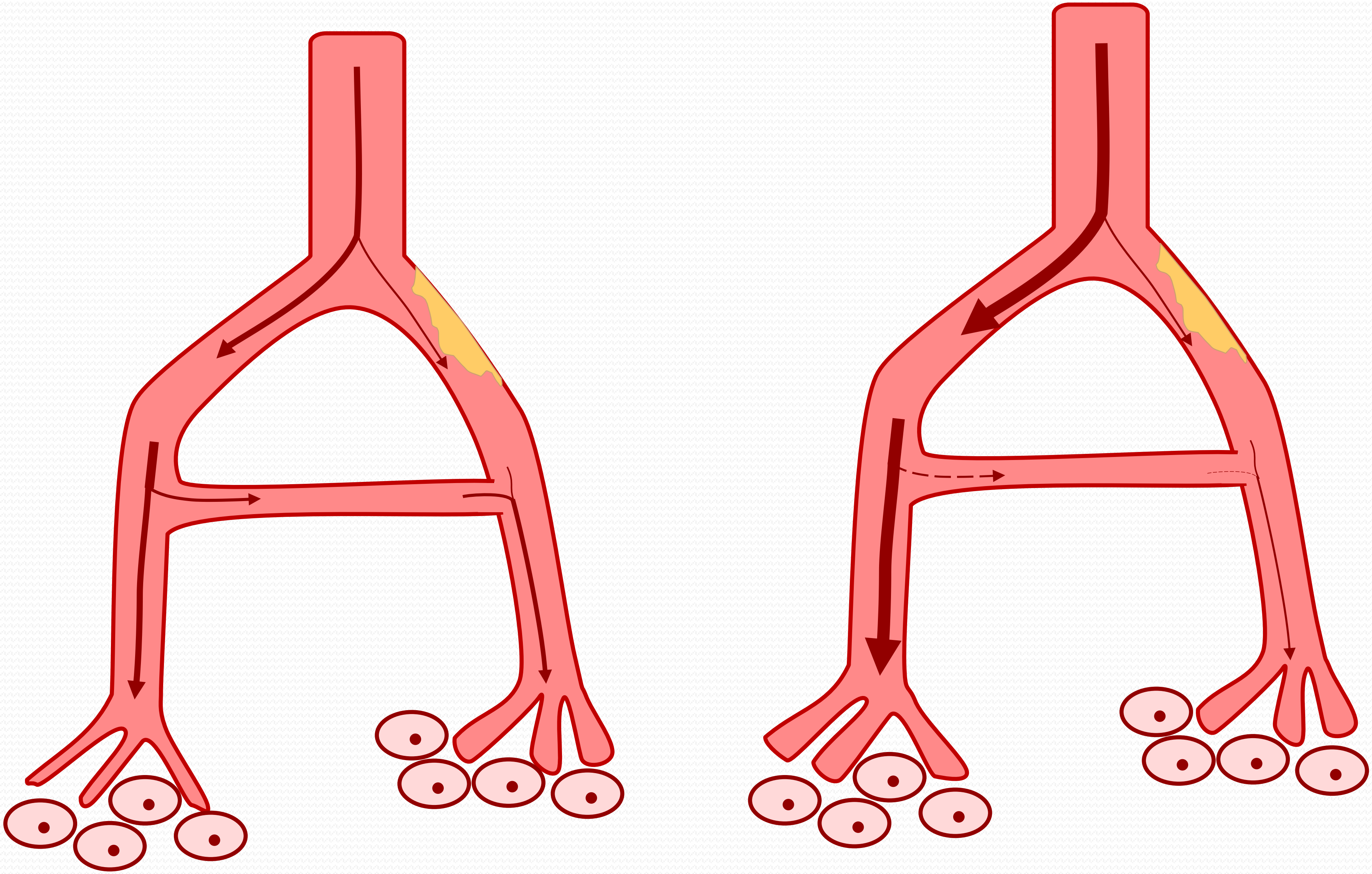


Boron & Boulpaep: Medical Physiology

Coronary steal phenomenon

Rest

Physical exercise, stress, vasodilator use



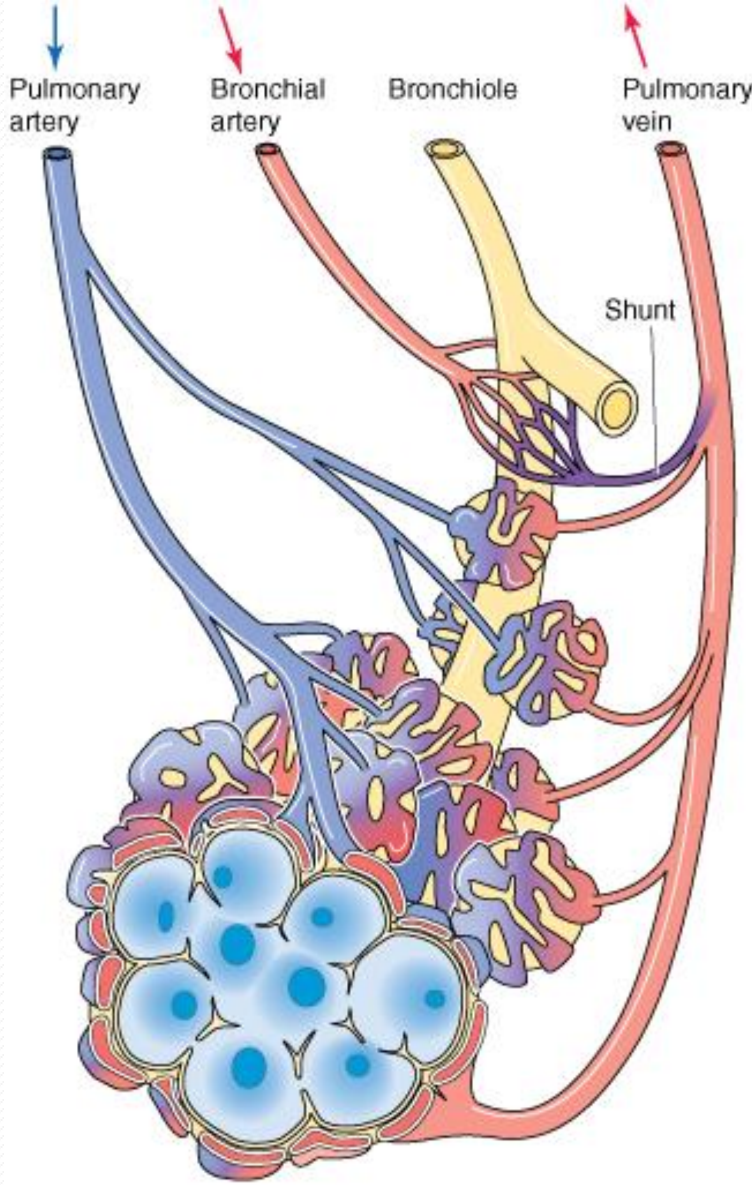
Regulation

Vasodilation	Mechanism	Vasoconstriction
↑P_{CO_2} ↓pH ↓P_{O_2} ↑adenosine ↑K^+	**Peripheral:** • <u>Metabolic</u>	↓P_{CO_2} ↑pH ↑P_{O_2} ↓adenosine ↓ K^+
Absence of stretch	• Myogenic	Stretch
Histamine Kinins NO PGI_2, PGE_2 EDHF	• Humoral	Serotonin TxA_2 Leucotrienes Endothelin
Symp NS Parasymp NS	**Central:** • Neural	Symp NS
E (β_2) ANP, BNP	• Hormonal	E, NE (α_1) R-A system Vasopressin

Blood flow to lungs

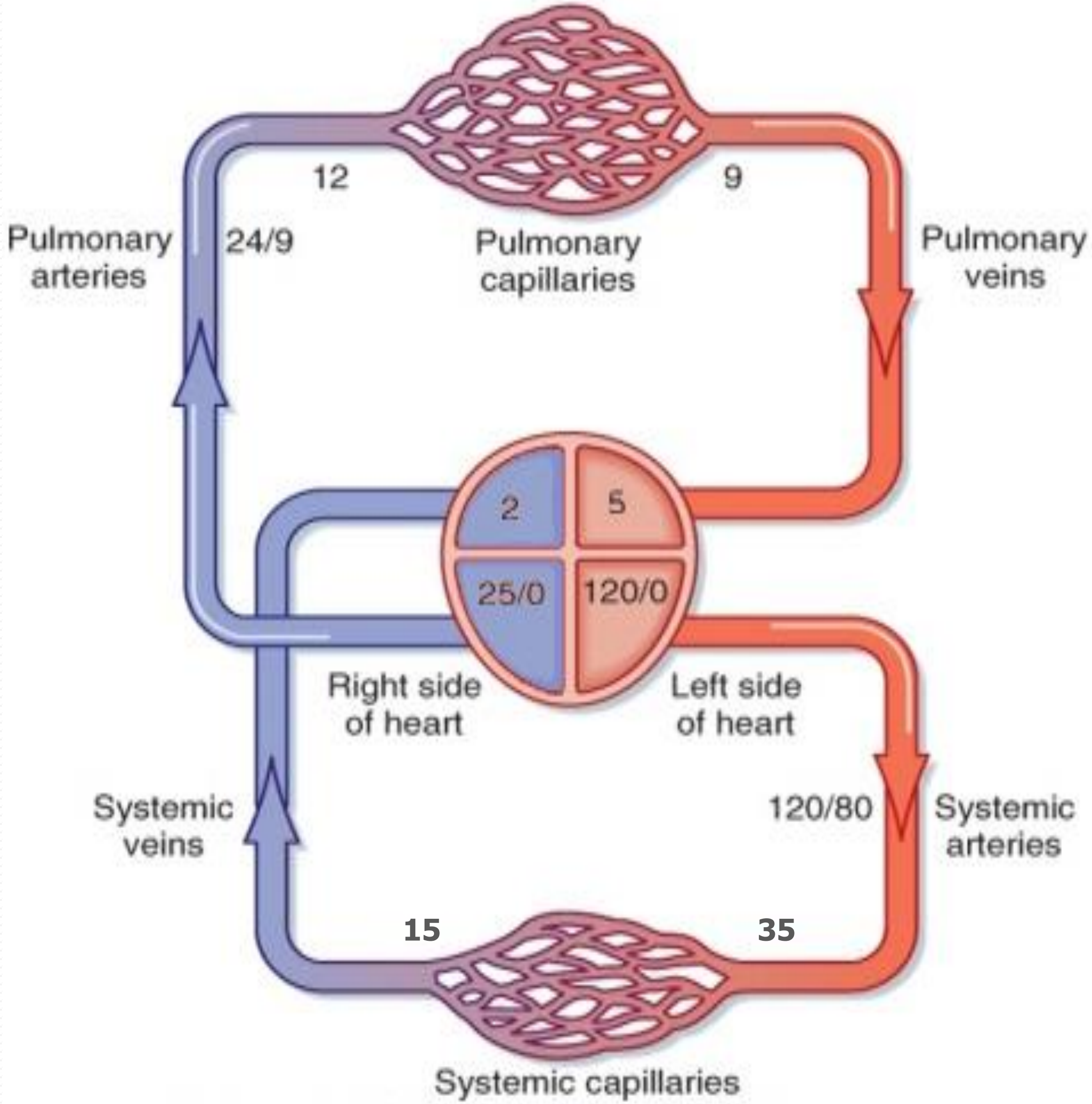
Blood flow to lungs

- Bronchial circulation
  - From aorta
  - Low flow-high pressure
  - 1-2 % from cardiac output
  - Supplies bronchi to terminal bronchioles, pleura
- Pulmonary circulation
  - From right ventricle
  - High flow-low pressure
  - 100% from cardiac output
  - Supplies respiratory bronchioles and alveoli



Pulmonary blood flow

- Low resistance,
- Low blood pressure,
- Depends on gravity,
- Hypoxic vasoconstriction

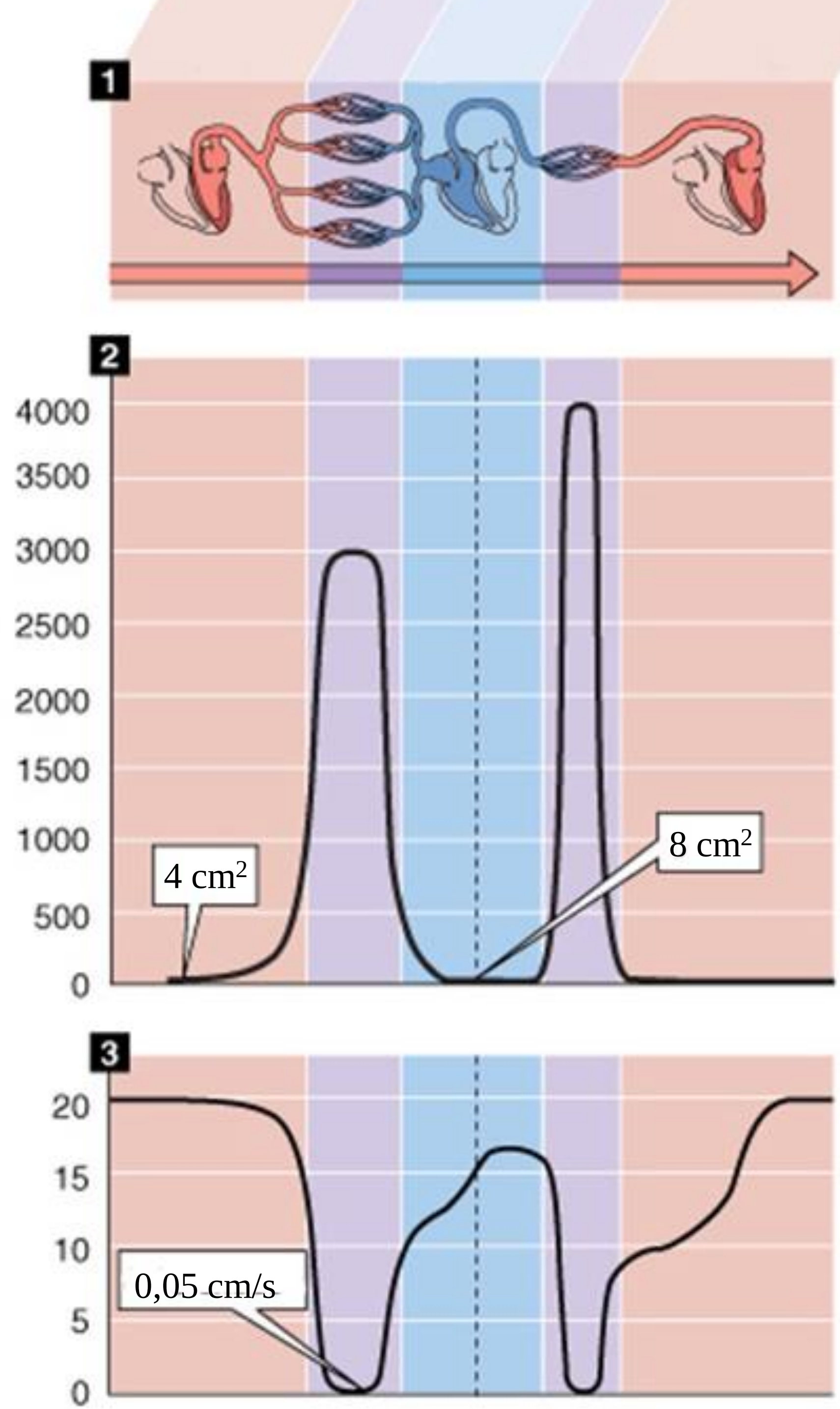


Koeppen & Stanton: Berne and Levy physiology 6th edition

Small circuit of the circulation

Summary cross-sectional area (cm²)

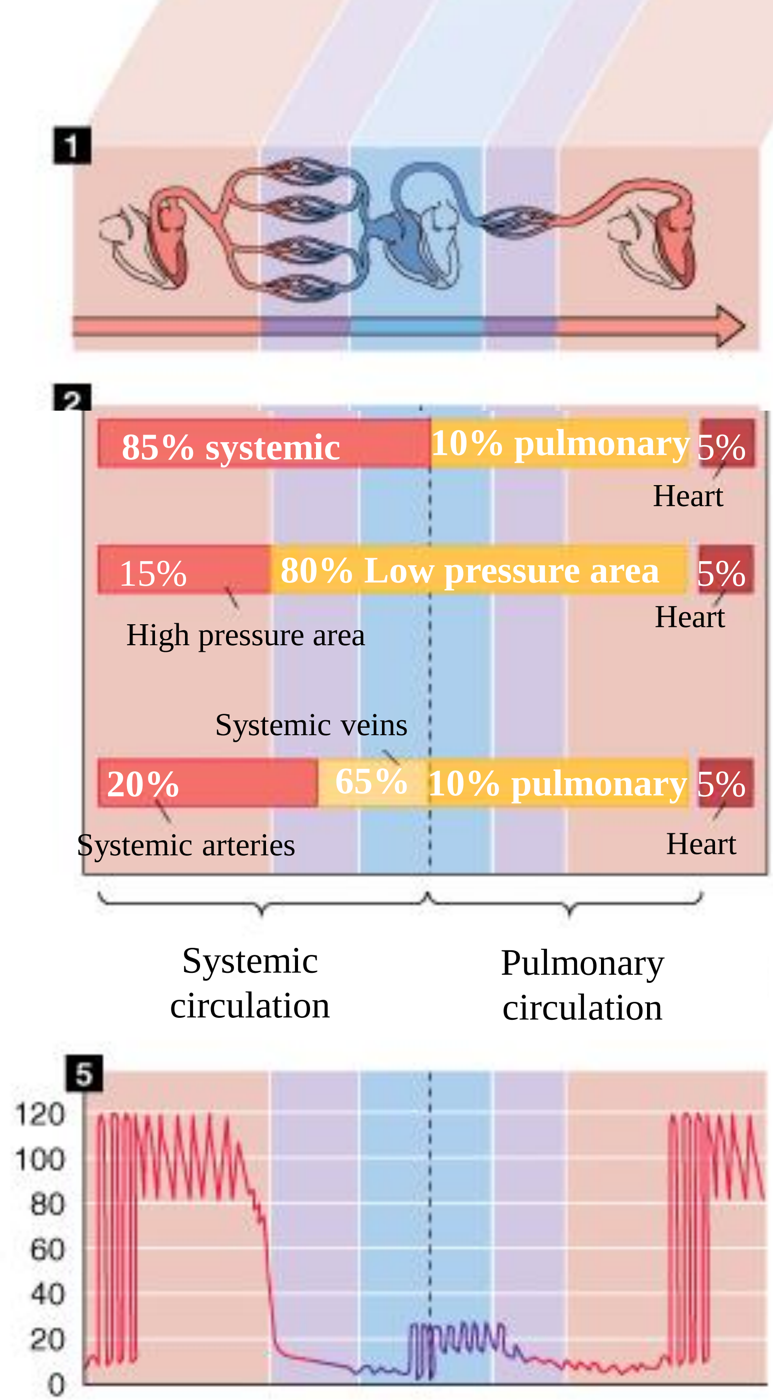
Linear velocity of blood(cm/s)



Small circuit of the circulation

Blood volume distribution

Blood pressure (mmHg)

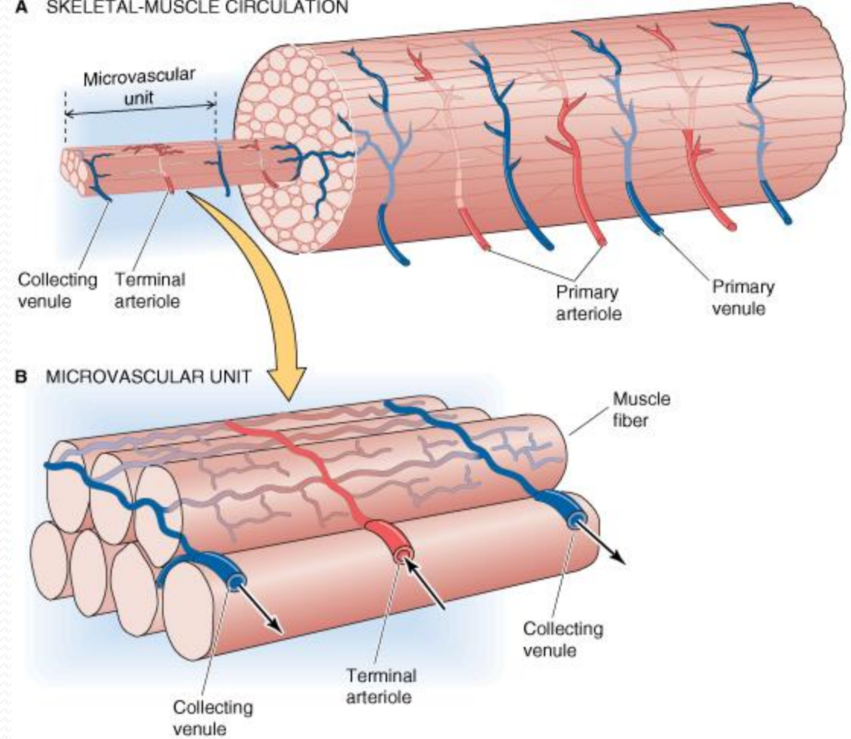


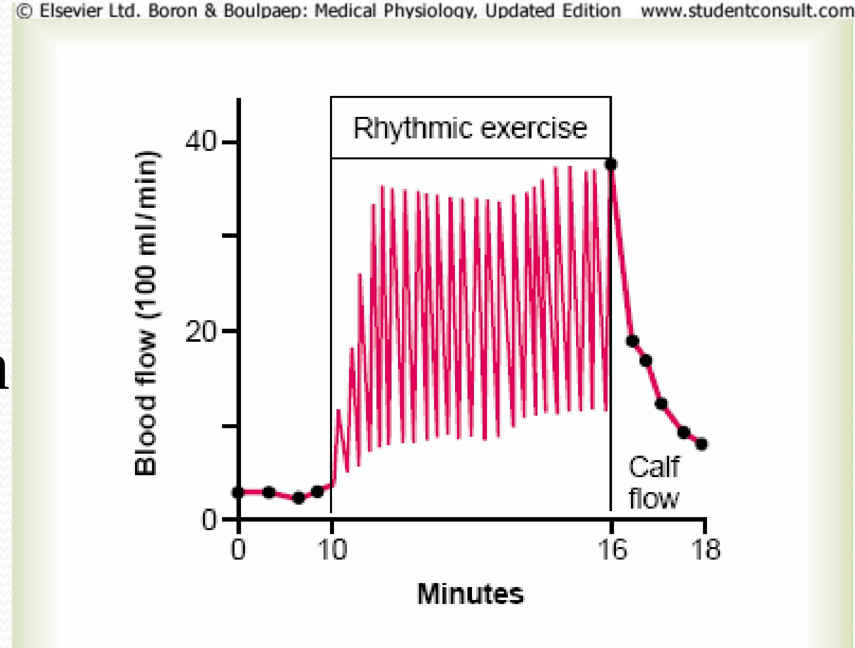
Koeppen & Stanton: Berne and Levy physiology 6th edition

Skeletal muscle blood flow

Blood flow to skeletal muscles

- 21% of cardiac output
- 3-5 ml/min/100 g at rest
- 50-80 ml/min/100g at maximal exercise
- In the oxidative part of the skeletal muscle 300-400 ml/min/100g
- During the contraction phase lower than during the relaxation
- In rhythmic exercise greater than in the static



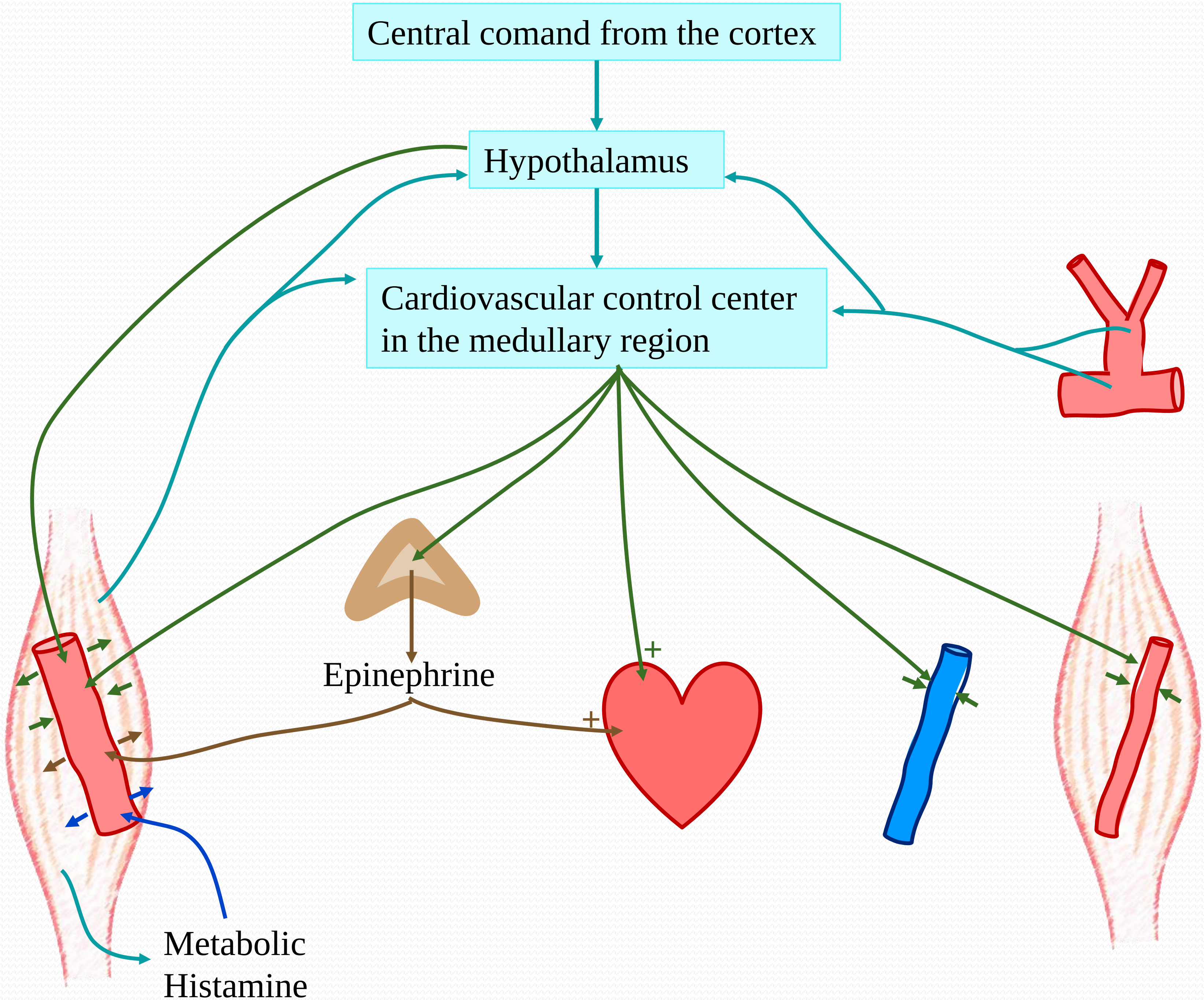


Guyton and Hall Textbook of Medical Physiology, 13th Edition, Saunders, 2015

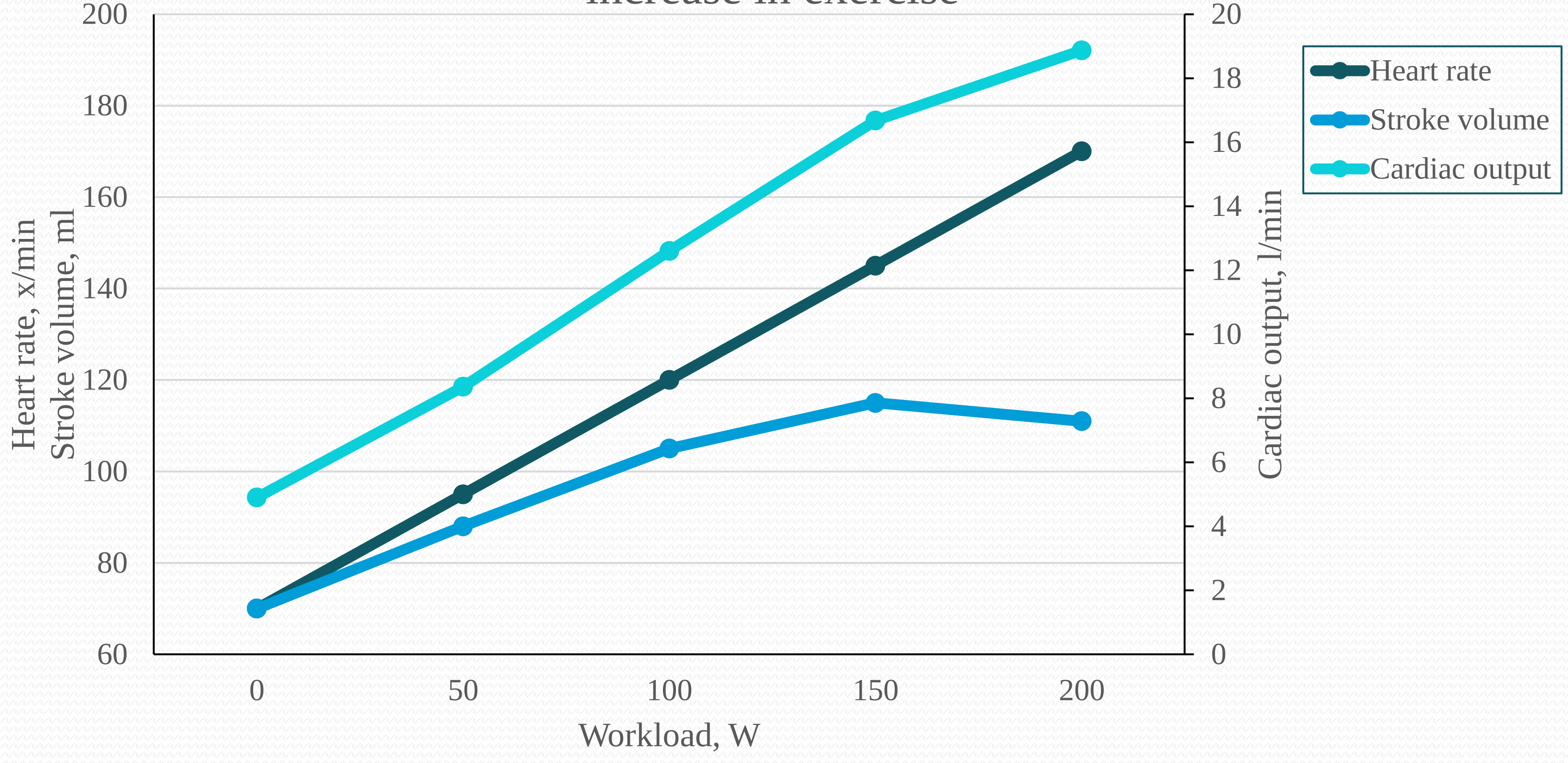
Regulation

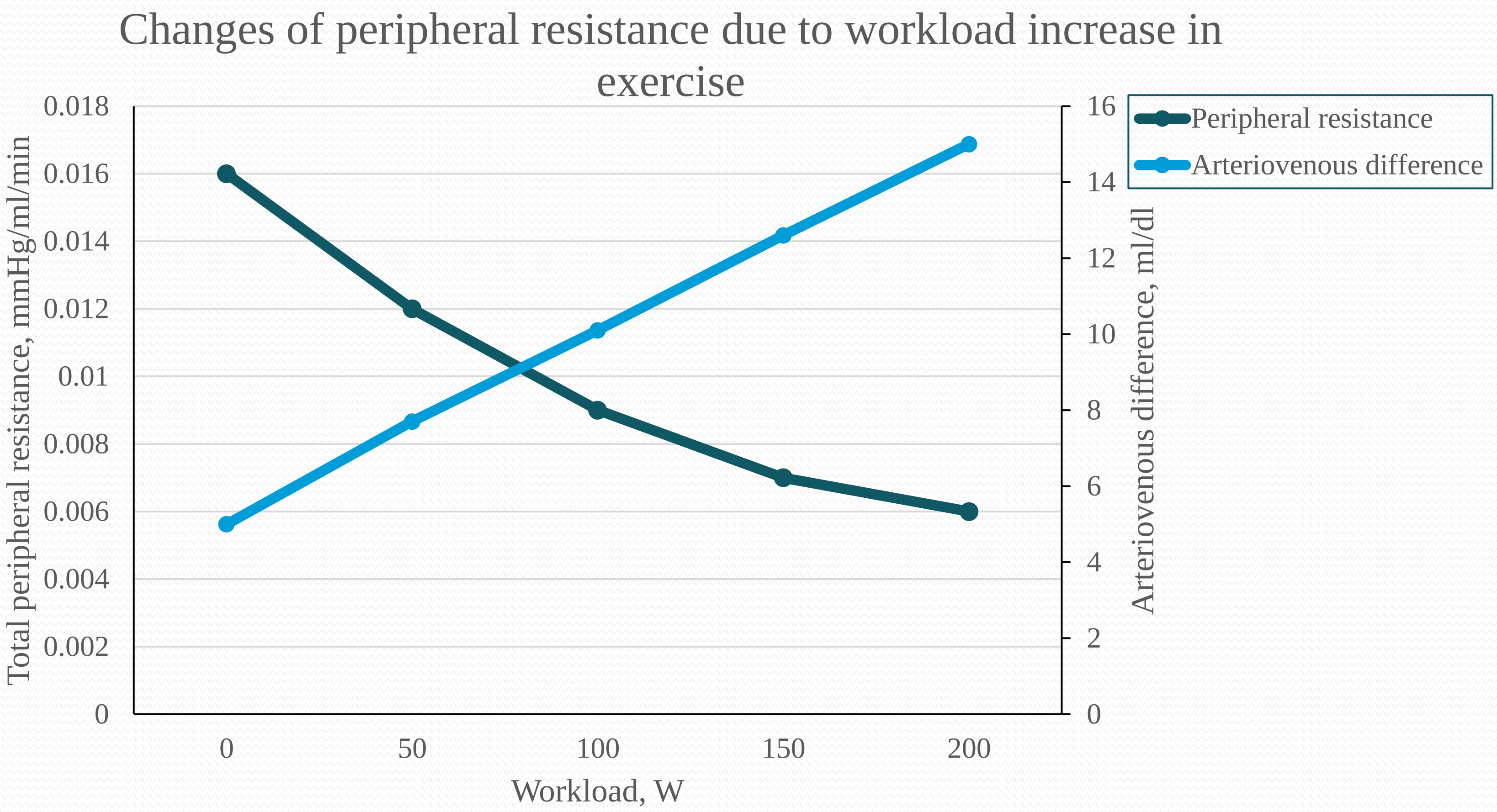
- Peripheral:
  - <u>Metabolic</u>
    - $\uparrow P_{CO_2}$, $\downarrow pH$, $\downarrow P_{O_2}$, $\uparrow$adenosine, $\uparrow K^+$
    - $\downarrow P_{CO_2}$, $\uparrow pH$, $\uparrow P_{O_2}$, $\downarrow$adenosine, $\downarrow K^+$
  - Myogenic
    - Absence of stretch
    - Stretch
  - Humoral
    - Histamine, Kinins, NO, PGI_2, PGE_2, EDHF
    - Serotonin, TxA_2, Leucotrienes, Endothelin
- Central:
  - Neural
    - Symp NS, Parasymp NS
    - Symp NS
  - Hormonal
    - E (β_2), ANP, BNP
    - E, NE (α_1), R-A system, Vasopressin

Changes in the cardiovascular system during exercise

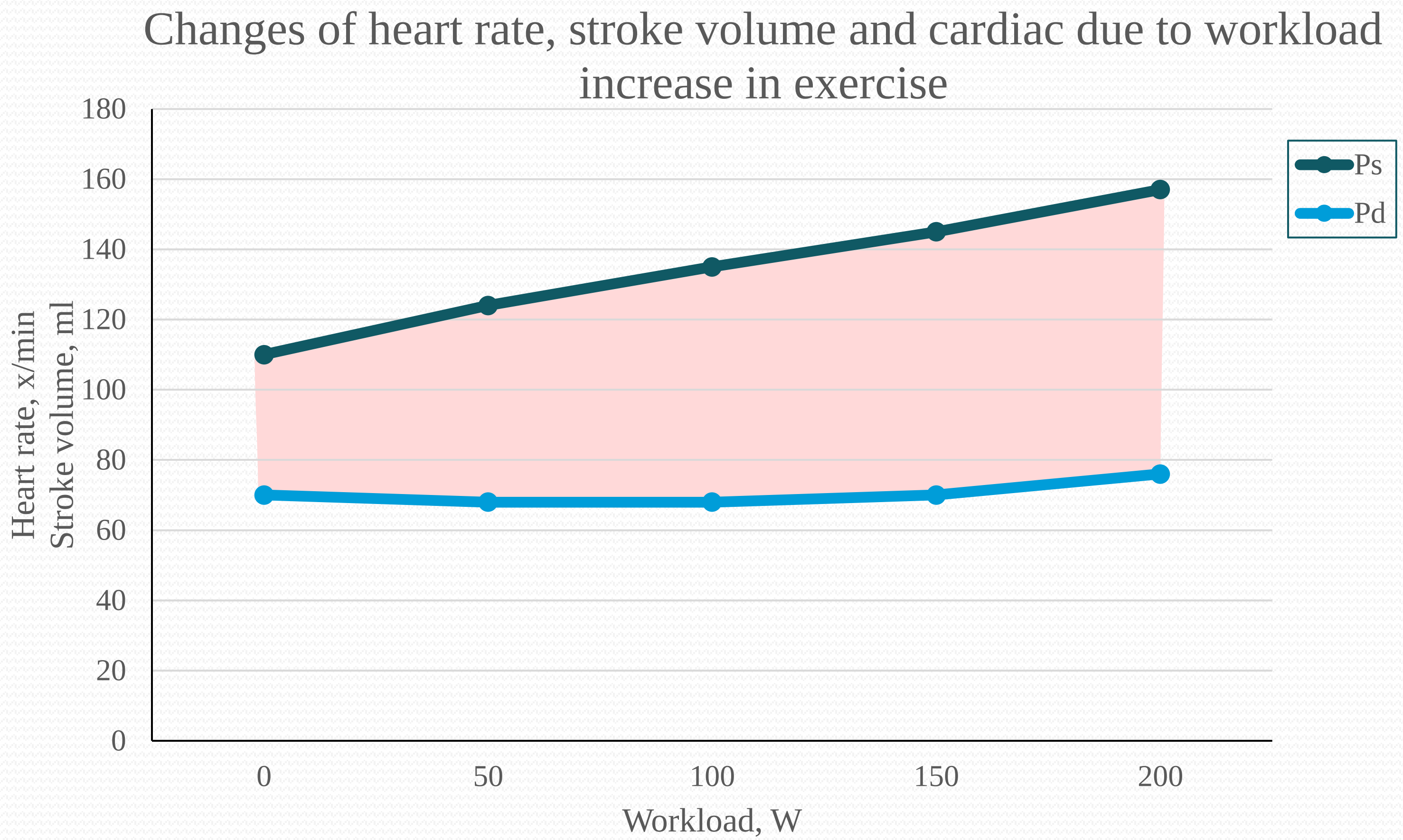

Central comand from the cortex
Hypothalamus
Cardiovascular control center in the medullary region
Epinephrine
+
+
Metabolic
Histamine

Changes of heart rate, stroke volume and cardiac due to workload increase in exercise

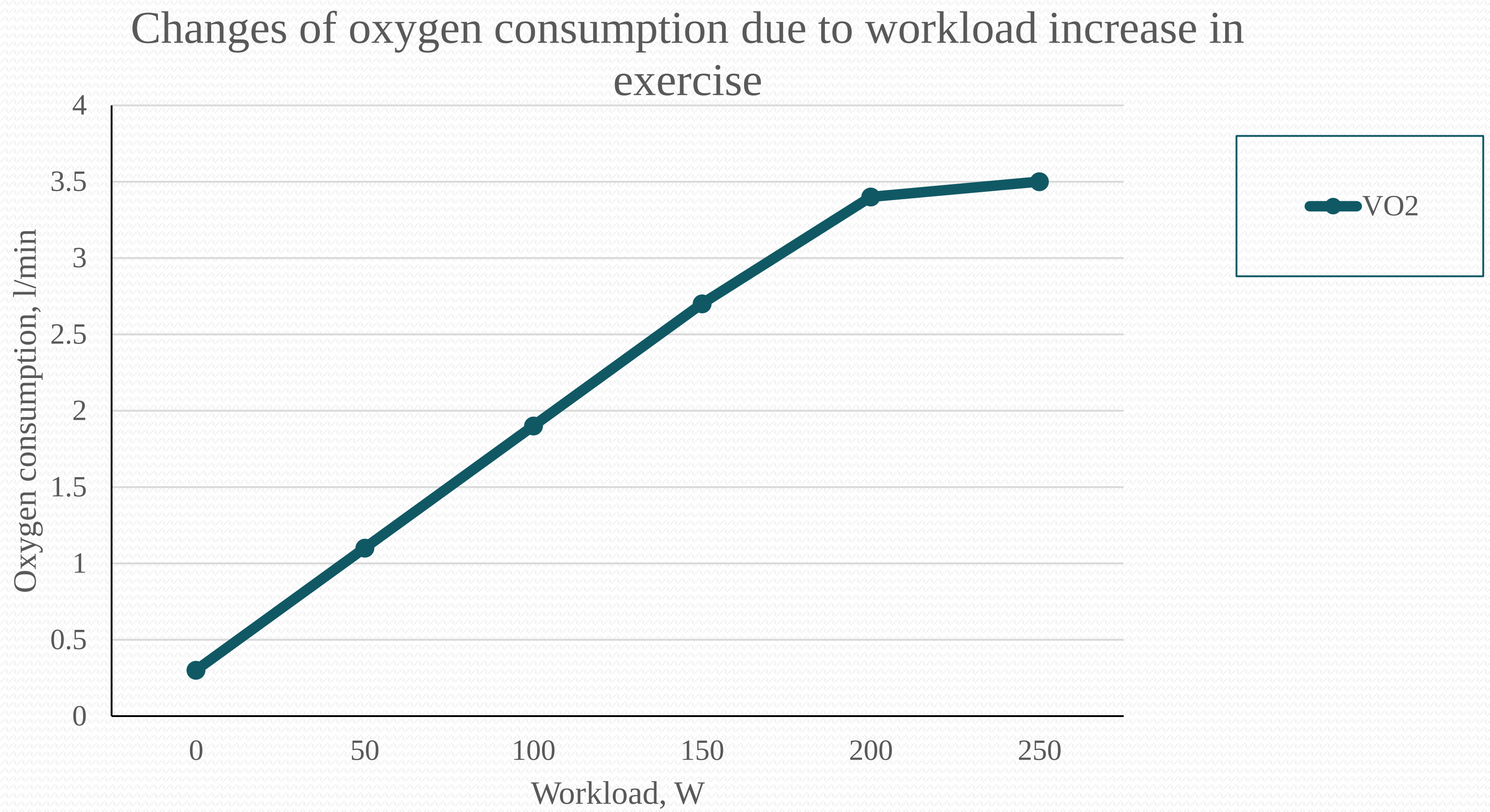




Changes of peripheral resistance due to workload increase in exercise
Total peripheral resistance, mmHg/ml/min
0.018
0.016
0.014
0.012
0.01
0.008
0.006
0.004
0.002
0
Arteriovenous difference, ml/dl
16
14
12
10
8
6
4
2
0
0
50
100
150
200
Workload, W
Peripheral resistance
Arteriovenous difference



Changes of heart rate, stroke volume and cardiac due to workload increase in exercise
Heart rate, x/min
Stroke volume, ml
180
160
140
120
100
80
60
40
20
0
0
50
100
150
200
Workload, W
Ps
Pd



Changes of oxygen consumption due to workload increase in exercise
Oxygen consumption, l/min
4
3.5
3
2.5
2
1.5
1
0.5
0
0
50
100
150
200
250
Workload, W
VO2

Maximal oxygen uptake

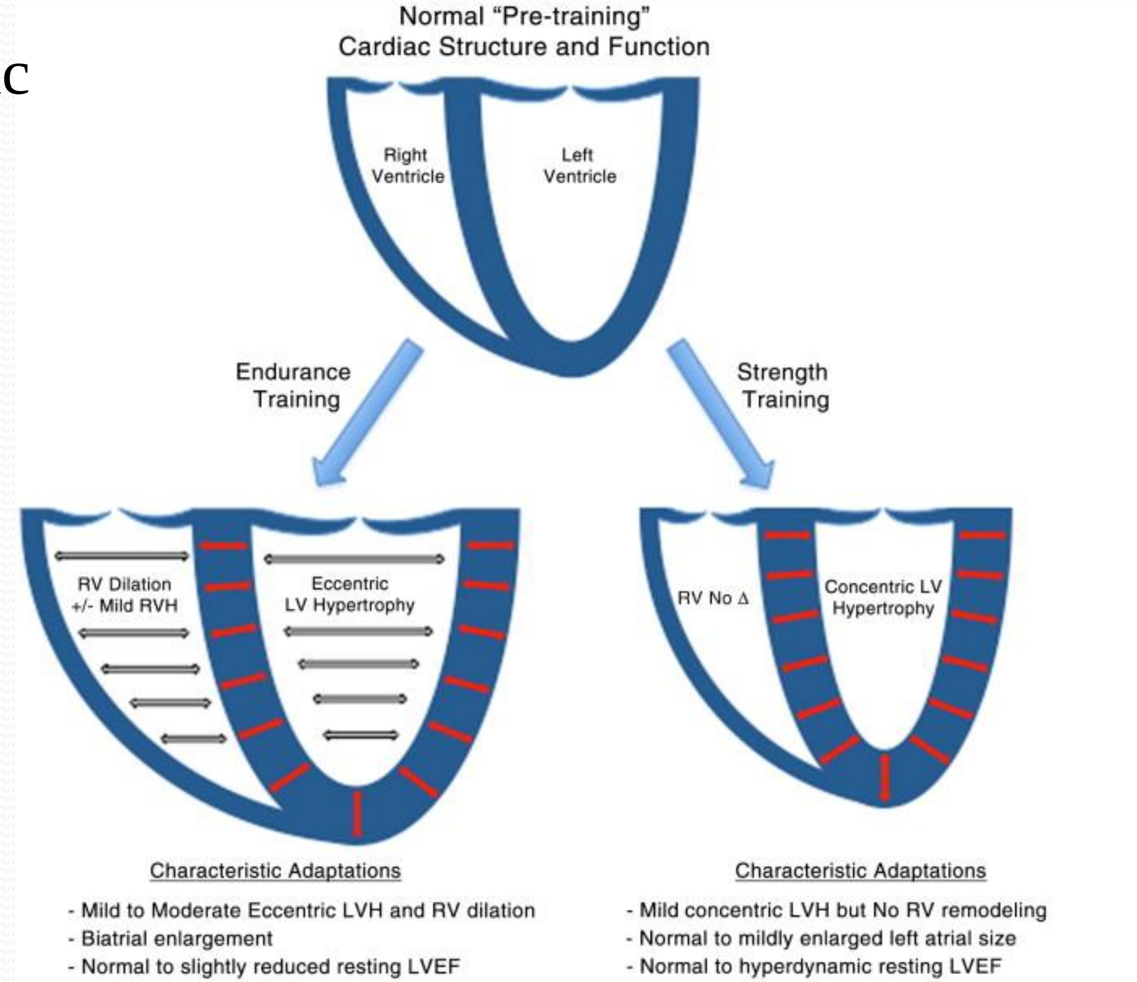
- Maximal oxygen consumption during exercise
  - Untrained 2-3 l/min
  - Trained – up to 6.5 l/min
- Average:
  - Men 35-45 ml/min/kg
  - Women 30-40 ml/min/kg

Limiting factors for maximal oxygen uptake

- Oxygen use in skeletal muscles
- Oxygen delivery
  - Respiratory – increases function until ~65% of maximal capacity
  - Heart – increases function until about ~90% of maximal

Heart adaptation to exercise

- Increased parasympathetic influence
- Decreased sympathetic influence



From Weiner RB, Baggish AL. Exercise-induced cardiac remodeling. *Prog Cardiovasc Dis* . 2012;54:380

Skeletal muscle adaptation to exercise

- Decreased peripheeral reesistance in muscles
- Increased density of capillaries
- Increased amount of myoglobin
- Increased number and activity of mitochondria
- Increased enzyme activity