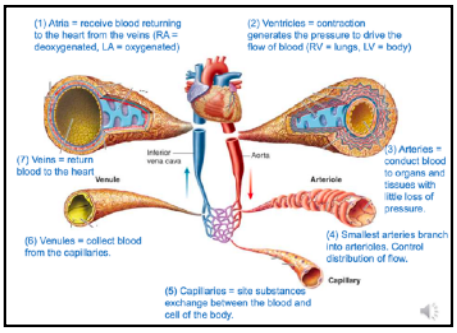
Cardiovascular System 1 (W1)

Overview of CVS, Excitation and Action Potentials (L1)

Anatomy of CVS

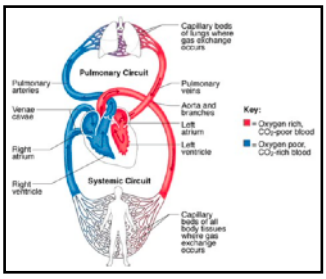


1. **Atria** = receive blood returning to the heart from the veins (RA = deoxygenated, LA = oxygenated)
2. **Ventricles** = contraction generates the pressure to drive the flow of blood (RV = lungs, LV = body)
3. **Arteries** conduct blood to organs and tissues with little loss of pressure
4. Smallest arteries branch into **arterioles**. Control distribution of flow
5. **Capillaries** = site substances exchange between the blood and cell of the body
6. **Venules** = collect blood from the capillaries
7. **Veins** = return blood to the heart
8. **Inferior vena cava** and **superior vena cava**. Deoxygenated blood from the body return to the heart through this vein
9. **Pulmonary vein** = bring oxygenated blood from the lungs to the heart
10. **Pulmonary artery** = transport deoxygenated blood from RV to lungs.

What is the cardiovascular/circulatory system?

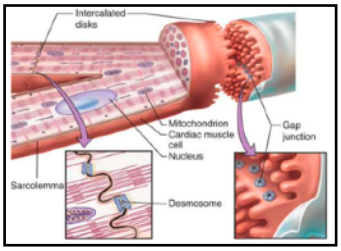
- Tubes through which the blood flows:
  - **Blood vessels**
- Pump to produce blood flow:
  - **Heart** (muscular pump)
- Fluid in the system:
  - **Blood**

Two circuits: the pulmonary and systemic circulations



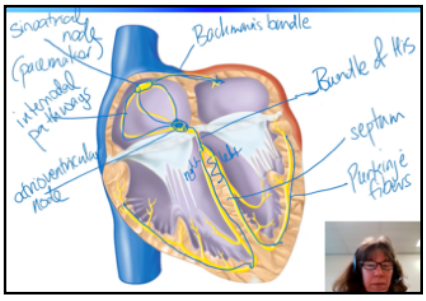
- Superior vena cava and inferior vena cava connect to right atria. Bring deoxygenated blood from the body
- Right ventricle transports deoxygenated blood through pulmonary artery to heart for oxygenation (**pulmonary circuit**)
- Oxygenated blood travels through pulmonary veins to left atria. Oxygenated blood leaves left ventricle through aorta and branches to body (**systemic circuit**)

Spread of electrical activity (excitation) through the heart

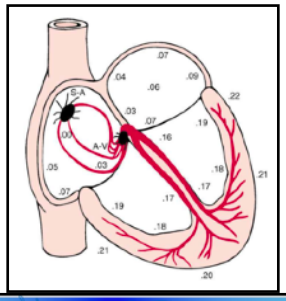


- **Electrical conduction**: cardiac myocytes are connected via **gap junctions**
- Muscle fibres are connected via **intercalated disks**
- Gap junctions allow for the passage of ions from one cell to the next
- **Desmosome**: **mechanical connection**. Glue cells together and hold them together

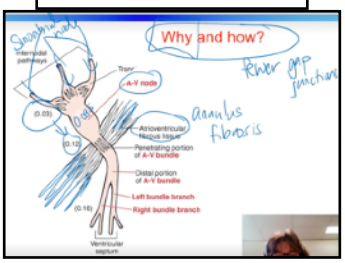
Excitation of the heart:



- **Sinoatrial node** - excitation of heart is initiated here
- Pacemaker cells here that spontaneously generate action potentials
- Internodal pathways between sinoatrial node and the **atrioventricular node**
- **Backmann's Bundle** are specialised muscle cells that carry electrical impulse from right atrium to left atrium
- **Bundle of His** branches around Septum into **Right** and **Left** Bundle of His
- Then electrical signal passed up ventricular walls from the bottom of the heart through **Purkinje fibres**



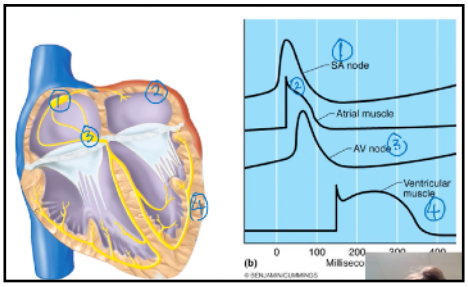
Transmission of the cardiac impulse through the heart: (sec)
- Atrial depolarisation takes ~0.09 seconds
- Process of ventricular excitation takes ~0.06 seconds once the electrical impulse reaches the Bundle of His



Slow conduction through the atria-ventricular node:
- Slower because there are **fewer gap junctions** between the atrio-ventricular cells
- Allows sufficient time for atria to be excited and contract before the ventricles below are excited

Spread of excitation through the heart:
1. Excitation originates in the **Sinoatrial node**
2. **Internodal pathways** in the atria
3. **Atrioventricular node** (slowed conduction ~0.05m/s)
4. **Bundle of His** (two branches, left and right)
5. **Purkinje** fibres (rapid conduction ~3-5m/s)

Cardiac action potentials cause the excitation of the heart
- Micro electrode inserted into intracellular fluid of cardiac muscle cell (from sinoatrial node) which records the membrane potential (cardiac action potentials)
- Voltage difference across the cell membrane = membrane potential

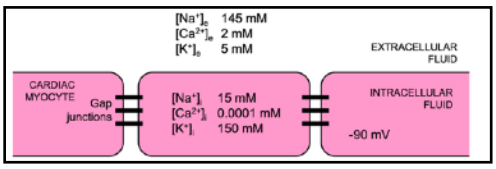


Spontaneous generation of 'pacemaker' action potentials in Sinoatrial and atrioventricular nodes:
- Different shapes
- Different strengths
- **Atrial** and **ventricular** muscle have a flat line beginning known as the **resting potential**
- **Nodal action potentials** (pacemaker action potentials) do **not** have a stable resting potential
  - Slow depolarisation called a **pacemaker potential**)

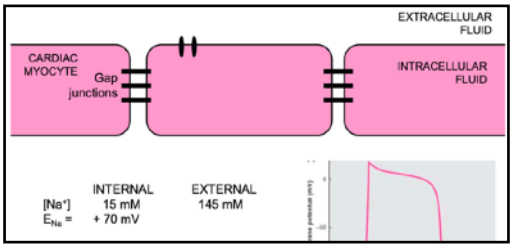
Sinoatrial node pacemaker and ventricular action potentials:
- **Ventricular action potential** = stable resting membrane potential, plateau phase (stays high before shooting back down to RMP)
- **Pacemaker action potential** = no stable resting potential (pacemaker potential), less negative maximum diastolic potential (MDP)
- Most negative point of **ventricular action potential is -90mV**. Most negative point of **sinoatrial node is -65mV**. This point is the **maximum diastolic potential (MDP) = -65mV**

Depolarisation, repolarisation and hyperpolarisation
- **Depolarisation**: When membrane potential is moving in the positive direction. Usually from -90mV to +15mV
- **Hyperpolarisation**: When membrane potential is moving in the negative direction. Usually from +15mV to -90mV
- **Repolarisation**: membrane potential at the end returns back to RMP

Ionic mechanisms underlying the **ventricular action potential**:
Ventricular resting membrane potential
- **Extracellular**
  - **[Na+]** = 145mM (HIGHER)
  - **[Ca2+]** = 2mM (HIGHER)
  - [K+] = 5mM (LOWER)
- **Intracellular** (-90mV potential)

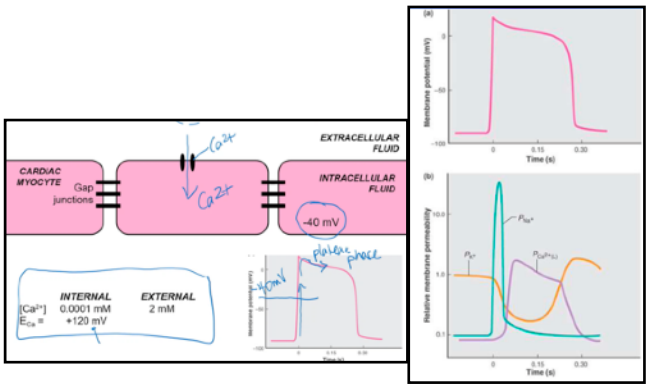


- [Na+] = 15mM
- [Ca2+] = 0.0001mM
- **[K+]** = 150mM



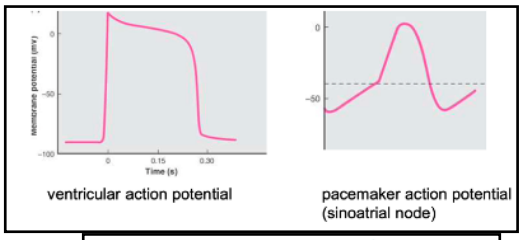
Ventricular action potentials (depolarisation)
- Depolarisation = opens **"Fast" voltage-sensitive Na+ channels**
- **Sodium** moves form outside of the cell to inside
  - Causes upstroke of ventricular action potential

Ventricular action potentials (depolarisation and plateau)
- Depolarisation and plateau = **'slow' voltage-sensitive Ca2+ channels**
- Intracellular fluid has membrane potential of -40mV
- Ca2+ goes through channels down concentration gradient (outside to inside cell)
- Depolarisation stops at +15mV
- Slow closing of Ca2+ voltage-sensitive channels results in **plateau phase** of AP

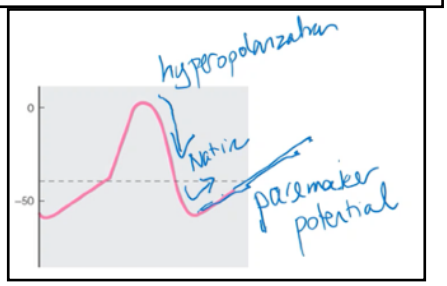


Ventricular action potential (repolarisation)
- Repolarisation = **voltage-sensitive K+ channels**
- Open at **-40mV** during **depolarisation**
- K+ leaves the cell into the extracellular fluids, cause ventricular muscle cell membrane potential to become less positive and force membrane potential to become RMP.

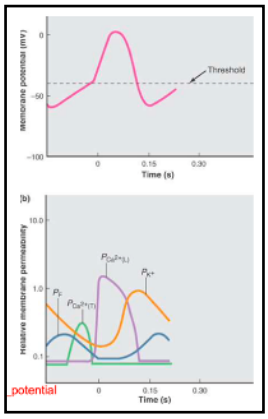
Ionic mechanisms underlying the spontaneous **Sino-atrial node (pacemaker) action potential**
- The puffer fish contains a tetrodotoxin (TTX) = a selective inhibitor of fast Na+ channels
- What will TTX do to a **ventricular** action potential?
  - Inhibit depolarisation of AP
- What will TTX do to a **pacemaker** action potential?
  - NOTHING. Fast Na+ voltage-sensitive channels are not involved in pacemaker action potential

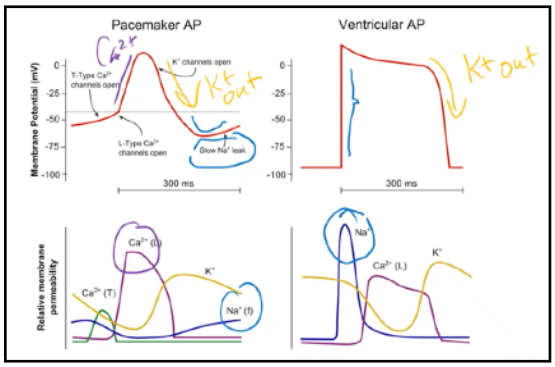


What is the pacemaker (or funny) current?
- Called the 'f' for **funny** or 'h' for hyperpolarisation **current**
- **SLOW inward flux of Na+ at -45mV**, cause hyper polarisation
- Pacemaker potential, before depolarisation, not stable



Sino-atrial node (pacemaker) action potential:
- **Pacemaker potential**
  - Initiated by **inward Na+** (**leaky channels**)
  - Followed by **inward Ca2+** (transient, **T**, short)) - during depolarisation
  - Gradual decrease in outward K+
- **Upstroke** = slow **Ca2+ influx** (**L**)(-45mV)
- **Repolarisation** = outward K+ (-40mV)





Cardiac pacemaker and ventricular action potentials:

- Why is it that the heart can beat in isolation of the body (pacemaking)?
  - Sinoatrial node cells **spontaneously** generate pacemaker action potentials
- T-type Ca2+ channels open, L-type cause depolarisation. Hyperpolarisation from K+ leaving, slow Na+ leak causes depolarisation straight away after hyper polarisation

The electrocardiogram and autonomic control of the heart (L2)

The electrocardiogram (ECG)

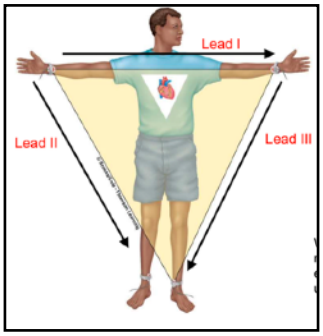
- A record of the hearts electrical activity, recorded from the surface of the body
- As excitation sweeps over the heart at any instant some parts of the heart will be positively charged while other parts are negatively charged
- This causes currents to flow in the medium surrounding the heart
- Because the body is a very good conductor these small currents can be detected at the body surface
- The ECG is a recording of these small currents and reflects the depolarisation and repolarisation of different regions of the heart

The ECG = clinical diagnostic tool:

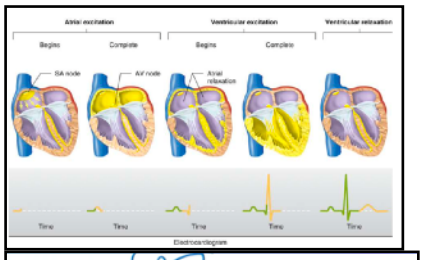
- Used by cardiologists to determine:

1. The anatomical orientation of the heart and the relative sizes of its chambers
2. Disturbances in cardiac rhythm and conduction
3. The extent and location of ischaemic (blockage of blood supply) damage to the myocardium
4. The effects of drugs or abnormal concentrations of various plasma electrolytes on the heart

Recording the ECG = standard bipolar limb leads:

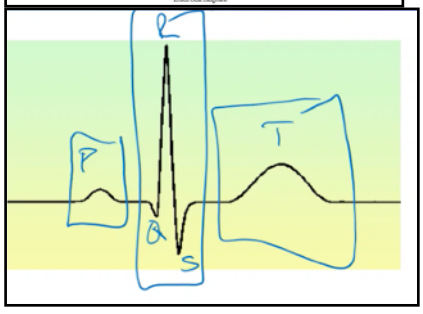


- Each ECG lead 'views' the electrical potential of the heart from different angles:
  - Lead I (0 degrees)
    - Right arm (-ve)
    - To left arm (+ve)
  - Lead II (60 degrees)
    - Right arm (-ve)
    - To left leg (+ve)
  - Lead III (120 degrees)
    - Left arm (-ve)
    - To left leg (+ve)
- When a wave of depolarisation moves towards the recording (+ve) electrode, the ECG trace shows an upward deflection



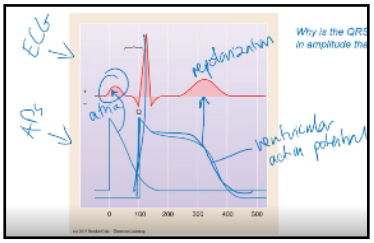
What does the ECG look like?

- Atrial excitation (slight raise of ECG, phase 1)
- Ventricular excision (large raise of ECG, phase 2)
- Ventricular relaxation (medium raise of ECG, phase 3)



Normal ECG = 3 phases

1. **P WAVE** = excitation of the atria
   - atrial depolarisation
2. **QRS COMPLEX** = excitation of the ventricles
- ventricular depolarisation, 3 points (relaxation of atria is covered by QRS complex
3. **T WAVE** = recovery (repolarisation) of the ventricles
- ventricular repolarisation

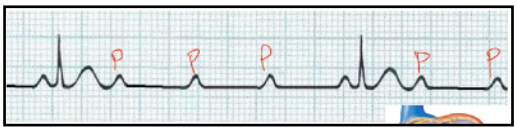


ECG and cardiac action potentials:
- The ECG is a composite recording of all of the action potentials produced by the nodal and myocardial cells
- Why is the QRS complex larger in amplitude than the P wave?
  - Ventricles contain more muscle mass than atria

Disorders of cardiac excitation (cardiac arrhythmias or abnormal cardiac rhythms):
Major causes of cardiac arrhythmias
1. Shift of the pacemaker from the sinoatrial node to other pacemaking regions
2. Abnormal impulse formation in the sinoatrial node
3. Blocking or delay of conduction of the impulse through the heart
4. Spontaneous generation of abnormal impulses in any region of the heart (e.g. ventricular fibrillation)

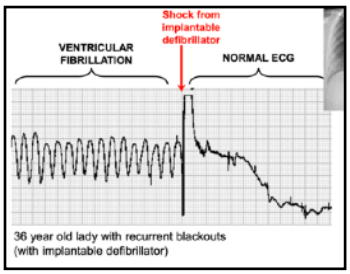
Shift of the primary pacemaker from the SA-node:
- SA-node normally sets the heart rate because its pacemaker cells have the **fastest** intrinsic rate of firing = 'follow the leader' - **intrinsic firing rate of SA-node is 70-100bpm**
- Therefore, the sinus node is normally the PACEMAKER of the heart = called **sinus rhythm**
- SA-node: pacemaker APs, 70-100 APs per minute (fastest)
- AV-node: pacemaker APs, 40-60 APs per minute
- Purkinje: pacemaker APs, 15-40 APs per minute
- Heart rate set by SA-node, the fastest auto rhythmic tissue
  - Other pacemaker cells will "follow the leader"
- If SA-node stops working, AV-node (second fastest) will take leadership and will set the heart rate
- If AV node stops working, SA-node generates 70bpm for atria, but Purkinje fibres will generate 30bpm for ventricles. Atria will beat at different speed to ventricles

Complete atrioventricular conduction block:



- **P wave** dissociated from QRS complexes. Doesn't follow pattern
- Conditions that can block the impulse through the AV-node
1. Ischaemia
2. Compression of the AV-node by scar tissue
3. Inflammation of the AV-node (fever)
4. Extreme stimulation of the heart by the vagus/parasympathetic nerves

Spontaneous generation of abnormal impulses in any region of the heart
- Ectopic focus
- Randomly, Purkinje fibre can increase rate to 140bpm, now the fastest pacemaker in the heart and dictate the rate at which the heart beats



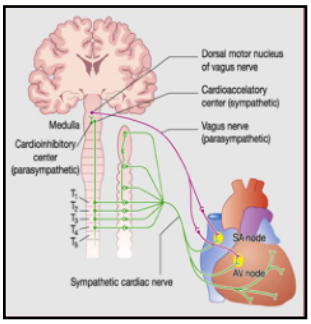
Ventricular fibrillation
- VF = fatal consequence of myocardial ischaemia and electrocution

Do you understand the excitation of the heart?
- The sinoatrial node is irreversibly damaged:
  - The atrioventricular node will now initiate the excitation of the heart, and the heart rate will be about 50 bpm

Autonomic control of the heart
- As you do exercise, heart rate increases

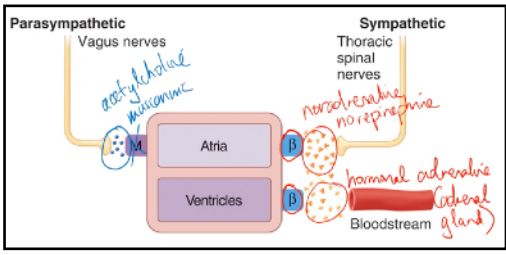
Heart rate increases during exercise
- HR increase in linear fashion to increase O2 delivery to active muscle
- Exercise training decreases resting HR. Trained athletes: resting HR as low as 40bpm
- Maximum HR not altered (decrease with age)

- Return of HR to normal post exercise is indicative of aerobic fitness



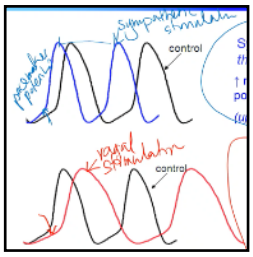
<u>Autonomic control of sinoatrial node pacemaking (heart rate)</u>
- Autonomic innervation of the heart:
- Activation of **cardiac parasympathetic nerves** (**vagus**):
  - **Decrease rate** of sinoatrial node pacemaking (decrease HR)
  - Slows conduction through atrioventricular node (AV-node)
  - Start in cardioinhibitory centre in Medulla, travel through vagus nerve and enter at AV-node and SA-node
- Activation of **cardiac sympathetic nerves**:
  - **Increase rate** of sinoatrial node pacemaking (increase HR)
  - Speeds up conduction through AV-node
  - Increase force of contraction (ventricular muscle)
  - Begin at cardioaccelatory centre in Medulla, travel through sympathetic cardiac nerves that innervate SA-node, AV-node and ventricular muscle

<u>Autonomic neurotransmitters and cardiac receptors:</u>
- **Parasympathetic** - **vagus nerves**
  - Innervate SA-node and AV-node
  - Neurotransmitter released is **acetylcholine** and acts of muscarinic receptors
- **Sympathetic** - **thoracic spinal nerves**
  - Innervate SA-node, AV-node and ventricular muscle
  - Neurotransmitter released is **noradrenaline** and acts on **beta receptors**
  - Also **hormonal adrenaline** released from adrenal gland that act on **beta receptors** in **ventricular muscle**



- What happens if you damage the autonomic nerves innervating the heart? Will the heart still beat?
  - Yes. Excitation of heart results from spontaneous excitation of pacemaker action potentials in SA-node. Nerves regulate the rate of pacemaking

<u>Autonomic nerves modulate heart rate (SA-node pacemaking):</u>
- Sympathetic nerve activation = the 'accelerator'
  - **Increase** of generation of pacemaker action potentials, thus HR
  - (Up to 230bpm, tachycardia = HR > 100 bpm)
- Parasympathetic (vagal) nerve activation = the 'brakes'
  - **Decrease** of generation of pacemaker action potentials, thus HR
  - (Down to 20 bpm; bradycardia = HR<60 bpm)



<u>Resting heart rate involves parasympathetic (vagal) nerve activation:</u>
- Parasympathetic - vagus nerves
- In experiment: Block sympathetic + parasympathetic nerve
  - Cause HR to increase to ~100bpm from ~70bpm
- Known as vagal tone

<u>Autonomic control of heart during exercise:</u>
- Increase in plasma epinephrine/adrenaline
- Increase activity of sympathetic nerves to heart
- Decrease activity of parasympathetic nerves to heart
- Heart rate increased by:

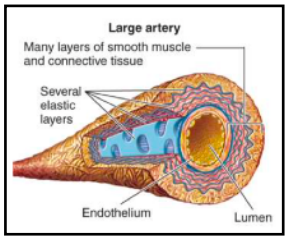
1. Reducing parasympathetic input to SA (vagal withdrawal)
2. Increasing sympathetic input to SA-node

Cardiovascular System 2 (W2)

Arteries (L1)

Left ventricular contraction ejects blood into the aorta and the systemic circulation

- Excitation of the heart (ECG)
- Is followed by ventricular contraction
- Which leads to an arterial pulse

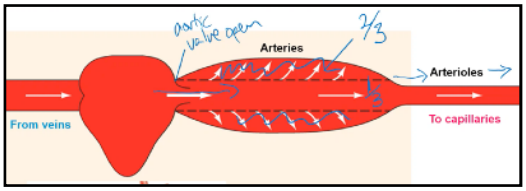


Arteries are large diameter elastic tubes

1. Arteries are **elastic tubes**
   - They act as pressure reservoirs to maintain blood flow through tissues during diastole
2. Arteries have **large diameter**
   - They provide a low resistance pathway for conducting blood to organs

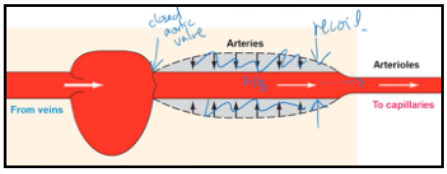
Arterial pressure is pulsatile:

- Flow of blood out of the heart is intermittent (aortic valve closed in-between contractions) but blood flow through tissues and organs of the body is continuous



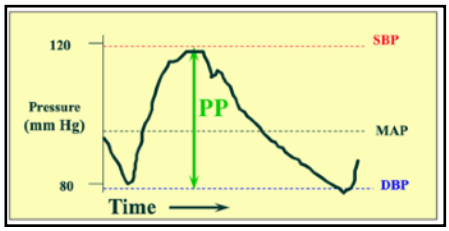
Systolic blood pressure

- Heart contracting and emptying (systole)
- Aortic valve is open
- 2/3 of blood stretches arteries, 1/3 of blood goes down into arterioles and capillaries



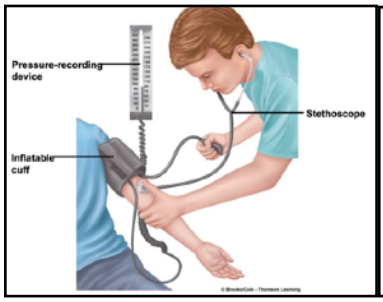
Diastolic blood pressure

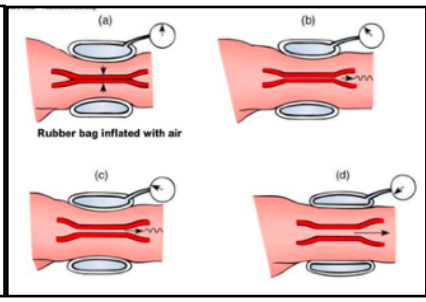
- Heart relaxing and filling (diastole)
- Aortic value is closed
- Stretched values of arteries recoils and remaining 2/3 of blood goes into arterioles
- Blood continues to flow through systematic arteriole during diastole because of elastic recoil of the walls of the arteries which had been stretched by blood entering the arteries during systole



Aortic Pressure Trace:

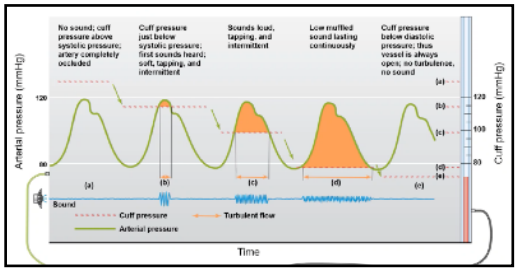
- SBP = Systolic BP (120 mmHg)
- DBP = Diastolic BP (80 mmHg)
- PP = pulse Pressure = SBP - DBP
- MAP (Mean Arterial Pressure) = DBP + 1/3(PP) = 80+1/3(40) = 93mmHg
- Dichrotic notch (little dip and then rise near peak of graph)
  - Aortic valve closes at this moment, results in decrease of pressure





Measurement of blood pressure using auscultation (listening to the sounds of the body):

- Inflated well above systolic pressure
- No flow of air
- Slight release of pressure results in turbulent flow
- At low pressures, flow of blood becomes streamlined blood flow
- We can hear the sounds of turbulent flow



Turbulent flow is noisy = Korotkoff sounds: