The specifics of some organ circulations …

Milan Chovanec

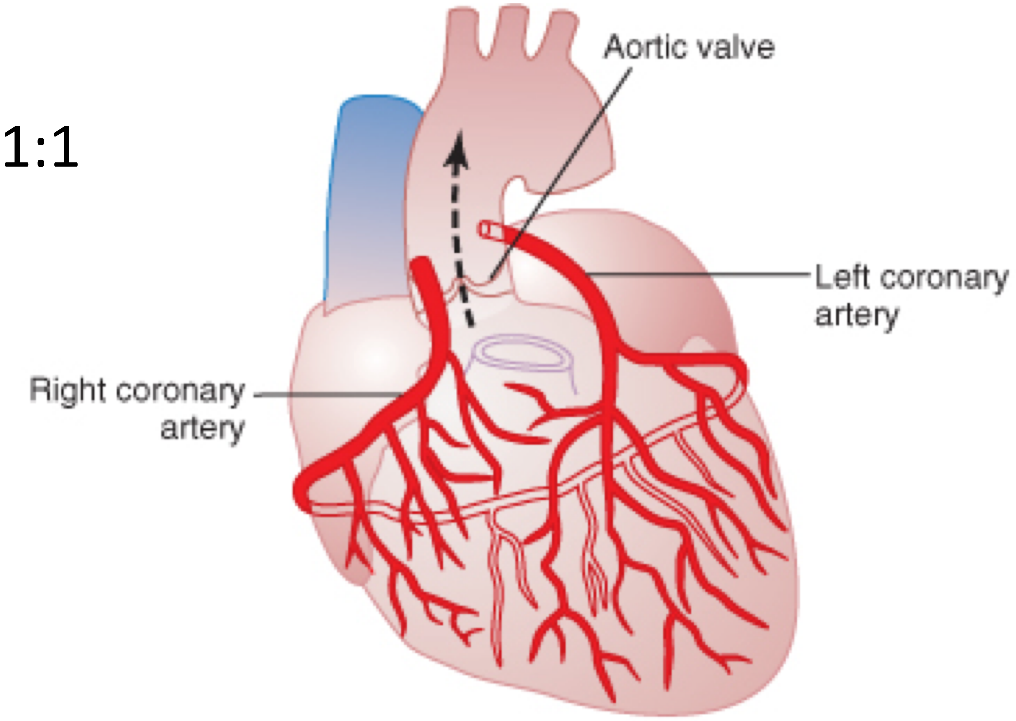
Department of Physiology, 2. LFUK in Prague

Cardiocenter, Na Homolce Hospital, Prague

- Blood supply to the heart, coronary flow
- Pulmonary circulation
- Skeletal muscle perfusion
- Brain perfusion

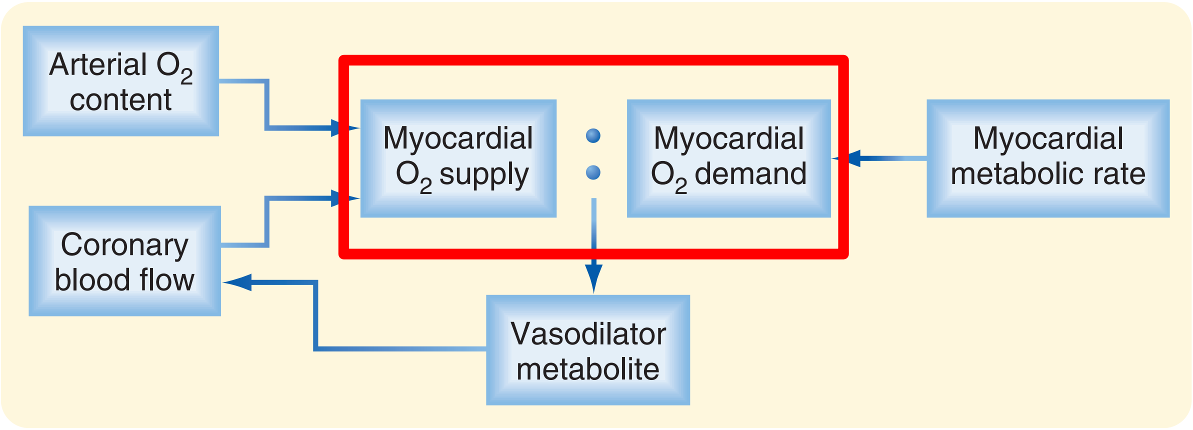
Coronary flow

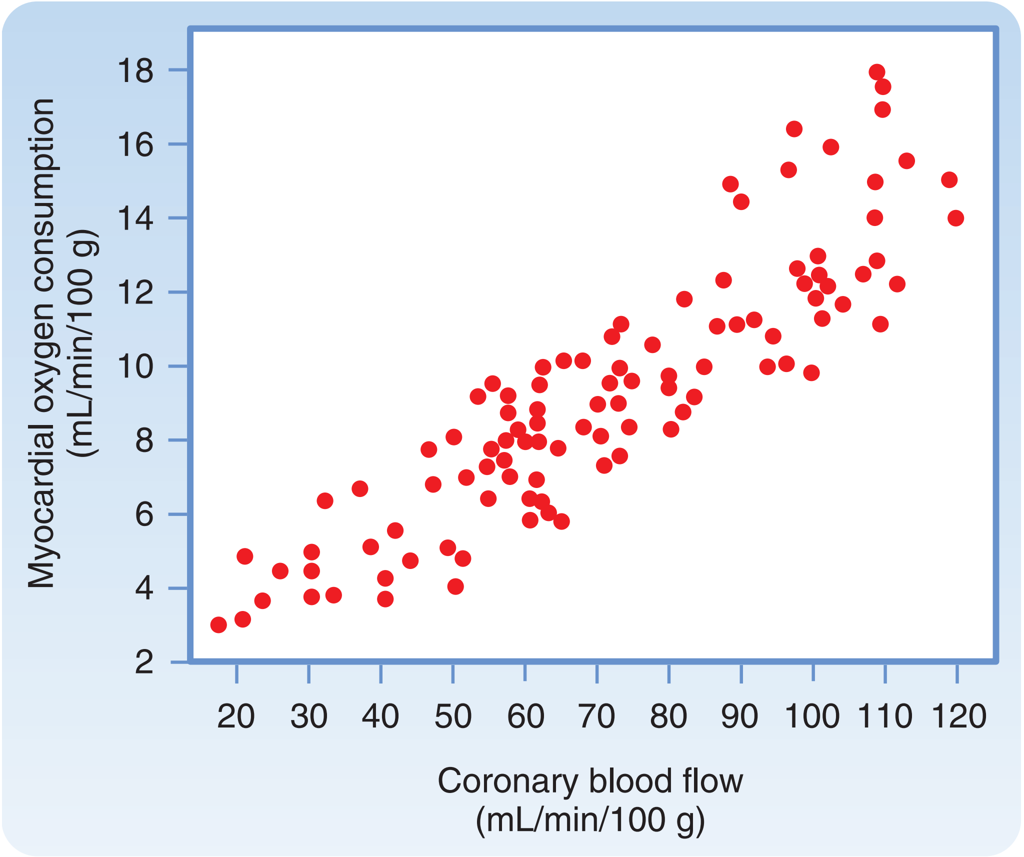
- 5% CO i.e. cca 250 ml/min (under resting conditions)
- Dense vascular supply: muscle fiber/capillaries 1:1
- Lateral flow:
  - 50%: right-sided type
  - 30%: balanced type
  - 20%: left-sided type



Coronary flow – suply vs. Demand of O_2

MYOCARDIAL OXYGEN BALANCE

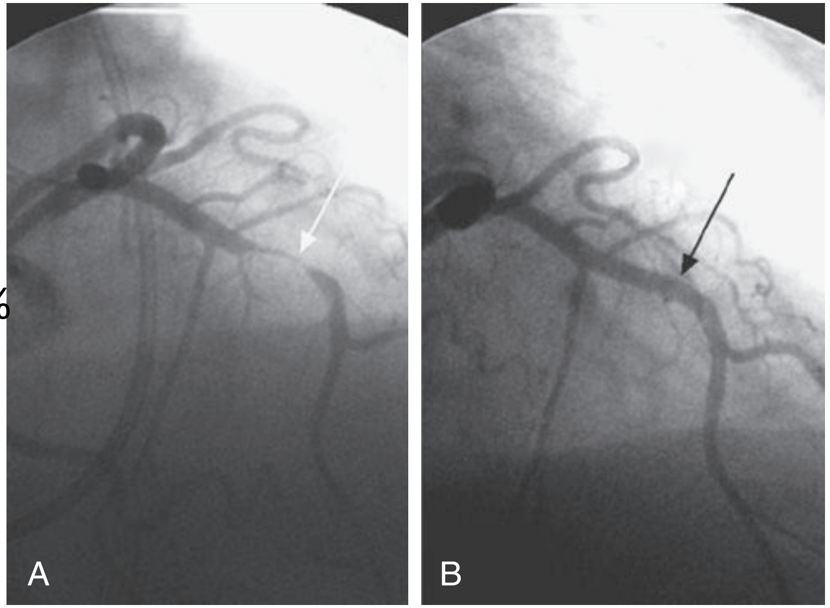




Coronary flow

O_2 consumption in tissues = increase in O_2 extraction from blood + increase in flow

- **Maximum extraction of O2 already in resting conditions, extraction of approx. 70-80% of flowing O2**
- Increasing the supply of O2 to the myocardium is possible only by increasing the flow
- The increase in flow is very sensitive to obstructions in the vessels - atherosclerosis….
- $RT = R_A + R_a + R_c + R_v + R_V$ share of individual resistances:1% + 70% + 20% + 8% + 1%
- An obstacle in the area of Ra will cause a large change in the resistance of the entire system - a decrease in flow... (physiological regulation, see below)
- SKG: shows only the vessels in the RA region, i.e. only a very large constriction (>75%) will significantly affect the flow rate…. (atherosclerosis,...)



Selective coronarography (SKG) **Percutaneous coronary intervention (PCI)**

Coronary flow – the flow regulation

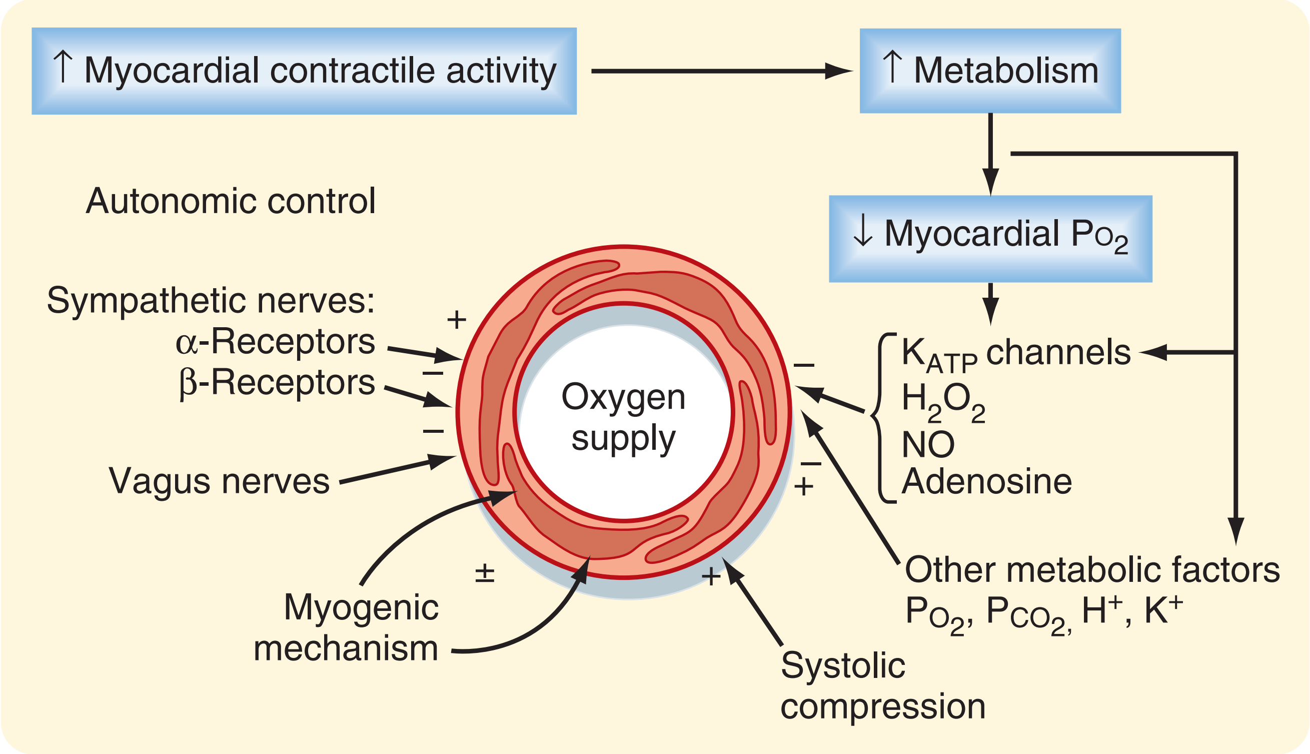
(vessels from the area of R_a – small arteries, arterioles)

- **<u>Nervous</u>** regulation: sympathetic/parasympathetic

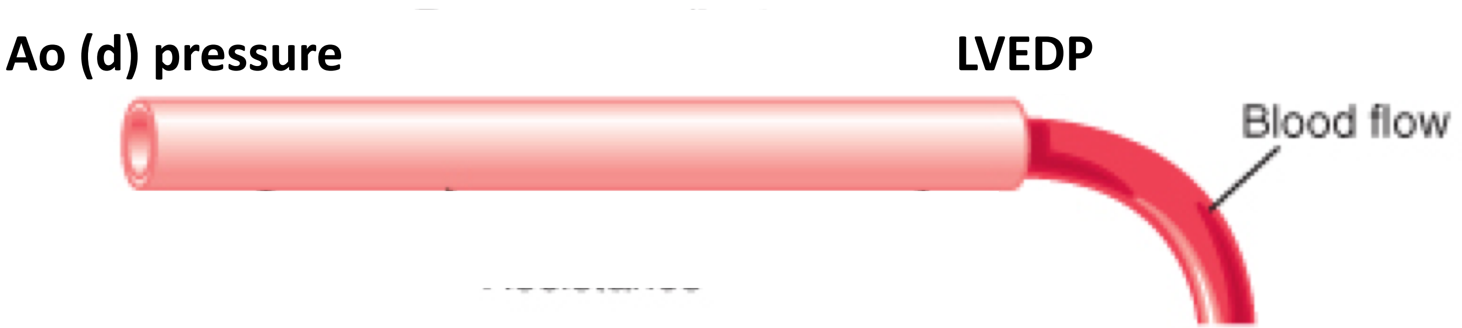
  α-adrenergic receptors (vasoconstriction)

  β-adrenergic receptors (vasodilation)

- **<u>Chemical</u>** regulation: pH, CO_2, lactate, PG…
- Myogenic
- Extravascular compression…

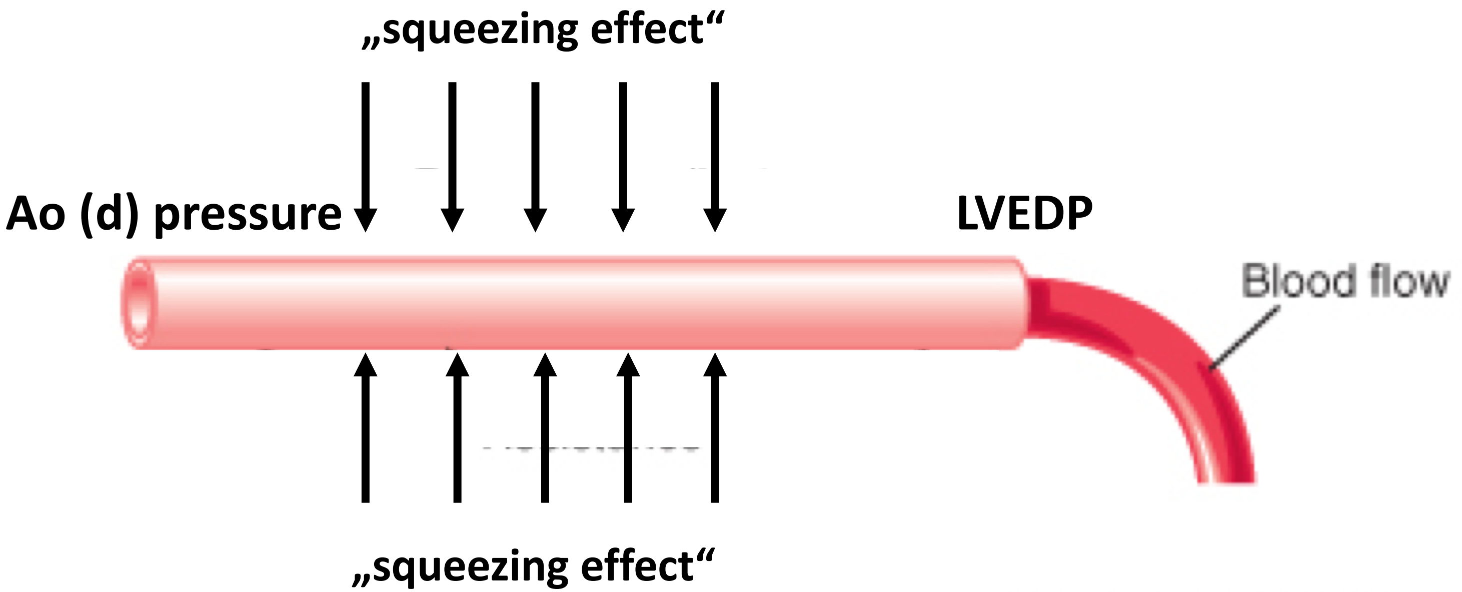


Coronary flow



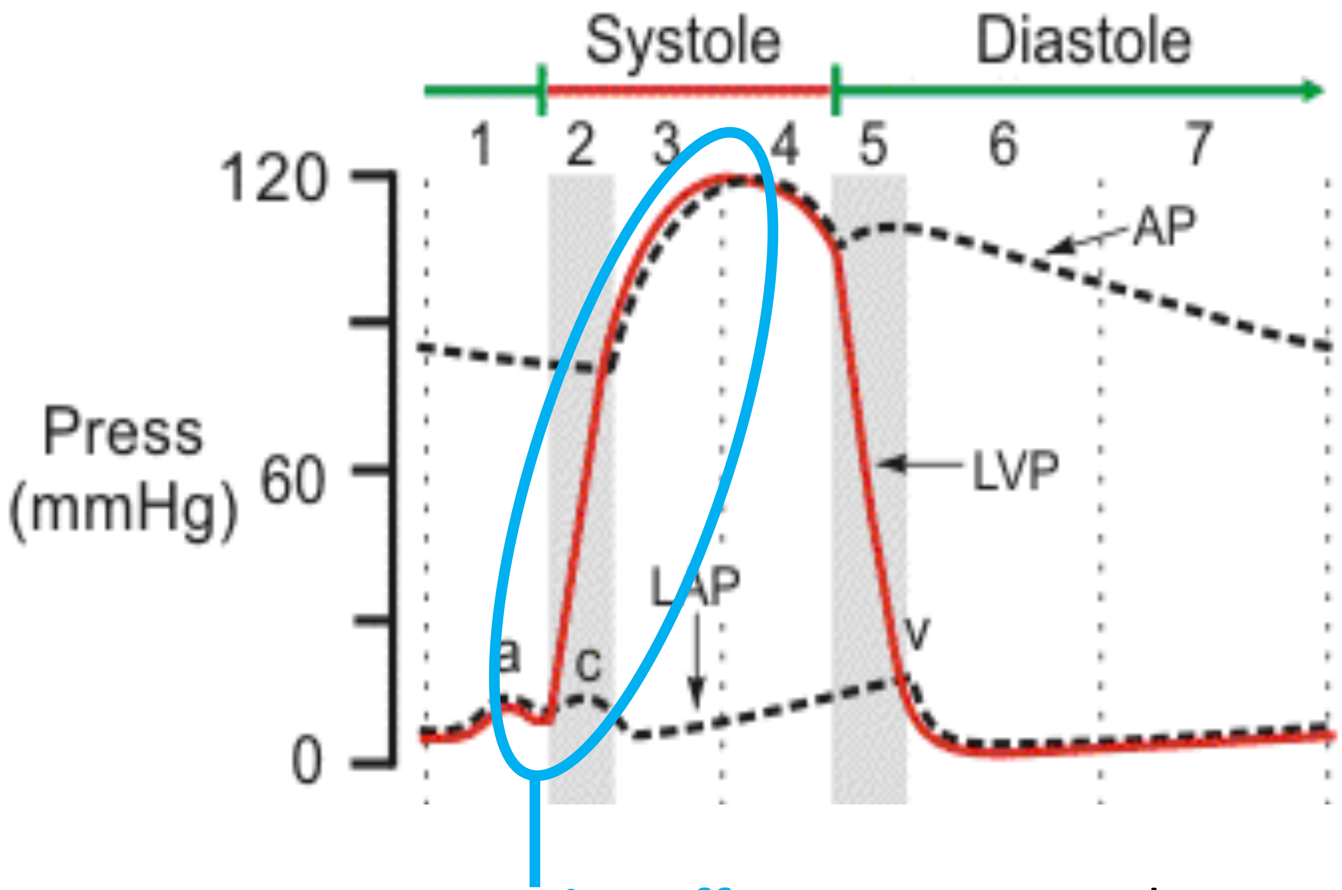
Upraveno z: © Elsevier. Guyton & Hall: Textbook of Medical Physiology 11e - www.studentconsult.com

Coronary flow



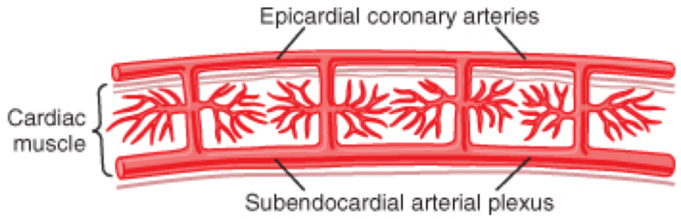
Upraveno z: © Elsevier. Guyton & Hall: Textbook of Medical Physiology 11e - www.studentconsult.com

Coronary flow



Sqeezing effect – extravascular compression

Coronary flow– “squeezing effect“



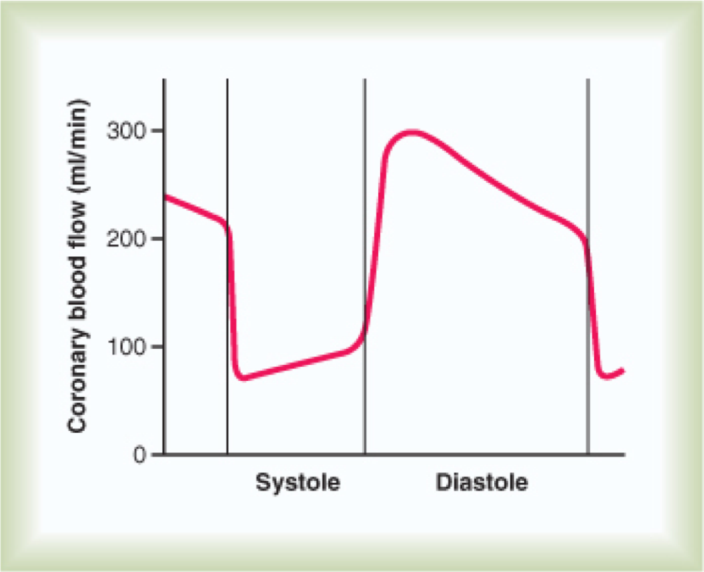
Minimally limited Q

Systole of LV

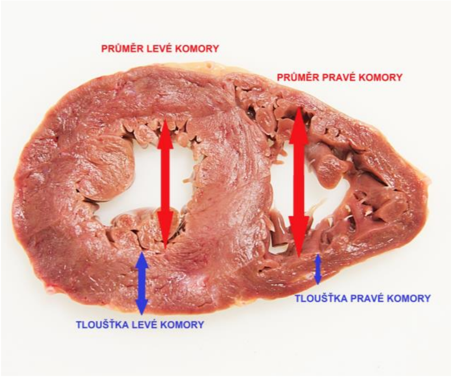
Very limited Q

Diastole of LV

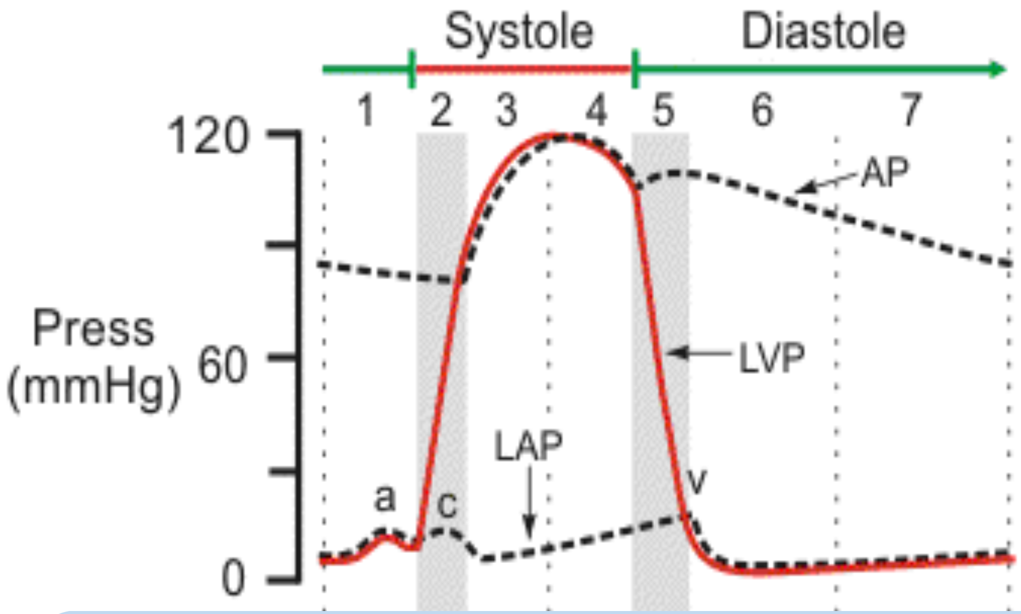
Not affected by LV contraction



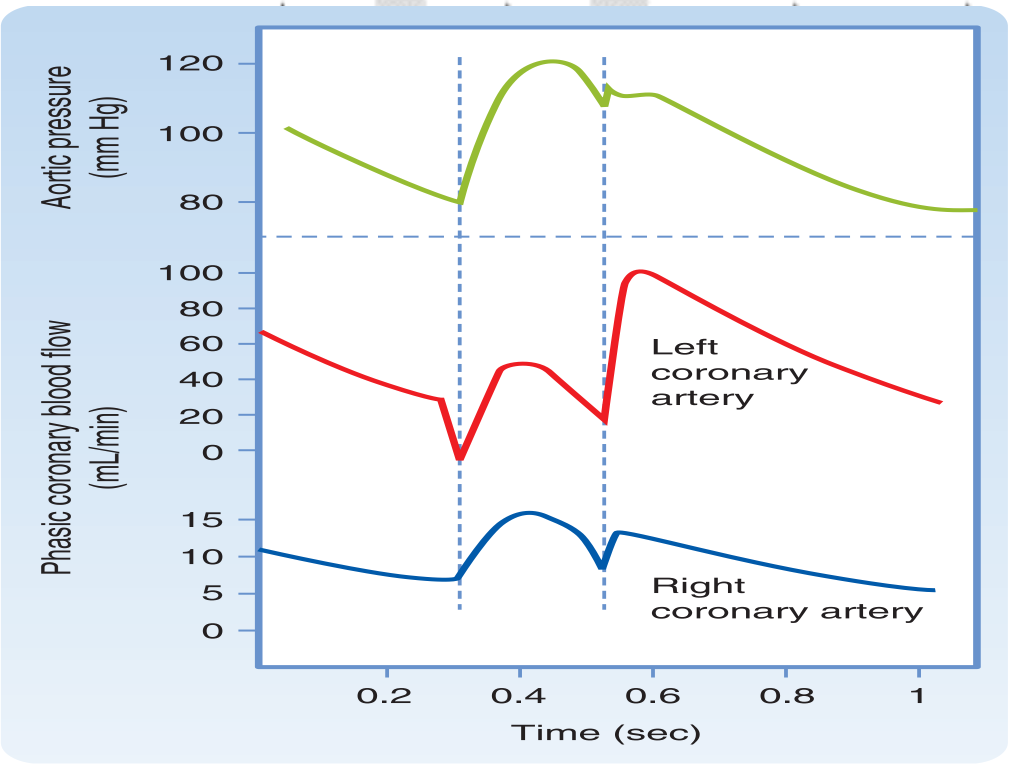
Not affected by squeezing effect in the right ventricle



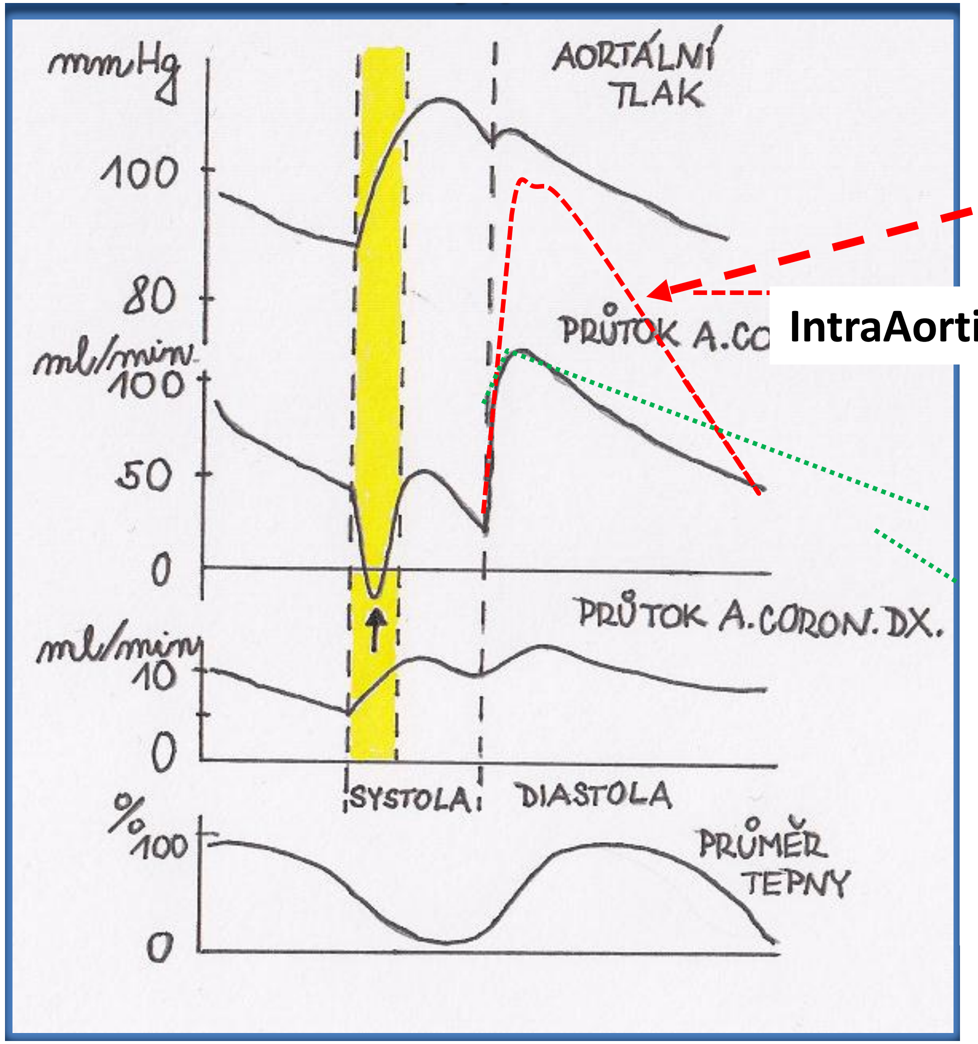
The heart cycle



Coronary flow

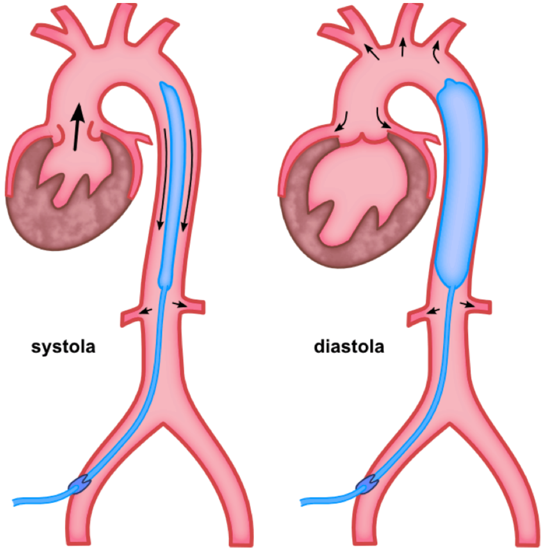


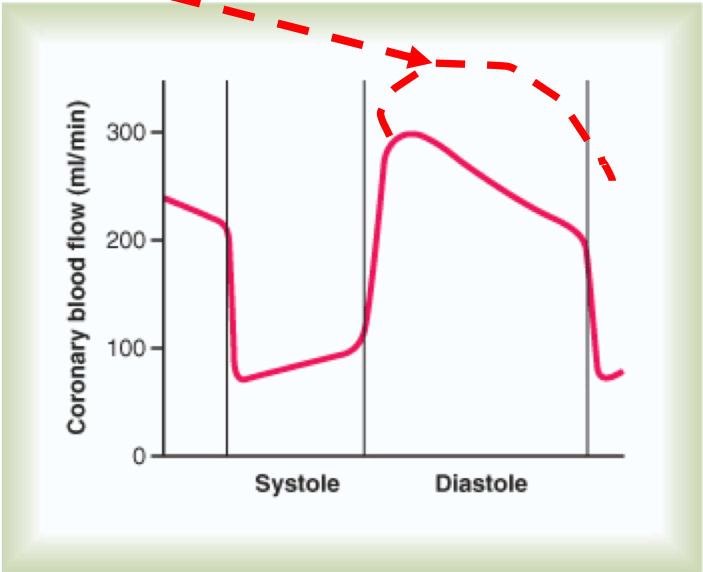
Coronary flow



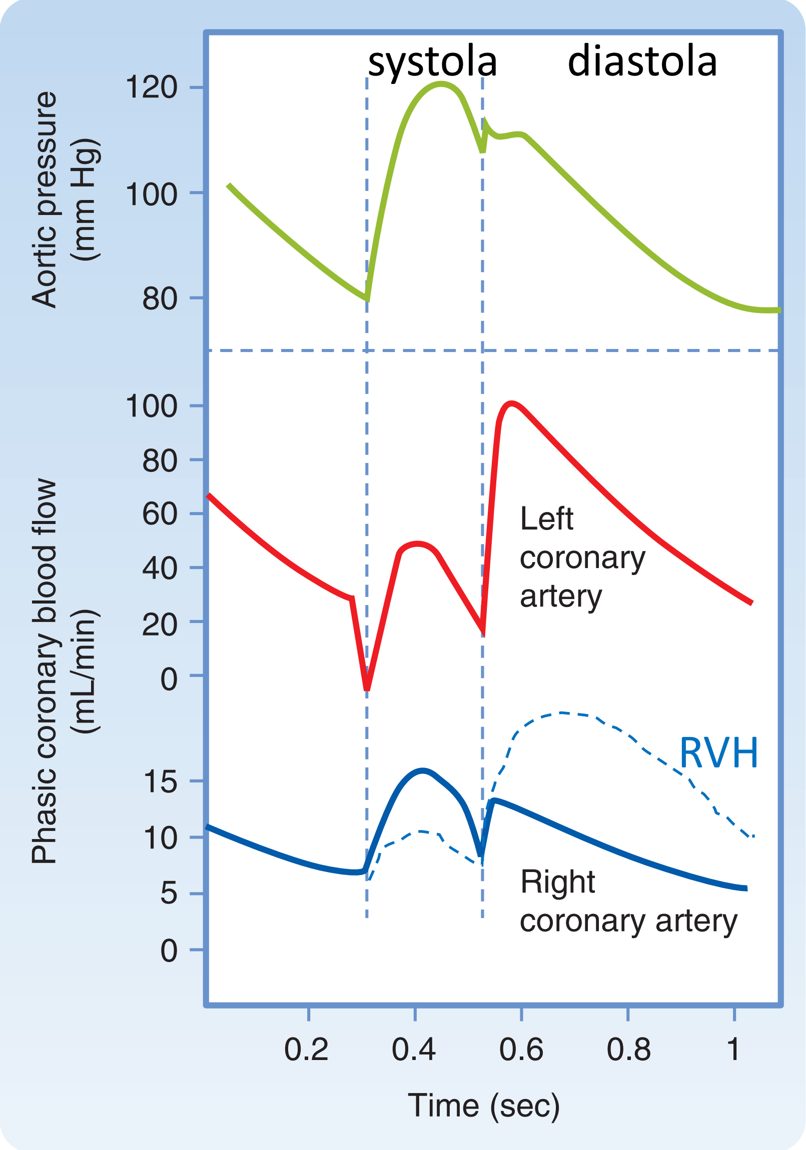
IABP

IntraAortic Baloon Contrapulsation





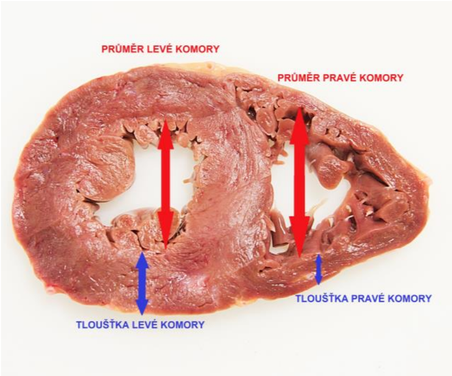
Coronary flow – pathology

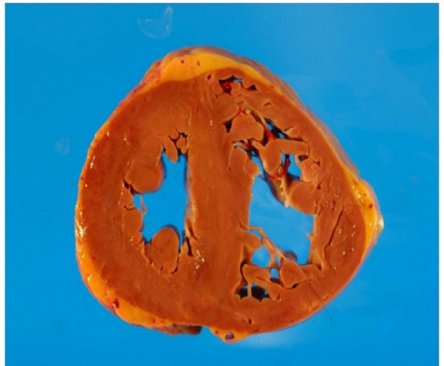


- Tachycardia (shortening of diastole)
- RV hypertrophy (RVH)….
- Aterosclerosis (PCI…)

- IABK….
- Nitrates: production of NO = vasodilation….⬆ Q

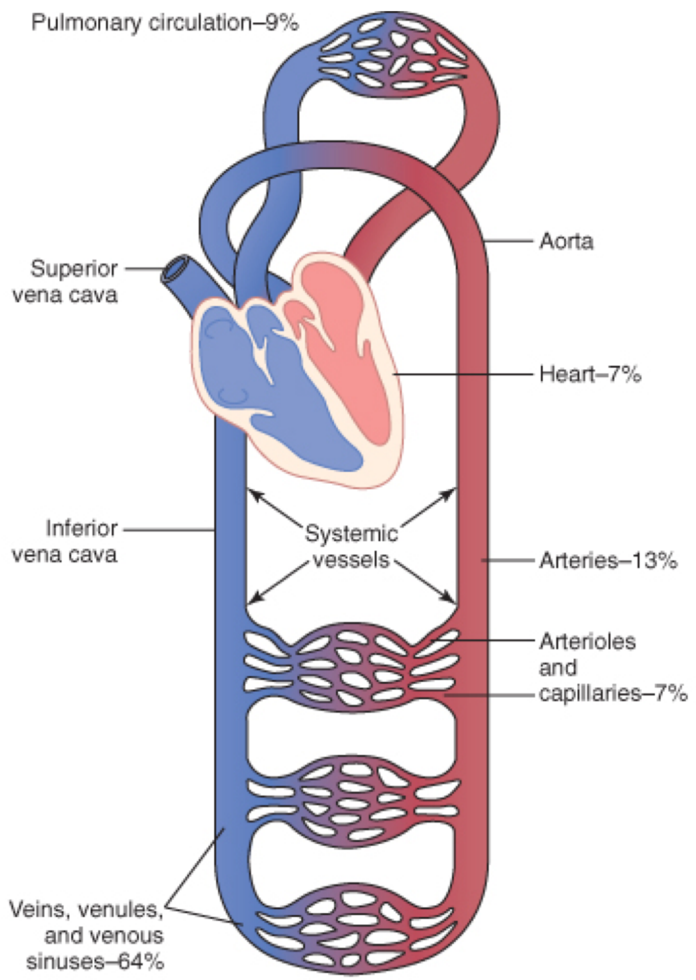
Fysiolol.



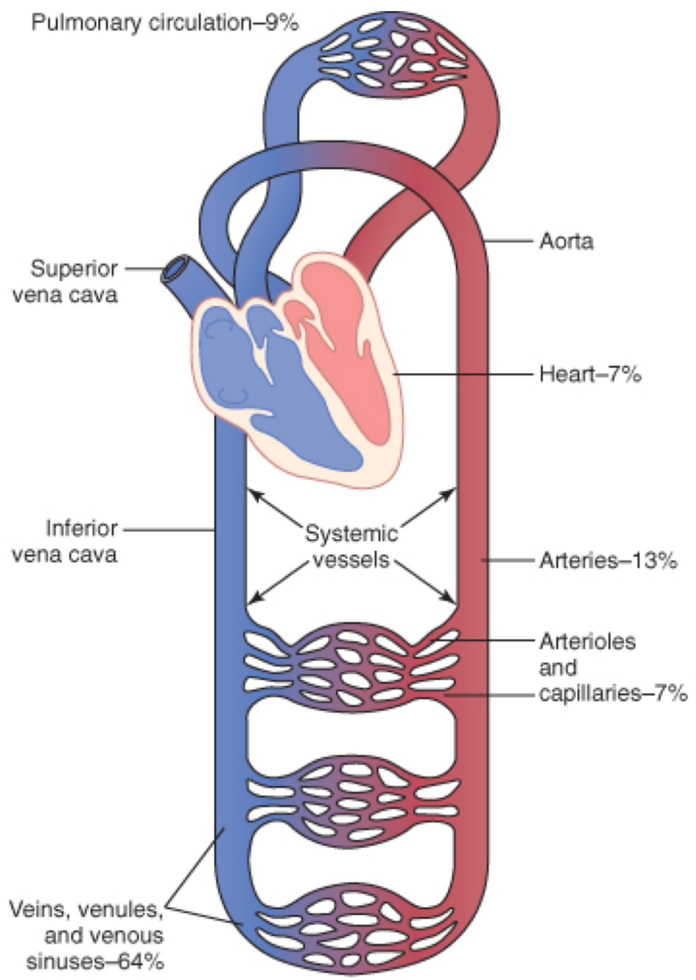


RVH

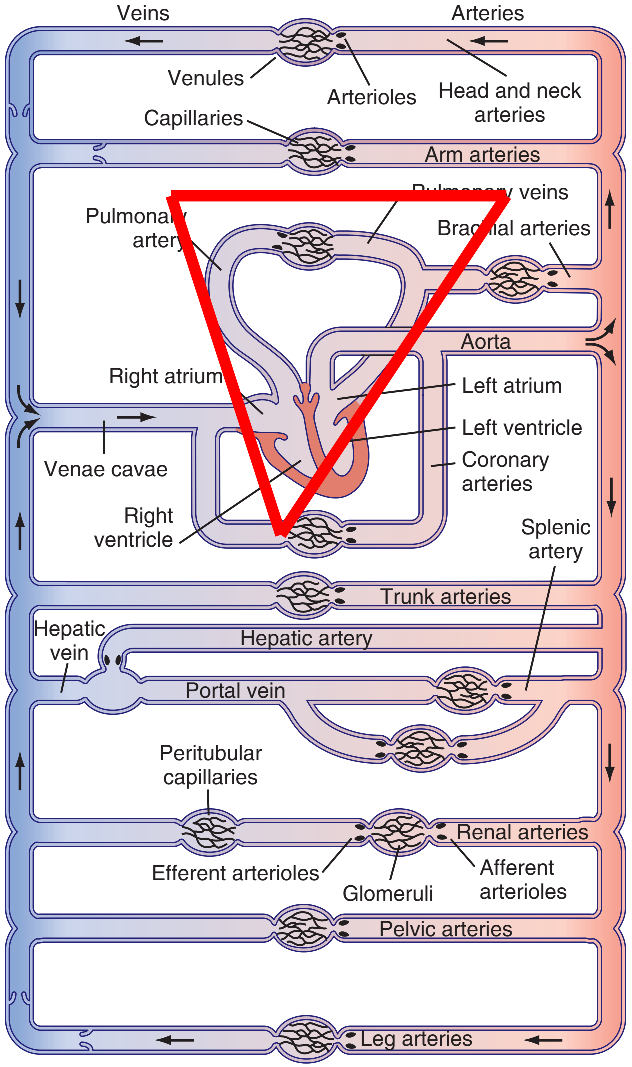
Pulmonary circulation



Pulmonary circulation



© Elsevier. Guyton & Hall: Textbook of Medical Physiology 11e - www.studentconsult.com



Pulmonary circulation vs. Systemic circulation

pulmonary : systemic circulation = serial arrangement!!!

	Pulmonary circulation	Systemic cirkulation
Flow (Q)	**equal**	**equal**
Resistance (R)	▼	▲
Perfusion pressure (∆P)	▼	▲
Vessels #	▼	▲
Vascular tonus	▼	▲
Velocity of flow	▲	▼
Shear stress	▲	▼
SMC	▼	▲
Resting NO production	none	present

Pulmonary circulation – structure v. function

- Function: O_2 from blood to tissues vs. O_2 from the environment into the blood
- response to hypoxia (vasoconstriction / vasodilation)
- HPV

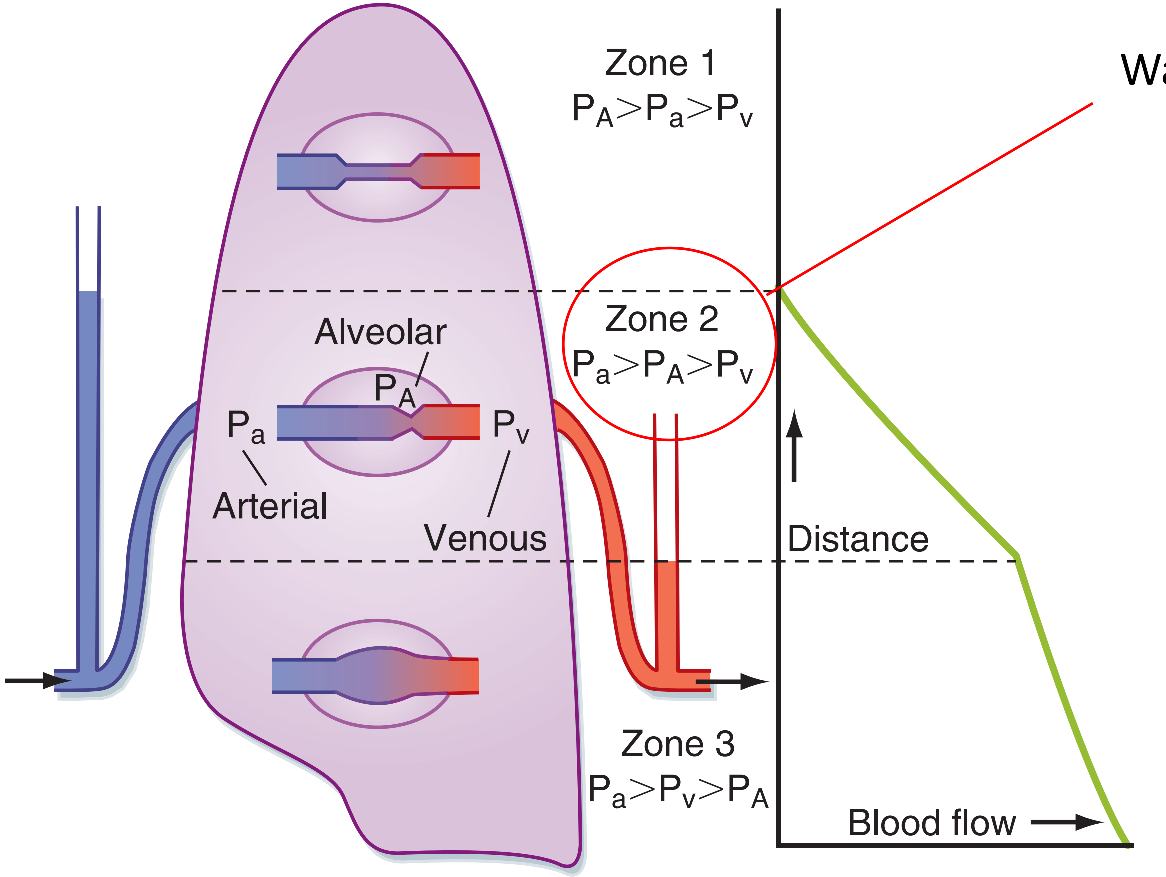
- Low resistance (low pulmonary vascular tone)
- NO production (continuous NO / when damaged)

Pulmonary circulation

- Lower basal vascular tone of pulmonary arterioles
- Less hungry muscle in arterioles
- Contraction of PASMC's – Ca2+ sensitization
- Vessel diameter depends on intramural + extramural (alv.) pressure (West zone)
- Response to hypoxia: Vasodilation vs. Vasoconstriction
- HPV

- Arteries / Veins, different structure, lower pressures... thinner heart wall
- SMC absent or not circular compared to systemic c.

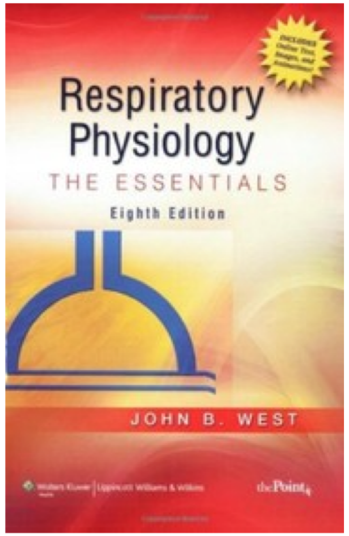
Pulmonary circulation– perfusion (West‘s zones)

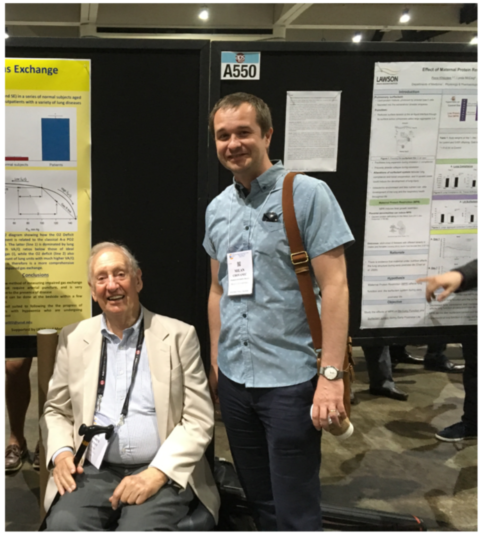


Waterfall effect

Decreased inspiration pressure
in arteficial ventilation improves venous return
and improves pulmonary circulation

John B. West





Pulmonary circulation – reaction to acute hypoxia (HPV)

- Systemic circulation:

hypoxia = vasodilation

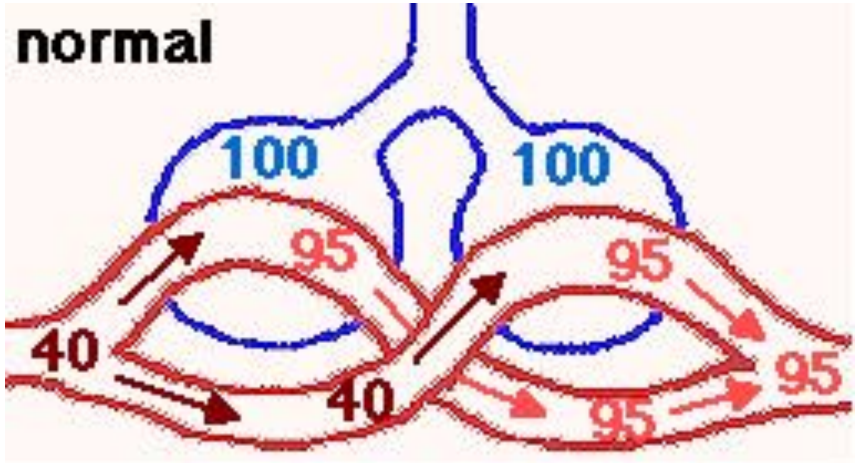
(lack of O_2) = (increased blood flow, increased O_2 supply)

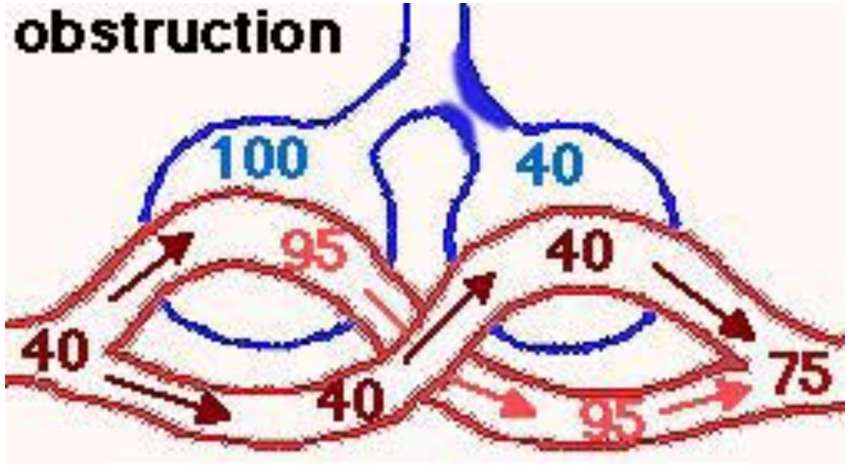
- Plicní cirkulace:

hypoxia = vasocostriction

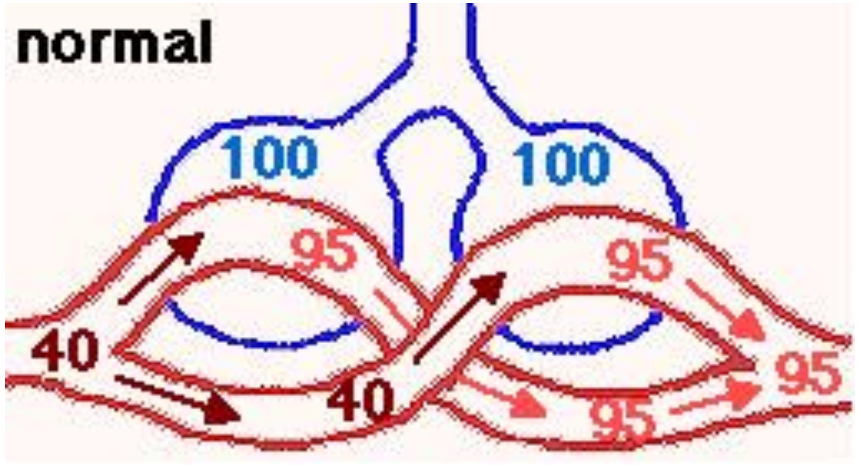
1. vasodilatation would increase hypoxia and this would be disadvantageous for the organism
2. Insufficiently ventilated areas of lung tissue (pulmonary alveoli)
3. HPV - hypoxia-induced closure of K1.5 - channels, depolarization, vasoconstriction of PASMC

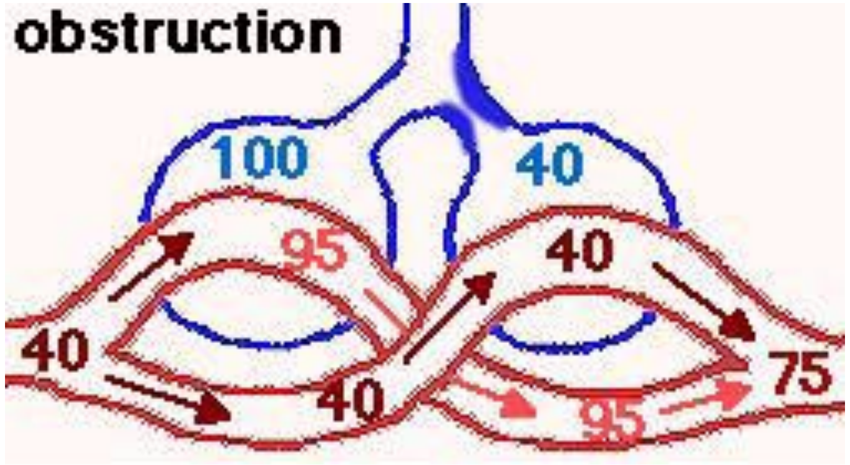
Pulmonary circulation – reaction to acute hypoxia (HPV)

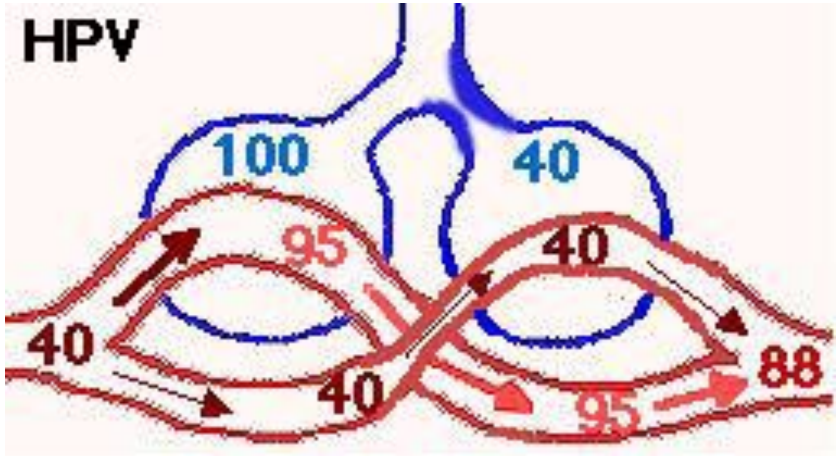




Pulmonary circulation – reaction to acute hypoxia (HPV)







Pulmonary circulation – chronic hypoxia

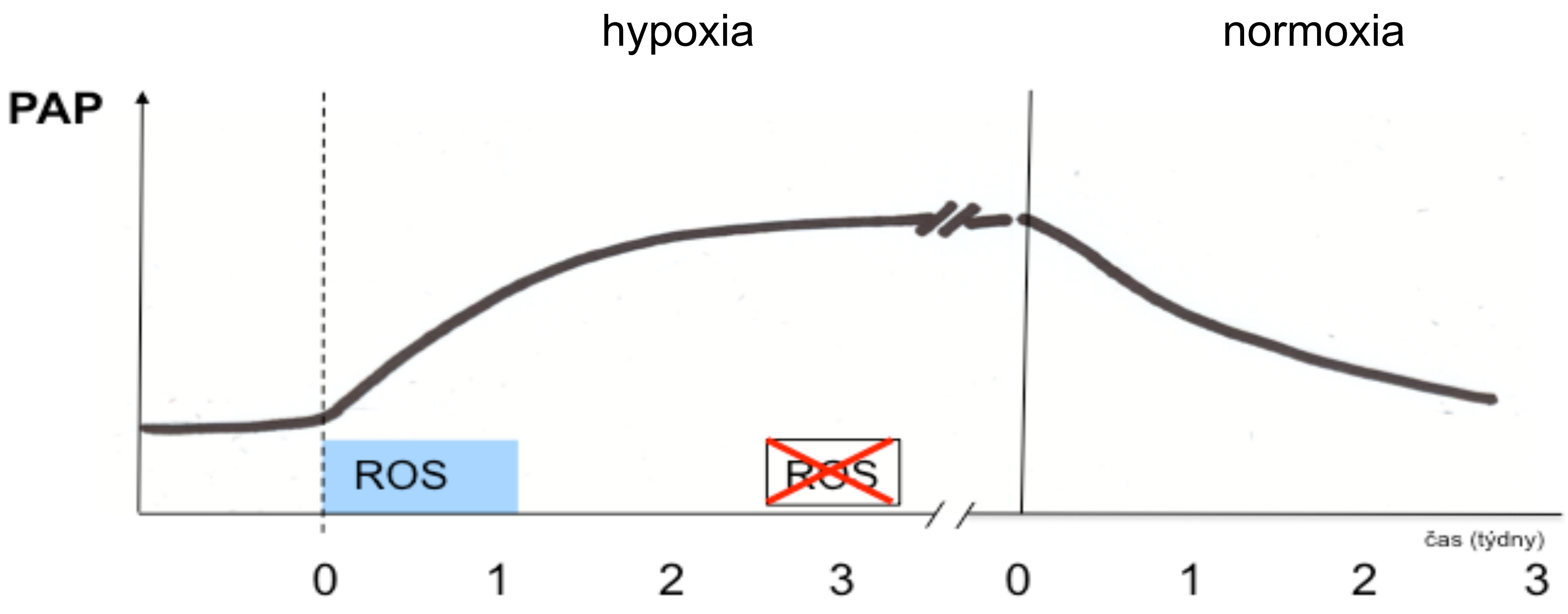
- Different reactions to exposure of chronic v. akute hypoxia

- Chronic hypoxia:

  - the entire lung tissue is exposed to long-term effects of hypoxia
    it is not progressive
  - ROS production is damaged during development
  - production of NO (eNOS, iNOS) started
  - NO synthase (NOS): production of NO but also superoxide
  - protection of the alveolocapillary membrane from increased
    perfusion?

Pulmonary circulation – chronic hypoxia

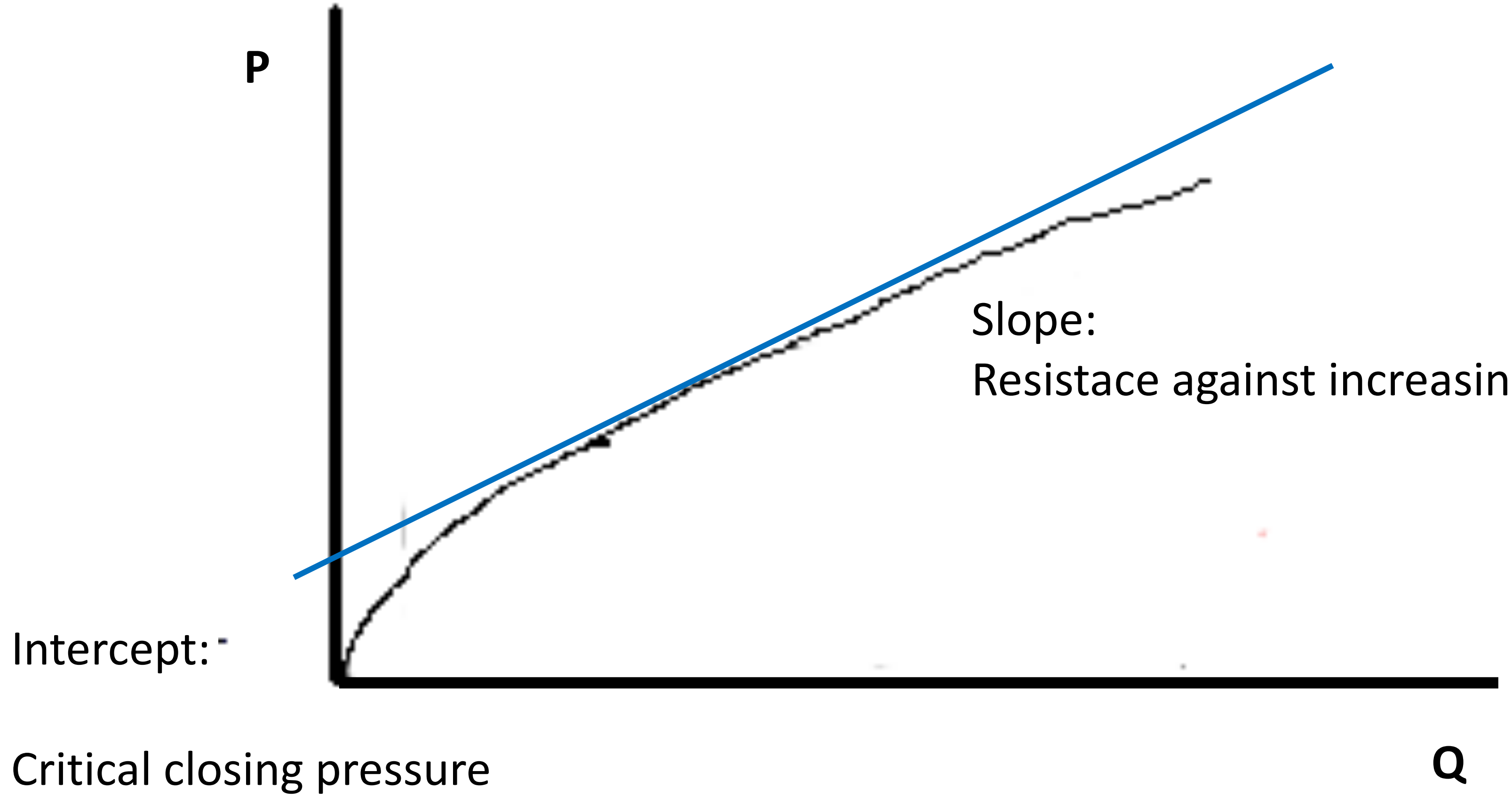
Hypoxic pulmonary hypertension (HPH)
VASOCONSTRICTION + REMODELLING pulmonary arterioles



Obrázek č.1: **Schéma rozvoje hypoxické plicní hypertenze.**

PAP – střední krevní tlak v plicnici, ROS – období, kdy se na rozvoji HPH podílí volné kyslíkové radikály (reactive oxygen species)
Schéma je zveřejněno s laskavým svolením Prof. MUDr. Jana Hergeta, DrSc., Ústav fyziologie 2.LFUK v Praze.

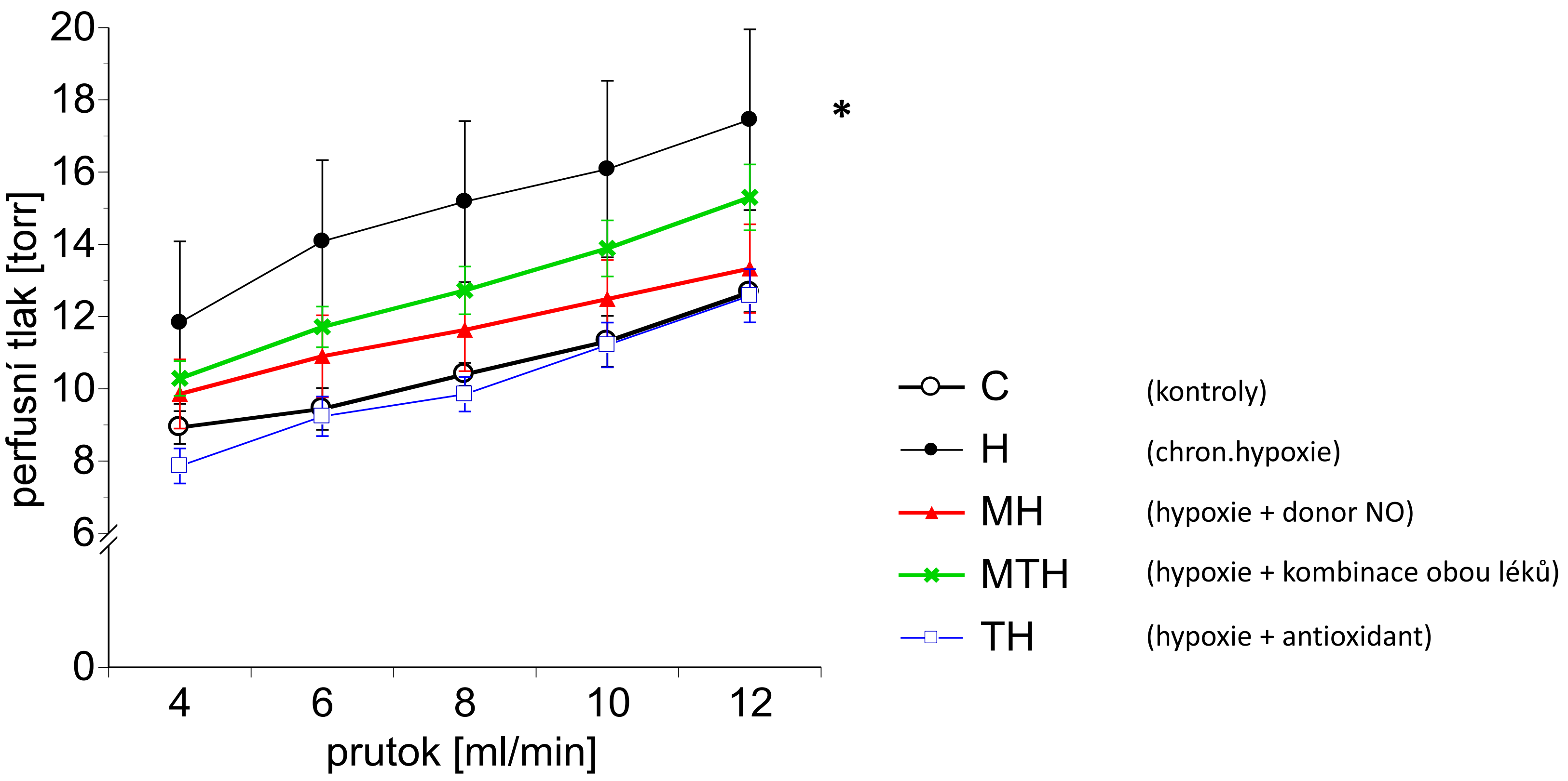
Pulmonary circulation – perfusion



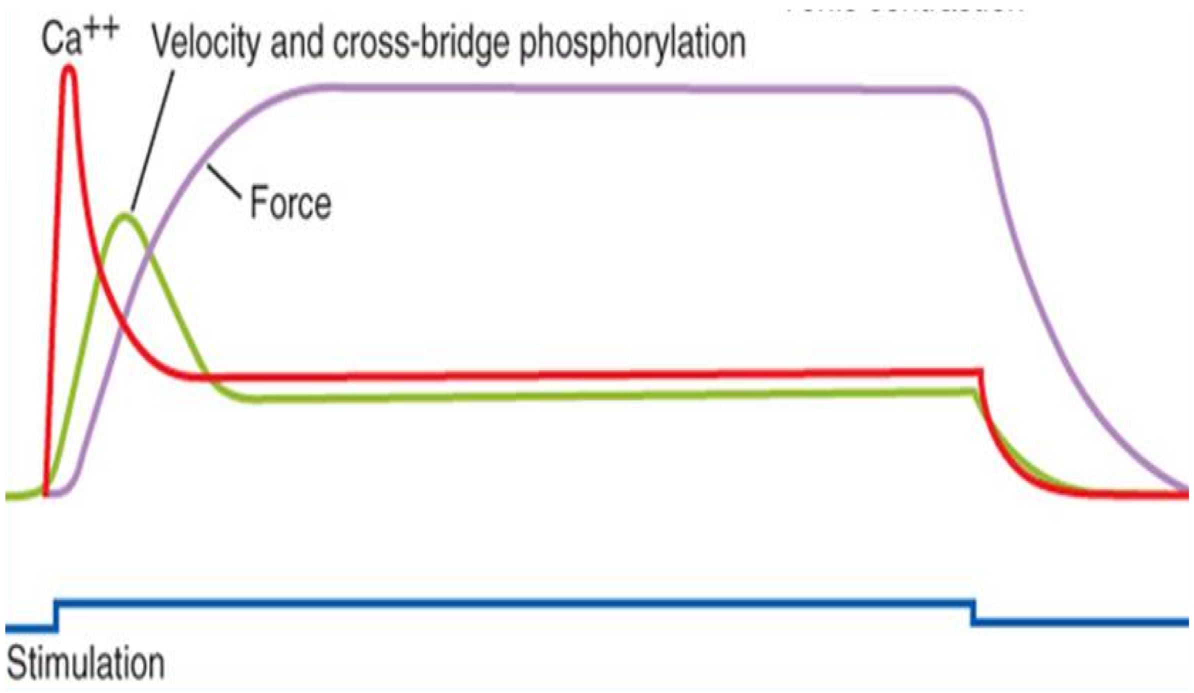
Critical closing pressure
of the PASMCs

P = intercept + slope Q

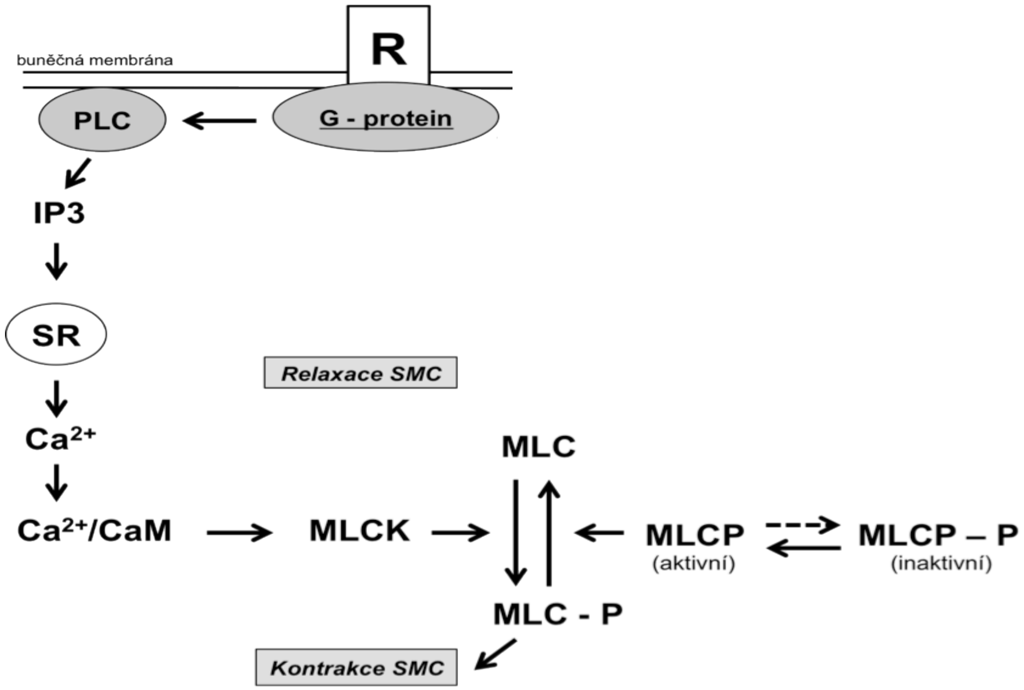
HPH in adult experimental male Wistar rats



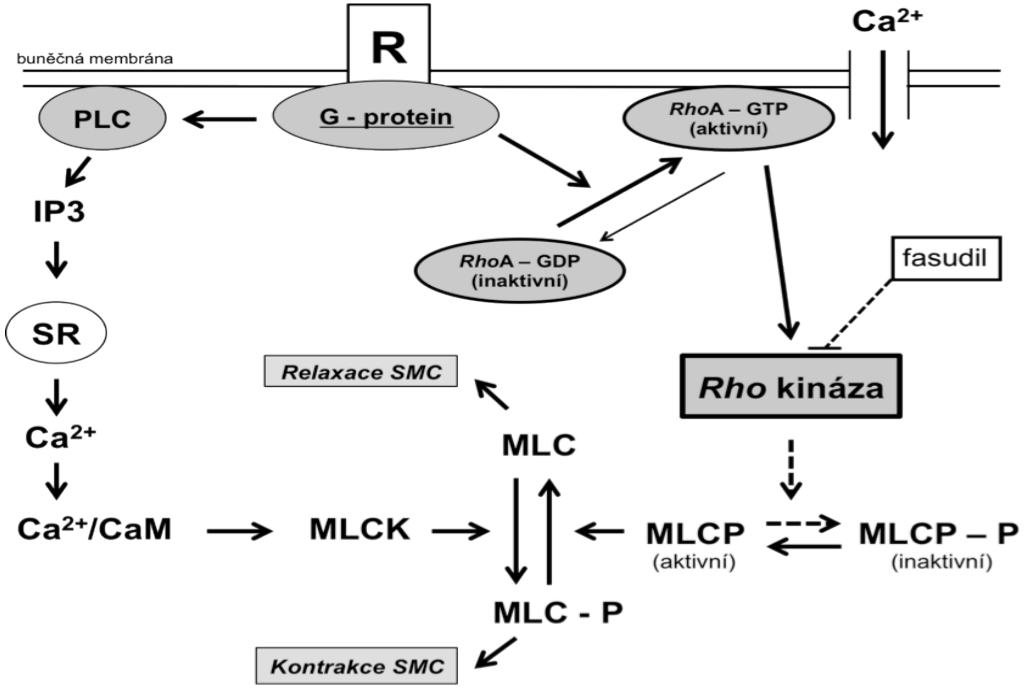
Pulmonary circulation – PASMC vasoconstriction: Ca^{2+} sensitisation



Somlyo & Somlyo, Nature, 1994



Pulmonary circulation – PASMC vasoconstriction: Ca^{2+} sensitisation



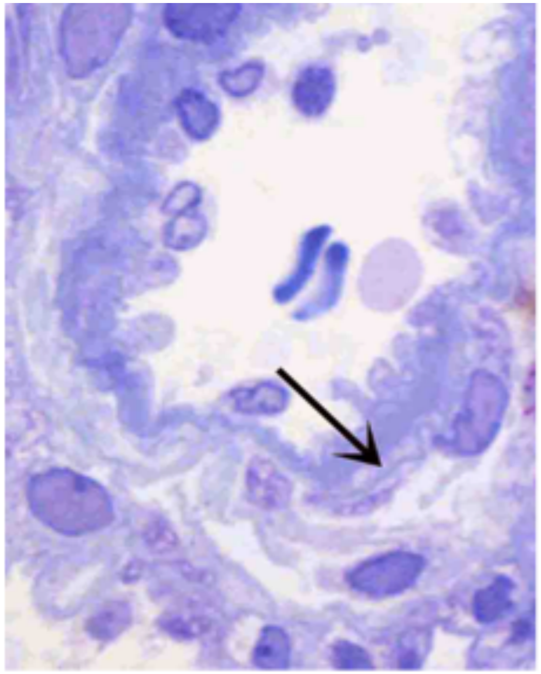
Obrázek č. 3: **Kontrakce hladké svaloviny aktivovaná G-proteiny.**

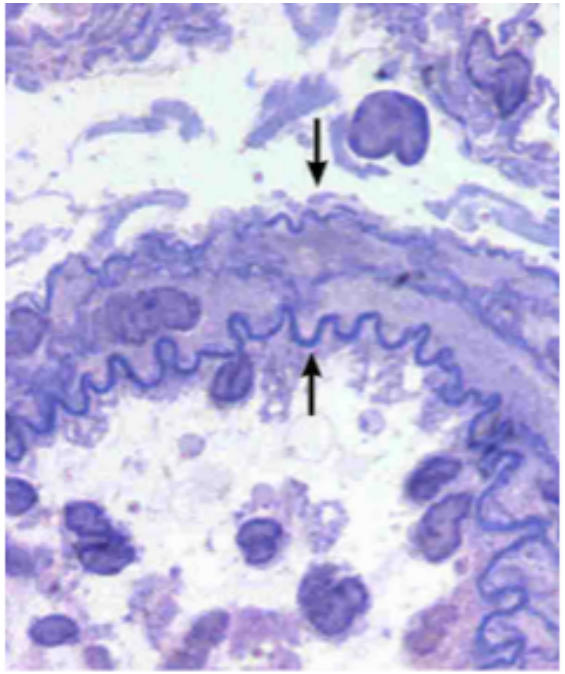
MLC: lehké řetězce myozinu (myosin light chain), MLCK: kináza lehkých řetězců mozinu, MLCP: fosfatáza lehkých řetězců myozinu, R: membránový receptor spřažený s G-proteinem, PLC: fosfolipáza C, IP3: inozitol-1-3-5-trisfosfát, SR: sarkoplazmatické retikulum, CaM: kalmodulin, -P: fosforylace

Převzato a modifikováno z: Nagaoka T, et al., Am J Respir Crit Care Med, 2005, 171, 494-499

Pulmonary circulation – SMCs in pulmonary arterioles

fysiology





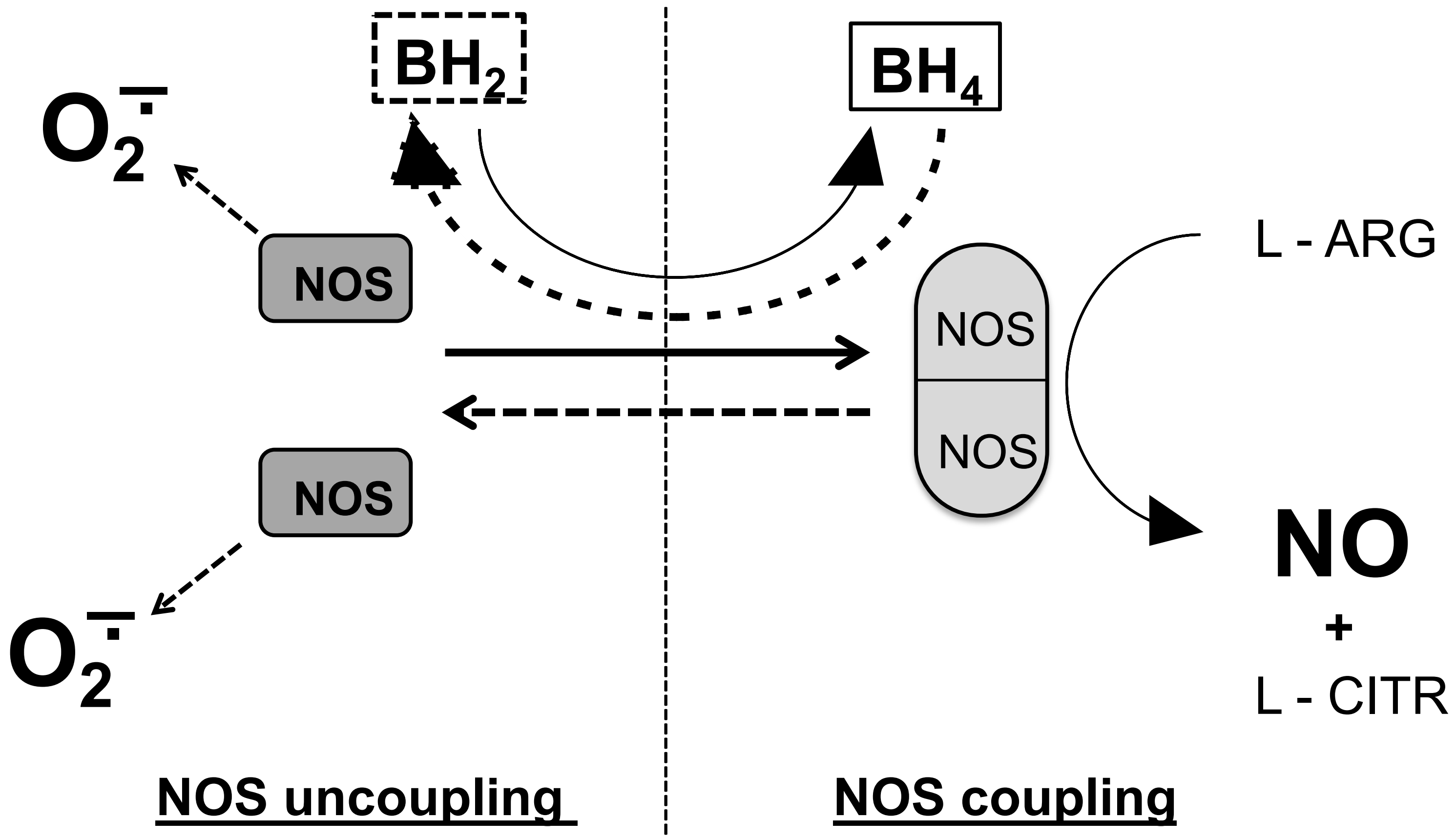
HPH

Obrázek č. 2: **Histologické zobrazení remodelovaných periferních plicních arteriol („double laminated vessels“).**

Vlevo: neremodelovaná periferní plicní arteriola s nerozšířenou tunica media (dlouhá šipka). Vpravo: remodelovaná periferní plicní arteriola působením chronické hypoxie se zbytnělou tunica media a viditelnou lamina elastica externa a interna (malé šipky). Barvení Toluidinová modř. Značka = 20 μm

Obrázek je zveřejněn s laskavým svolením Doc. MVDr. Luďka Vajnera, CSc, Ústav histologie a embryologie, 2.LFUK v Praze.

Pulmonary circulation – NO / superoxide production



Obrázek č. 4: Fyziologie NO syntázy a produkce NO.
$O_2^{\cdot -}$ - superoxid, **NO** – oxid dusnatý, **NOS** – syntáza oxidu dusnatého, **L-ARG** – L-arginin, **L-CITR** – L-citrulin, **BH_2** – dihydrobiopterin, **BH_4** -tetrahydrobiopterin

Skeletal muscles

- Muscle fibers types: red (slow) – high capacity of OXFOS

  white (fast) – lower capacity of OXFOS

- Perfusion of the muscle depends on the constriction/dilation of the precapillary sphincters

- Resting conditions: 1,5-4,5 ml/min/100g

- Intensive physical acitivity: increasing of flow 15-20x, 70-90ml/min/100g

- Regulation of muscle flow:
  1. Nervous (symp/parasymp)
  2. **Local factors, products of metabolism: adenosin, ADP, pH, lactate, temperature, CO_2 …**

Skeletal muscle – nervous regulation

- $\boldsymbol{\alpha}$-adrenergic receptors, regulation of SVR, arterioles ($\boldsymbol{\alpha}_1$), precapillar arterioles ($\boldsymbol{\alpha}_2$)
  - activation: NOR … vasoconstriction (increase of resistance, increase BP)

- $\boldsymbol{\beta}$-adrenergic receptors: $\boldsymbol{\beta}_1$ – heart, skeletal muscle

  $\boldsymbol{\beta}_2$ – heart, lungs, skeletal muscle, kidneys…
  - activation: A, Salbutamol, Clenbuterol … vasodilation (increase flow)

- Sympathetic nerve endings = NOR

- Adrenal medulla = A + NOR

Physical activity– circulation changes

1. Sympathetic activation with an effect on the entire circulation: **α** + **β** receptors

2. Increase BP: **α** – receptors (vasoconstriction, increase SVR)

3. increase CO: **β** – receptors (inotropy, chronotropy…)

Physical activity– circulation changes

- Increased sympathetic activation / decreased parasympathetic activation
- Cerebral cortex - initiation of muscle movement

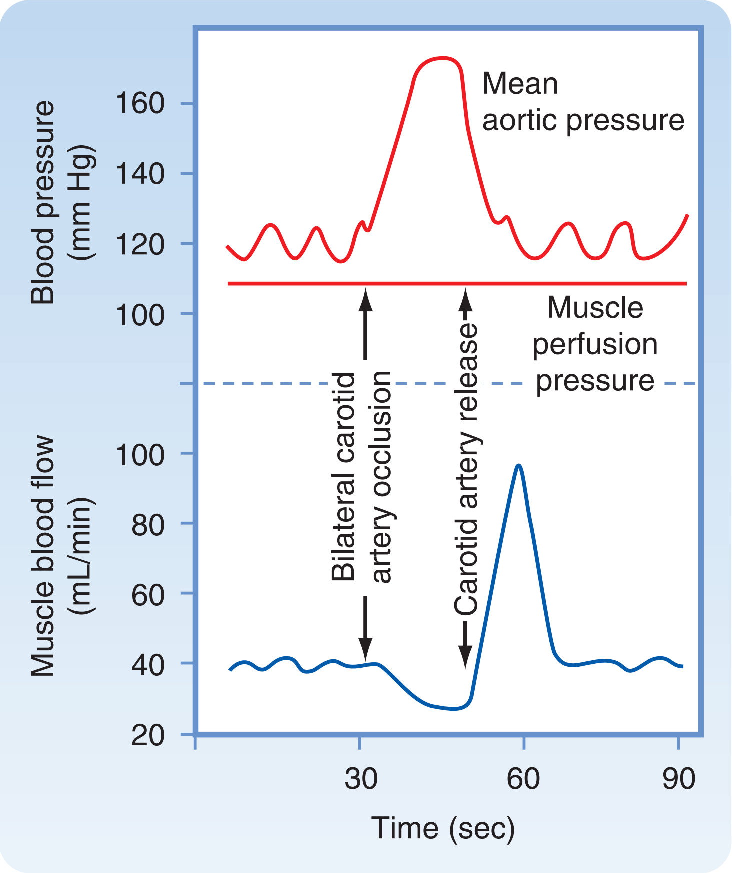
1. Increased heart function, CO: inotropy, chronotropy

2. Vasoconstriction of peripheral arterioles, increase in SVR except for 2 (3) organs:
    - Skeletal muscles: local products of metabolism lead to local vasodilation...!!!
    - Coronary + Cerebral circulation: a little effect of sympathetic activation (no receptors)

3. Vasoconstriction of capacitive vessels - veins, increase in venous return

Skeletal muscles

Vascular muscle tone depending on the activity of baroreceptors in the Sinus Caroticus



Low SVR - high sympathetic activation - low muscle perfusion

and vice versa

- Response to a shock state without initial activation of skeletal muscles.
- Muscles locally without products of metabolism
- Circulation preferences of vital organs: brain + heart
  (by circulation with minimal sympathetic activation)…

Cerebral circulation

- 50 ml/min/100g …. 750 ml/min …. 15% CO
- 20 ml/min/100g – hypoxia
- < 10 ml/min/100g – brain death

- Cerebral perfusion pressure (CPP) = MAP - ICP

- CBF - autoregulation

Cerebral circulation

- CPP – autoregulation in narrow range: decrease – ischemia

  increase – increase ICP (10-15 mmHg)

- CPP = MAP - ICP
- CBF = CPP / CVR