Physiology 1A

Local and Regional Blood Flow

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Key points from this lecture:

Understand the concept of autoregulation of blood flow and the main theories developed to explain it: myogenic, metabolic and endothelium-dependent regulation.

Appreciate the role of several hormones (angiotensin II, bradykinin, histamine) in controlling systemic and local blood flow.

Understand the main mechanisms modulating blood flow in the skin, heart, skeletal muscle, lungs and brain.

Reference: Stanfield Ch. 14 pp. 402-409.

Local and regional control of blood flow

CNS, autonomic nerves control systemic blood pressure.

Individual tissues and organs can control their flow according to their requirements.

- O_2 delivery, CO_2 removal
- glucose, amino acids, fatty acids
- pH / ion balance
- transport of hormones, other special substances
- organ function: skin (heat loss)
  kidney (blood vol and osmolarity)

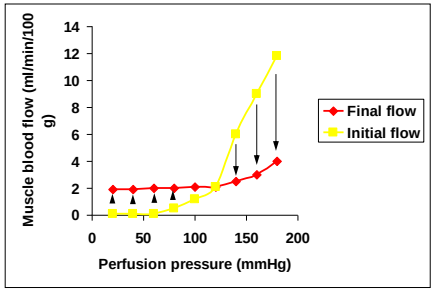
Generally, greater metabolic activity = greater flow

Organ / Tissue	% CO	ml/min	ml/min/100g
Brain	14	700	50
Heart	4	200	70
Bronchi	2	100	25
Kidneys	22	1100	360
Liver	27	1350	95
Muscle (inactive)	15	750	4
Bone	5	250	3
Skin (cool weather)	6	300	3
Thyroid gland	1	50	160
Adrenal gland	0.5	25	300
Other tissues	3.5	175	1.3

Intrinsic control of local blood flow:

Autoregulation

Local flow in tissue or organ remains constant in face of fluctuations in pressure.



Perfused dog hindlimb

Step to pressure from control pressure (100 mmHg)

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How?

1.<u>Myogenic theory.</u>

Vessels (arterioles) constrict or dilate in response to changes in intra-luminal pressure:
Myogenic response.

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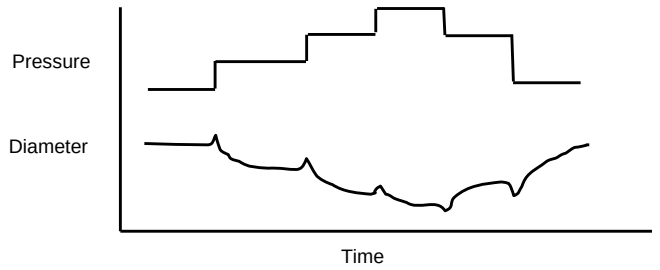

Increased pressure → Increased wall stretch / tension → Constriction → Reduced flow

Decreased pressure → Decreased stretch / tension → Dilation → Increased flow

Myogenic: independent of endothelium / neurohumoral factors

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<u>2. Metabolic Theory</u>

Pressure decreases → Flow decreases

'Subtheories'
2a. Oxygen deprivation
2b. Vasodilator formation

Other nutrients ? ← Tissue [O_2] (oxygen tension) decreases → Vasodilator substances formed

? ?

Vessel dilates → Flow increases

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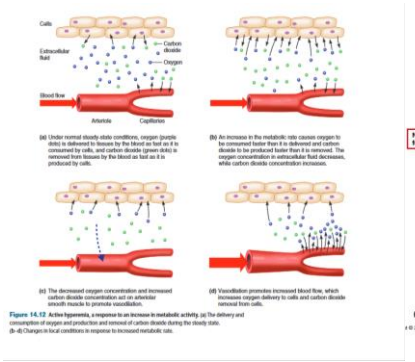
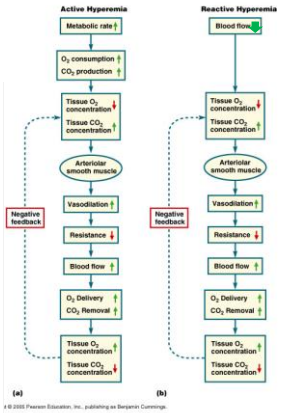
Active and reactive hyperemia: vasodilator formation

Changes in tissue metabolic activity or local blood flow result in altered concentrations of local vasoactive substances (incl. O_2, CO_2).
Effect is to match blood flow to metabolic requirements.





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Candidate substances:

Adenosine – coronary, skeletal muscle vessels

$\downarrow PO_2 \longrightarrow \uparrow$ ATP metabolism → Adenosine → Dilation

CO_2 / H^+ $\quad H_2O + CO_2 \rightleftharpoons H_2CO_3 \rightleftharpoons H^+ + HCO_3^-$

K^+ - released from active skeletal muscle, high brain activity

Organic phosphate (PO_4^{2-})
- released from active skeletal muscle

Histamine, prostacyclin

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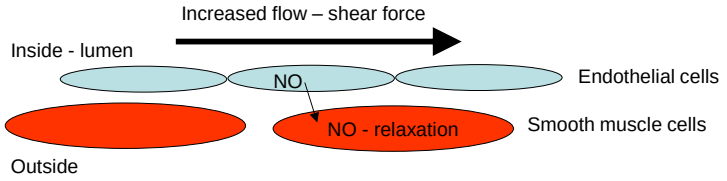
3. Endothelium – mediated regulation

Endothelium responds to changes in flow rate (pressure gradient).
Increased flow ⟶ dilation
Mediated by nitric oxide (NO) release



Muscle cells relax – dilation of vessel

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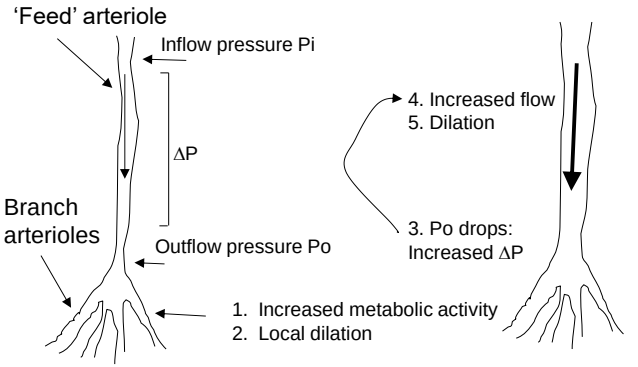
Physiological role of flow-mediated dilation: Upstream signalling



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Extrinsic control of local blood flow:
Neural / hormonal influences

Neural: mainly sympathetic nerve stimulation

Neurotransmitter (noradrenaline) constricts arterioles
(α-adrenoceptors) ⟶ Reduces flow

Can have 'local' effects (i.e. no change in systemic pressure)

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Parasympathetic stimulation:

Some blood vessels in head, face, genitalia, bladder, large bowel.

Hormones

Adrenaline, noradrenaline from adrenal gland.

Adrenaline dilates skeletal muscle, coronary arterioles. Constricts others

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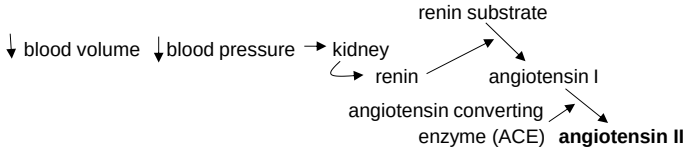
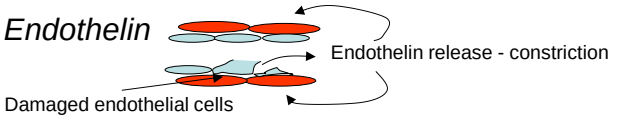
Angiotensin II



Very potent constrictor of arterioles.
Acts systemically.

Endothelin



Very potent local constrictor. Long-lasting effects.

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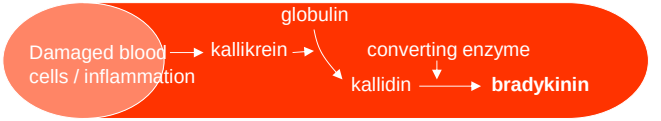
Bradykinin



Potent vasodilator
Increases capillary permeability (local oedema)
Short half-life (inactivated by ACE)

Histamine

Released by tissues in inflammation, allergic reaction. Potent local vasodilator

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Control of particular circulations

Coronary circulation

Mechanical compression during systole reduces blood flow; most occurs during diastole.

Aortic pressure (AP) determines flow in coronary vessels:

Increased AP ⟶ increased flow

Coronary arterioles dilate with increased metabolic activity of the heart ⟶ increased flow-adenosine

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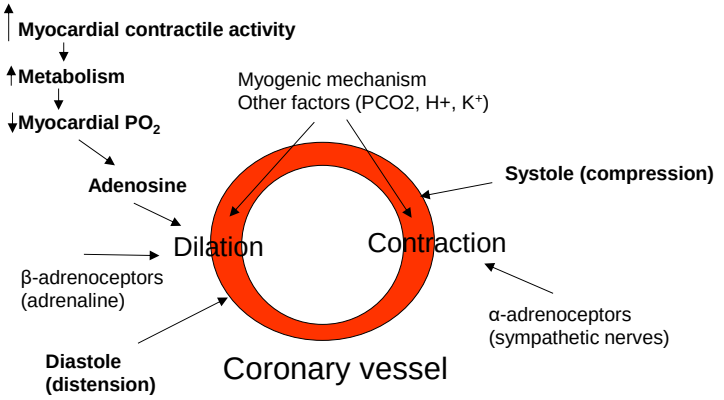

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Skin circulation

Skin is site of heat loss - Temperature control

Apical skin (nose, ears, lips, hands, feet) has many arteriovenous anastomoses – thick muscular-walled arterioles with dense sympathetic innervation.

Non apical skin – no A-V anastomoses, but strong sympathetic innervation
Sweat glands

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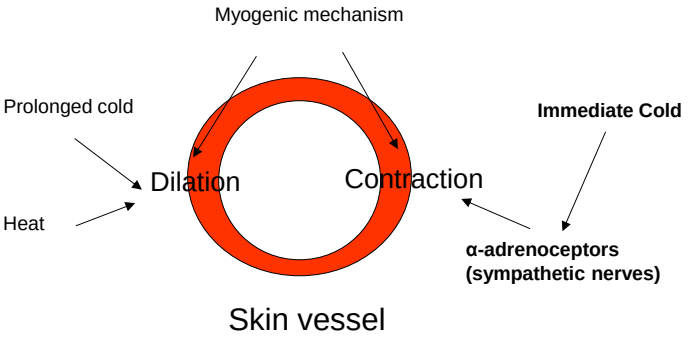

Skin colour

Pale: low venous blood content
Red / 'ruddy': high venous blood content
Ashen / grey: arterial constriction and low HbO_2
Dark purple: venous engorgement and low HbO_2

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Skeletal muscle circulation

Skeletal muscle flow may increase 50x during exercise (5 - 250 ml/min/100g tissue)

Blood flow is coupled to O_2 consumption

Therefore metabolic activity / metabolites control diameter

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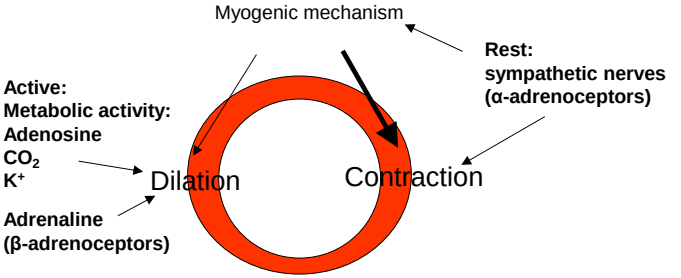
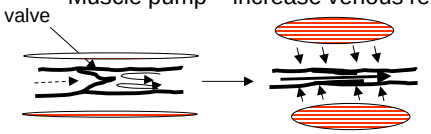


Skeletal muscle vessel

Muscle pump – increase venous return



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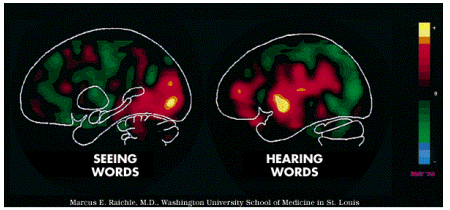
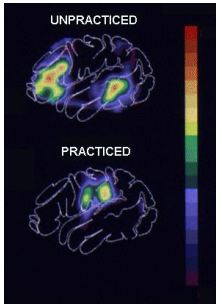
Cerebral circulation

PET scans show fine localised control of blood flow



Marcus E. Raichle, M.D., Washington University School of Medicine in St. Louis

The PET scan on the left shows two areas of the brain (red and yellow) that become particularly active when volunteers read words on a video screen: the primary visual cortex and an additional part of the visual system, both in the back of the left hemisphere. Other brain regions become especially active when subjects hear words through ear-phones, as seen in the PET scan on the right.



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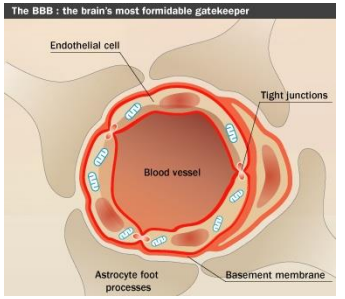
Blood-brain barrier – endothelial cells in capillaries have tight junctions between them. Nothing can cross apart from gases, water



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For brain blood flow:

Sympathetic stimulation is <u>weak</u> and relatively unimportant.

Metabolic control is most important, particularly $P(CO_2)$. Also adenosine, K^+

Myogenic mechanisms contribute to very tight <u>autoregulation</u> of cerebral blood flow

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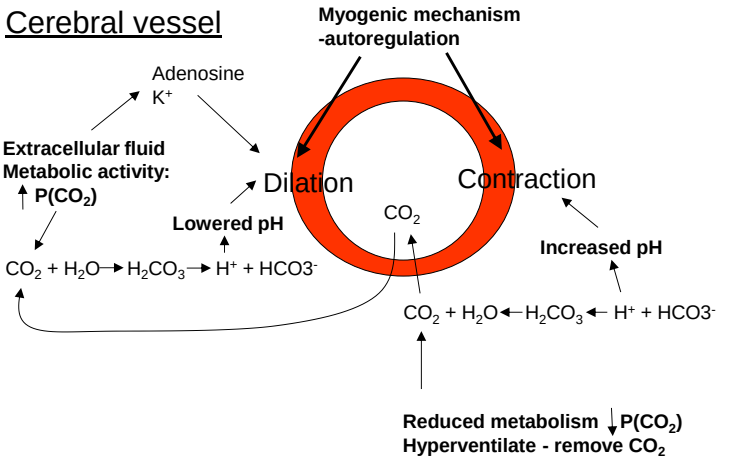
<u>Cerebral vessel</u>



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<u>Pulmonary circulation</u>

Gas exchange

- low basal tone
- no autoregulation
- little effect of sympathetic nervous stimulation
- no metabolic regulation (very high flow / low requirements)

Flow is coupled to alveolar ventilation (O_2 available)

Local hypoxia ⟶ local vasoconstriction

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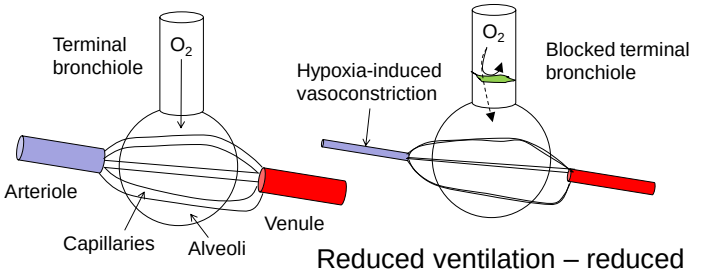
Ventilation / perfusion ratio (V/Q) is maintained.



Normal ventilation / perfusion

Reduced ventilation – reduced perfusion due to hypoxic vasoconstriction

Slow constriction (~30 min). Endothelium?

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Lecture summary:

- Autoregulation of blood flow is the maintenance of 'local' blood flow by a tissue in response to changes in metabolic requirements or systemic pressure. Autoregulation probably involves myogenic, metabolic and endothelium-dependent mechanisms.

- Blood flow in the coronary and skeletal muscle circulations is determined by the mechanical effects of compression and distension and metabolic hyperemia, mediated primarily by adenosine in the coronary circulation.
- Adrenaline is an important vasodilator in active skeletal muscle.
- Cutaneous circulation is controlled principally by sympathetic nerve activity, in response to temperature.
- Cerebral blood flow is not moderated by sympathetic nervous activity, but relies on local metabolites, principally CO_2 and K^+.
- Pulmonary blood flow is matched to the oxygen saturation of surrounding alveoli. Hypoxia causes pulmonary vasoconstriction, mediated by subtances released from the endothelium.