Breathing, circulation and blood

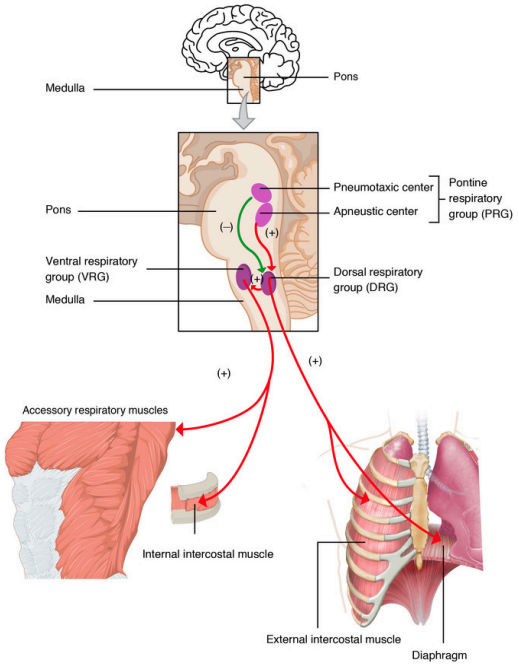
Y1 SEMESTER 1

Breathing, Ventilation and the Cardiovascular system

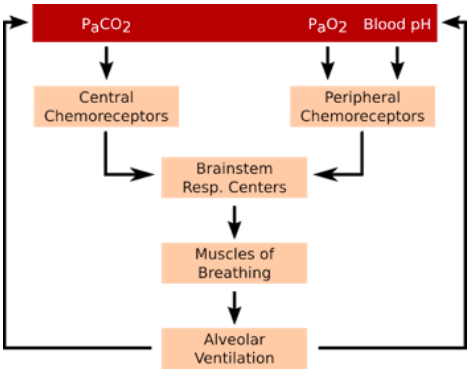
We have tried our best to keep all our notes accurate and up to date. However this is the first year these notes have been sent out so we would love your help to improve them. If you notice any mistakes or have any edit suggestions, please email me s1803407@ed.ac.uk

Breathing

- Respiration is made up of two general processes:
  - **external respiration** - the absorption of oxygen and the removal of carbon dioxide from the body as a whole
  - **internal respiration** - utilization of oxygen at a cellular level and the production of carbon dioxide



- Spontaneous respiration is controlled by medulla (respiratory pacemaker) in the brainstem
  - The medullary rhythmicity area: two regions of interconnected control centres
    - Made up of the *dorsal respiratory group* (DRG) and the ventral *respiratory group* (VRG)
    - The DRG integrates info from chemoreceptors for co2 and pressure, and signals VRG to alter breathing rhythm

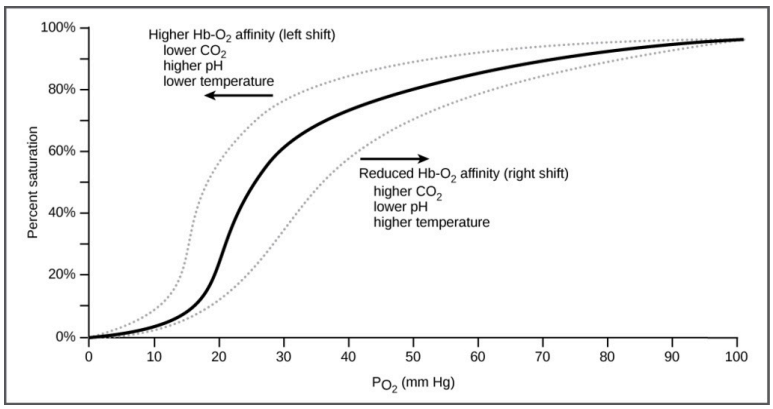


- Respiratory centres affected by other stimuli (e.g. stimuli from chemoreceptors)
  - Feedback information to the medullary rhythmicity area comes from sensors like *central chemoreceptors in the brain* and *peripheral chemoreceptors located in the carotid bodies and aorta*
    - Large increases in arterial PCO2 stimulate the peripheral chemoreceptors in the aorta and carotid bodies, resulting in faster breathing with greater volume of air exchange. Decreased arterial PCO2 inhibits the central and peripheral chemoreceptors leads to inhibition of medullary rhythmicity area (MRA) and slower respiration
    - Peripheral chemoreceptors respond **quickly** to changes in :
      - Arterial pO2
      - Arterial [H+] (pH)
      - Arterial pCO2
    - Central chemoreceptors respond **slowly** to changes in:
      - pCO2

+ Central chemoreceptors are less sensitive to ongoing changes in pH as compared to the peripheral chemoreceptors because the cerebrospinal fluid and interstitial fluid of the brain is separated from buffers in the blood by the blood-brain barrier

Gas Exchange

- Efficient gas transfer requires a large surface area of contact between the alveoli and capillaries. There is extensive branching in blood vessels and bronchioles.This allows for 2 large surface areas to be in contact with each other.
- Oxygen just diffuses across alveolar membranes, moving down a partial pressure gradient.
- Oxygen is carried in the blood in two forms: dissolved and bound to haemoglobin (Hb) (much more efficient).
    - 1.5% is dissolved in plasma
    - 98.5% is bound to haemoglobin
    -
- The oxygen affinity (ie the capacity for Hb to hold onto oxygen) is influenced by the environment
    - This is due to the structure of haemoglobin in which the binding of the first O2 molecule to each molecule slightly changes the conformation of the protein, increasing the oxygen affinity of the other 3 subunits

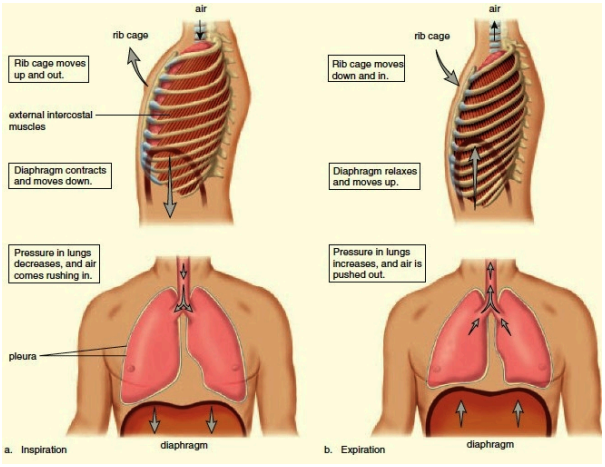


    - This can be visualised using an oxygen saturation curve
        - https://gpnotebook.com/simplepage.cfm?ID=-476446676
    - If the curve is shifted to the right, this means that the oxygen affinity of Hb is reduced (ie it gives up oxygen to the tissues easier). This can occur due to:
        - **Increase in CO2**
        - **Increase in temperature**
        - **Decrease in pH**
        - **Increased in 2,3 DPG**

Ventilation

- Two phases: inspiration and expiration
- Air moves in and out of the lungs because of the existence of a pressure gradient (where pressure in one place is different than another). Fluid always moves down a pressure gradient: this is the **primary principle of ventilation**
    - When atmospheric pressure (101.3kPa) is greater than the pressure in the lungs, air flows down the gas pressure gradient into the lungs from the atmosphere.
    - The pulmonary ventilation mechanism has to establish two gas pressure gradients: one where alveolar pressure (P_A) is lower than atm for inspiration and one where P_A > atm for expiration
        - These pressure gradients are established by changes in the size of the thoracic cavity: produced by contraction + relaxation of respiratory muscles
        - Expansion in the volume of the thorax results in a decreased intrapleural pressure which leads to a decrease alveolar pressure

- **Inspiration** : contraction of the diaphragm or the contraction of the diaphragm and the external intercostal muscles produces inspiration
    - As the diaphragm contracts it descends
    - Contraction of the external intercostal muscle pulls the anterior of the ribs up and out (like a bucket-handle movement). This also elevates the sternum and enlarges the thorax
    - Contraction of the sternocleidomastoid, pectoralis minor and serratus anterior muscles can aid in the elevation of the the sternum during forceful inspiration



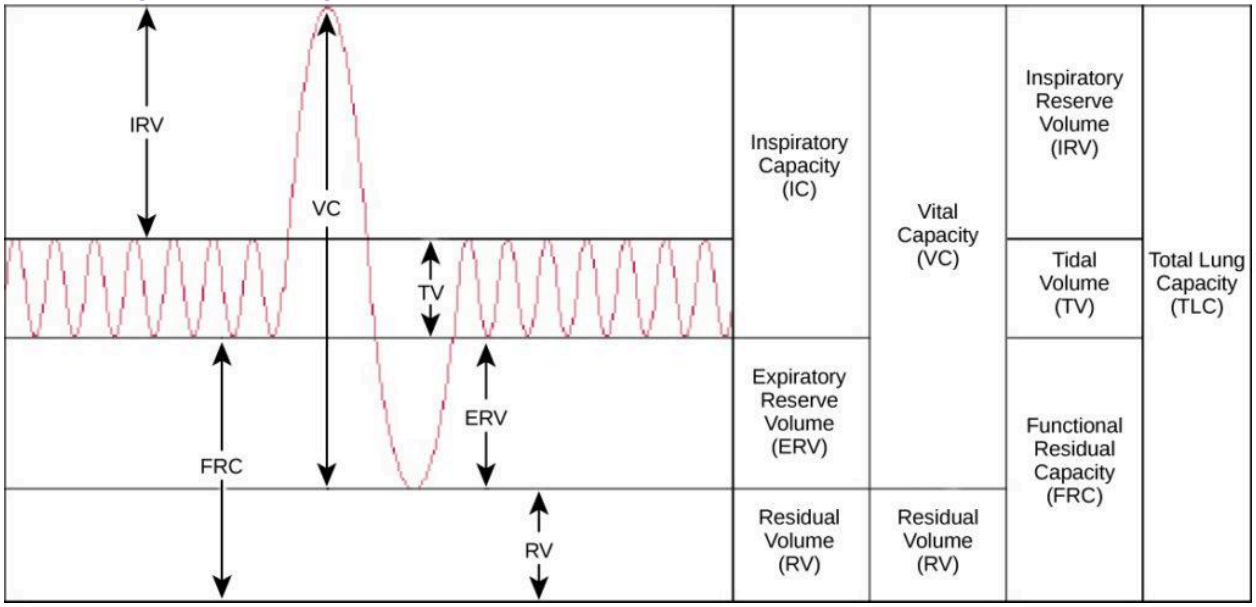
- **Expiration**: ordinarily a passive process that begins when the pressure gradients are reversed
    - The inspiratory muscles relax, decreasing the size of the thorax and increasing P_{IP}
        - Note that the pressure between the parietal (thorax lining) and visceral (lung lining) pleura is always negative and less than alveolar pressure in order to overcome the collapse tendency of the lungs
    - As alveolar pressure increases, a positive pressure gradient from the alveoli to the atm is established and expiration occurs.
        - In forced expiration, the contraction of the abdominal and internal intercostal muscles can increase alveolar pressure
        - The tendency of the thorax and lungs to return to their pre-inspiration volume is a physical phenomenon called **elastic recoil**

- The ability of the lungs and thorax to stretch (referred to as **compliance**) is essential to

normal respiration

- Surface tension (resulting from the attractive forces between water molecules in surfactant produced by Type II pneumocytes) in important in preventing alveolar collapse

Spirometry + Pulmonary Volumes and Capacities



- Pulmonary volumes and capacities are frequently measured using a spirometer
-
    - The volume of air exhaled normally after a typical inspiration: **tidal volume (TV)**
        - Typically 500mL for an adult at rest
    - After an expiration of tidal air, an individual can still force more air out of their lungs: this additional volume is called the **expiratory reserve volume (ERV)**
        - An adult typically has an ERV of between 1000 to 1200 mL
    - The **inspiratory reserve volume (IRV)** is the amount of air than can be forcibly inspired over a normal inspiration
        - Measured by having an individual exhale normally after a forced inspiration
        - Normal IRV: 3300mL
    - The amount of air that cannot be forcibly expired is known as **residual volume (RV)**
        - RV is normally about 1200mL
    - **Vital capacity (VC): IRV + TV + ERV**
        - Represents largest volume of air an individual can move in and out of the lungs
        - How large a vital capacity can depend on many factors: size of the thoracic cavity, posture + more
        - Excess fluid in the pleural/abdominal cavities also decreases vital capacity
        - Emphysema also decreases vital capacity: alveolar walls become stretched and lose their elasticity
        - **Inspiratory capacity (IC): TV + IRV**
            - Maximal amount of air an individual can inspire after a normal expiration
        - **Functional Residual Capacity (FRC): ERV + RV**

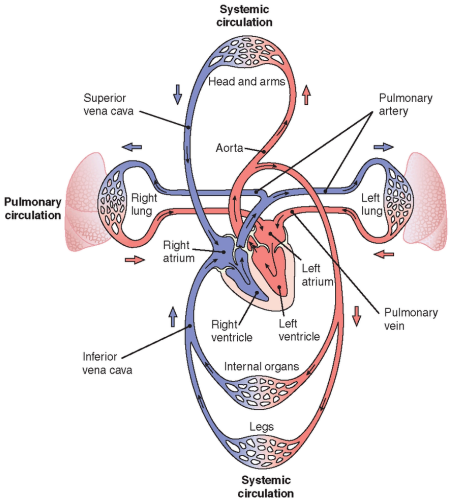
        - Amount of air left in the lungs at the end of a normal expiration w/o contracting expiratory muscles
- Forced Expiratory Volume (FEV) test is another application of spirometry
    - Can determine the presence of a respiratory obstruction by measuring the volume of air expired per second during forced expiration
        - The volume forcefully expired during the first second (FEV_1)
        - is normally 83% of the vital capacity
        - FEV_2 , the total volume expired during the first 2 seconds, is about 94% of the VC.
        - By the end of the third second, FEV_3 , 97% of the vital capacity should have expired.

Respiratory Diseases

- **Restrictive pulmonary disorders:** restriction of the alveoli and reduced compliances leading to decreased lung inflation
    - Hallmark of these: decreased lung volume and capacities (inspiratory reserve volume and vital capacity
    - Causes: exposure to contaminants, immunological diseases, obesity and metabolic disorders
    - Patients classically experience dyspnoea
    - Therapy: eliminating the cause of the restriction, ensuring adequate gas exchange, and improving exercise tolerance
- **Obstructive pulmonary disorders**
    - Obstructive disorder may obstruct inspiration and expiration while restrictive disorders mainly restrict inspiration
    - Chronic Obstructive Pulmonary Disease (COPD)
        - Have chronic trouble breathing, visibly hyperinflated chests
        - Chronic bronchitis and emphysema is commonly seen
        - Tobacco use is the primary cause of COPD
        - Acute respiratory failure, heart failure and vascular resistance are possible outcomes
        - Can be managed w bronchodilators and corticosteroids
    - Bronchitis
        - Person produces excessive tracheobronchial secretions that obstruct airflow and the bronchial mucus glands are enlarged
        - RIsk factors: smoking, decline of pulmonary function w age, environmental exposure
    - Emphysema
        - Air spaces distal to terminal bronchioles are enlarged as a result of damage to lung connective tissue
        - Alveoli enlarge, rupture and fuse into large irregular spaces
    - Asthma
        - Recurring inflammation of mucus membranes and spasms of the smooth muscle walls in the bronchial air passages
        - The inflammation and contractions narrow airways
        - Dyspnoea is a major symptom but hyperventilation, headaches, numbness, and nausea can occur
        - Can be treated using bronchodilators or anti-inflammatory medication

Cardiovascular System

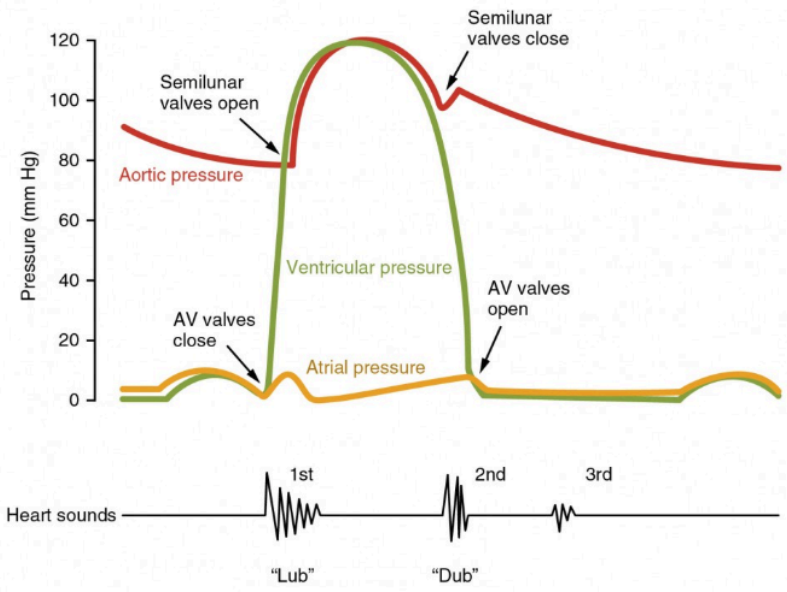
- The cardiovascular system is comprised of two major circuits:
    1. **The pulmonary circuit**
        - Smaller circuit: through pulmonary artery to the lungs to heart through the pulmonary veins
            - Low pressure (25/10mmHg)
    2. **The systemic circuit**
        - Larger systemic circulation leaving through the aorta, branches going to many organs and returning through large veins and vena cava
        - Output first exits through the aorta, then moves to large arteries (elastic), then smaller arteries (muscular), then arterioles, then capillary beds, then venules, then small veins, then large veins then come back into the heart through the vena cava
            - Higher pressure (120/70mmHg)



The Heart

- The heart acts as the pump of both circuits
    - Tracing the path of blood through the heart: enters right atrium through vena cava, flows through the tricuspid valve into right ventricle. Blood then flows through the pulmonary semilunar valve into the pulmonary artery which takes blood to the lungs. The blood enters the heart through the pulmonary vein which deposits the blood into the left atrium. From here, it passes through the bicuspid valve to the left ventricle. From here, it is pumped into the aorta
    - *Source: https://courses.lumenlearning.com/suny-ap2/chapter/cardiac-cycle/*

        - When the excitatory signals spread to the atria from the sinoatrial node, atrial systole occurs. The myocardium of the left and right atria contract and pump blood into the ventricles.
        - Note: there is a drop in ventricular pressure that occurs during ventricular diastole that allows the atrioventricular valves to open and the contents of the atria to fill the ventricles. This is responsible for the majority of ventricular filling. The effects of atrial systole are minor and additive.
        - The myocardium of the atria then relaxes and the atria enter atrial diastole.
        - When the ventricles are filled with blood, in early ventricular systole, the pressure in both ventricles increases as the ventricular myocardium contracts. This rises above the pressure in the atria and causes the atrioventricular valves to close, preventing blood flow back into the atria.



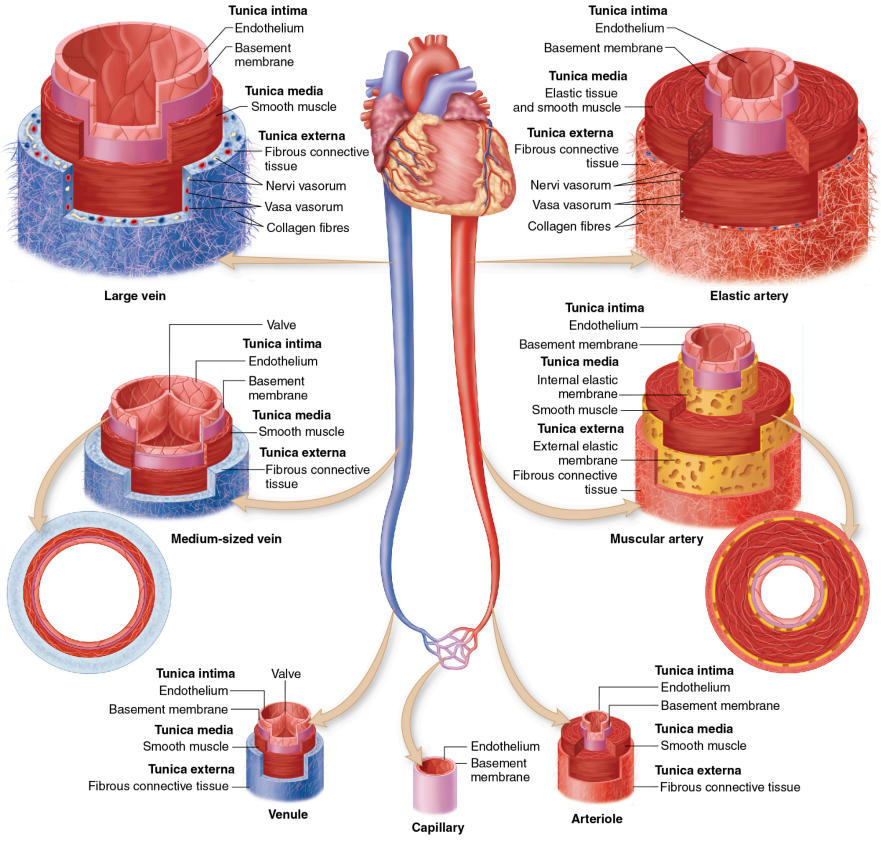
- When the atrioventricular valves close, the ventricular pressure rapidly increases from 0-80 mmHg. The atrial pressure also increases slightly.
- In late ventricular systole, the semilunar valves open to allow blood to flow down its pressure gradient through the aorta and pulmonary trunk. The ventricular pressure increases further (80-120 mmHg) then begins to curve back down. Aortic pressure also increases from roughly 80 -120 mmHg.
- The opening of the semilunar valves causes the atrial pressure to decrease back down, then very slowly rise again.
- In ventricular diastole, the ventricles relax and the semilunar valves close. The closure of the semilunar valves causes the aortic pressure to fall back down to roughly 100 mmHg and the ventricular pressure to decrease rapidly. This allows the atrioventricular valves to open again, which causes a decrease in the atrial pressure and the aortic pressure (which decreases back down to roughly 80 mmHg).

- Cardiac Output = Heart Rate (HR) x Stroke Volume (SV)
  - CO will also match venous return (ie. what leaves the heart will return)
    - Venous return = amount of blood entering ventricle in diastole, determined the preload

        - Preload: determined by venous capacitance and venous filling; can be seen as ‘stretch’ on the heart before systole
    - SV is influence by contractility (force of contraction) and end diastolic volume (volume of blood in ventricle at the end of diastole

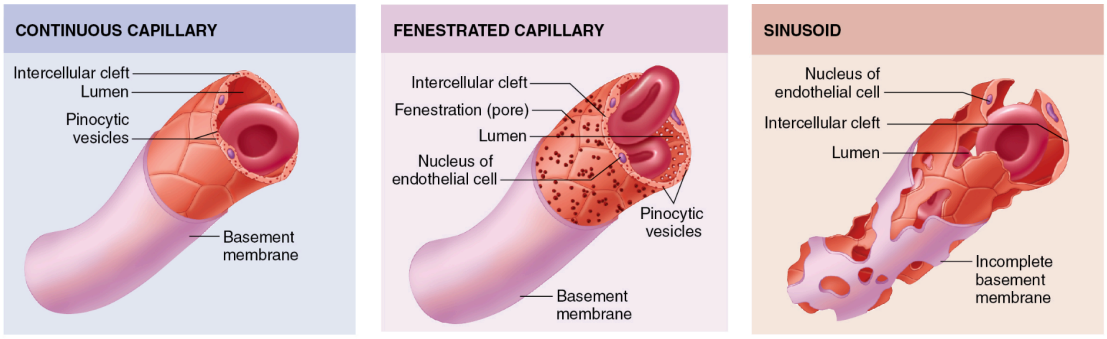
Blood Vessels

- Blood is transported through the body through blood vessels



    - **Arteries**: vessels that carry blood away from the heart
        - **Elastic Arteries:** largest in the body, includes aorta and major branches
            - Acts like a “wind kessel” because of elastic recoil: constant pressure on the fluid (blood) so it moves and comes out continuously, despite the fluctuations of the pump (heart).
            - Elastic recoil allows blood to keep moving between cycles of the heart
        - **Muscular arteries:** smaller in diameter than elastic arteries but thicker walls (due to thick muscle layer)
            - Vascular smooth blood muscle has basal vascular tone (ie degree

of constriction experienced by a blood vessel relative to its maximally dilated state/amount of dilation/constriction) so it can relax or constrict to regulate blood flow and pressure
        - There are sympathetic messages (e.g. alpha adrenergic vasoconstrictors, beta-2-adrenergic, angiotensin II, endothelin, histamine, nitric oxide and prostaglandins) that can affect muscle tone
- **Arterioles (also called resistance vessels):** smallest arteries
    - Key role in regulating blood flow through the variable contraction of smooth muscle in their walls which increases resistance
    - Arterioles are an area of bottleneck due to the low flow rate and low cross sectional area
- **Metarteriole:** short connecting vessels that connects an arteriole to capillaries
    - Proximal ends encircled by regulatory valves called precapillary sphincters that can relax or contract to change blood flow into capillary networks



- **Capillaries**: carry blood from arterioles to venules
    - When blood enters the capillary bed, forces favour filtering fluid **out** into the tissue bed, facilitating exchange of substances. At the venous end, forces favour tissue fluid **re-entering** the capillary
        - At the arterial end, hydrostatic pressure (35mm/Hg) is greater than oncotic pressure/osmotic drag that tries to stop fluid leaving vessels(25mm/Hg) which leads to a net flow **out** into tissues. At the venous end, there is a smaller hydrostatic pressure (15mm/Hg) than osmotic pressure (25mm/Hg) which leads to a net flow **into** the capillaries
            - When these forces (called starling forces) don't function normally, there can be an accumulation of fluid in interstitial spaces: "oedema"
                - Increased hydrostatic pressure can be caused by heart failure, venous obstruction and incompetence in valves on veins

        - Decreased oncotic pressure can be caused by protein loss (nephrotic issues, protein losing enteropathy) or lower protein synthesis (hepatic diseases/failure, malnutrition, acute illness)
        - Other causes of starling dysfunction include increased capillary permeability and lymphatic dysfunction
    - Veins: vessels that carry blood towards the heart. One-way valves are found in the veins to prevent potential backflow. Veins tend to be thinner walled and more susceptible to collapse (much less elastin compared to arteries)
        - **Veins** collapse into a non-circular cross section which allows ofth vein to have a range of capacities
        - **Venules**: small-diameter vessels closest to capillary beds
        - **Small veins (also known as capacitance vessels)**: hold highest proportion of blood volume in systemic circulation due to ability to stretch (capacitance)
- **Laminar flow** describes how blood flows through vessels in which the liquid next to the surface of the vessels don't move very fast. Each successive layer towards the centre slip past at increasing speeds so flow is fastest at the centre of the tube
    - Flow is affected by the size, diameter and length of the tube and viscosity of the liquid
    - **Pouseille's equation** describes the flow (Q) through a rigid tube [ie. a blood vessel] (radius R, length L) due to a pressure gradient:

Q	Flow rate
P	Pressure
r	Radius
η	Fluid viscosity
l	Length of tubing

        - $$Q = \frac{\pi \mathrm{Pr}^4}{8\eta l}$$
    -