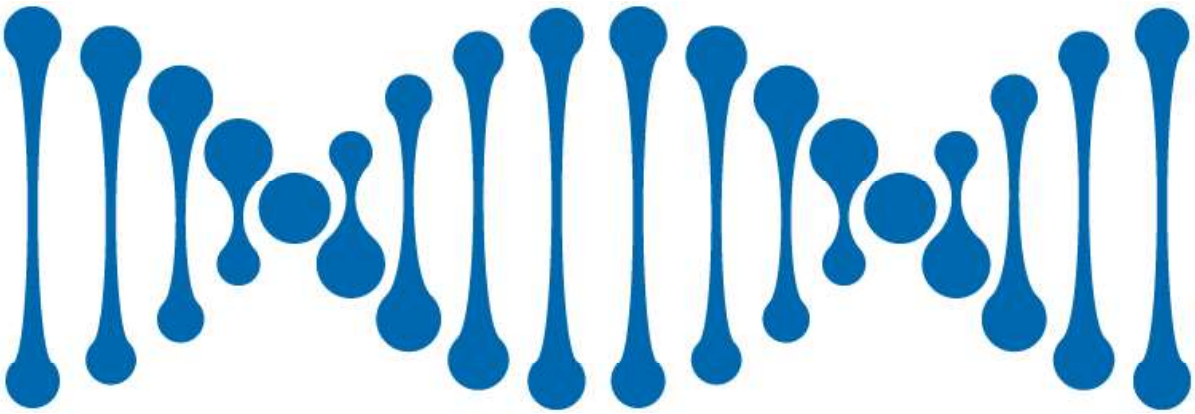

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Integrated Physiology A (PHSI2X05)

Course Notes

Anonymous
University of Sydney
2018

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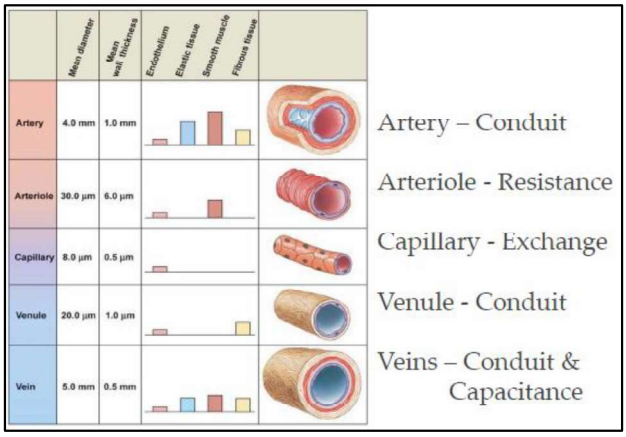
Topic 5: Cardiovascular Physiology

Lecture 1: Introduction and haemodynamics

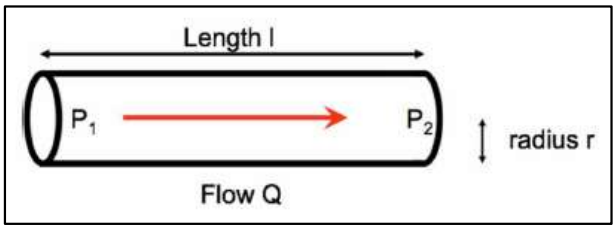
In the body, arteries travel away from the heart and veins travel towards the heart, regardless of the degree of oxygenation. Cardiac output is distributed throughout the arteries to the arterioles, then to the capillaries, before travelling back to the heart through the venules and the veins.

The right side of the heart pumps deoxygenated blood to the lungs, known as pulmonary circulation. The left side of the heart pumps oxygenated blood around the body, known as systemic circulation. Systemic circulation begins with either the ascending aorta to the brain, or the descending aorta to the rest of the body.

Oxygen diffusion occurs across capillary beds. In some organs where large amounts of blood must be filtered (such as the kidney), capillary beds can be in parallel. In other organs (such as the brain and the arms), capillary beds are in parallel, meaning blood goes through one or the other, and not both.



- Arteries are conduits that have pulsatile flow to deliver blood to the arterioles.
- Arterioles are resistance vessels made of smooth muscle. These can be easily controlled by the nervous system to vasodilate or vasoconstrict to change blood flow.
- Capillaries are exchange vessels, where oxygen is offloaded for metabolic processes, and carbon dioxide is loaded. Substrates are also unloaded, and metabolites loaded.
- Venules are conduits, much like arteries.
- Veins are capacitance vessels, meaning they have large compliance. If needed, they will expand to accommodate a large blood volume.



In a blood vessel with the properties pictured left, the driving force is a pressure gradient across the length of the vessel. Blood will flow when a positive gradient is present.

According to Ohm's Law (V=IR), the pressure gradient $\Delta P = P_1 - P_2 = QR$, where R is the resistance due to Poiseuille's Law ($R = 8nl/\pi r^4$, where n is the viscosity, l is the length and r is the radius. The important thing to remember is that a change in radius will cause a quartic change in resistance (for example, if radius changes from 2 to 1, resistance will increase by a factor of 16).

To calculate the resistance of vessels in series, just add the resistances together. However, for the resistance of vessels in parallel: $\frac{1}{R_{tot}} = \frac{1}{R_1} + \frac{1}{R_2} + \frac{1}{R_3} + \cdots$

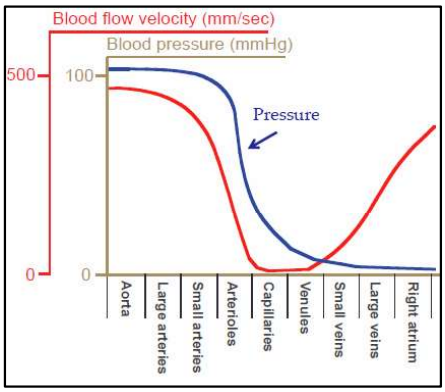
Therefore, the total resistance of vessels in parallel is lower than any of the individual resistances in series. Arteries and veins have relatively low resistance as they can change size, and capillaries have low resistance as there are many in parallel.

In systemic circulation,

- ΔP = mean arterial pressure (MAP) – right atrial pressure (RAP). RAP is usually 0 mmHg, meaning ΔP = MAP. Since the heart spends more time relaxed (in diastole) than contracted (in systole), MAP = diastolic pressure (DP) + $\frac{1}{3}$ (systolic pressure (SP) – DP).
- Q = total flow of circulation = cardiac output (CO)
- R = total resistance of circulation = total peripheral resistance (TPR)

And so, according to $\Delta P = QR$, **MAP (– RAP) = CO × TPR**.

Blood flow refers to the volume of blood per unit time, while flow velocity refers to the distance of blood per unit time (a.k.a. speed). Flow velocity is fast in all vessels except the capillaries, where it slows to allow exchange.



Pictured left is the pressure and flow velocity across the vessels. Note that pressure must continually drop to allow blood flow. The largest pressure drop is across the arterioles, and is directly controlled by smooth muscle constriction. Also notice right atrial pressure (RAP) is almost zero.

The flow velocity dips to one thousandth of the aorta in the capillaries.

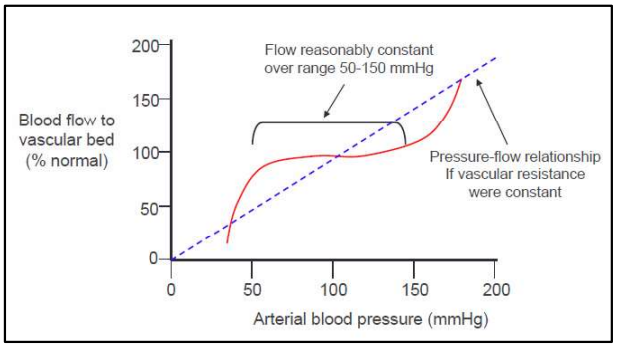
Most of our blood volume sits in the veins (65%!). The elastic properties of the vessel can be measured by determining the relationship between pressure and volume of that vessel. This is called capacitance (or compliance), where $C = \Delta V / \Delta P$. Venous capacitance is around 20 times that of arterial capacitance.

There are many factors that affect arteriole diameter, which are listed in the below table.

Vasoconstriction	**Vasodilation**
Local factors	Local factors
Increased myogenic activity	Decreased myogenic activity
Increased [O_2]	Decreased [O_2]
Decreased [CO_2] and other metabolites	Increased [CO_2] and other metabolites
	Histamine release
Cold	Heat
Autonomic nerves	Autonomic nerves
Increased sympathetic stimulation	Decreased sympathetic stimulation
Circulating hormones	Circulating hormones
Vasopressin, angiotensin II	Adrenaline, noradrenaline

For example:

Increase in muscle metabolic activity
→ increase in O_2 consumption, CO_2 and metabolite production
→ decrease in [O_2], increase in [CO_2 + metabolites]
→ vasodilation of arterioles
→ increase in local blood flow
→ increase in rate of O_2 supply and CO_2 +metabolites removal
→ [O_2] and [CO_2 + metabolites] returns to normal.



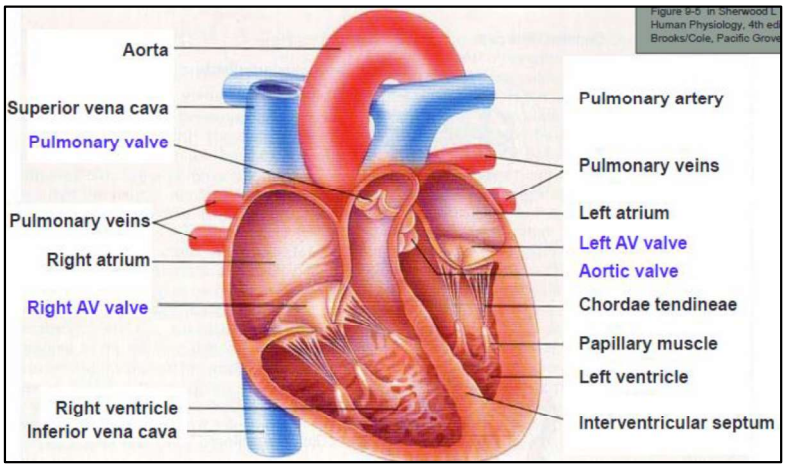
If changes in resistance didn't occur, the relationship between blood pressure and flow would be linear. However, this is not the case, as pressure needs to remain reasonably constant. The relationship pictured left is caused by vasoconstriction and vasodilation.

Sympathetic nerves (vasomotor) nerves innervate all vessels except capillaries. Innervation varies according to type of vessel (most in arterioles) and according to region (most in skin, least in brain). Most sympathetic nerves are vasoconstrictors, and are activated by noradrenaline (making them adrenergic). They are tonically active, which means that when relaxed, vasodilation occurs – marked effect when pharmacological blockage introduced. Often, it is controlled via reflex (more on the baroceptor reflex later).

Adrenaline and noradrenaline (a.k.a. epinephrine and norepinephrine) are released from the adrenal medulla. Adrenaline acts on β receptors to cause vasodilation. Noradrenaline works on α receptors to cause vasoconstriction.

Vasopressin (antidiuretic hormone, ADH) is released from the pituitary in response to haemorrhage or similar, and causes vasoconstriction. Another drug, angiotensin is the most potent vasoconstrictor agent known (more on this later).

Lecture 2: Mechanical events of the cardiac cycle

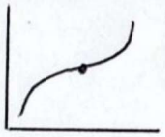


The structure of the heart is pictured left. Deoxygenated blood returns to the heart via the superior and inferior vena cava. It enters the right atrium, and then through the tricuspid AV valve in to the right ventricle. Blood then moves into pulmonary circulation through the pulmonary semi-lunar valve.

Concepts in Physiology – Handwritten Summary

CONCEPTS IN PHYSIOLOGY

- Homeostasis is a 'set of steady states' in which an organism operates comfortably.
- Energy input is required to maintain homeostasis.



  - The further the displacement, the more energy required to return to equilibrium.
- Constant input of energy, water and ions is necessary to maintain steady states
- Communication between parts of the body is also essential.
- Membranes are a barrier between extracellular and intracellular fluid (ECF / ICF)
- Made of phospholipid bilayer, hydrophilic head outwards, hydrophobic tail inwards.
- Small hydrophobic molecules can pass through, but everything else is obstructed:
  - large hydrophobic molecules
  - proteins
  - ions
  - charged molecules
  - polar molecules.
- Transporters modify permeability
- Receptors interpret intercellular signals.
- Cytoskeletal proteins attach to the membrane, providing structural support, and:
  - adoption of specialised shapes
  - motility and shape change
  - contraction and relaxation
  - stretching and relaxation
- Red blood cells change shape to carry oxygen and carbon dioxide.
- Movement across a membrane is down the electrochemical gradient, which is the net of electrical and chemical gradients.
- Movement against requires energy.
- Osmolarity is the concentration of solute per volume: eg KCl at 1M = 2Osm.L^{-1} as ionisation

Transporters

a) Channel proteins - water filled pore:

Open (eg. aquaporin) → locked open (down gradient)

Closed → ligand-gated.

b) Carrier Proteins - two + step movement:

Uniport	Antiport	Symport
facilitated diffusion	two substrates in opposite directions	two substrates in same direction
down gradient	up gradient	either gradient
eg. glucose transporter	Na^+ K^+ ATPase	SALT transporter

- Hyperosmotic → ↑water inside = hypotonic
- Hyposmotic → ↓water inside = hypertonic
- Isosmotic → water = in and out.

- Negative feedback loops move towards homeostasis.
- Positive feedback loops move away from homeostasis.
- Negative feedback is dynamic and fast.

eg. ↓ temp → nerve → brain → response

- Postive example: baby pushing on uterus stimulates contractions.
- Chemical signalling:
  - input
  - transduction
  - response.
- input
  - endocrine: between body parts
  - autocrine: same cell type nearby
  - paracrine: other cells nearby
- Transduction: signalling cascade
- Response: - motility + shape change
  - differentiation
  - proliferation
  - nutritional storage + use
  - signal release.
- Signalling can also occur across gap junctions and membranes (contact-dependent).
- Receptors: - receptor-channel (change in conformation)
  - receptor-enzyme
  - a protein-coupled receptor
  - integrin receptor

Eg. successive phosphorylation: kinase transforms a product, which then acts as an enzyme itself.

- All circuits with cell must be integrated.
- Circuits are moderated: product often release a down-regulator or deactivate the kinase.

(1)

- Haemoglobin has four Haem rings with Fe^{2+} ion to bind to oxygen (98%)
- Oxygen easily crosses membranes: High pO_2 in lungs, low in cell. Low pCO_2 in lungs, high in cell.
- Anaerobic metabolism
  - cytoplasm
  - small amounts of ATP
  - lactate.
- Aerobic metabolism
  - mitochondria
  - CO_2
  - Use NADH and $FADH_2$ to strip electrons and form ATP in electron transport chain.