Regional Circulation (pulmonary, skin, muscle, cerebral, splanchnic)

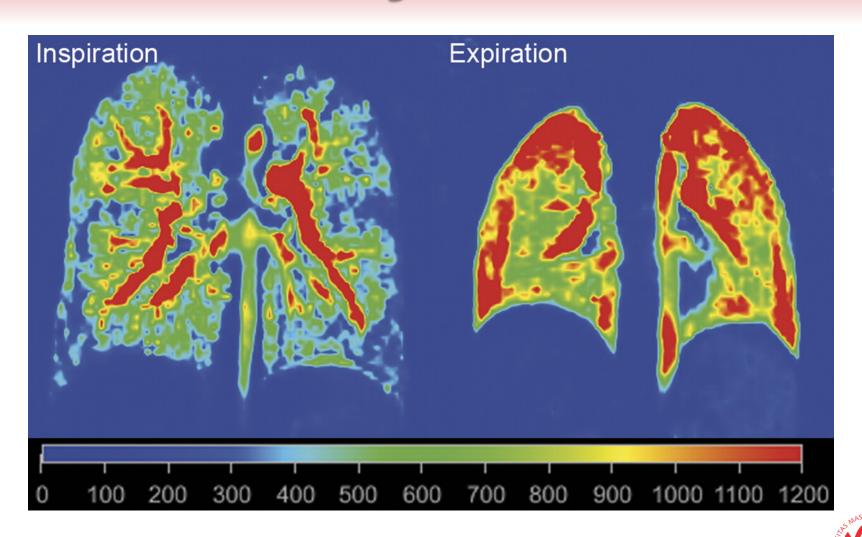
Assoc. Prof. MUDr. Markéta Bébarová, Ph.D.

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Regional Circulation

- an organ may be supplied by two blood inflows:
 - the nutrient circulation
 - the functional circulation
- various ways of anatomical and functional adaptation of an organ-specific circulation to provide the optimal function of the organ
- varying impact of particular ways of regulation of the blood flow (~ vasal tone) in various organs



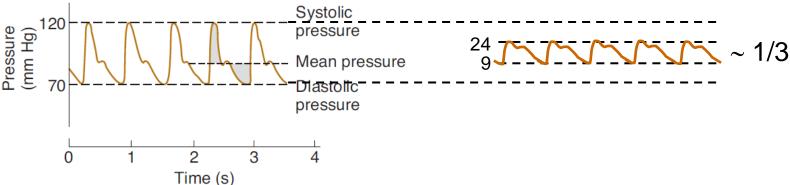
 Blood flow through lungs is virtually equal to the blood flow through all other organs.

Functions:

- provide the gas exchange
- blood reservoir
- mechanical, chemical and immunological filter



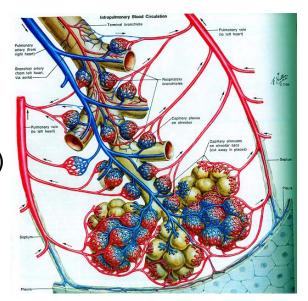
- Arteries (differences compared to the arteries in the systemic circulation)
 - bigger total cross-section of all pulmonary arteries
 - smaller thickness of the vessel walls
 - arterioles have a thin muscle layer → lower resistance (1/10 of the resistance in systemic circulation; the smallest during a mild inspiration), lower decrease of blood pressure in this part of bloodstream
 - high compliance





Capillaries

- wide, abundant anastomoses form a net surrounding alveoles
- time of passage ~0.75 s (gas exchange)
- area of perfused capillaries: at rest
 ~60 m², at intensive exertion ~90 m²



http://www.percussionaire.com/historyreview.asp

Veins

- high compliance
 (blood reservoir, autoregulatory mechanism at maintaining the blood pressure during orthostasis in lying position, about 400 ml of blood moves to lungs → ↓ vital capacity)
- failure of the left heart → ortopnoe

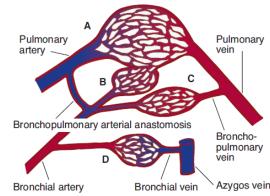


Nutrient circulation

aa. bronchiales, vv. bronchiales , vv. pulmonales (physiological arteriovenous shunt + Pulmonary part of blood from coronary capillaries → saturation of blood with oxygen in

the systemic circulation 98%, the stroke volume in the left ventricle by

1-2% bigger than in the right ventricle)

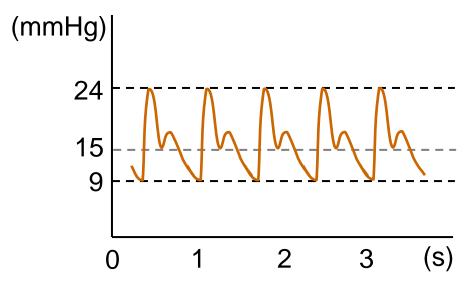


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Lymphatic vessels

fast transport of proteins and various particles from the peribronchial and perivascular tissue $\rightarrow \downarrow$ formation of the tissue fluid ~ prevention of the pulmonary edema

- Blood pressure in the pulmonary bloodstream
 - pressure in a. pulmonalis



- pressure in pulmonary capillaries measured as the pulmonary artery wedge pressure (~7.5 mmHg)
- pressure in pulmonary veins pulsates between 1 and 6 mmHg (as the pressure in left atrium)

Factors affecting the fluid filtration into intersticium:

Minimal filtration in pulmonary capillaries physiologically!

- pressures in intersticium and pulmonary capillaries capillary pressure about 10 mmHg, oncotic pressure 13 mmHg
- 2. permeability of pulmonary capillaries
- Pulmonary edema inhibits effective gas exchange.



- Regulation of blood flow in lungs
 - A. Systemic mechanisms
 - B. Local mechanisms



- Regulation of blood flow in lungs
 - A. Systemic mechanisms
 - 1) Neural regulation
 - sympathetic nerve fibers
 through α₁ rec. vasoconstriction
 (small impact on resistance, *i.e.* pressure, but decrease capacity of the lung bloodstream, ~empty lung blood reservoir)
 - through α_2 and β_2 rec. vasodilation NO
 - parasympathetic nerve fibers (M₃ rec. → relaxation NO)
 - 2) Humoral regulation (circulating substances)

vasoconstriction: adenosine (A_1) , endothelin (ET_A) , angiotensine II vasodilation: adenosine (A_2) , endothelin (ET_B) , histamine (H_1, H_2)

Regulation of blood flow in lungs

B. Local mechanisms

chemical (metabolic) autoregulation
 opposite reaction compared to systemic circulation
 (↓ pO₂ – also systemic hypoxia, ↑ pCO₂, ↓ pH, histamine → vasoconstriction → deviation of perfusion from the non-ventilated alveoli within 5-10 min)

unknown mechanism, key role likely playes surrounding lung tissue, maybe degranulation of basofile granulocytes releasing vasoactive substances (namely histamine)

works also in opposite way: obstruction of perfusion in a part of lungs $\rightarrow \downarrow pCO_2 \rightarrow constriction$ of influent bronchus to provide optimal ratio of ventilation/perfusion)



- Regulation of blood flow in lungs
 - C. Passive factors
 - cardiac output
 physical exertion → ↑ cardiac output → saturation of haemoglobin is stable, opening of so far non-perfused capillaries → ↑ blood flow through lungs and total amount of O₂ delivered to body
 - gravity

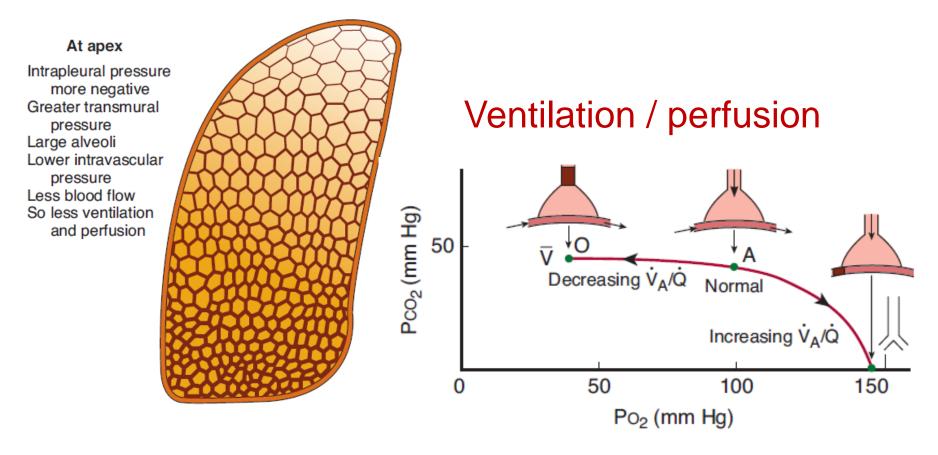


- Blood distribution in lungs gravity
 - irregular due to action of the hydrostatic pressure
 - pulmonary apexes about 15 cm above the orificium of a. pulmonalis, hydrostatic and arterial pressure is approx. equal → minimal blood flow
 - blood flow increases from apex to base in a linear way
 - † total blood flow (e.g. physical exertion) ~ apex báze equivalent † flow through individual regions



- Blood distribution in lungs gravity
 - irregular due to action of the hydrostatic pressure
 - pulmonary apexes about 15 cm above the orificium of a. pulmonalis, hydrostatic and arterial pressure is approx. equal → minimal blood flow
 - blood flow increases from apex to base in a linear way
 - intensive physical exertion → ↑ cardiac output even 6times → opening of so far unperfused capillaries → pressure in a. pulmonalis increased only slightly (decreased work of the right heart + prevention of formation of the pulmonary edema due to increased capillary pressure)

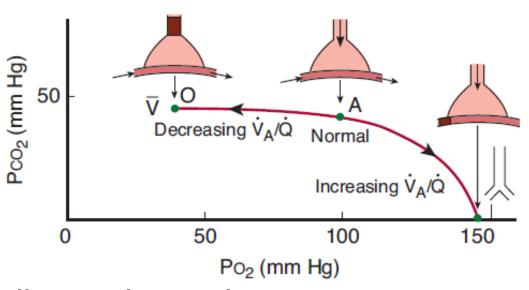






- Defective ratio of ventilation and perfusion
 - most often cause of hypoxic hypoxia in clinical practise
 - blood flow through non-ventilated alveoli → right-left shunt (deoxygenated blood directly to the left heart) → ↓ arterial blood saturation with O₂

Ventilation / perfusion



 content of CO₂ usually not changed (compensatory hyperventilation in other alveoles)



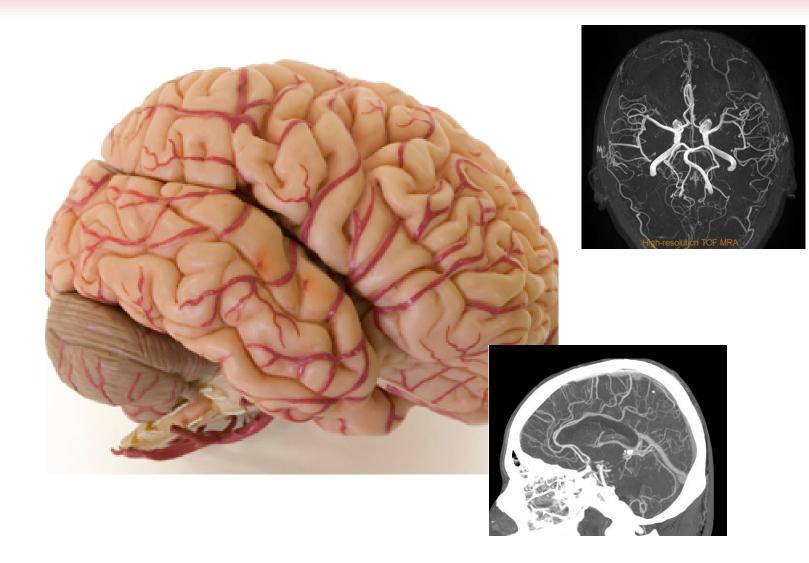




TABLE 34–1 Resting blood flow and O_2 consumption of various organs in a 63-kg adult man with a mean arterial blood pressure of 90 mm Hg and an O_2 consumption of 250 mL/min.

		Blood Flow		Arteriovenous	Oxygen Consumption		Resistance (R units) ^a		Percentage of Total	
Region	Mass (kg)	mL/min	mL/100 g/min	- Oxygen Difference (mL/L)	mL/min	mL/100 g/min	Absolute	per kg	Cardiac Output	Oxygen Consumption
Liver	2.6	1500	57.7	34	51	2.0	3.6	9.4	27.8	20.4
Kidneys	0.3	1260	420.0	14	18	6.0	4.3	1.3	23.3	7.2
Brain	1.4	750	54.0	62	46	3.3	7.2	10.1	13.9	18.4
Skin	3.6	462	12.8	25	12	0.3	11.7	42.1	8.6	4.8
Skeletal muscle	31.0	840	2.7	60	50	0.2	6.4	198.4	15.6	20.0
Heart muscle	0.3	250	84.0	114	29	9.7	21.4	6.4	4.7	11.6
Rest of body	23.8	336	1.4	129	44	0.2	16.1	383.2	6.2	17.6
Whole body	63.0	5400	8.6	46	250	0.4	1.0	63.0	100.0	100.0

^aR units are pressure (mm Hg) divided by blood flow (mL/s).

Reproduced with permission from Bard P (editor): Medical Physiology, 11th ed. Mosby, 1961.

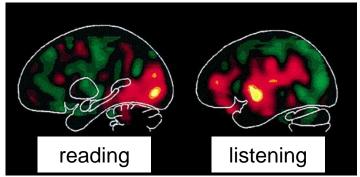


• provides:

constant sufficient blood supply
 intensive oxidative metabolism of the grey matter
 (40% of the brain matter), is metabolically more active
 – the grey matter is very sensitive to hypoxia!
 (black-out during several seconds of the brain ischemia, irreversible damage during several minutes)

2) dynamic blood redistribution

neuronal activity and, thus, the rate of metabolism of particular regions of the grey matter notably varies (metabolic hyperaemia)





- provides:
 - 1) constant sufficient blood supply
 - 2) dynamic blood redistribution

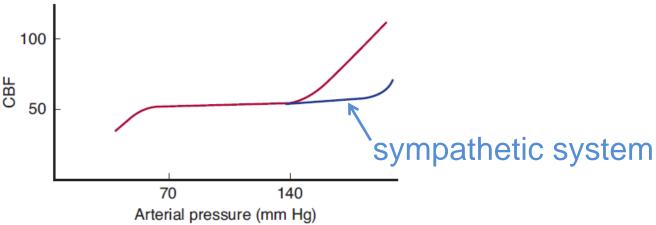
Cover of these specific demands of brain, namely of its grey matter, requires both anatomical and functional adaptation of the cerebral circulation.



- Anatomical specialities of cerebral circulation:
 - circulus arteriosus cerebri
 (interconnection of main cerebral arteries by anastomoses)
 - 2) very high density of capillaries (3000 4000 capillaries / mm² od the grey matter)
 - ~ minimalization of diffuse distance for gases and other substances
 - 3) very short arteriols (almost 1/2 of the vasal resistance falls on arteries which are abundantly innervated)



- Functional adaptation of cerebral circulation:
 - 1) high and stable blood flow (grey matter: 1 l/kg/min)
 - 2) high O_2 extraction (35%)
 - 3) well developed autoregulation (myogenic and metabolic)



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- Functional adaptation of cerebral circulation:
 - 1) high and stable blood flow (grey matter: 1 l/kg/min)
 - 2) high O_2 extraction (35%)
 - 3) well developed autoregulation (myogenic and metabolic)
 - 4) high reactivity on changes of CO₂ concentration
 - 5) local vs. total hypoxia
 - 6) innervation

sympathetic vasoconstr. fibers (norepinephrine, neuropeptide Y) parasympathetic cholinergic fibers (acetylcholine, VIP) sensoric fibers (substance P, CGRP; migraine headache)

Special physical conditions of cerebral circulation:

1) solid cover of brain by skull

Ultimate value of actual blood volume in brain, of cerebral tissue and liquor is constant (Monro-Kelli theory).

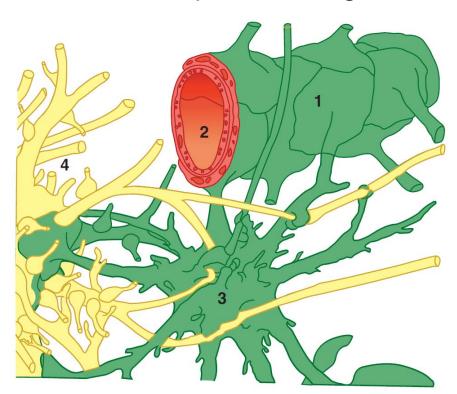
- → flow may be increased only by acceleration of the blood flow, not by an increase of capacity of the bloodstream
- → Cushing reflex (tumour, bleeding)

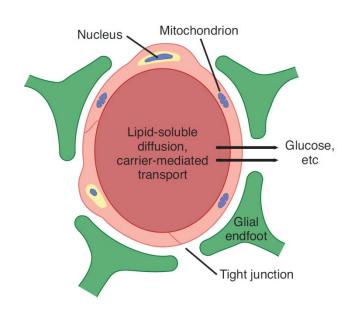
2) gravity

orthostatic reaction (lower central venous pressure + decreased stroke volume → hypotension → postural syncope)

Blood-brain barrier

cerebral capillaries – tight inter-endothelial connections









Blood-brain barrier

By free diffusion:

- → lipophilic substances (O₂, CO₂, xenon; unbound forms of steroid hormones)
- → water (aquaporins; osmolality of blood and cerebrospinal fluid is identical!)
- → glucose the main source of energy for neurons (free diffusion would be slow – accelerated by GLUT)

By transcellular transport (regulated):

- \rightarrow ions (e.g. H⁺, HCO³⁻ vs. CO₂!)
- → transporters for thyroid hormones, some organic acids, choline, precursors of nucleic acids, aminoacids, ...

Blood-brain barrier

Many drugs and peptides pass the capillary wall as well but they are immediately transported back to the blood by a nonspecific transporter - glycoprotein P – located in apical membranes of endothelial cells.

Functions:

- maintenance of constant composition of the neuron environment
- protection of brain against endogenic and exogenic toxins
- prevention of loss of neurotransmitters to the bloodstream



Cerebrospinal fluid

- fills the brain chambers and subarachnoidal space
- volume ~150 ml,
 rate of production ~550 ml/d (exchange 3.7times/day)

Cerebrospinal fluid is constantly of a composition different from plasma.

Sul	bstance	CSF	Plasma	Ratio CSF/Plasma	
Na ⁺	(meq/kg H ₂ O)	147.0	150.0	0.98	
K ⁺	(meq/kg H ₂ O)	2.9	4.6	0.62	
Mg ²⁺	(meq/kg H ₂ O)	2.2	1.6	1.39	
Ca ²⁺	(meq/kg H ₂ O)	2.3	4.7	0.49	
CI ⁻	(meq/kg H ₂ O)	113.0	99.0	1.14	
HCO ₃ ⁻	(meq/L)	25.1	24.8	1.01	
Pco ₂	(mm Hg)	50.2	39.5	1.28	
рН		7.33	7.40		
Osmolality	(mosm/kg H ₂ O)	289.0	289.0	1.00	
Protein	(mg/dL)	20.0	6000.0	0.003	
Glucose	(mg/dL)	64.0	100.0	0.64	
Inorganic P	(mg/dL)	3.4	4.7	0.73	
Urea	(mg/dL)	12.0	15.0	0.80	
Creatinine	(mg/dL)	1.5	1.2	1.25	
Uric acid	(mg/dL)	1.5	5.0	0.30	
Cholesterol	(mg/dL)	0.2	175.0	0.001	

Cerebrospinal fluid

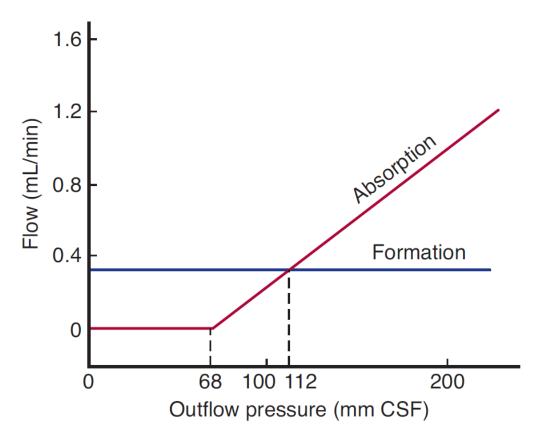
Function:

 protection of brain (together with menanges)

Outer table of skull Trabecular bone Inner table of skull Dura mater Subdural (potential) space Arachnoid Subarachnoid space Arachnoid trabeculae Artery Pia mater Perivascular spaces Brain

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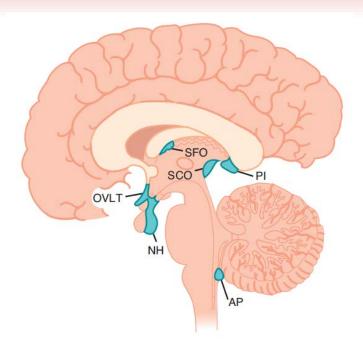
Cerebrospinal fluid







- Paraventricular organs
 - ~ brain regions where the blood-brain barrier is missing (fenestrated capillaries)
 - neurohypophysis + neighbouring ventral part of eminentia medialis
 - area postrema (AP)
 - organum vasculosum laminae terminalis (OVLT)
 - subfornical organ (SFO)



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Regions secreting polypeptides into the bloodstream (oxytocin, vasopressin, hypothalamic hormones), chemoreceptive zones (AP), osmoreceptive zones (OVLT).



- Measurement of cerebral blood flow
 - Kety method
 - Fick principle, method of indicatory gas
 - nitrous oxide N₂O

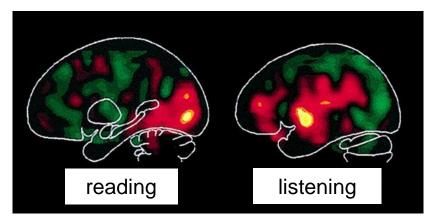
N₂O concentration in the venous blood

cerebral blood flow = $\frac{N_2O \text{ removed from blood by brain / time}}{\text{average arteriove nous difference of } N_2O$

→ average blood flow through all perfused regions!



- Measurement of cerebral blood flow regional PET (positron emission tomography)
 - a substance labelled by radionuclides with a short half time
 - the substance is injected, the increase and following decrease of its concentration is evaluated by scintillation detectors placed around the head
 - e.g. labelled 2-deoxyglucose its consumption is a good indicator of the flow



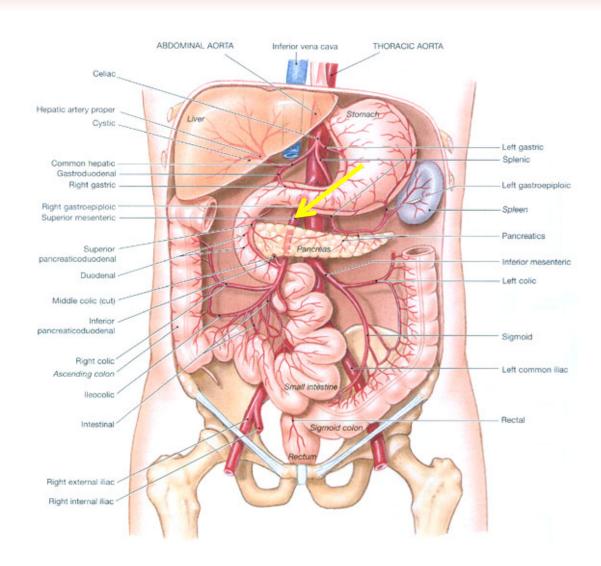


- Measurement of cerebral blood flow regional PET (positron emission tomography)
 - a substance labelled by radionuclides with a short half time
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 - e.g. labelled 2-deoxyglucose its consumption is a good indicator of the flow

fMRI (functional magnetic resonance)

- better resolution
- reduced haemoglobin becomes paramagnetic, change the signal emitted by blood, we can measure the amount of oxyand deoxyhaemoglobin as an indicator of the blood flow

Splanchnic Circulation





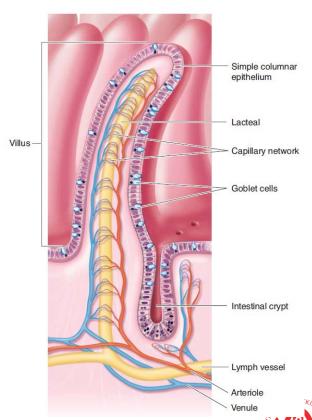


- blood flow through GIT including liver and pancreas
- blood flow through spleen
- Main functional roles:
 - metabolic function of GIT
 - blood reservoir
 - special (e.g. spleen removal and degradation of old/altered erythrocytes)



- Blood reservoir
- due to the high capacitive ability of splanchnic vessels – notable impact on the systemic regulation of circulation (BP)
- at rest ~20% of the total blood volume
- rich innervation with sympathetic vasoconstrictive fibers α rec. → vasoconstriction at ↑ activity of sympathicus or ↑ concentration of circulating catecholamines → even 350 ml of the blood emptied into the systemic circulation during several minutes! → stabilization of stroke volume and BP (hypotension bleeding, intensive physical exertion, ...)

- Intestinal circulation
 (a. coeliaca, a. mesenterica superior and inferior)
- small arterioles form a submucous plexus from which branches enter musculature and intestinal villi
- countercurrent exchange of substances between arteriole and venule in the villus (water, Na+, O₂)



- Intestinal circulation (a. coeliaca, a. mesenterica superior and inferior)
- Regulation of blood flow:
 - metabolic vasodilation (mediators: adenosine, ↓
 [K+]_e and ↑ osmolarity)
 (functional hyperaemia during digestion: induced by GIT hormones gastrin and cholecystokinin and by resorbed substances glucose and fatty acids)
 - neural regulation almost exclusively sympathicus, α > β rec. → vasoconstriction (during defense reaction, blood diverted from GIT to muscles and heart by vasoconstriction)



- Intestinal circulation
 (a. coeliaca, a. mesenterica superior and inferior)
- Regulation of blood flow:
 - metabolic vasodilation (mediators: adenosine, ↓
 [K+]_e and ↑ osmolarity)
 - neural regulation almost exclusively sympathicus, $\alpha > \beta$ rec. \rightarrow vasoconstriction

During ischemia, the metabolic vasodilation will be present regardless of vasoconstrictory action of sympathetic system (the so called autoregulatory escape).

- Hepatic circulation (v. portae, a. hepatica)
- 25% of the cardiac output (~1.5 l/min)
 - ¾ v. portae, ¼ a. hepatica

- portal circulation 2 capillary bloodstreams in series:
 - 1) <u>in intestinal villi</u> resorption of water-soluble substances from the intestine
 - in liver sinusoids high permeability (large gaps between endothelial cells), also for proteins synthesized in liver and released to circulation

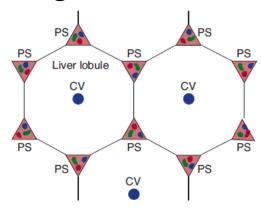
- Hepatic circulation (v. portae, a. hepatica)
- 25% of the cardiac output (~1.5 l/min)
 - ¾ v. portae, ¼ a. hepatica

Regarding O₂ supply, the ratio is opposite!

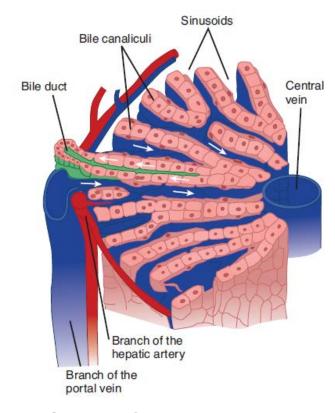
- portal circulation 2 capillary bloodstreams in series:
- the portal blood which has already passed the first capillary bloodstream in the intestine has ↓ O₂ content → a. hepatica represents the nutrition hepatic circulation (interrupted blood flow → lethal liver necrosis)



- Hepatic circulation (v. portae, a. hepatica)
- terminal portal venules and hepatic arteriols empty into a net of sinusoids in liver lobuli, the mixed blood leaves lobuli through the central vein



• functional unit - acinus



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- Hepatic circulation (v. portae, a. hepatica)
- pressures different from other tissues:

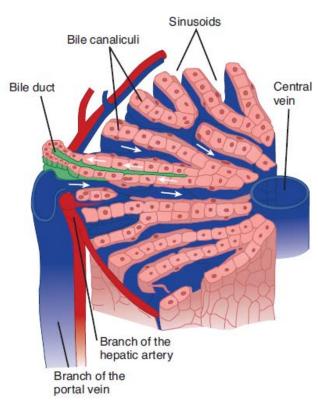
- a. hepatica: 90 mmHg

- v. hepatica: 5 mmHg

- *v. portae*: 10 mmHg

- sinusoids: 2.25 mmHg (big pressure reduction due to high resistance in branches of *a. hepatica*)

Pressure in sinusoids below pressure in *v. portae*!



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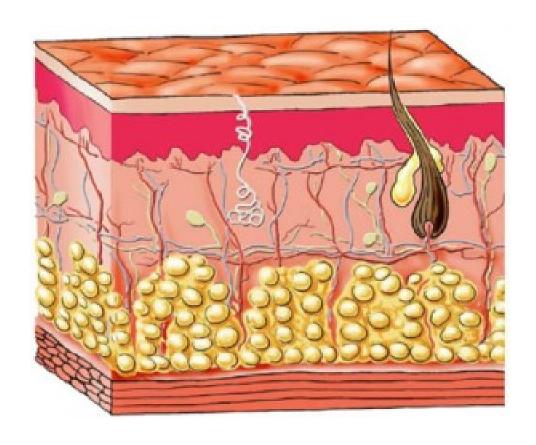
- Hepatic circulation (v. portae, a. hepatica)
- due to sudden pressure ↓ in a. hepatica → inverse regulation of blood flow in v. portae and a. hepatica:
 - between meals: many sinusoids collapsed, flow in v.
 portae low, adenosine formed constantly and washed less → dilation of terminal hepatic arterioles
 - after a meal: flow in v. portae ↑, adenosine washed faster → constriction of hepatic arterioles, higher flow in v. portae also opens so far collapsed sinusoids → pressure in v. portae does not ↑ too much (protection against fluid loss in highly permeable liver tissue)
- increased hepatic pressure (cirhosis) → ascites

- Hepatic circulation (v. portae, a. hepatica)
- Regulation of blood flow:
 - neural: sympathetic vasoconstrictive fibers α
 rec. → vasoconstriction
 - metabolic: adenosine → vasodilation
 - passive: ↑ BP → passive dilation of portal vein radicles → ↑ liver blood amount congestive heart failure → extreme venous congestion diffuse noradrenergic discharge due to ↓ BP → constriction of portal vein radicles → ↑ portal pressure → blood flow bypasses most of liver and enters systemic circulation

- Hepatic circulation (v. portae, a. hepatica)
- flow in a. hepatica and in v. portae are complementary - reciprocal compensation of changes but incomplete due to different way of autoregulation:
 - a. hepatica ability of autoregulation
 - v. portae not able to autoregulate
- sufficient O₂ supply is essential for liver function! ↓
 flow → ↑ O₂ extraction
 (reserve for ↑ O₂ extraction anatomical setting of
 hepatic circulation, arteries and veins distant → no ↓ of
 arterial O₂ by countercurrent exchange)

- Hepatic circulation (v. portae, a. hepatica)
- hepatic lymphatic circulation
 - formation of almost ¾ of the body lymph
 - lymph rich on proteins (many plasmatic proteins are formed in hepatocytes + proteins from plasma due to the high permeability of sinusoids)







- Skin blood flow considerably varies (0.02-5 l/min).
- Regulation of skin blood flow:
 - Sympathetic nerve fibers
 - Humoral local factors
 (histamine → vasodilation, serotonine → vasoconstriction)



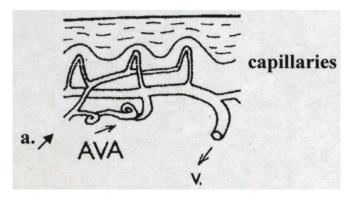
- Metabolic demands of skin small (decubitus)
- Maintenance of body temperature
 - warm supply from the core (dependent on blood inflow)
 - warm loss (conduction, convection, radiation, evaporation)
 - poikilothermic tissue (toleration of strong warm fluctuation, 0 45°C)

Arteriovenous anastomoses

- Protection against environment
- Maintenance of mean blood pressure



- Arteriovenous anastomoses
 - specific structural adaptation
 - convoluted muscle vessels directly connecting arteriols and venules (low-resistance shunt)



Honzíková N - Poznámky k přednáškám z fysiologie (1992)

- regulated by sympathetic vasoconstrictive nerve fibers (their activity regulated by the centre for thermoregulation located in hypothalamus)

- Reaction on a temperature change:
 - direct impact of a temperature change on the vessel tone
 - 2) excitation of skin thermoreceptors
 - 3) excitation of thermoreceptors in brain

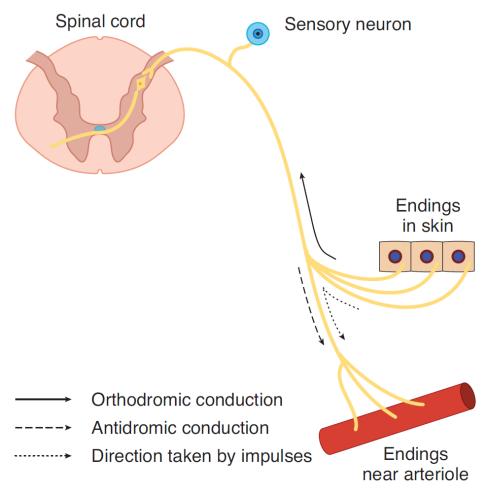


reflex modulation of sympathetic vasoconstrictive activity



Axon reflex

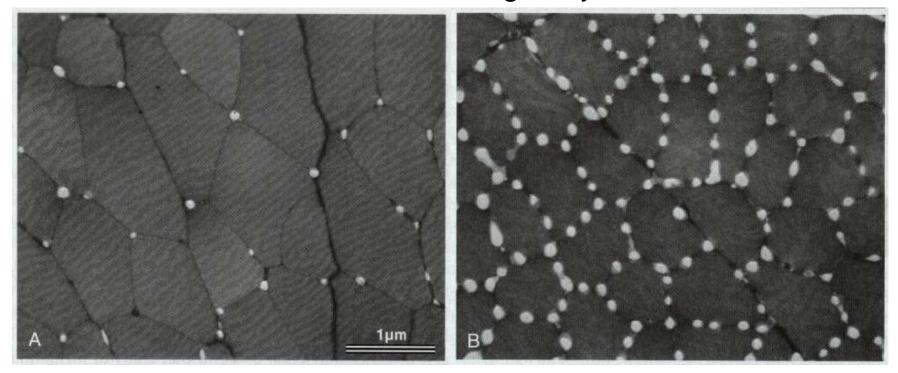






unstimulated muscle

regularly stimulated muscle



Guyton and Hall. Textbook of Medical Physiology, 12th edition



Function:

1) Blood supply of muscles

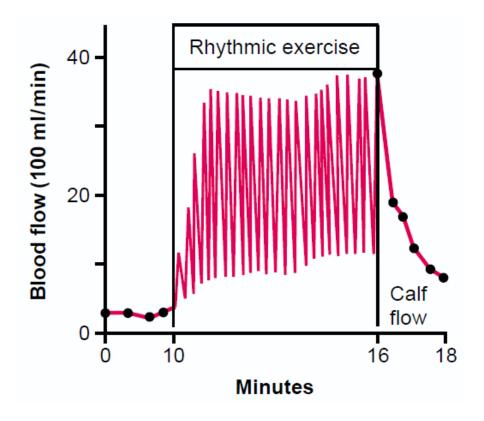
O₂ and nutrients supply, namely glucose wash of metabolites (CO₂) and metabolic heat the resting blood flow − 18% of the cardiac output *vs.* even 90% at intensive exertion (the local blood flow ↑ even 20times; opening of capillaries closed at rest)

2) Regulation of blood pressure

skeletal muscles – 40% of the body weight → resistance of the muscle bloodstream has a high impact on the total peripheral resistance



The blood flow during muscle activity is intermittent.





- The blood flow during muscle activity is intermittent.
- During the tetanical contraction, the blood flow may be almost stopped.
 - O₂ content in myoglobin is sufficient for about 5-s to 10-s lasting ischemia. Anaerobic glycolysis follows, lactate is formed and cumulates (fatique, pain).
- Muscle pump (massage of the deep veins during contractions, increase of the venous return)



- Regulation of the muscle blood flow:
 - Neural regulation dominates at rest
 - 2) Local chemical regulation dominates at physical exertion



- Regulation of the muscle blood flow:
 - 1) Neural regulation

dominates at rest

rich innervation by tonic active sympathetic vasoconstrictive fibers (norepinephrine) → high tone of arteriols at rest ~ big dilation reserve

activity regulated from baroreceptors (baroreflex) – noted impact on regulation of total peripheral resistance (orthostasis, hypovolaemia $\rightarrow \downarrow$ flow even to only 1/5 of the resting flow)

norepinephrine – at low dose vasodilation (baroreceptors), at high doses vasoconstriction (α receptors) epinephrine – vasodilation (more β receptors)

- Regulation of the muscle blood flow:
 - 1) Neural regulation

dominates at rest

sympathetic cholinergic vasodilatory fibers

(resistant vessels in muscles and skin) $\rightarrow \uparrow$ flow even before the start of muscle activity \sim anticipation of the muscle activity during the stress reaction (+ vasoconstriction in other locations – prevention of sudden drop of the blood pressure)



- Regulation of the muscle blood flow:
 - 2) Local chemical regulation

dominates at physical exertion

release of K⁺ from contracting muscles $\rightarrow \uparrow$ concentration of K⁺ in intersticium + \uparrow osmolarity (also lactate)

- + \downarrow pO₂ (and nutrients) + \uparrow pCO₂ + \downarrow pH (also lactate)
- → metabolic vasodilation

almost linear increase of the flow with increasing metabolic activity



- Sufficient release of energy for the muscle activity is dependent on:
 - 1) increased blood flow (~increased O₂ supply)
 - 2) increased O₂ extraction (from 25 to 80%)



Anaerobic glycolysis

The amount of formed lactate is proportional to O_2 deficiency (oxygen debt).

lactate → acidosis → metabolic vasodilation + pain (nociceptive C fibers) – the pain terminates the intensive muscle load

hyperaemia persists after the end of muscle work→ lactate washed and mostly metabolized in liver to glycogen + primary source of energy for the heart

- Local vasodilation in contracting muscles
 - $\rightarrow \uparrow$ blood flow
 - → ↑ capillary pressure + ↑ osmolarity (K+, lactate)
 - → ↑ filtration → edema in contraction muscles

