بسم الله الرحمن الرحيم

Physiology Team 436
Cardiovascular Block

Review File

This work is intended for **review** of the Cardiovascular block lectures.

قال ﷺ:" دعوةُ ذِي النُّونِ الَّتي دعا بها فِي بطنِ الْحوت، لا إله إِلَّا أنت سبحانك إني كُنت من الظالمين لم يَدْعُ بها مسلم في كربة إلا استجاب اللهُ له "

Color Index:
Text – Important - Very important – Formulas - Values

Done by:
Laila Mathkour - Jawaher Abanumy
Reviewed by: Lulwah Alshiha

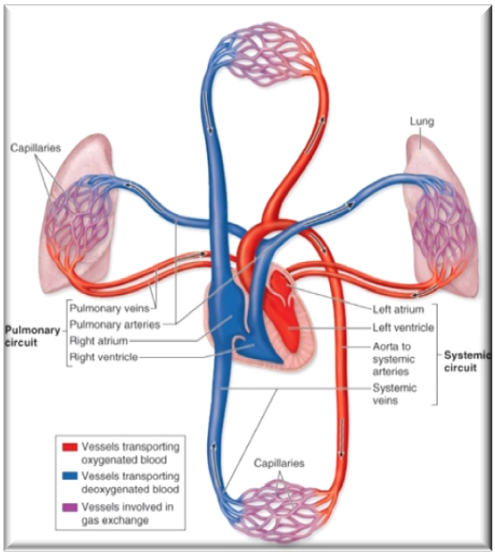
دعواتكم لنا بالتوفيق

Lecture #1,2 Contractile Mechanisms in Cardiac Muscle, Cardiac Electrical Activity

Cardiovascular System

Components

- Heart
- Blood Vessels



It is a closed system in which blood circulates. Therefore, we call it circulatory system

Function

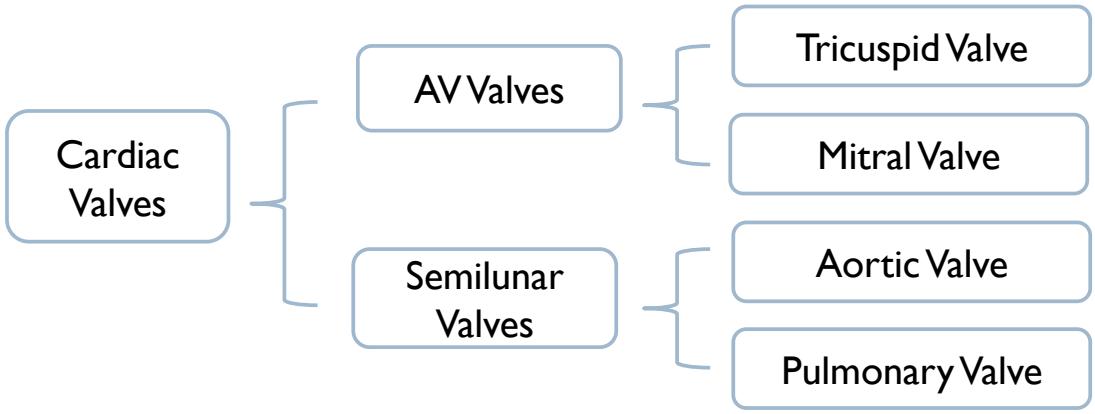
- Delivery of O2, glucose and other nutrients to active tissues.
- Removal of CO2, Lactate and other waste from active tissues.
- homeostatic mechanisms
- Adjustment of oxygen and nutrient supply in different physiologic states.
- Transport of metabolites and other substances to and from storage sites.
- Transport of hormones, antibodies and other substances to site of action.
- Defense
- Thermo-regulation

The Heart as a Central Pump

- The heart contains 4 chambers:
  - 2 atria (right and left)

    Thin-walled, low pressure chambers that act as reservoirs for their respective ventricles (not important as pumps)
  - 2 ventricles (right and left)

    Principle pumps of the CVS capable of generating flow with pressure. (The thickness of the ventricular wall is related to pressure generated: left thicker than right)



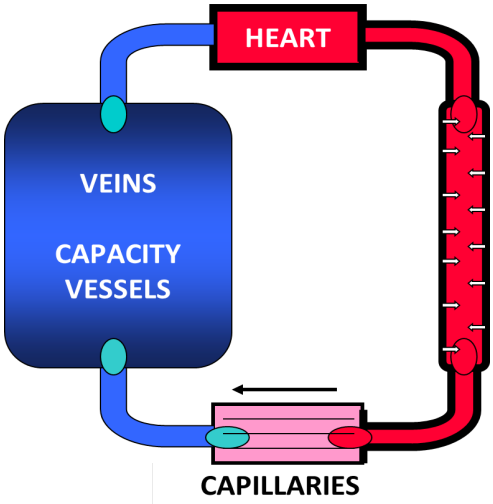
- For effective pumping, the heart must be functioning properly in five basic respects:

1. The contractions of individual cardiac muscle cells (myocytes) must occur at regular intervals and be synchronized (not arrhythmic).
2. The valves must open fully (not stenotic**).
3. The valves must not leak (not insufficient or regurgitant).
4. The ventricular contractions must be forceful (not failing).
5. The ventricles must fill adequately during diastole.

Blood Vessels and Circulation

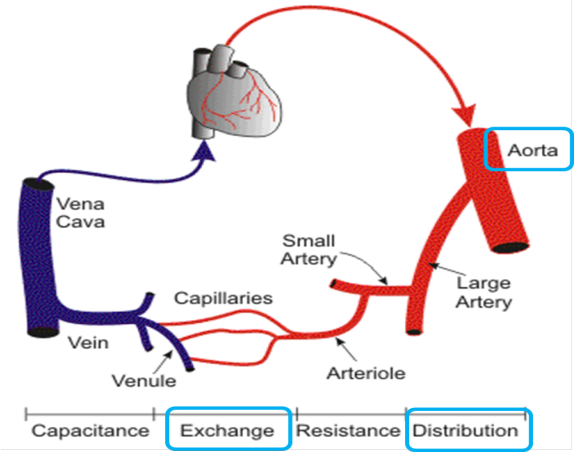
VEINS
Are also called (Volume reservoirs)

(HIGH COMPLIANCE)
(LOW PRESSURE)
MORE BLOOD VOLUME



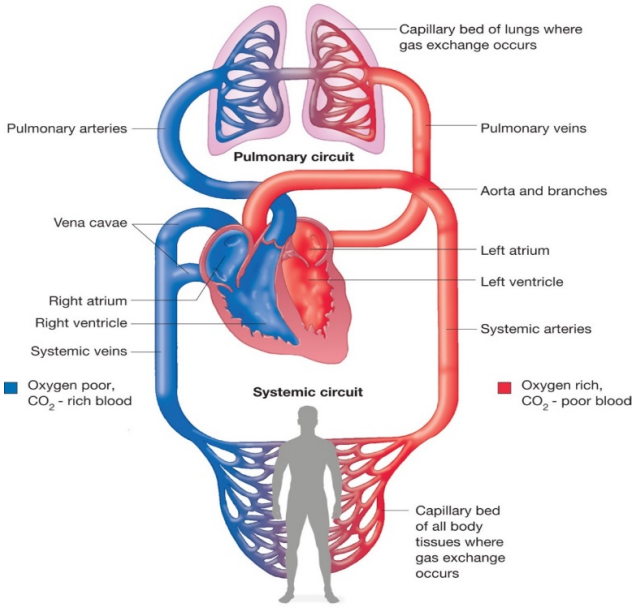
ARTERIES
Are also called (Pressure reservoirs)

(LOW COMPLIANCE)
(HIGH PRESSURE)
LESS BLOOD VOLUME



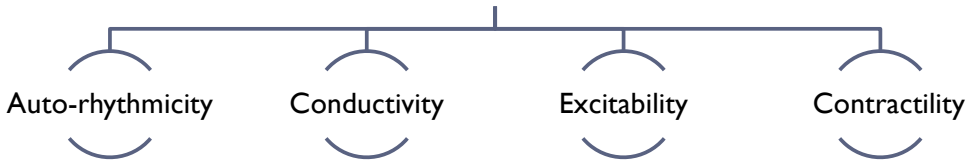
COMPLIANCE: is the property of undergoing elastic deformation , as change in volume when subjected to an applied force.

Systemic Circulation	Pulmonary Circulation
Starts at **Left Ventricle**	Starts at **Right Ventricle**
Ends at **Right Atrium**	Ends at **Left Atrium**
These 2 circulation are connected in series.	



How the Heart Performs its Function as the Central Pump of the CVS

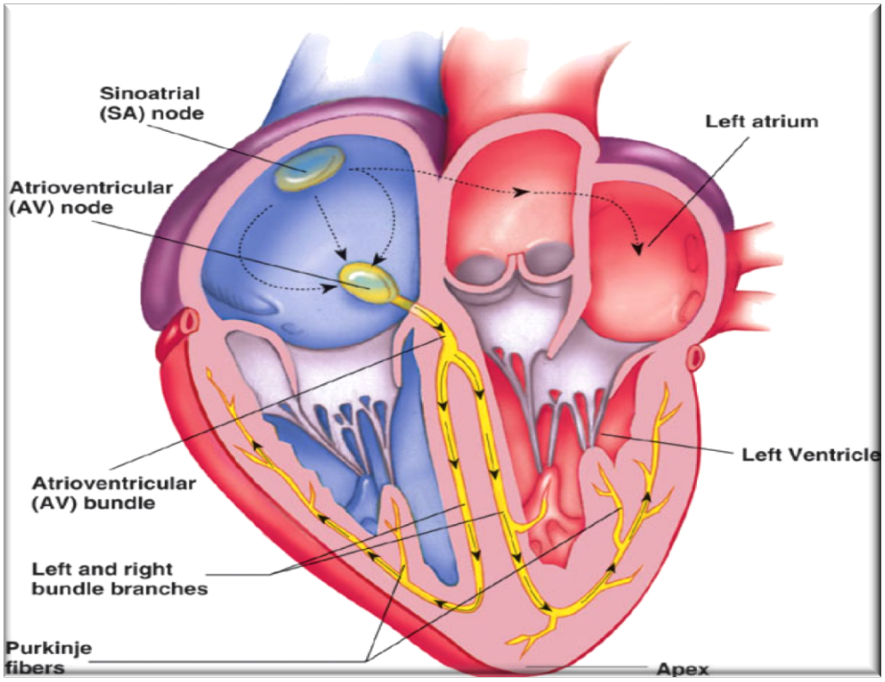
- The heart has four basic properties which are essential for its functioning as the central pump of the CVS:



- There are 2 main types of cells in the heart:
  - Cells of the specialized <u>conduction</u> system.

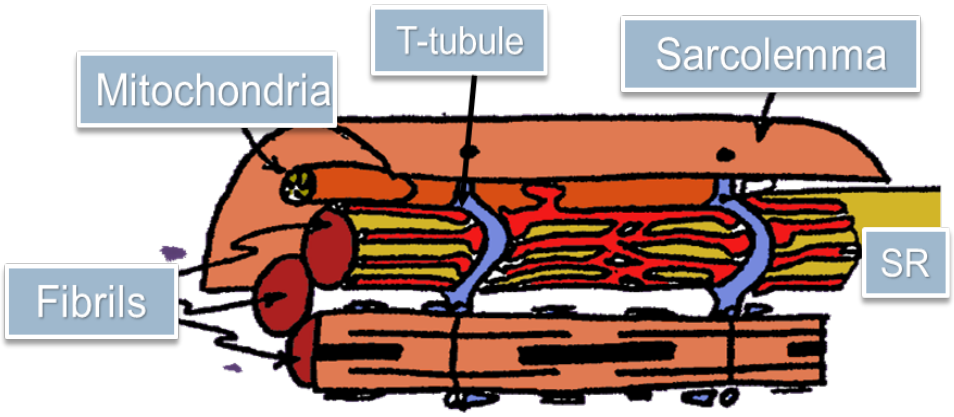
    (SA node, AV node, AV bundle, Left & Right Bundle Branch, Purkinje fibers)
  - <u>Contractile</u> cells (myocytes; working cells).

    (wall of atria & inter-arterial septa and wall of ventricle & inter-ventricular septa)



Ultrastructure of Myocyte

- The cardiac muscle cells (fibers; myocytes) branch and interdigitate, but each is a complete unit surrounded by a cell (plasma) membrane (sarcolemma).
- Where the end of one muscle fiber abuts (adjoin) on another, the membranes of both fibers parallel each other through an extensive series of folds. These areas are called intercalated disks (intercalated discs: cell membranes, separate individual cardiac muscle cells from one another).
- Thus, each fiber is separated from its neighboring fibers by its sarcolemma (laterally) and by the intercalated disks (end-to-end).

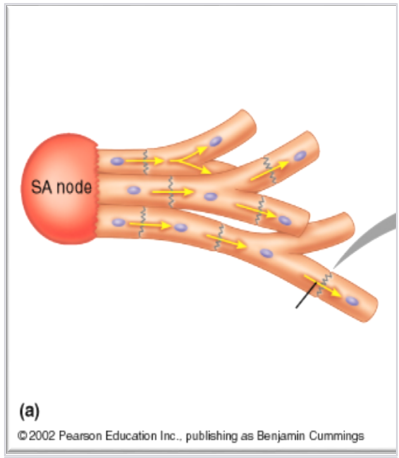


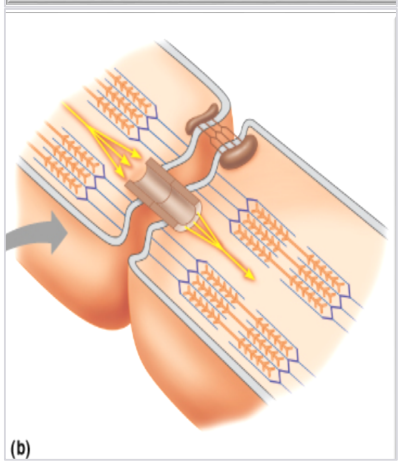
- Gap junctions: are trans-membrane channel proteins, connecting the cytoplasm of the neighboring cardiac muscle cells.
  - They allow free diffusion of ions between neighboring cells.
  - Action potentials can also travel from one cardiac muscle cell to another.
- So intercalated discs allow passage of current through cells, this mechanism ensures electrical coupling of the cells.

Mechanical Coupling and Electrical Coupling

intercalated discs enable **synchronization** of contraction of cardiac muscle by:

- Providing mechanical coupling
  - Desmosomes resist stretching and prevent detachment of the cardiac fibers during contraction.
- Providing electrical coupling
  - Allows free diffusion of ions between neighboring cells. Action potentials can also travel from one cardiac muscle cell to another.





Differences between cardiac and skeletal muscles

Cardiac Muscle	Skeletal Muscle
T system in cardiac muscle is located at the Z lines of the sarcomeres	T system in skeletal muscle is located at the A–I junction
The sarcoplasmic reticulum makes complexes with the transverse tubular membrane at dyad junction	The sarcoplasmic reticulum makes complexes with the transverse tubular membrane at triad junctions.

Resting Membrane Potential (RMP)

Resting membrane potential: is an intracellular potential of the resting myocyte and is found to be –80 mV to –90 mV.

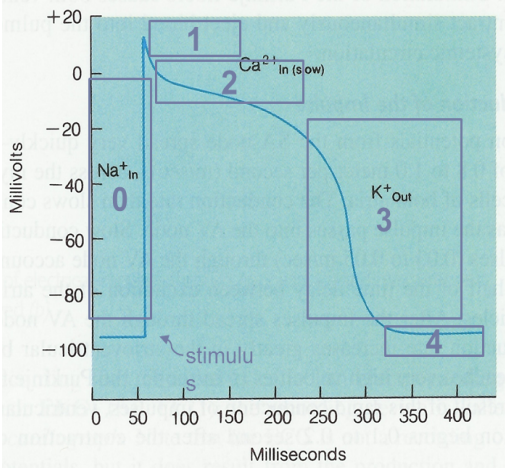
- **In atrial and ventricular cells:** this RMP is stable until external stimulation is applied.
- **In SA node cells (in particular) and many conduction fibers:** the RMP is not stable, drifting towards zero at times.
- **Electrical potentials arise from:**
  1. Differences in the concentrations of ions across the membrane.
  2. The presence of selective ion-conducting channels spanning the membrane, namely K^+, Na^+, and Ca^{2+}.

Resting Ventricular Myocytes	
Intracellular concentration	***Extracellular concentration***
Na+: 10 mm/L	Na+: 140 mm/L
K+: 140 mm/L	K+: 4 mm/L
Ca++: 0.0001 mm/L	Ca++: 1.2 mm/L

- In resting conditions: membrane is permeable to K^+ only.
- K^+ diffuses out of cell (efflux) down a concentration gradient.
- Negatively charged ions (phosphate and proteins) cannot leave cell creating negative intracellular charge
- **RMP is due to K^+ efflux (very IMP)**

Action Potential in Cardiac Muscle

- Duration of cardiac action potential is 0.4 seconds



Phases of cardiac Action Potential	Ionic changes
0- Rapid depolarization (+20 mV)	Fast sodium channels opens → Na^+ influx
1- Partial repolarization (5-10mV)	Opening of K^+ channels → K^+ out
2- Action potential plateau (0 mV)	Slow calcium channels opens → Ca^{2+} influx
3- Repolarization (back to RMP)	K^+ out

Cont.

Excitability : is the electrical response to excitation (stimulation).
When an excitable tissue is excited, it responds by generating action potentials.
Cardiac action potentials can be broadly classified into two types, termed:
Fast-response.
Slow-response potentials.

What causes the Plateau in the Action Potential?

1. **The main cause is slow calcium channels**: slow to open & remain open for several tenths of a second → Large quantity of calcium ions flow into the interior of the cardiac muscle fiber → maintains prolonged period of depolarization → causing the plateau in the action potential.

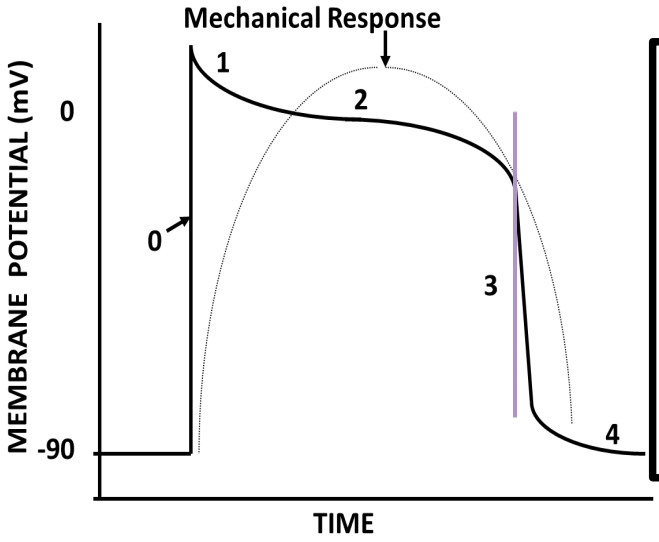
2. **Another factor** to maintain the plateau phase is the **decreased permeability** of the cardiac muscle membrane for potassium ions → decrease outflux of potassium ions during the action potential plateau.

Differences Between Fast-Response and Slow-Response Action Potentials

	Fast Response Action Potential	Slow Action Potential
Found in	1. Atrial 2. Ventricular 3. His-Purkinje cells	1. Sinus node 2. Atrioventricular (AV) node
Phases found	All phases of action potential are present (0/1/2/3/4)	Phases 1 & 2 are absent (phase 0/3/4 are found)
RMP(Phase 4)	Stable; voltage is constant	voltage slowly decreases (drifting towards zero with time)
Phase 0	Rapid depolarization with a substantial overshoot	Slower initial depolarization, lower amplitude overshoot
Phase 1	- A rapid reversal of the overshoot potential	Absent
Phase 2	Long plateau	Absent
Phase 3	Repolarization	Repolarization
Phase 4	Stable , resting membrane potential	Slowly depolarizing "resting" potential
Conduction Velocity	Rapid	Slow

Fast-Response Action Potential

Phase	Due to
Phase 0 – Very rapid depolarization	Na^+ influx through voltage-gated (fast) Na^+ channels
Phase 1 – Early partial repolarization	• Inactivation of (fast) Na^+ channels • K^+ begins to move out of cell
Phase 2 – Plateau	➢ Permeability of slow (ca+2) channels • L-type calcium channels ➢ Chemical & Electrical forces of K^+ & Ca^{2+} balanced; • K^+ out of cell = Ca^{2+} into cell
Phase 3 - Repolarization	➢ Inactivation of slow (Ca^{2+}) channels ➢ ↑ conductance of K^+ out of cell • Polarity of the cell interior becomes more (-)
Phase 4	Resting state; RMP established



During Phase 2 - plateau:
Catecholamines → ↑ inward current of Ca (by phosphorylating DHPR)

Ca^{2+} channel blocker drugs → ↓ inward current

Refractory Period of Cardiac Muscle

	Absolute Refractory Period	Relative Refractory Period
Definition	Cardiac muscle cannot be excited while it is contracting	Cardiac muscle can be excited by strong stimulus
Benefit	Long ARP	-
Time	Depolarization and 2/3 repolarization	Repolarization
Duration	0.25 - 0.3 sec	0.05 sec

- Long absolute (effective) refractory period will prevent cardiac muscles from being tetanized.
- The duration of the effective refractory period is approximately equal to the duration of the mechanical event.

Cardiac Muscle is a Syncytium

- Cardiac muscle functions as a syncytium as each muscle cell is electrically connected to its neighboring cells through the gap junctions.
- Thus, stimulation of a single myocyte:

  → the action potential spreads from cell to cell through the gap junctions.

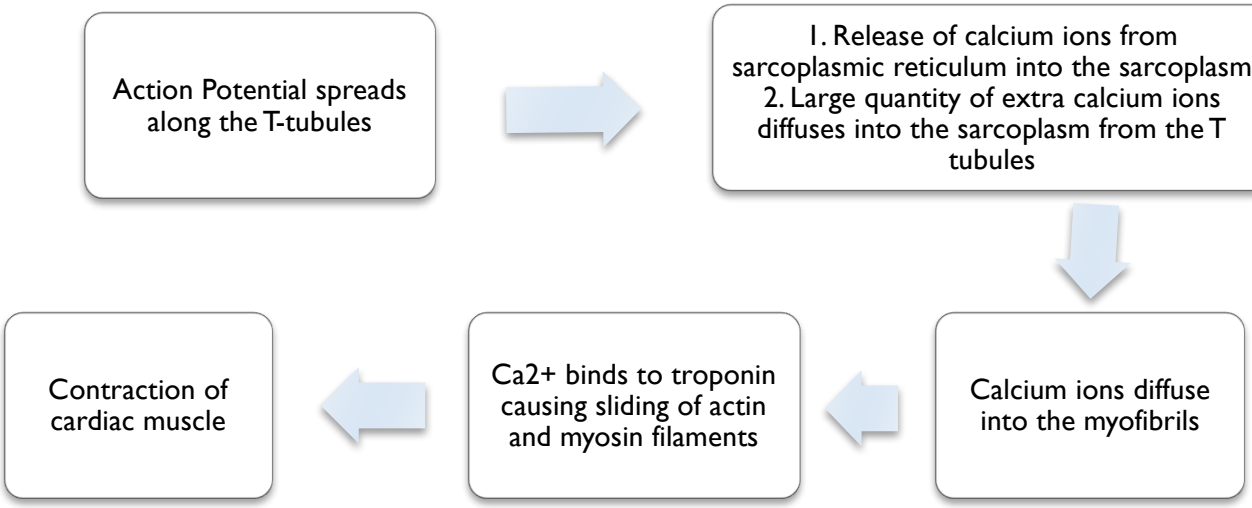
  → synchronous contraction of all the myocytes.
- The atrial syncytium is separated from the ventricular syncytium by the fibrous tissue surrounding the valvular openings (fibrous skeleton of the heart).

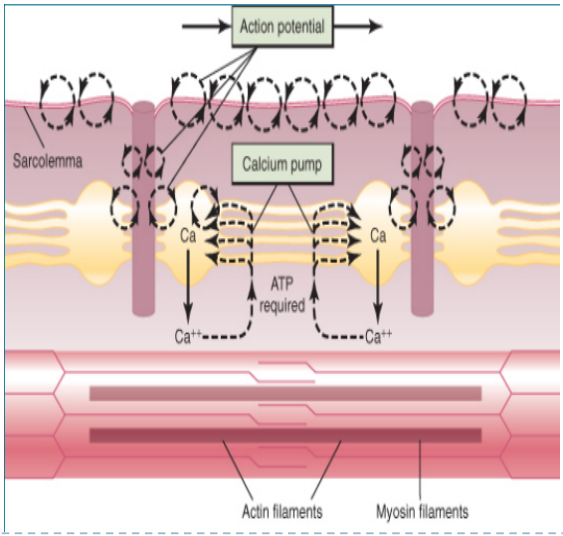
Contraction Cycle

- **Contraction cycle:** it is the continuous cycling of cross-bridges.
- As long as calcium concentrations remain high, actin and myosin cross-bridges interact to produce contraction of the muscle, similar to that seen in skeletal muscle.
- ↑ Ca → ↑ contraction ↓ Ca → ↓ contraction
- Skeletal muscle is susceptible to rigor (تيبس) if no ATP is present in the muscle cell to bind to the myosin head and allow it to **detach** from the actin filament.
- Cardiac muscle is unlikely to ever undergo rigor, due to the large amounts of mitochondria producing ATP.

Excitation Contraction Coupling

- Excitation – Contraction Coupling: is the mechanism by which the action potential causes muscle contraction.
- Action potential spreads to the interior of the cardiac muscle fiber along the transverse (T) tubules.
- The T tubules of cardiac muscle have a diameter 5 times as great as that of the skeletal muscle tubules.
- The strength of contraction of cardiac muscle depends to a great extent on the concentration of calcium ions in the extracellular fluids.
- At the end of the Plateau of the action potential → calcium ions are pumped back into the sarcoplasmic reticulum and the T-tubules → contraction ends (repolarization)





- Each contraction involves the hydrolysis of an ATP molecule for the process of contraction and sliding mechanism.
- Cardiac muscles are continually contracting and require substantial amounts of energy.
- The energy is derived from ATP generated by oxidative phosphorylation in the mitochondria.
- The myocytes contain large numbers of mitochondria.

Factors Affecting Cardiac Contractility

Positive ionotropic effects:	Negative Ionotropic effects:
• These are the factors/mechanisms that increase the cardiac contractility. • Sympathetic stimulation (catecholamines) • Calcium ions	• These are the factors/mechanisms that decrease the cardiac contractility. • Parasympathetic stimulation (vagal – of the vagus nerve- stimulation) • Acetylcholine

1. Sympathetic stimulation:

- Catecholamines interact with beta-adrenergic receptors → activation of adenylyl cyclase. This increases intercellular levels of cAMP.
- cAMP activates protein kinases which promote the phosphorylation of L-type Ca2+ channels.
- Phosphorylation of L-type Ca2+ channels increases the influx of Ca2+ during the action potential and hence more Ca2+ is released from the sarcoplasmic reticulum.

2. Parasympathetic stimulation:

- Interaction of acetylcholine with muscarinic receptors on cardiac muscle cell, and Inhibition of the release of norepinephrine from neighboring sympathetic neurons.
- Interaction of acetylcholine with muscarinic receptor inhibits adenylyl cyclase → ↓ intracellular levels of cAMP.
- The reduction in cAMP leads to a reduction in Ca2+ influx during the action potential , and thus a decrease in contractility.
- The reduction in contractility induced by parasympathetic stimulation is seen primarily in the atria.

Cardiac electrical activity

The Autorhythmicity, Excitability and Conductivity are Electrophysiological properties of the heart

Excitability

The Contractility is **Mechanical property of the heart (mechanical response to excitation)**

Cardiac electrical activity

Autorhythmicity

Contractility

Generating rhythmical electrical impulses independent of any extrinsic stimulation . Impulse generate in SA node

Conductivity

The conduction system specialized cells of the heart carry cardiac impulses rapidly to the myocytes in the atria, and after a pause, to the myocytes in the ventricles.

The atria contract about one sixth (1/6) of a second ahead (before) of ventricular contraction. To allow filling of the ventricles before they pump the blood into the circulation

Contain of

SA node

Bachmann's Bun

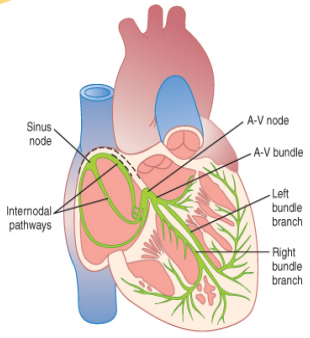
internodal pathway

AV node

AV bundle (Bundle of His)

Left and right bundle branches

Purkinje fibers



Potassium Equilibrium Potential

Potassium : is the generator of the resting membrane potential.
Intracellular concentration of K^+ is 140 and extracellular concentration is 4 → efflux of K^+ down concentration gradient.
This causes the intracellular charge to be negative due to :

1. K^+ efflux
2. negative intracellular ions (mainly organic phosphates and intracellular proteins) not being able to accompany the K^+ ions.

The Nernst Equation

It describes: the balance of electrical and chemical forces across a cell membrane. And we use to calculate Potassium Equilibrium Potential.

$$Em = 61.5 \log 10 \frac{[X]e}{[X]i}$$

Note the subscript 'e' is usually replaced by 'o'.

Em = (equilibrium potential for particular ion)
[X]e = concentration of ion in ECF
[X]i = concentration of ion in ICF

According to Nernst equation:
Membrane permeable to potassium:

- $E_K = 61.5 \log_{10} \frac{4}{140} = -95$ mV

Membrane permeable to sodium:

- $E_{Na} = 61.5 \log_{10} \frac{140}{10} = +71$ mV

Ion	Extracellular concentrations (mM)	Intracellular concentrations (mM)*	Equilibrium potential (mV)
Na^+	145	10	70
K^+	4	135	−94
Ca^{++}	2	10^{-4}	132

- E_K to K+ = -95 mV
- RMP = -90 mV
- We can conclude from the values that the RMP is mainly due to potassium efflux and not sodium influx.
- **But if RMP is caused by K efflux, why aren't they equal?**
  RMP increased because small amounts of Na diffused into cell. The diffusion of Na is called background currents

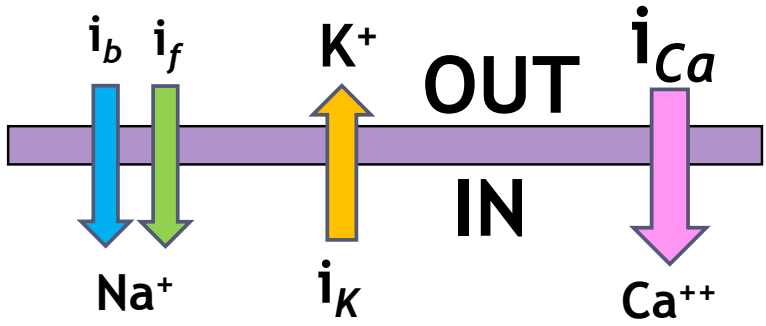
Electrical Activity of The Pacemaker. Auto-rhythmicity

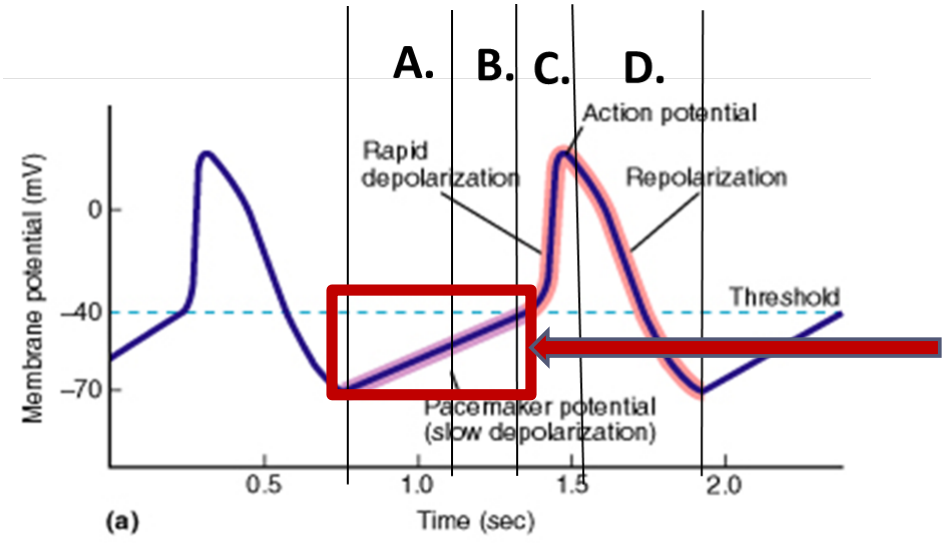
The decay of pacemaker potential with time is caused by:		
Early stage		**Later stage**
A small current of Na^+ flow into the cell. This current can be (i_f and i_b):	Membrane permeability to K^+ gradually falls. As a result the outward background current i_k falls progressively This will allow the inward currents (i_f **and** i_b) to dominate increasingly.	Ca^{2+} current in the later part.

I_f a specialized pace maker current termed

I_b the inward background current

f= funny channels: channels for sodium on SA membrane)





As time passes, pacemaker potential decays (decreases in negativity)

Conduction of Impulses.
Conductivity

SA Node

- **Location:** in the superior lateral wall of the right atrium near the opening of the superior vena cava.
- **Functions:** Pacemaker of the heart
  - Its rate of rhythmic discharge is greater than any other part in the heart.
  - Highest frequency.
- SA Node Is capable of originating action potentials.

AV Node

- **Location:** in the posterior wall of the right atrium.
- **Function:** delay (stopping) in the conduction of impulses (0.1 sec).
- This allows time for the atria to empty the blood into the ventricles before ventricular contraction begin.

The Purkinje system

- **Purkinje fibers** are very large fibers.
- Transmit action potentials at a very high velocity (1.5-4.0 m/sec).
- Highest speed of conduction.
  - Very high permeability of gap junctions → ions are transmitted easily from one cell to the next → enhance the velocity of transmission
- Ventricular muscle contract at almost the same time.

Conduction Velocity (CV) in heart

CV depends on: current spread, hence, diameter and number of gap junctions between cells (larger diameter, more gap junctions → faster conduction).

Purkinje fibers: have **very large diameter** and **more gap junctions** with high permeability.

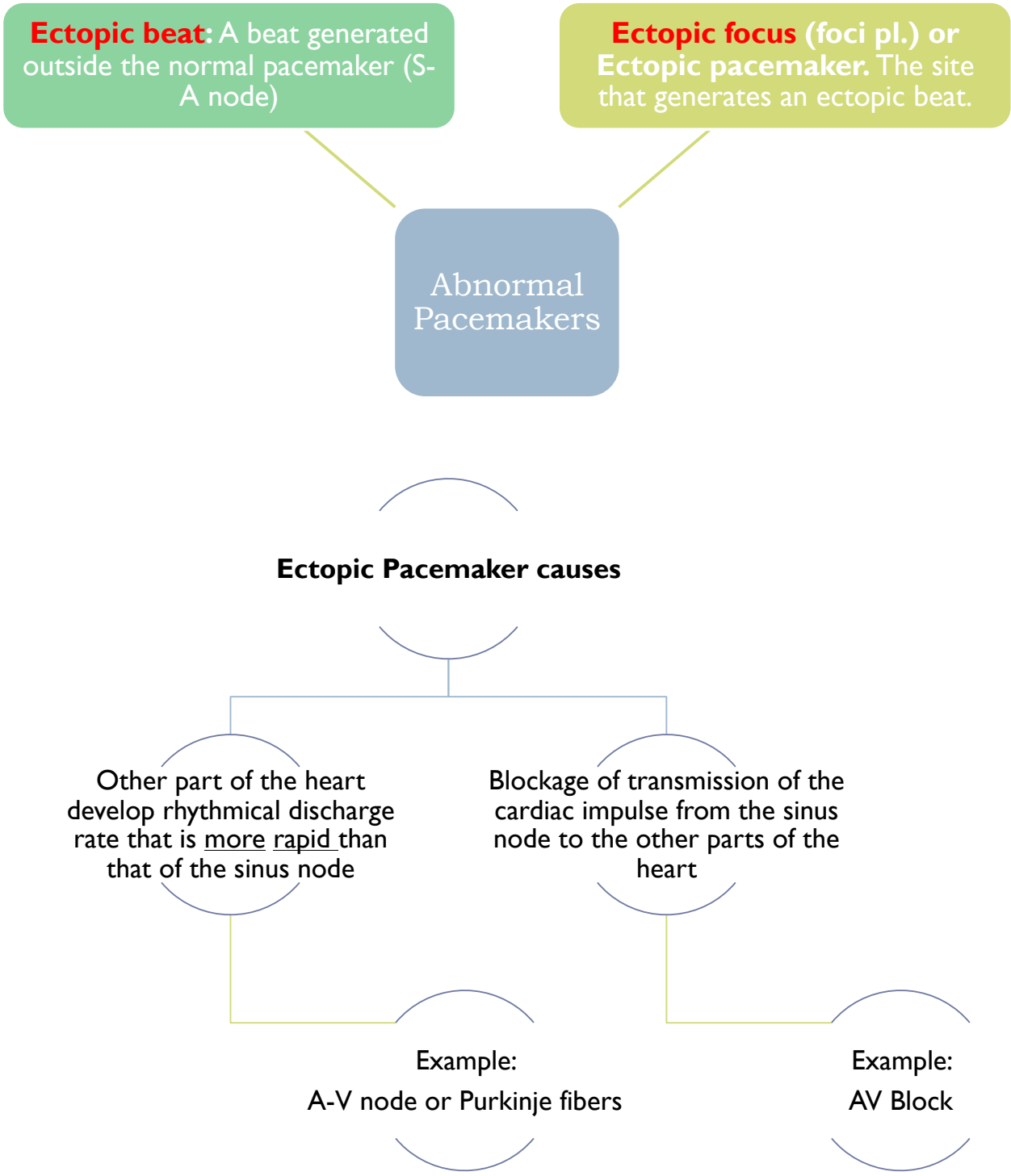
AV node and bundle (Bundle of His): have small diameter and few gap junctions.

The **high conduction** velocity of Purkinje fibers is to ensure that the ventricular myocytes contract at almost the same time.

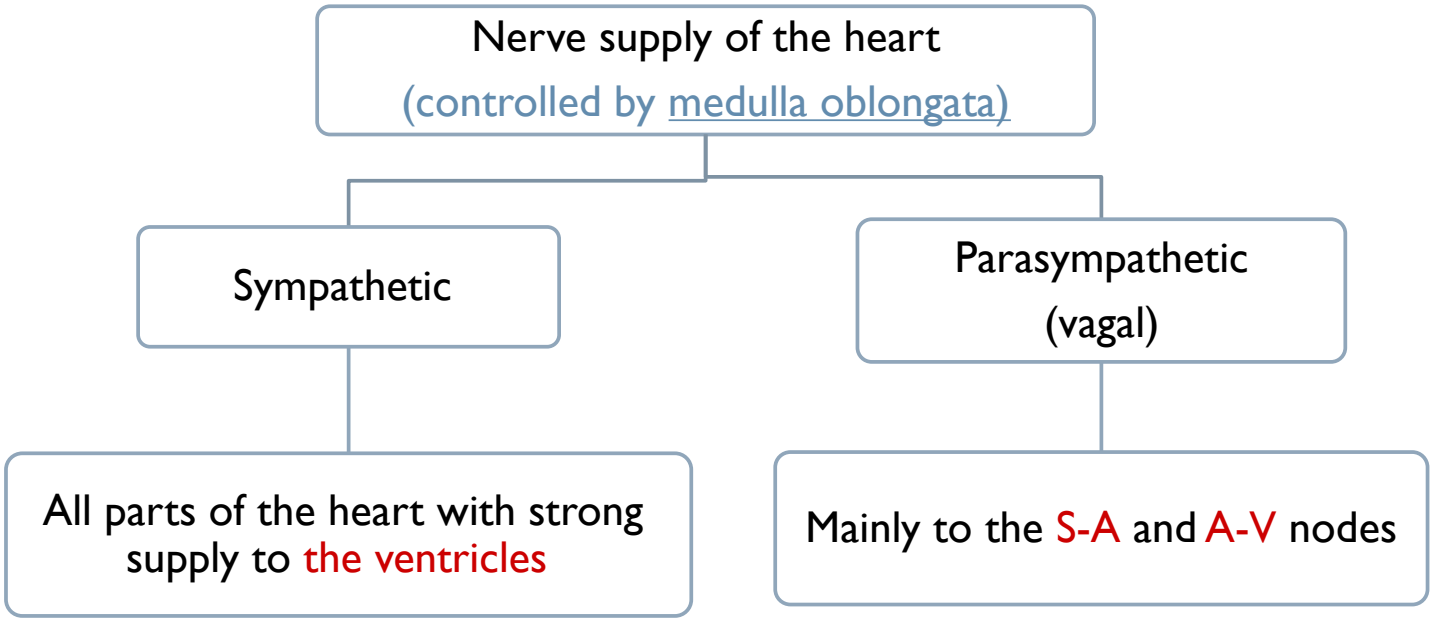
Approximate CV:

SA node	0.05 m/sec
Atria	0.3m/sec (internodal pathway 1.0m/sec)
AV node	0.05m/sec
Bundle of His	1 m/sec
Purkinje system	4 m/sec
Ventricular muscle	1 m/sec

Abnormal Pacemakers



Control of the heart Rhythmicity and impulse conduction by the cardiac nerves



Increase the :

- Rate of rhythm of the S-A node.
- Transmission (conduction) of the impulses to the A-V node.
- Force of contraction.

Decrease rate of rhythm of the S-A node and transmission of impulses to the A-V node.

Strong stimulation of the vagi:

- Stop the rhythmical excitation completely by the S-A node.
- Block transmission of cardiac impulses completely from the atria to the ventricle.

Ventricular Escape: some point in the Purkinje fibers develops a rhythm of its own

Lecture #3,4,5,10 Cardiac Cycle, ECG, Heart sounds and murmurs

Valves of the Heart

- There are 4 valves. Found at entry & exit of each ventricle.
- Each Ventricle has an entrance and an exit which are guarded by Cardiac Valves. The valves allow blood flow in only one direction.
- When the AV valves are open, Semilunar valves are closed and the opposite is true. Opening and closure of the valves is based on the pressure gradient across the valves.
- AV valve cusps are held by the Chorda Tendinea to Papillary muscles; this is to limit movements and eversions of the valves during ventricular systole.
- While the papillary muscles are connected to the AV valves they DO NOT open or close them.

The Cardiac Cycle; The Heart Beat

- The cardiac cycle (heart beat) is a sequence of events that take place in the heart in each beat and consists of alternate periods of systole (contraction and emptying) and diastole (relaxation and filling).
- When the heart rate is 72 Beat/min the duration of the cardiac cycle is 0.8 sec. The duration is shortened with increase in HR (Heart Rate).
- The atria and ventricles go through separate cycles of systole and diastole. Contraction happens with excitation, whereas relaxation follows the subsequent repolarization.
- Ventricle contraction generate pressure which is responsible for orderly blood movement.
- The **Ventricles are flow and pressure generators**. (Blood flows from an area of high pressure to an area of low pressure.)
- The actual pump is the ventricles.

Events During the Cardiac Cycle

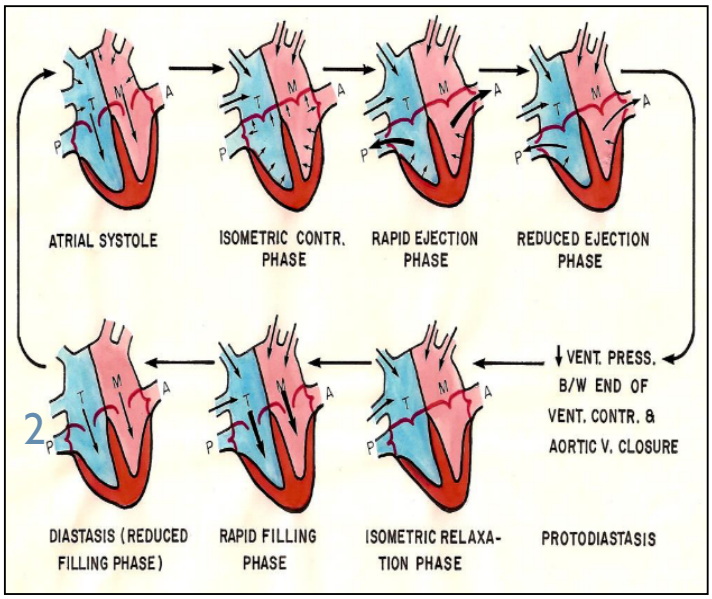
Electrical Events → Mechanical Events → Pressure Changes → Volume Changes → Heart Sounds

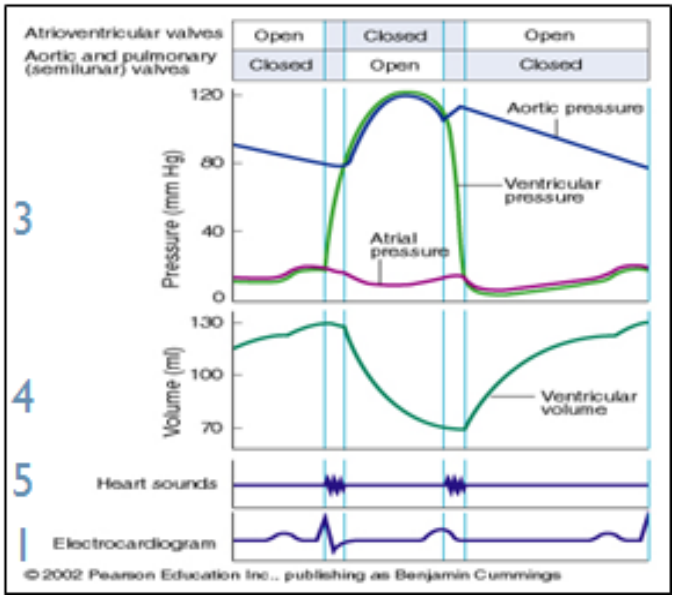
Events are the same in the right & left sides of the heart, but with lower pressures in the right side.

Electrical event ⟶ Excitation and ECG changes

Contraction followed by relaxation ⟶ Mechanical event

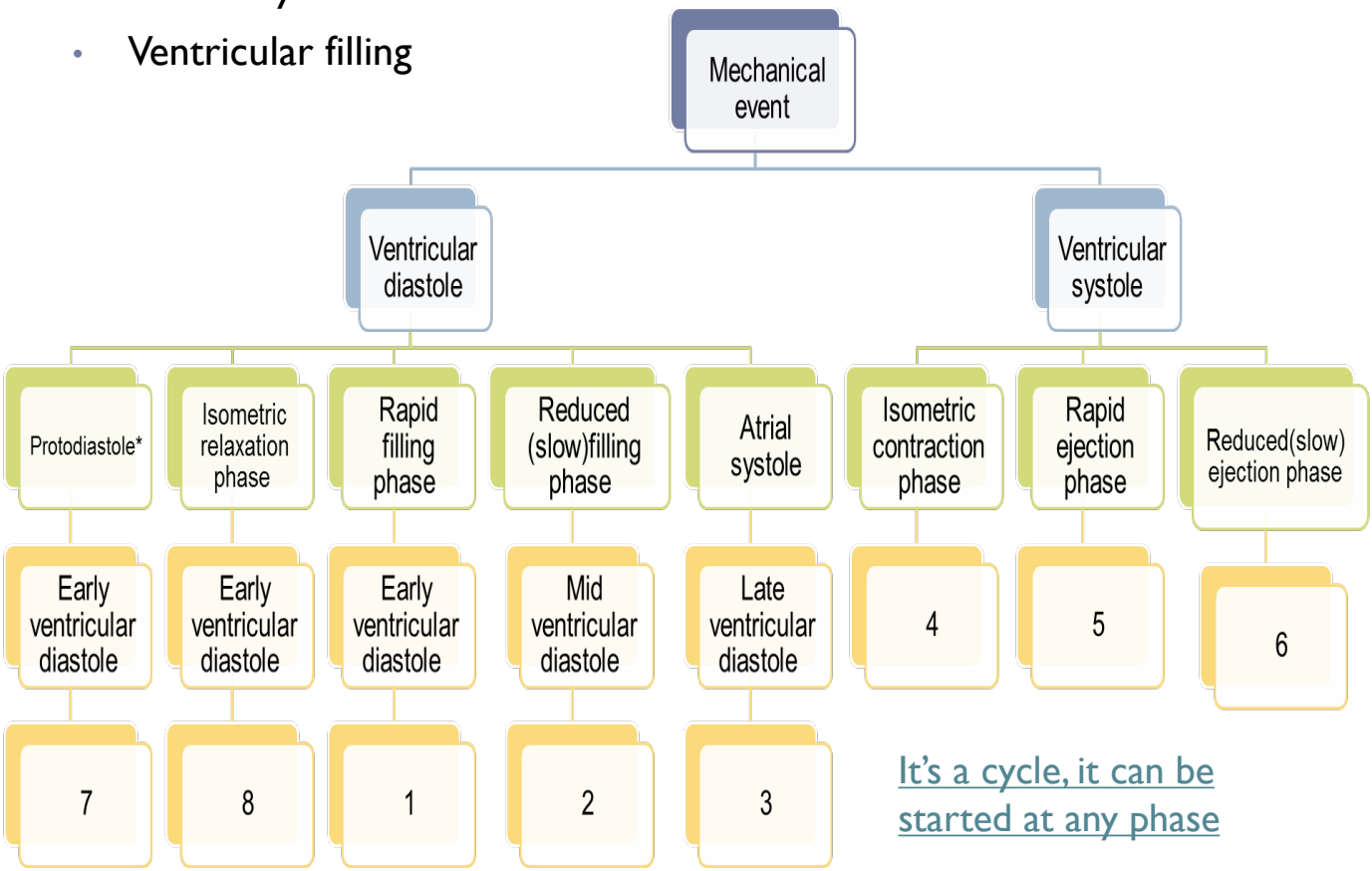
- Ventricular pressure changes
- Ventricular volume changes
- Valve closure ↓ Heart sound
  - عندما تغلق valve يظهر صوت القلب
  - Valve opening
- Aortic Pressure changes
- Right atrial pressure changes
  - Jugular venous waveforms





Mechanical Events (Phases) During the Cardiac Cycle

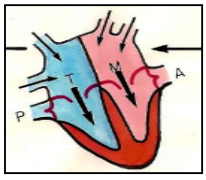
- Each cardiac cycle (heartbeat) consists of 2 major periods (phases):
  - Systole (contraction) and Diastole (relaxation).
  - repeated in (Relaxation) next beat (Contraction).
- The atria and ventricles go through separate cycle of Systole and Diastole.
- Normally, diastole is longer than systole.
- Tissues receive blood during systole and diastole
  - Ventricular systole= 0.3 sec
  - Ventricular diastole= 0.5 sec
  - Atrial systole= 0.1 sec
  - Atrial diastole = 0.7 sec
- Importance of the long ventricular diastole?
  - Coronary blood flow
  - Ventricular filling



Mechanical Events (Phases) During the Cardiac Cycle

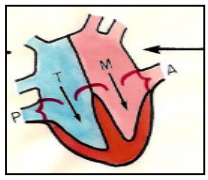
(Phase 1): Rapid Filling Phase; Early Diastole

- The SA Node did not reach threshold which means it did not get the AP yet
- The atrium is still also in diastole.
- The continuous inflow of blood results in increased pressure at the atrium which exceeds the pressure of the ventricles → opening the mitral cusp (bicuspid)
- Atrial pressure > ventricular pressure.
- This pressure differential, the AV valve is open, and blood flows directly from the atrium into the ventricle.
- 60-70 % of the blood passes Passively to the ventricles along pressure gradient resulting in:
- Increase in ventricular volume rapidly
- Increase in Ventricular pressure
- Decrease in Atrial pressure
- 3rd heart sound is heard



(Phase 2): Reduced Filling Phase (diastasis); Mid Diastole

- AV valves are still open
- The remaining atrial blood flows slowly into the ventricles.
- LV volume ↑ (slowly.)
- LV pressure gradually ↑(Because of filling)



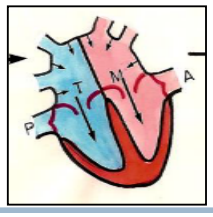
Atria	Ventricles	AV Valves	SL Valves	ECG
Diastole	Diastole	Opened	Closed	T-P interval

- Aortic pressure is still decreasing

Mechanical Events (Phases) During the Cardiac Cycle

(Phase 3): Atrial Systole; Late Ventricular Diastole

- Preceded by atrial depolarization.
- The SA node reaches threshold and fires
- Atrial contraction (-At end of ventricular diastole- systole duration 0.1) → rise in atrial pressure which is see as a wave.
- The atrial pressure exceeds the ventricle pressure means AV valve remains open and semilunar is closed.
- More blood is squeezed into the ventricle
- Tops off last 27-30% of ventricular filling ≈ 40 ml → rise in ventricular pressure.
- Here it reaches EDV=average 135ml.
- In this phase blood cannot enter the atria which result in back flow to the jugular vein
- (which make us see the pulse)
- A 4th heart sound is heard here.
- Aortic pressure is still ↓.
- At ECG we see it as P wave.



Atria	Ventricles	AV Valves	SL Valves	ECG
Systole	Diastole	Opened	Closed	P wave

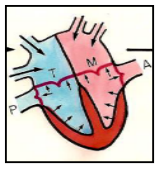
Effect of Atrial Contraction on Ventricle Filling

- At rest: Atrial contraction adds little extra blood to the ventricles.
- During Exercise: When the heart rate is high, ventricle filling time is reduced. Atrial contraction adds a substantial amount of blood to the ventricles.

Mechanical Events (Phases) During the Cardiac Cycle

(Phase 4): Isovolumetric Ventricular Contraction

- The impulse passes through the AV node and specialized conduction system to excite the ventricles → ventricular depolarization → QRS complex in the ECG
- At the beginning of ventricular systole period between closure of AV- vs. & opening of Semilunar- vs. Preceded by ventricular depolarization. Starts with closure of AV- vs.
- This is followed by ventricular contraction → ventricular pressure immediately exceeds atrial pressure → The AV valve is closed → 1st heart sound is heard.
- The aortic valve is still closed.
- Ventricular pressure must continue to increase before it exceeds aortic pressure to open the aortic valve.
- Because no blood enters or leaves the ventricle, the ventricular chamber remains at constant volume, and the muscle fibres remain at constant length.
- This period lasts about 0.04 - 0.05 s, until the pressures in the left ventricle exceeds the pressures in the aorta (80 mm Hg) and the aortic valve opens.
- During isovolumetric contraction, the AV valves bulge into the atria, causing a small but sharp rise in atrial pressure → c wave in the atrial pressure curve.
- Aortic pressure is still ↓.
- Ventricular pressure ↑.

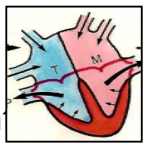


Atria	Ventricles	AV Valves	SL Valves	ECG
Diastole	Systole	Closed	Beginning: closed End: opened	QRS complex

- Ventricle is a closed chamber.
- Volume in ventricle = EDV
- Ventricle contracts with no changes in volume.

Mechanical Events (Phases) During the Cardiac Cycle

(Phase 5): Rapid (maximum) Ejection Phase



- Contraction of the ventricle → ↑ intraventricular pressure. When ven pressure exceeds aortic pressure, i.e., at ≈ 80 mmHg → the aortic valve is forced open → ejection of blood begins. Semilunar valve is open
- Ejection is rapid during this phase, then slowing down as systole progresses during the slow ejection phase (next phase).
- Ventricular volume decreases substantially as blood is rapidly pumped out.
- The ejected volume is the SV. ≈ 75% of SV is ejected during this phase.
- the remaining volume is the ESV (averages about 65 ml).
- Blood is forced into the aorta faster than blood is draining off into the smaller vessels at the other end → ↑ of aortic pressure.
- Peak pressures in the left ventricle is about 120 mm Hg. Late in systole, pressure in the aorta actually exceeds that in the left ventricle, but for a short period momentum keeps the blood moving forward.
- The atria are in diastole . The **AV valves** are pulled down by the contractions of the ventricular muscle, and atrial pressure drops → x decent in the atrial pressure curve.

(Phase 6): Slow (Reduced) Ejection Phase

- This is the last phase of ventricular systole, atria are in diastole
- Ejection is slow → ventricular volume ↓ more slowly.
- ≈ 25% of SV is ejected during this phase. Almost 25% of ventricular blood
- The intraventricular pressure declines somewhat before ventricular systole ends.

Mechanical Events (Phases) During the Cardiac Cycle

(Phase 6): Slow (Reduced) Ejection Phase (Cont..)

- Aortic valve closes at the end of this phase, as a result of:
- ↓ Ventricular pressure < aortic pressure
- When LV pressure 110 mmHg (Aortic back pressure& Aortic-v closes)
- The atria are in diastole.

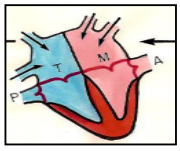
(Phase 7): Protodiastolic Phase

- The T wave on the ECG signifies ventricular repolarization occurring at the end of ventricular systole.
- The already falling ventricular pressures drop more rapidly. This is the period of protodiastole, which lasts for a very short period of time; ≈ 0.04 s.
- Physiologists have different opinion about the existence of this phase. Physiologists believe in its existence think that the aortic valve has not yet closed by the end of the slow ejection phase and that the protodiatolic phase is the period between the end of ventricular systole and closure of the aortic valve.
- Thus, protodiastole ends when the momentum of the ejected blood is overcome and the aortic valve closes, setting up transient vibrations in the blood and blood vessel walls
- → second heart sound (S2).
- After the valves are closed, pressure continues to drop rapidly during the period of isovolumetric ventricular relaxation, which follows.
- The atria are still in diastole. The atrial pressure continues to rise due to continuous venous return. However, atrial pressure is still lower than the ventricular pressure .

Mechanical Events (Phases) During the Cardiac Cycle

(Phase 8): Isovolumetric Ventricular Relaxation

- In beginning of diastole when the aortic valve closes, the AV valve is not yet open, because the ventricular pressure still exceeds atrial pressure, so all valves are once again closed for a brief period of time and no blood can enter or leave the ventricle. Preceded by ventricular repolarization.
- Period between closure of semilunar-vs& opening of AV-vs.
- The muscle fibre length and chamber volume remain constant.
- As the ventricle continues to relax → the pressure steadily falls.
- The atria are still in diastole. The atrial pressure continues to rise due to continuous venous return → v wave in the atrial pressure curve. However, atrial pressure is still lower than the ventricular pressure.
- The mitral valve opens at the end of this phase.
- This phase thus represents the beginning of diastole and it's the quiescent period between closure of the aortic valve and opening of the mitral valve.
- It lasts for ≈ 0.04 sec.



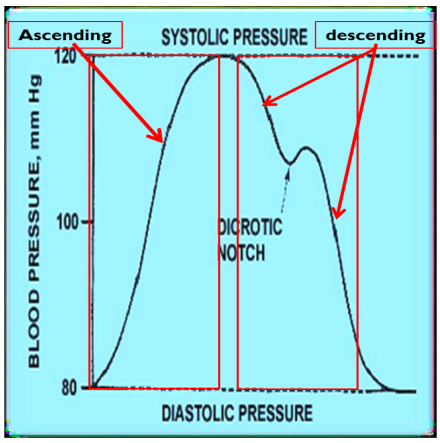
Atria	Ventricles	AV Valves	SL Valves
Diastole	Diastole	Beginning: closed End: opened	Closed

- LV is a closed chamber, i.e. relax with no changes in volume.
- Volume of blood in ventricle = ESV.
- AV- vs open at the end of this phase.

Changes in Aortic Pressure

Ascending or anacrotic limb

- This coincides with the 'rapid ejection phase'.
- The amount of blood that enters aorta > the amount that leaves
- Aortic pressure ↑ up to 120 mmHg



Descending (Catacrotic) Limb

- Passes in 4 stages:

↓Aortic pressure	• This coincides with the 'reduced ejection phase' • The amount of blood enters aorta < leaves
Dicrotic notch (incisura)	Due to closure of aortic valve • There is sudden drop in aortic pressure. • This notch is seen in the aortic pressure curve at end of ventricular systole.
Dicrotic wave	Due to elastic recoil of the aorta • Slight ↑ in aortic pressure
Slow ↓ aortic press	Up to 80 mmHg Due to continuous blood flow from aorta→ systemic circulation

Pulse Pressure

- Maximum aortic pressure = Systolic pressure (SP)= 120 mmHg
- Minimum aortic pressure = Diastolic pressure (DP)= 80 mmHg
- Pulse pressure (PP)= SP – DP= 120 – 80= 40 mmHg
- An increase in pulse pressure can indicate a hardening of the arteries. (arteries are pressure reservoirs).

AP Changes During the Cardiac Cycle

Wave				
upward deflection			downward deflection	
a wave	c wave	v wave	x descent (wave)	y descent (wave)
Atrial systole: ↑ atrial pressure during atrial systole (contraction)	+ve as a result of bulging of AV valve into the atria during 'isovolumetric contraction phase' -ve as a result of pulling of the atrial muscle & AV cusps down during 'rapid ejection phase', resulting in ↓ atrial pressure	Atrial diastole or ↑ venous return (VR) +ve: atrial pressure ↑ gradually due to continuous VR -ve as a result of ↓ atrial pressure during 'rapid filling phase'	Downward displacement or movement of AV valves during 'reduced ejection phase'	↓ atrial pressure during 'reduced filling phase'

Ventricular Volume Changes

Phases	Ventricular volume
1. Atrial systole	↑
2. Isometric contraction phase	Constant
3. Rapid ejection phase	↓ rapidly
4. Reduced ejection phase	↓ slowly
? Protodiastole	Constant
5. Isometric relaxation phase	Constant
6. Rapid filling phase	↑ rapidly
7. Reduced filling phase	↑ slowly

LV Pressure-Volume Loop:

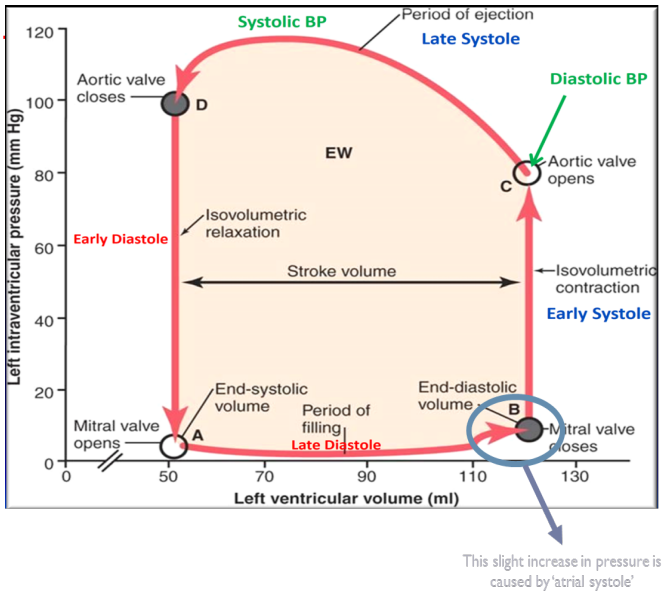
- Correlation of intra-ventricular changes in volume & pressure that occur during one cardiac cycle.
- Ventricular systole and diastole can be divided into early and late phases.

	Systole	Diastole
Early	Isovolumetric Contraction	Isovolumetric Relaxation
Late	Isotonic Contraction (Ejection phase)	Isotonic Relaxations (Filling phase)

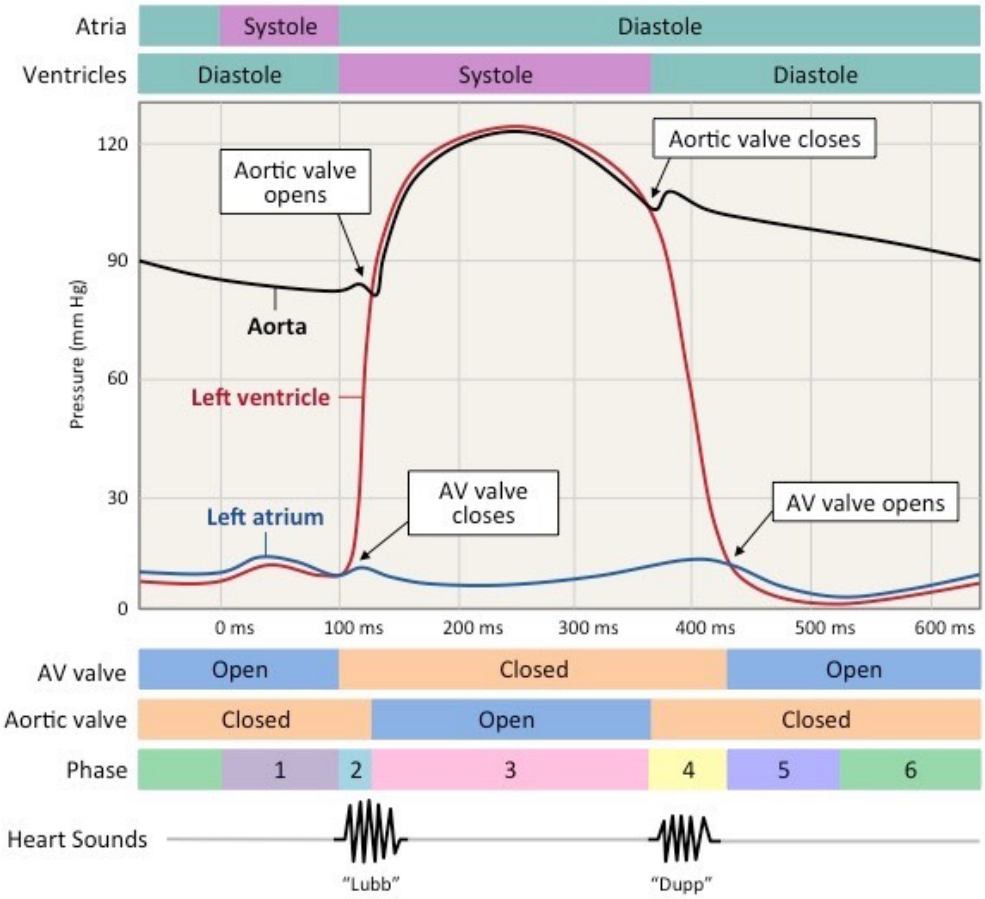
Cont.

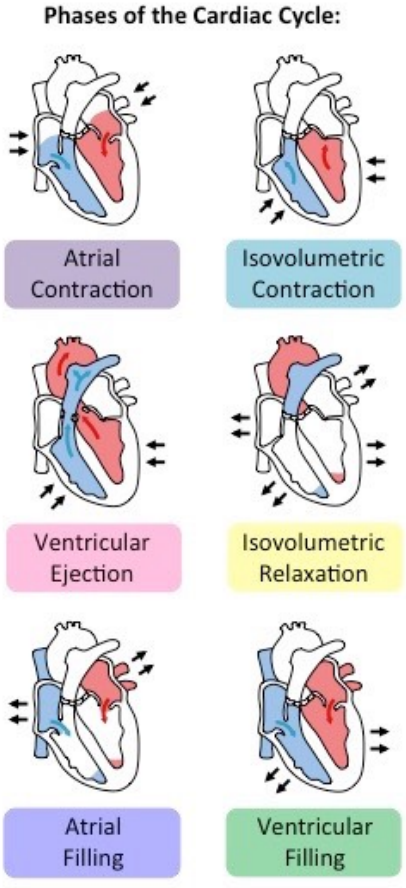
What you should remember about Pressure - Volume Loop

- Closer & opening of mitral & aortic- vs during each phase.
- Beginning of systole (B) & end (D.)
- Early & late systolic periods.
- Beginning of diastole (D) & end (B.) Early & late diastolic periods.
- Diastolic filling occurs between points A & B.
- Ejection occurs between points C & D.



Summary





ECG or EKG "Electrocardiogram"

If a recording electrode is applied on any point on the surface of the trunk, it will detect electrical waves reflecting the electrical activity in the heart. These electrical waves may be as small as 1 mv and are amplified, recorded on ECG paper / monitor / computer and stored.

When there are no propagating potentials, no waves are recorded.

is a recording of the electrical activity of the heart.

ECG

Types of information we can obtain from an ECG:

- Heart rate
- Normal intervals
- Rhythm
- Cardiac axis

Methods for Recording Electrocardiograms:

1- Computer-based and electronic display

2- Pen recorder and a moving sheet

Two electrodes are required

Active electrode	Reference electrode
Applied to a recoding point on the surface of the body.	serves a reference to the active electrode.

A positive wave is recorded when depolarization is propagating towards the electrode or when repolarization is propagating away from the electrode.

A negative wave is recorded when depolarization is propagating away from the electrode or when repolarization is propagating towards the electrode.

Cont.

- ECG is a diagnostic tool that records the electrical activity (action potentials) generated by the heart from chest surface, per unit time.
- To produce normal sinus rhythm, (3) criteria must be met:
  1. Action potential must originate in SA- node.
  2. SA nodal impulse must occur regularly at a rate of 60 – 100 impulses per minute.
  3. Activation of myocardium must occur in correct sequence & correct timing & delays.

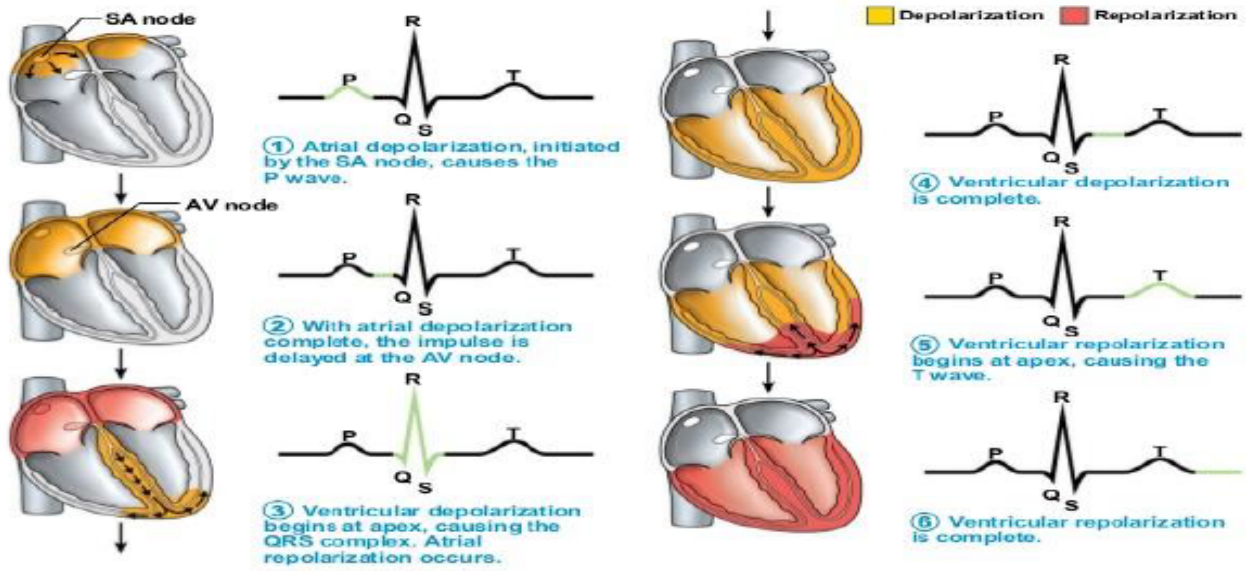
SA node rate: 60-100 b/min. Under vagal influence 70-80 b/min.

Action Potential	spread through the atria.	atrial contraction	The impulse then reaches AV-node, His Bundle & the Purkinje system to the farthest point in ventricles	Ventricles contract
Originates in SA-node at time zero. Atrial depolarization	It takes a total of (0.1 sec.)	For 0.1 sec.	0.08 - 0.1 sec	For a total time period of (0.3 sec.)

- In normal ventricles , current flows: From *negative* → *positive*,
- From the *base* toward → the *apex*

From *electronegative inner surface* → *electropositive outer surface*

- An electrode placed near the base of the heart is electronegative, and near the apex is electropositive
- The first area that depolarizes is the ***ventricular septum***



The Normal Electrocardiogram (ECG)

- The vertical calibration lines: Voltage(millivolt)
- 1 small square in the vertical calibration = 1 mm = 0.1 mv.
- 5 small lines (large square) = 0.5 mV.
- The horizontal calibration lines: Time (seconds)
- 1 inch(25 small lines) = 1 second
- Each inch is divided by 5 dark vertical lines
- The interval between the dark lines (large squares 5mm)= 0.2 second
- thin line (small squares 1mm)= 0.04 second

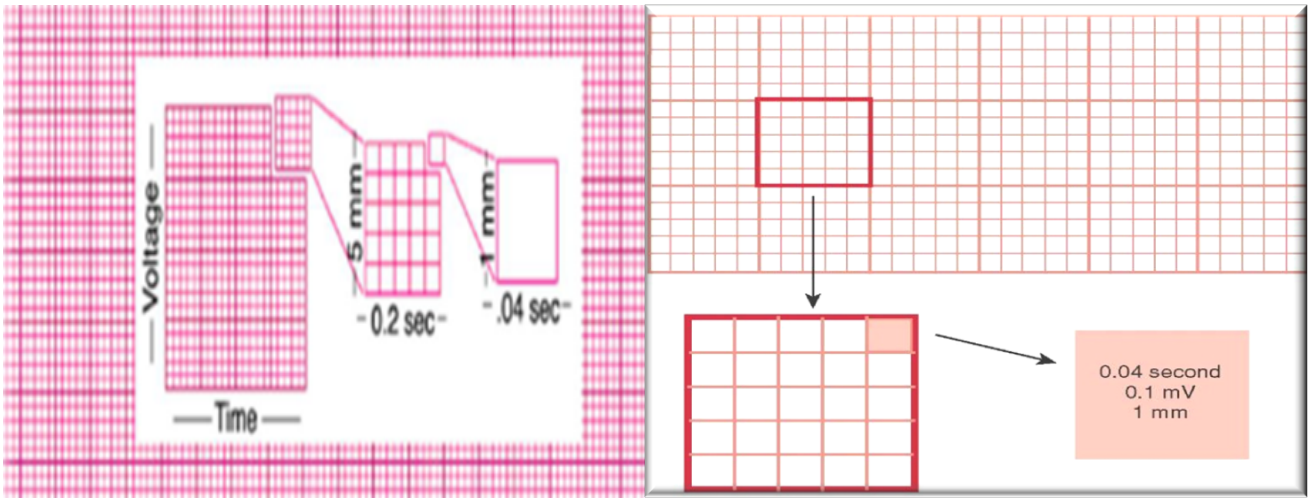
The depolarization wave spreads through the heart

↓

electrical currents pass (from bass to apex) into the surrounding tissue

↓

part of the current reaches the surface of the body



Normal Rate and Rhythm; Sinus Rhythm

- ✓ Impulses originate in the SA node regularly at a rate of 60-100 beats per minute in adults.
- ✓ P waves upright, uniform in size and contour from beat to beat.
- ✓ Each P is followed by a QRS complex with a resulting P:QRS ratio 1:1.
- ✓ All complexes are evenly spaced.
- ✓ PR interval is constant and within normal range.

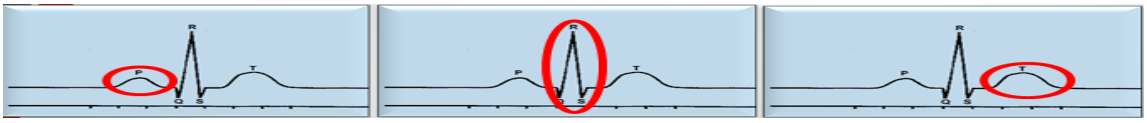
ECG waves

One heartbeat is normally recorded as:

- 3 waves: P-wave, QRS complex, T-wave

  3 positive waves (P,R,T) & 2 negative waves (Q,S)
- 3 segments: PR segment, ST segment, TP segment
- 3 time intervals: P-R interval, Q-T interval, R-R interval

ECG Wave	P- wave	QRS complex	T- wave
Cause	Atrial depolarization P-wave is recorded before the onset of atrial systole	Ventricular depolarization QRS complex is recorded before the onset of ventricular systole (isometric contraction phase)	Ventricular repolarization T-wave is recorded before the onset of ventricular diastole (isometric relaxation phase)
Represent	-Time of electrical impulse from SA node to spread through atrial muscle. -Duration = 0.08 – 0.1 sec -Precedes atrial contraction by 0.01 - 0.02 sec	-Measured from beginning of Q wave till end of S wave. -Consists of 3 waves: •Q wave: (-ve): Produced by depolarization of interventricular septum. •R wave: (+ve): Produced by depolarization of ventricular wall. •S wave: (-ve): Produced by depolarization of the base of the heart. -Duration = 0.1 sec. -Precedes ventricular contraction by 0.02 sec. -Occurs after P-wave by 0.12-0.2 sec = PR interval	-Occurs during latter part of systole, before the onset of diastole. -Ventricular repolarization progresses from apex to the base of the heart. -Duration = 0.27 sec.



N.B. Atrial repolarization occurs at the same time with ventricular depolarization. But, since ventricular depolarization wave is giant, it masks the atrial repolarization wave

ECG Intervals

P-R interval

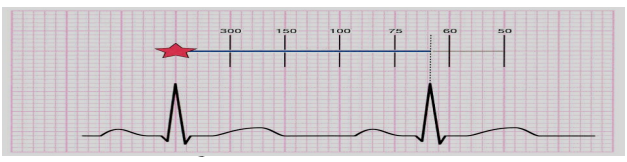
- P-R interval is the time from the initial depolarization of atria to the initial depolarization of ventricles.
- Time period measured from start of P- wave to start of QRS complex; Thus P-R interval includes P- wave & PR segment
- P-R interval range = 0.12-0.2 sec.
- An increase in conduction velocity through AV node will decrease P-R interval (sympathetic stimulation) & vice versa.

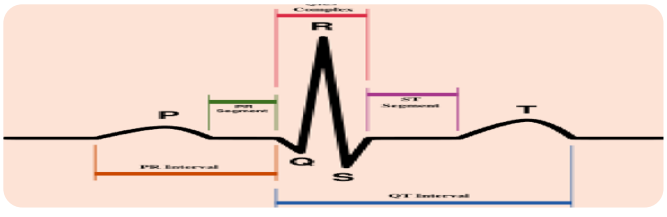
Q-T interval

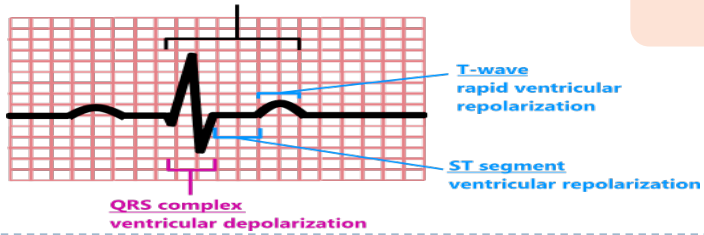
- The Q-T interval includes the QRS complex, ST segment & T- wave.
- It represents total time taken by ventricle to depolarize & repolarize [contraction of ventricles]
- Q-T interval range =0.35 – 0.45 sec.
- Approximate Refractory period of ventricle.

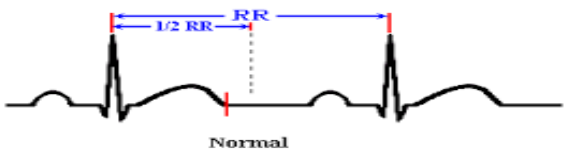
R-R interval

- The interval between two successive R- waves.
- It determines the heart rate & cardiac cycle length.
- Heart rate can be measured by counting the number of R- waves per minute.









ECG Segments

PR segment

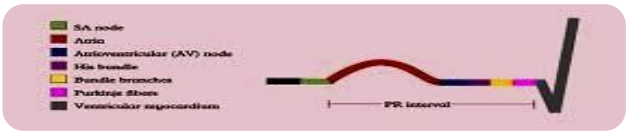
- P- wave is followed by brief isoelectric (zero voltage) flat portion of ECG that corresponds to AV- node conduction à PR segment.
- This segment correlates with conduction time through the AV- node & AV bundle or AV nodal delay = 0.13 sec.

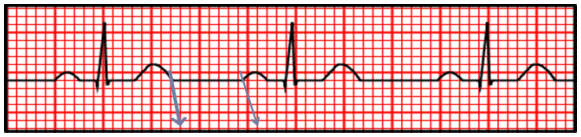
ST segment

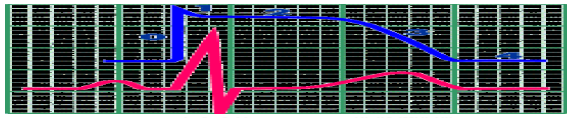
- Isoelectric segment follows the QRS complex, showing that there is no potential difference between areas of myocardium at this stage.
- At this time, both ventricles depolarized & roughly corresponds to the plateau phase of the ventricular action potential.
- J point: at end of QRS, zero reference potential for analyzing current of injury.

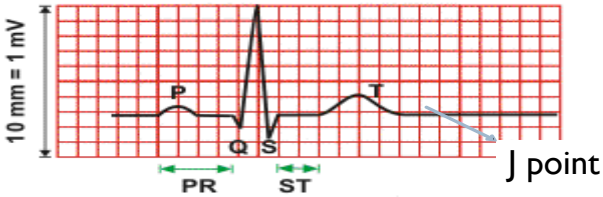
TP segment

- Time interval from ventricular repolarization till next atrial depolarization.
- Calculated from end of T- wave to beginning of P- wave.
- It represents ventricular filling.









No current flow in the heart during segment's time.

1. PR segment: AV- node delay.
2. ST segment: Cardiac muscle completely depolarized.
3. TP segment: Ventricular filling takes place.

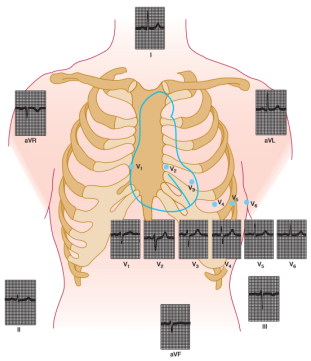
The ECG Leads

ECG leads

Lead: two wires and their electrodes to make a complete circuit

Bipolar Leads

The ECG is recorded from two electrodes These are the ECG records obtained when the active electrode is applied to a recording point and the reference electrode is applied to another recording point.



Unipolar Leads

These are the ECG records obtained when the reference electrode is at zero potential. The active electrode is applied to the recording points on the body surface.

I,II,III

Lead I: records the potential between left arm and right arm. The active electrode is at VL and the reference electrode is at VR.

Lead II: records the potential between left leg and right arm. The active electrode is at VF and the reference electrode is at VR.

Lead III: records the potential between left leg and left arm. The active electrode is at VF and the reference electrode is at VL.

Augmented Limb Leads (aVR, aVL, aVF)

The two limbs are connected to the negative terminal of the ECG,and the third limb is connected to the positive

When the positive terminal is on:

The right arm (aVR): inverted

The left arm (aVL)

The left leg (aVF)

All are similar to the standard limb leads

Chest Leads (V1,V2,V3,V4,V5, V6)

Recorded from the:

anterior surface of the chest (V1,V2,V3,V4,V5,V6)

Positive electrode on the chest

The indifferent electrode is the negative electrode connected to the right arm, left arm, and left leg

V1 and V2: QRS are mainly negative because the chest leads are nearer to the base of the heart

V3,V4 and V6 are mainly positive because the chest electrode are nearer to the apex

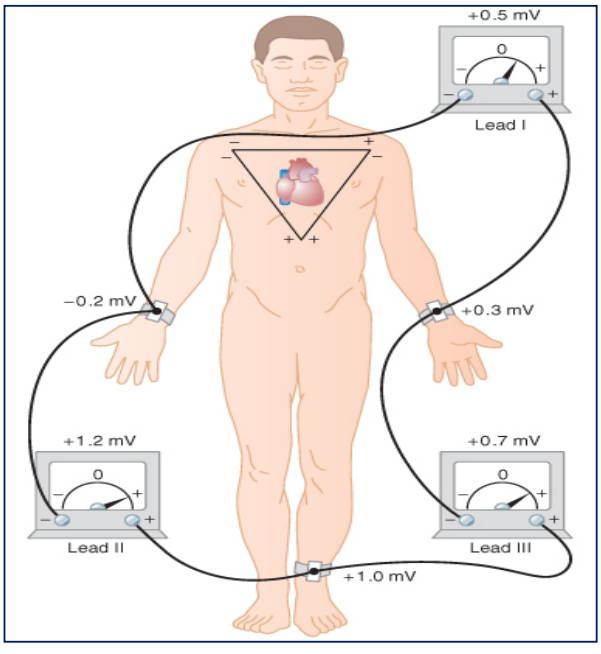
Einthoven's Triangle & law

Einthoven's Triangle:

- is drawn around the area of the heart
- The two apices at the upper part of the triangle represent the points at which the two arms connect electrically
- The lower apex is the point at which the left leg connects

Einthoven's Law:

- if the electrical potential of any two of the three bipolar limb leads are known, the third one can be determined mathematically by summing the first two (note the +ve and -ve signs)
- *The sum of the voltage in* *Lead I + Lead III= Lead*
- ***Einthoven's*** law: $E_I + E_{III} = E_{II}$



In the ECG, at any given instant, the potential of any wave in lead II is equal to the sum of the potentials in lead I and III.

Heart Sounds

- Detected over anterior chest wall by:

  1- Auscultation (Stethoscope.)

  2- Phonocardiography (sound recording device.)

- The 4 heart sounds can be detected:

  - 1st & 2nd heart sounds (usually audible)
  - 3rd & 4th heart sounds (of low pitch, usually not audible)

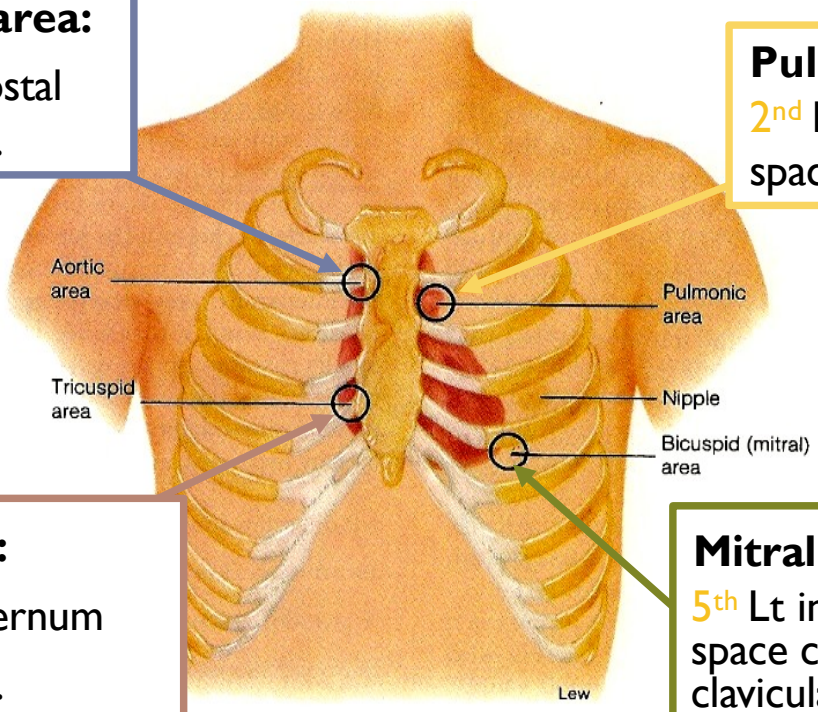
- Important for diagnosis of valvular heart diseases (murmurs)

Heart sounds windows:

It is best heard at 4 certain areas:

Aortic area:
2nd Rt costal cartilage.

Pulmonary area:
2nd Lt intercostal space.



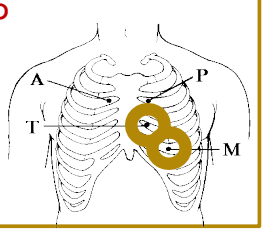
Tricuspid area:
lower part of sternum towards Rt side.

Mitral area:
5th Lt intercostal space crossing mid-clavicular line, or 9 cm (2.5-3 in) from sternum.

Heart Sounds

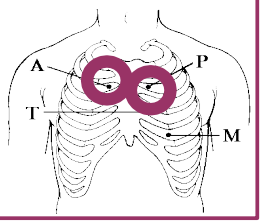
S1

- Due to closure of the atrio-ventricular valves. Very IMP
- It marks beginning of ventricular systole.
- Recorded at the beginning of the 'isovolumemetric contraction' phase.
- Long in duration (0.15 sec.) longest duration of all sounds. very imp
- Of low pitch and loud (LUB).
- Frequency range (25-35) (25-45 in boys' slides) Hz.
- Best heard at Mitral & Tricuspid areas.



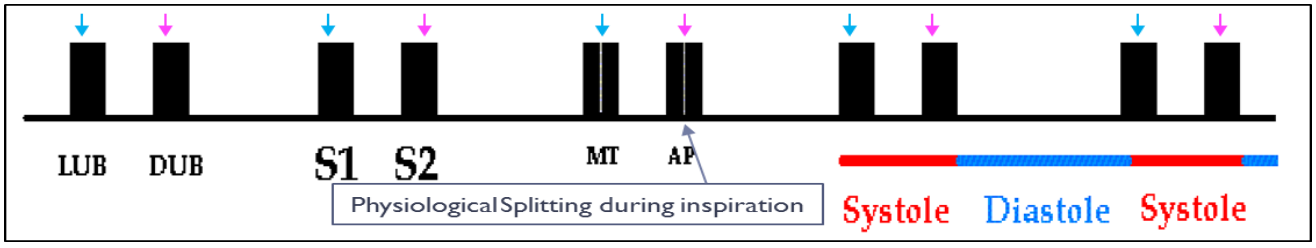
S2

- Due to closure of semilunar valves.
- Marks the beginning of ventricular diastole and end of ventricular systole.
- Recorded at the beginning of the 'isometric relaxation' phase.
- Short in duration (0.11-0.125 sec.) (0.12sec. in boys' slides).
- Of high pitch, soft, and sharp (DUB).
- Frequency : 50Hz.
- Best heard at Aortic & Pulmonary areas.



Physiological Splitting:

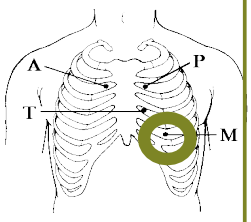
- S2 splits physiologically into 2 sounds during **inspiration.**
- This splitting occurs due to delay closure of pulmonary valve.

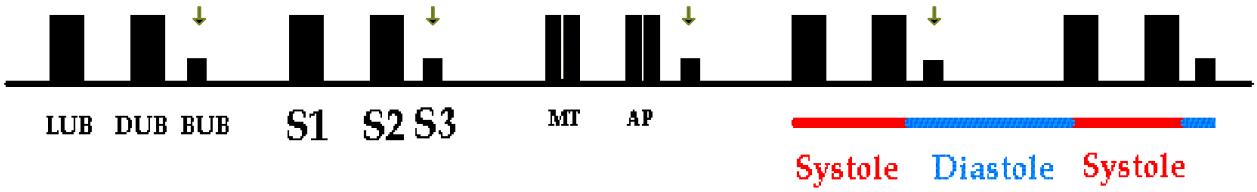


Heart Sounds

S3

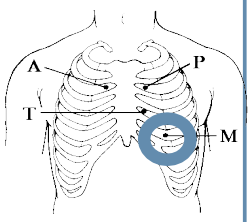
- Recorded during the 'rapid filling' phase, due to rush of blood into the ventricle. Very imp
- Duration 0.05 sec.
- S3 is usually not audible(soft and very low pitch)
- heard in children and young individuals.IMP
- Best heard at Mitral area.

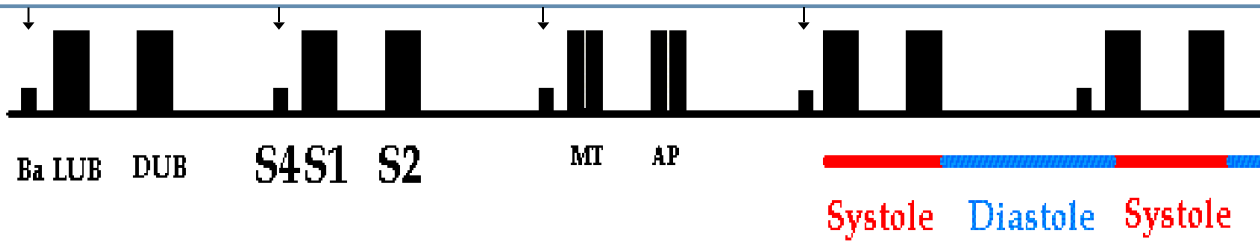




S4

- Recorded during 'atrial systole.'
- Duration 0.04 sec.
- S4 is usually not audible (very low pitch)
- Usually heard in elderly.IMP
- Best heard at Mitral area.





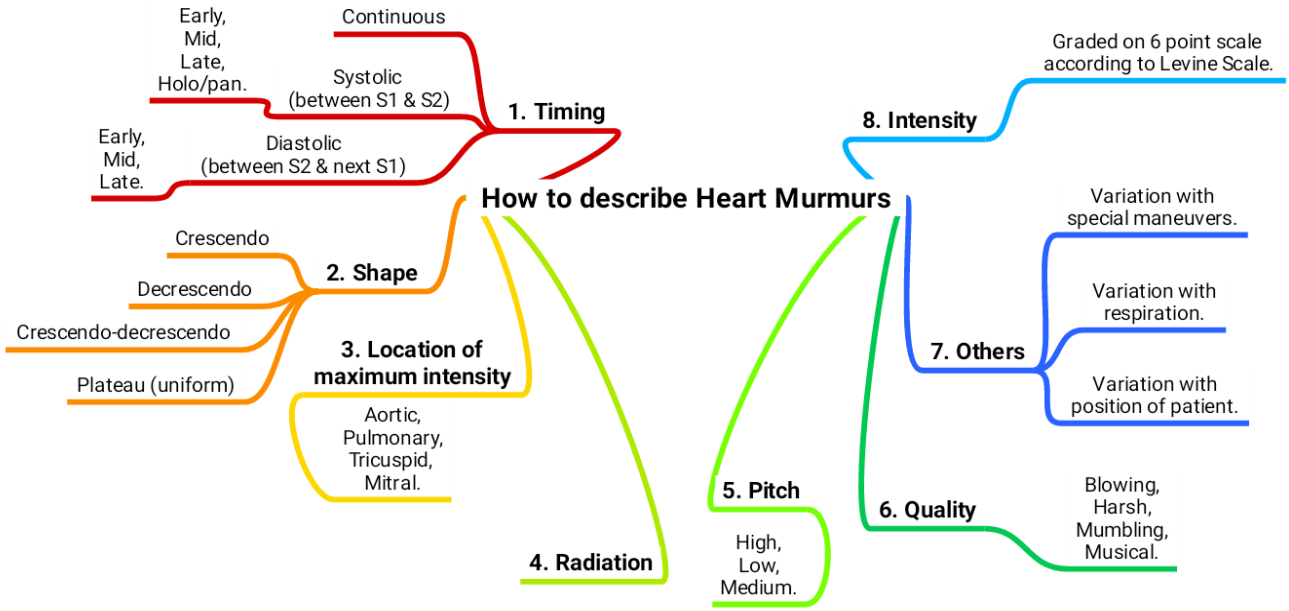
Significance of Heart Sounds

- Important for diagnosis of abnormal heart sounds **(murmurs).**
- Murmurs are longer than heart sounds.
- **What makes noises in the heart?**

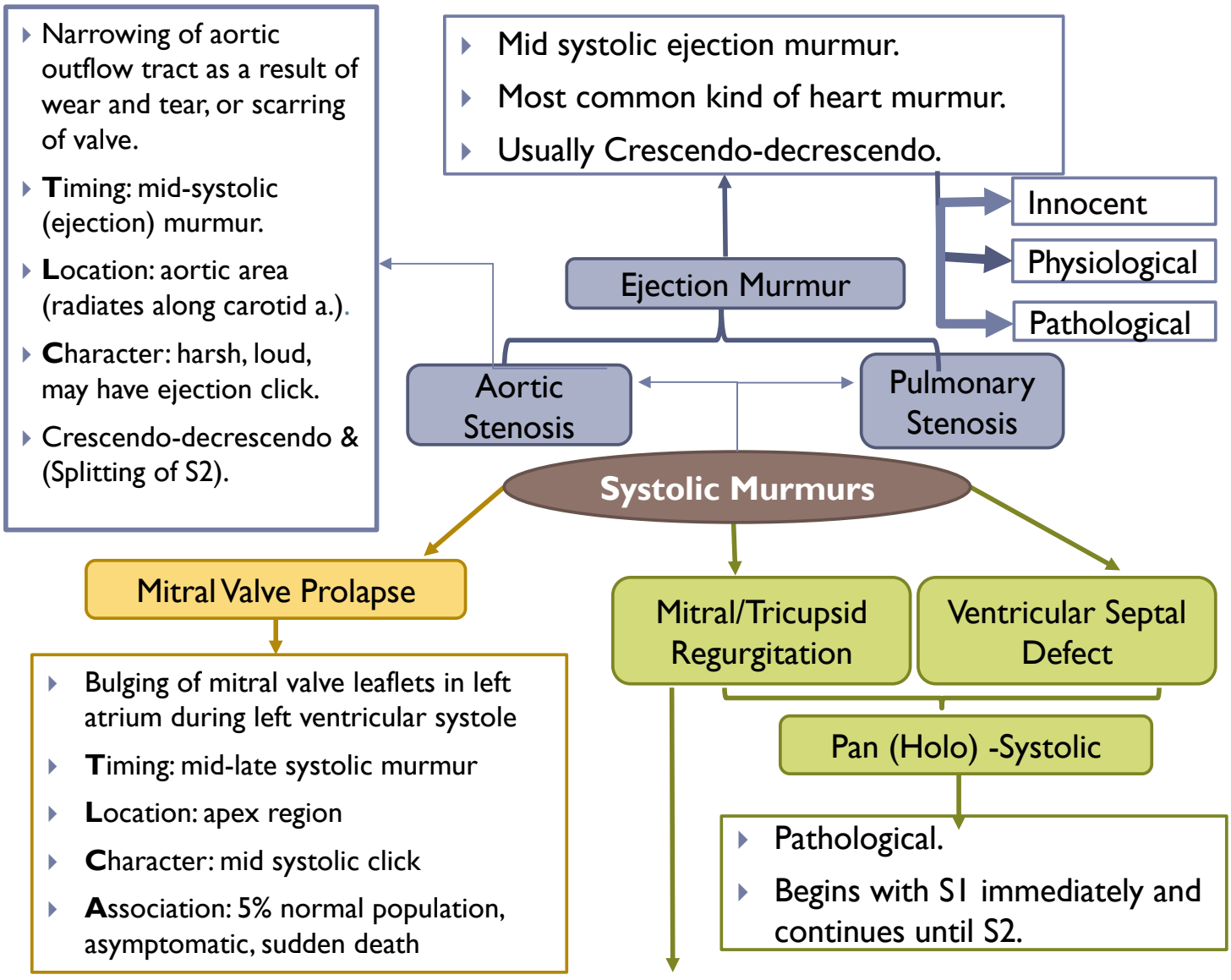
1. Valves closing (normal heart sounds)
   - Atrioventricular (S1)
   - Semilunar (S2)
2. Increased intra-cardiac hemodynamics (murmurs):
   - Blood striking left ventricle (S3,S4)
   - Increased blood flow across normal valves
   - Turbulent flow through abnormal valves/septal defects

Causes of Murmurs

Pathological murmurs	Physiological murmurs (normal murmurs)
• Turbulent flow through abnormal valves • Septal defect • Congenital • Tight valves (stenosis) • Leaky valves (regurgitation or insufficiency • Combination of Stenosis and Insufficiency.	• Increased blood flow across normal valves • Due to pregnancy, fever, anemia, hyperthyroidism, and children

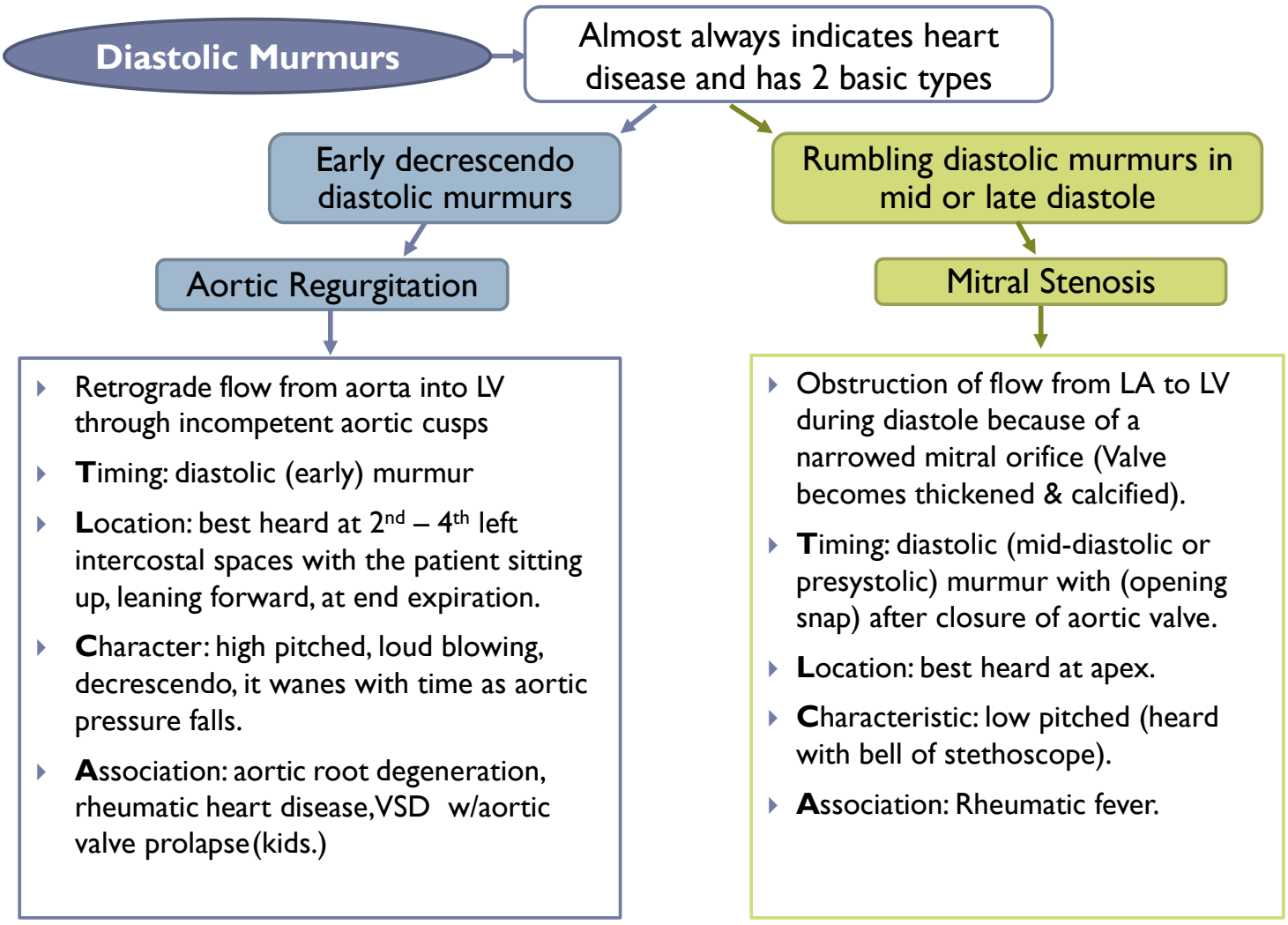


Systolic Murmurs



Pathophysiology of Systolic Murmurs

- Derived from harsh & ↑ turbulence in blood flow during systole.
- **Associated with:**
  1. ↑ flow across normal valve.
  2. ↑ flow into a dilated great vessel.
  3. ↑ flow across an abnormal valve, or narrowed ventricular outflow tract - e.g. aortic /pulmonary stenosis.
  4. ↑ flow across an incompetent AV valve - e.g. mitral/tricuspid regurgitation.
  5. ↑ flow across the inter-ventricular septum - e.g. VSD.



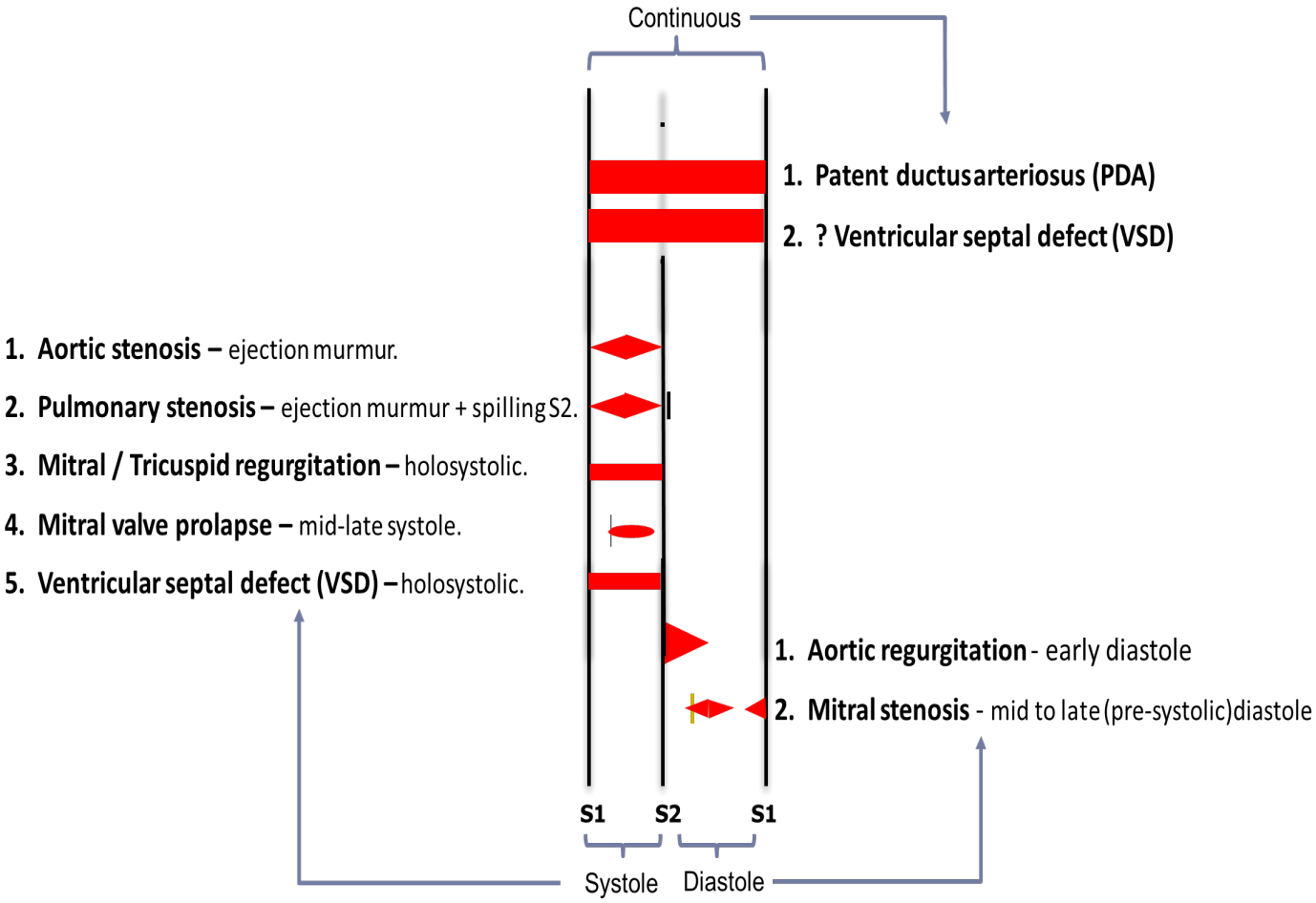
Continuous Murmurs

Continuous Murmurs

Begin in systole, peak near S2 & continue into all or part of diastole. Heard with:

- Ventricular Septal Defect (VSD)
- Patent Ductus Arteriosus (PDA)

Failure of closure of the duct between pulmonary artery & aorta.
Timing: continuous murmur.
Location: upper left sternal border.
Characteristics: machine-like.
Association: L to R shunt, cyanosis.



Lecture #6 Arrhythmias

Interpretation

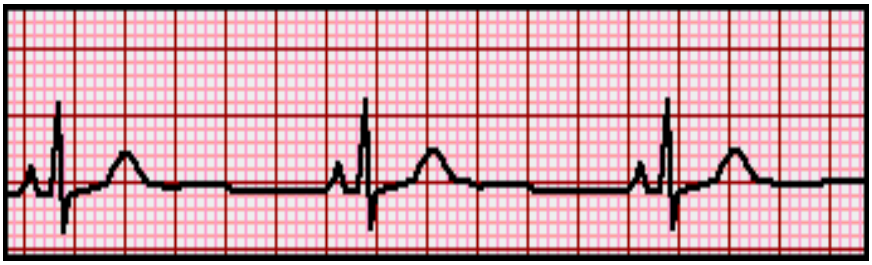
- Develop a systematic approach to reading EKGs and use it every time.
- The system we will practice is:
  - Heart Rate
  - Rhythm
    (including intervals and blocks)
  - Axis
  - Hypertrophy
  - Ischemia

Heart Rate

Rule of 300: Divide 300 by the number of boxes between each QRS = rate

- HR of 60-100 per minute is normal
- HR > 100 = tachycardia
- HR < 60 = bradycardia

Heart rate in picture below:(300 / 6) = 50 bpm



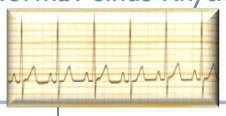
Number of big boxes	Rate
1	300
2	150
3	100
4	75
5	60
6	50

Cont.

Arrhythmias

Abnormal Sinus Rhythm

Normal sinus Rhythm

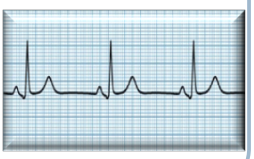


Abnormal cardiac Rhythms that Result From Impulse conduction block

regular
Single p-wave precedes every QRS complex
p-r interval is constant and within normal rang
P-P interval is constant

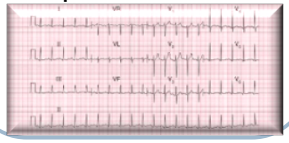
Bradycardia

slow heart rate
< 60 bpm
-Causes:
1.Parasympathetic stimulation .
2.Expiration.



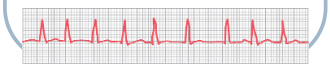
Tachycardia

an increase in the heart rate
Heart rate > 100 bpm
-Causes:
1.Increased body temperature.
2.Sympathetic stimulation.
3.Drugs: digitalis.
4.Inspiration.



Sinoatrial Block

Blockasde of the S-A node impulse before entering atrial muscle
-Causes:
1.Ischemia of the A-V node .
2.Compression of the A-V node by scar formation .
3.Inflammation of the A-V node
4.Strong vagal stimulation.

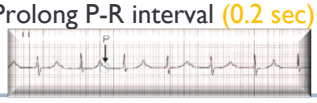


A-V Block

When impulse from the S-A node is blocked
Causes:1.Ischemia of the A-V node
2.Compression of the A-V node by scar formation.
4.Strong vagal stimulation

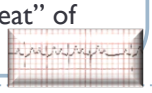
First degree block

Prolong P-R interval (0.2 sec)



Second degree block

P-R interval > 0.25 sec
only few impulses pass to the ventricles:
1.Atria beat faster than ventricles.
2."dropped beat" of the ventricles

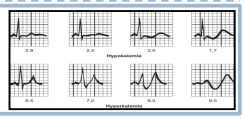
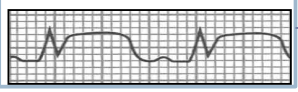
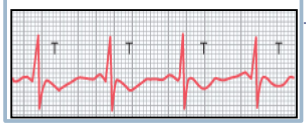
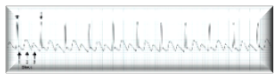
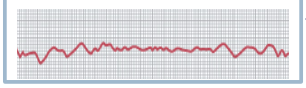


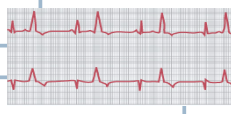
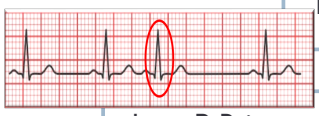
Third degree block

complete dissociation of P wave and QRS waves
ventricle escape from the influence of S-A node
atrial rate is 100 beats/min
ventricular rate is 40 beats/min
stokes-Adams syndrome

Cont.

Arrhythmias

- **Potassium and the ECG**
  - Hypokalemia: flat T wave
    Hyperkalemia: tall peaked T wave
    
- **Myocardial infarction**
  
  - Complete loss of blood supply to the myocardium resulting in necrosis or death of tissue : ST segment elevation , Deep Q wave
- **Ischemia and the ECG**
  
  - one of the common uses of the ECG is in acute assessment of chest pain .
    causes: restriction of blood flow to the myocardium(Reversible)
    angina pectoris (irreversible)
- **Atrial flutter**
  
  - A single large wave travels around and around in the atria.
    The atria contracts at high rate
- **Atrial fibrillation**
  - Same mechanism as ventricular fibrillation. it can occur only in atria without affecting the ventricles
- **Ventricular fibrillation**
  
  - The most serious of all arrhythmias
    causes: impulses stimulate one part of the ventricles, then another then itself
- **Atrial fibrillation**
  - Premature contraction , extraasystoles or ectopic beat result from ectopic foci that generate abnormal

- **Premature Ventricular Contractions (PVC)**
  
  - short P-R interval depending on how far the ectopic foci from AV
- **Premature Atrial**
  
  - short P-R interval depending on how far the ectopic foci from AV

Lecture #7,8 venous return, cardiac output

Venous Return

Factor controlling VR

- 1- Skeletal muscle pump → ↑ venous return.
2- Pressure drop during inspiration → ↑ venous return.
Forceful expiration (Valsalva maneuver)→ ↓ venous return.
3- ↑Blood volume → ↑ venous return.
4- ↑Pressure gradient → ↑ venous return.
5- ↑Venous pressure → ↑ venous return.
6- Gravity → ↓ venous return.

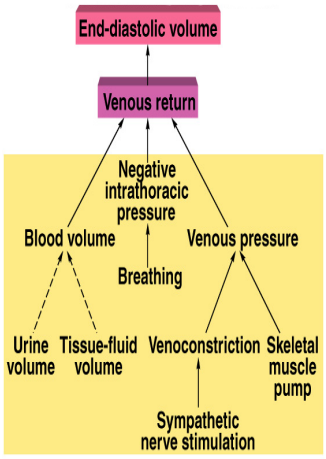
Depend on

1- Blood volume & venous pressure.

2- Venoconstriction caused by sympathetic NS.

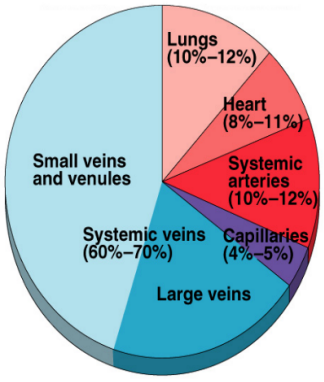
3- Skeletal muscle pumps.

4- Pressure drop during inhalation.



characteristic of the Veins

- Hold most of the body's blood (70% of blood is on the venous side as they are thin-walled) & are thus called capacitance vessels.
- Have thin walls & stretch easily to accommodate more blood without increased pressure (higher compliance).
Have only 0 - 10 mm Hg Pressure



Definition

is the quantity of blood flowing from large veins into the right atrium each min
Under steady state conditions, venous return (VR) must equal cardiac output (CO) when averaged over time because the cardiovascular system is essentially a closed loop. Otherwise, blood would accumulate in either the systemic or pulmonary circulations.
Venous return is determined by the difference in pressure between the venous pressure nearest to the tissues (MCP) and the (CVP).

Determinants of Venous Return

1. Blood Volume

At constant venous capacity, as the blood volume↑ → the MCP ↑ → ↑VR.

At constant venous capacity, as the blood volume ↓ → the MCP ↓ → ↓VR.

2. Venous Capacity

It is the volume of the blood that the veins can accommodate

At a constant blood volume, as the venous capacity ↑ → more blood spends a longer time in the veins instead of being returned to the heart → ↓ the effective circulating volume → ↓VR.

At a constant blood volume, as the venous capacity ↑ → the MCP ↓ → ↓VR.

As the venous capacity ↓ → ↑VR.

3. Sympathetic Activity

Venous smooth muscle is profusely supplied with sympathetic nerve fibers.

Sympathetic stimulation → venous vasoconstriction → modest ↑ in mean systemic filling pressure (MCP) → ↑VR.

Sympathetic stimulation → ↓ venous capacity → ↑VR.

4. Skeletal Muscle Activity

Skeletal muscle contraction → external venous compression → ↓ venous capacity → ↑VR

Skeletal muscle activity also counter the effects of gravity on the venous system.

5. Activity (Respiratory Pump: Thoracic Pump)

As the venous system returns blood to the heart from the lower regions of the body , it travels through the chest cavity .The pressure in the chest cavity is 5 mm Hg less than atmospheric pressure.

The venous system in the limbs and abdomen is subjected to normal atmospheric pressure.

Thus , an externally applied pressure gradient exists between the lower veins and the chest veins , promoting venous return.

6. Venous Valves

These valves permit blood to move forward towards the heart but prevent it from moving back toward the tissues.

These valves also play a role in counteracting the gravitational effects of the upright posture.

7- gravity

Venous compliance is high and veins readily expand with blood.Thus , upon standing from the supine position , most of blood volume shift occurs in the veins .

This decreases right ventricular filling pressure (preload),leading to decline in stroke volume by starling mechanism .

Left ventricular stroke volume also falls because of reduce pulmonary venous return (decreased left ventricular preload).this causes cardiac output and mean arterial pressure to fall.

If arterial falls appreciably upon standing ,this is termed orthostatic or postural hypotension .

This fall in arterial pressure can reduce cerebral blood flow to point where a person might experience syncope (fainting).

Pressures

Pressures

Central Venous Pressure (CVP)

CVP: is the venous pressure in the right atrium and the big veins of the thorax (= right atrial pressure (RAP) = jugular venous pressure).

Venous pressure is measured with a catheter inserted in the central venous system, usually SVC.

The normal range of the CVP = 0 - 4 mm Hg.

It is the force responsible for cardiac filling.

CVP is used clinically to assess hypovolaemia and during IV transfusion to avoid volume overloading.

CVP is raised in right-sided failure.

Mean Systemic Filling Pressure or Mean Circulatory Pressure (MCP)

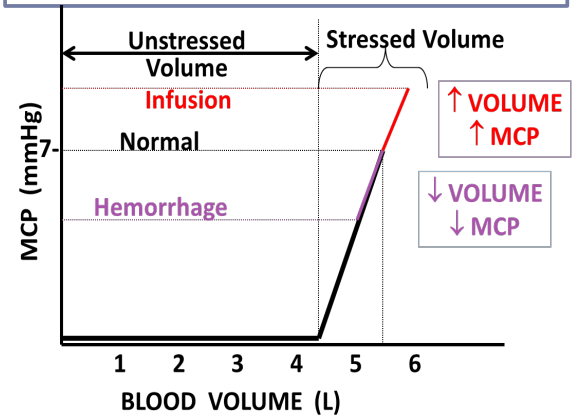
It is the pressure nearest to the tissues.

Its normal value is about 7 mmHg.

The value for right atrial pressure at which venous return is zero is called the mean systemic filling pressure. It is the point at which the vascular function curve intersects the X-axis (i.e. where venous return is zero and right atrial pressure is at its highest value).

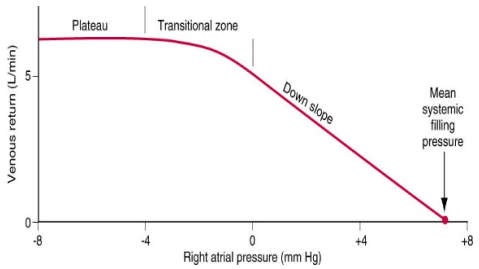
It is affected by:

1) Blood volume (it is directly proportional to blood volume).
2) Venous capacity (it is inversely proportional to the venous capacity).



Venous Return Curve (Vascular Function Curve)

Venous return (VR) curve relates VR to right atrial pressure.



Venous return is decreased when:

1. The right atrial pressure (RAP) is increased,
2. Pumping capability becomes diminished.
3. The nervous circulatory reflexes are absent.

The plateau is due to closure or collapse of the vein by increased negative pressure.

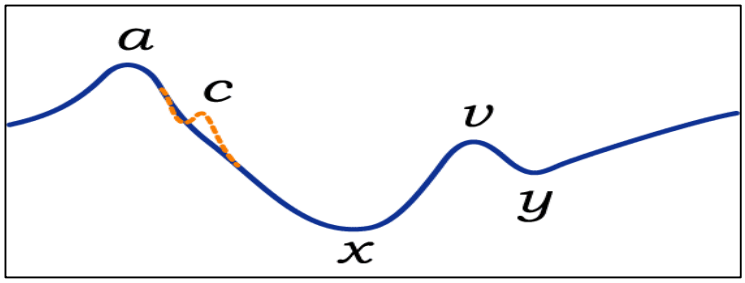
in Valsalva maneuver the intrapleural pressure becomes positive which is transmitted to the large veins in the chest → decrease venous return.

Jugular vein

Why Right Internal Jugular Vein?	Why Internal Jugular Vein (IJV)?	Pressure	Pulse
Right jugular veins extend in an almost straight line to superior vena cava, thus favoring transmission of the haemodynamic changes from the right atrium. The left innominate vein is not in a straight line and may be kinked or compressed between Aortic Arch and sternum, by a dilated aorta, or by an aneurysm.	IJV has a direct course to right atrium (RA). IJV is anatomically closer to right atrium (RA). IJV has no valves (Valves in EJV prevent transmission of RA pressure)	Vertical height of oscillating column of blood.	Defined as the oscillating (moving up and down) top of vertical column of blood in right internal jugular vein that reflects pressure changes in right atrium in cardiac cycle.

Normal Pattern of the Jugular Venous Pulse

The normal JVP reflects phasic pressure changes in the right atrium and consists of three positive waves and two negative descents.

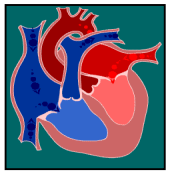


a WAVE
Venous distension due to RA contraction
Retrograde blood flow into SVC and IJV

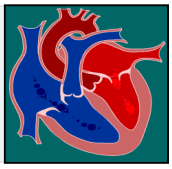
c WAVE:
is due to Ventricular contraction and resulting bulging of tricuspid valve into the right atrium during isovolumetric contraction.

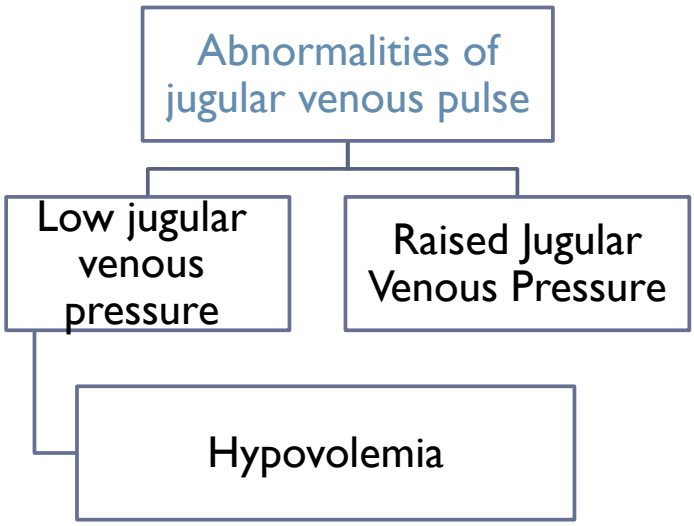
x DESCENT:
is due to atrial relaxation and the tricuspid valve moves downward.

v WAVE
is due to, Rising right atrial pressure when blood flows into the right atrium during ventricular systole when the tricuspid valve is shut.



y DESCENT
is due to the decline in right atrial pressure when the tricuspid valve reopens





Causes of a raised JVP may be classified into those due to:

1- Increased right ventricular filling pressure e.g. in heart failure, fluid overload.
2- Obstruction of blood flow from the right atrium to the right ventricle e.g. tricuspid stenosis
3- Superior vena caval obstruction e.g. retrosternal thyroid goiter.
4- Positive intrathoracic pressure e.g. pleural effusion, pneumothorax
The JVP usually drops on inspiration along with intrathoracic pressure.

Cardiac output

Cardiac Output (C.O)

Definition

C.O.: is the volume of blood flow ejected from the right or left ventricle per minute. = 5 L\min at rest.

Stroke volume: is the volume of blood ejected from each ventricle per beat. = 70 ml\beat at rest

Heart Rate = 72 beats\ min.

cardiac output = the volume of blood pumped by one ventricle per beat X the number of beats per minute:

Values

The cardiac output at rest is approximately 5 L/min.

Men:5.6, womens:4.9

The body's blood volume averages 5 to 5.5 liters.

Each ventricle pumps the equivalent of the entire blood volume each minute.

During exercise, the CO can **increase** to 20 - 25 liters/min and to as high as 35 - 40 liters/min in well trained athletes.

Regulation

C.O regulation: is well regulated according to tissue metabolic demands.

Basic determinant of C.O.: is the O_2 requirements of body tissues, for their metabolic rates.

Accordingly, if the metabolic rate is increased → the CO and VR are increased WHY? to maintain optimal O_2 supply to the active tissues.

Factors affecting & regulating cardiac output

1- Stroke volume

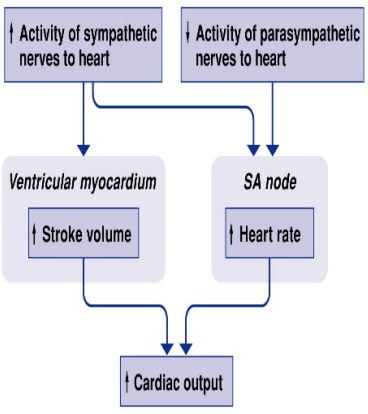
-Myocardial contractility (ventricular myocardiam)

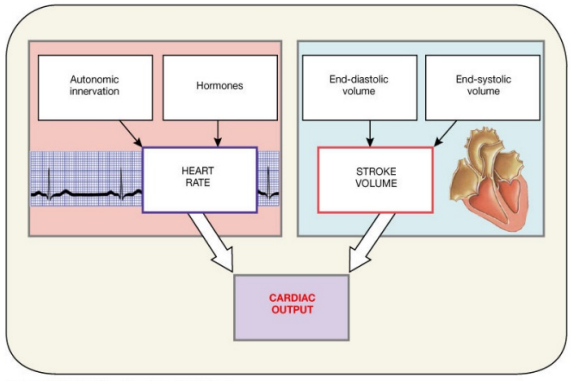
-Preload and afterload (End systolic/ diastolic volume)

2-Heart rate (decrease, increase)

-increase (Hormones, pregnancy, Sympathetic Nervous system, Decrease blood volume ,excersize)

Decrease: (High blood pressure or blood volume,Parasympathetic nervous system)





Physiological Changes In Cardiac Output

Moderate Exercise

HR increases to	200% of resting (140 bts/min)
SV increases to	120% (85ml)
CO increases to	240% (12L)

Severe Exercise

HR increases to	300% of resting (200 bts/min)
SV increases to	175% (125ml)
CO increases to	500% - 700% (25 - 35 L)

In athletes:

maximum CO may be 35L or more - can't increase maximum HR beyond 200 bts - hence - SV increases to 175 ml.

Physiological changes

- **During the first 3 hours after meal:** the CO is increased by ≈ 30% to enhance blood flow in the intestinal circulation.
- **Later months of pregnancy:** are accompanied by > 30% increase in CO due to increased uterine blood flow.
- **At environmental temperature** above 30 °C : the CO is increased due to increased skin blood flow.
- **At low environmental temperature:** CO is increased due to shivering that increases blood flow to the muscles.
- **Increased sympathetic activity:** during anxiety and excitement enhances the CO up to 50% - 100%.
- **Sitting or standing from the lying position:** deceases the CO by 20% - 30%.
- **Exercise:**

Pathological changes

Causes of low CO:

- Low VR (e.g., haemorrhage)
- Reduced contractility (e.g., heart failure)
- Tachyarrhythmias (e.g., atrial fibrillation and ventricular tachycardia)
- Marked bradycardia (e.g., complete heart block)

Causes of high CO:

- Hyperthyroidism: the increase in the CO is due to the high metabolic rate → vasodilatation →↑ CO to 50%+ of control.
- AV fistulas
- Fever
- Anaemia
- Anxiety

Cardiac Index and Cardiac Output

- ## Cardiac Index

It relates the **cardiac output** to body **surface area**.

Thus relating **heart performance** to the **size** of the individual.

The unit of measurement is liter per minute per square meter of body surface area **(L/min/m^2).**

- ## Cardiac Output Measurement

The Direct Fick's Method:

The amount or **volume of any substance** taken up by an organ or by the whole body is equal to:
(The arterial level of the substance – the venous level) X blood flow.

$$\text{Blood flow} = \frac{\text{Amount}}{(\text{Arterial level} - \text{Venous level})}$$

Methods for Measuring Cardiac Output

Cardiac output can be *measured* using the **Fick principle:**

- In the steady state, the cardiac output of the left and right ventricles is equal.

- In the steady state, the rate of O2 consumption by the body must equal the amount of O2 leaving the lungs in the pulmonary vein minus the amount of O2 returning to the lungs in the pulmonary artery.

- Total O2 consumption or the rate of O2 absorption by the lungs can be measured by the rate of disappearance of oxygen from respired air, using any oxygen meter.
- The amount of O2 in the pulmonary veins is pulmonary blood flow multiplied by the O2 content of pulmonary venous blood. Likewise, the amount of O2 returned to the lungs via the pulmonary artery is pulmonary blood flow multiplied by the O2 content of pulmonary arterial blood.
- O2 consumption = cardiac output × [O2] pulmonary vein – cardiac output × [O2] pulmonary artery
- Cardiac output = O2 absorbed by the lungs per minute/arteriovenous O2 difference

Lecture #9 stroke volume and heart failure

- **Stroke volume:** is the volume of blood pumped (ejected) by each ventricle per beat (during each ventricular systole), and it is about 70-80 ml/beat.
- **Factors Affecting It:**

1- End diastolic volume (EDV) (Preload):

- It is: the volume of blood present in each ventricle at the end of ventricular diastole.
- Preload: load on the muscle in the relaxed state.
- Normal amount: 120-130 ml, can be increased during diastole (filling of ventricles) to a volume of (120-130mL).
- Applying preload to a muscle causes:
  1- The muscle to stretch.
  2- The muscle to develop passive tension.

Mechanism:

The larger the EDV, the more the ventricle is stretched → the longer the initial myocardiac-fiber length before contraction → higher degree of overlap of thick and thin filaments → more cross-bridge interactions between myosin and actin → greater force on the subsequent cardiac contraction → greater SV.

The relationship is also explained by:

the greater sensitivity to calcium → at greater lengths.

EDV Depends on:

A- Filling time: the duration of ventricular diastole.
B- Venous return: the rate of blood flow during ventricular diastole.

2- End systolic volume (ESV):

It is: volume of blood present (that remains) in each ventricle at the end of ventricular systole.
Normal amount: 50-60 ml.

↑ End-Systolic Volume (ESV) → ↓ stroke volume

↓ End-Systolic Volume (ESV) → ↑ stroke volume

↑ preload → ↓ ESV

↑ Contractility → ↓ ESV

↑ Afterload → ↑ ESV

The Frank–Starling Principle (Starling's Law of the Heart)

- **Represent:** the intrinsic relationship between EDV and SV.
- **It is based on:** the length-tension relationship within the ventricle.
- **Mechanism:** if venous return increased → ventricular end diastolic volume (preload) is increased (increase both stroke volume & cardiac output) → ventricular fiber length is also increased → resulting in an increased 'tension' of the muscle.

→ ↑ Venous return → ↑ EDV

→ ↑ Force of ventricular contraction

→ ↑ Stroke Volume

→ ↑ Cardiac Output

Sum up definition: it is the ability of the heart to change its force of contraction and therefore stroke volume in response to changes in venous return.

Afterload

It is: the load on the muscle during contraction.
Represents: tension (force) which must be developed in the walls of ventricles (muscle) during systole to open the semilunar valves and eject blood to aorta /pulmonary artery.

Is increased by any factor that restricts arterial blood flow like:

1. Increased arterial blood pressure (systemic Arterial hypertension).
2. Vasoconstriction.

Is decreased by systemic Arterial hypotension.

When aortic pressure is reduced,→ velocity of shortening of the LV myocardial fibers increases so , reduced after load, the LV can eject blood more rapidly. → This increases the rate blood ejection → less blood is left within the LV at the end of systole → ↓ ESV.

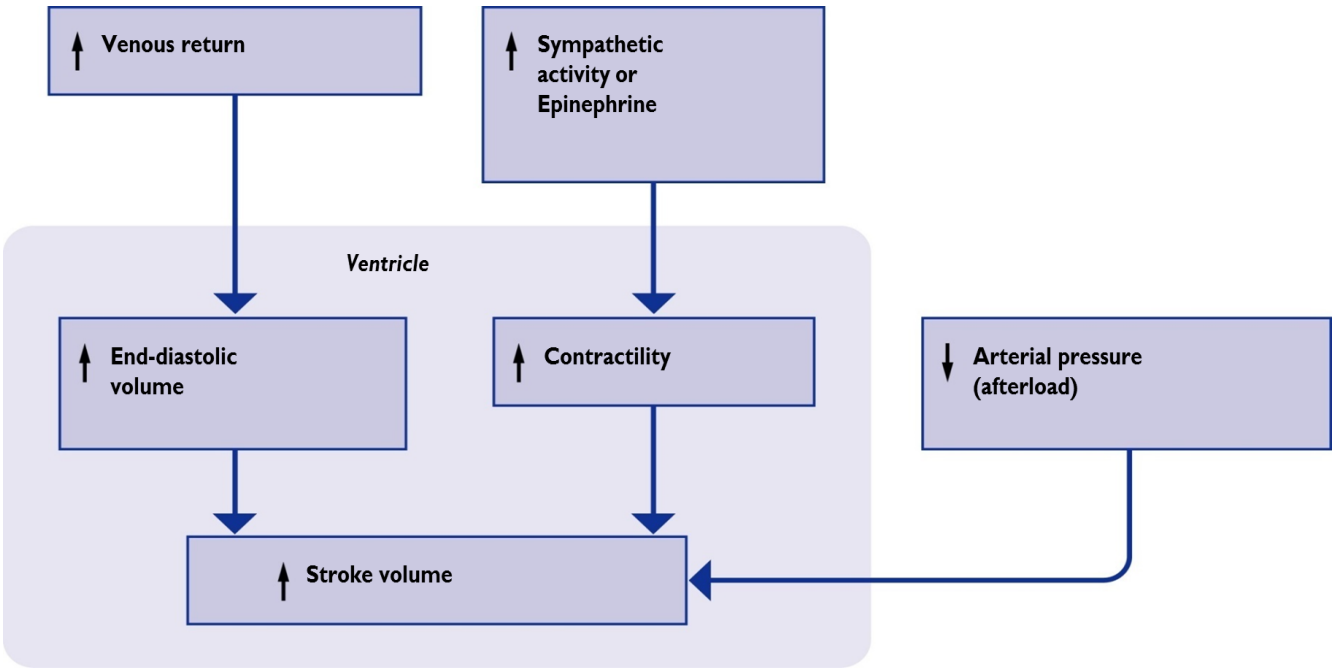
Thus, afterload ↓ , SV ↑ as a result of the ↓ in ESV.

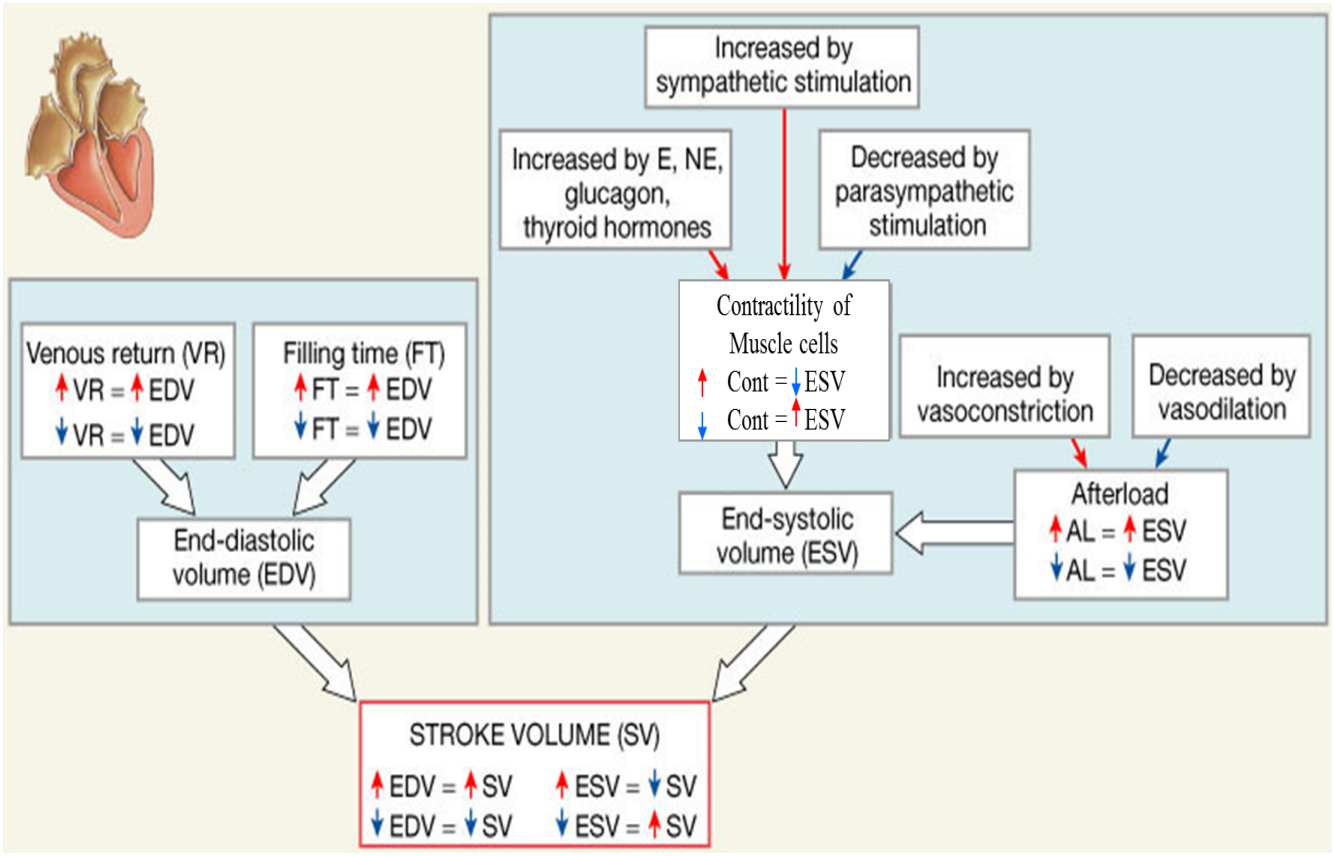
- The opposite is true with increased LV after load.

Left ventricular afterload = Mean aortic pressure

- LV afterload is increased in conditions of : 1- aortic stenosis 2- arterial hypertension
- The LV must respond and compensate to changes of afterload
- For example : LV work must increase in attempt to maintain the SV constant in the face of an increased afterload.

Factors Affecting Stroke Volume

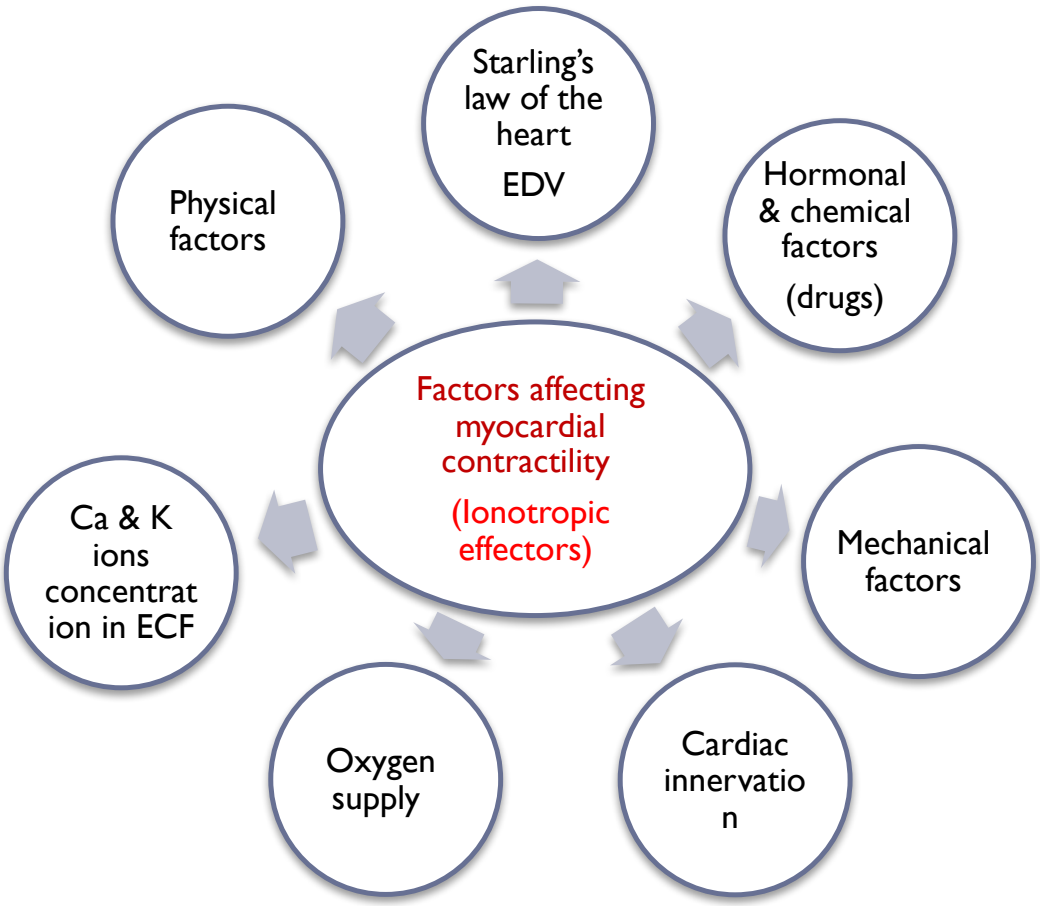




Myocardial Contractility (Inotropic State)

Inotropic effect of noradrenaline and adrenaline:

- **it is:** an intrinsic property of the myocardium independent of the preload. Thus, myocardial contractility can increase without an increase in pre-load.
- Changes in myocardial contractility are due to changes in the intracellular dynamics of calcium.
- Drugs that increase contractility usually provide more calcium and at a faster rate to the contractile machinery.
- More calcium will activate more cross-bridges and thereby strengthen the heart beat.



Heart failure

Heart failure

Diagnose

- Indicator for Diagnosing Heart Failure

Ejection Fraction (EF): is the percentage of blood that is pumped out of your heart during each beat.

How do we calculate EF ?
It is the fraction of end-diastolic volume ejected during a heart beat.

EF = stroke volume / end diastolic volume

70 ml / 130 ml = 0.54 "no unit"

- **Medical history is taken to reveal symptoms**
- **Physical exam is done**
- **Tests**

- Chest X-ray
- Blood tests
- "ECG"
- "Echo"
- X-ray of the inside of blood vessels (Angiogram)

causes

1- Impaired cardiac function
- Coronary heart disease
- Cardiomyopathies
- Rheumatic fever
- Endocarditis

2- Increased cardiac workload
- Hypertension
- Valvular disorders
- Anemias
- Congenital heart defects

3- Acute non-cardiac conditions
- Volume overload
- Hyperthyroidism, Fever, Infection

sign

- Respiratory sign:

Persistent Cough
Fluid [Breathing worsens with lying flat (orthopnea)
- Edema
- Tiredness, fatigue
- Lack of appetite/ nausea

Definition

It is the pathophysiological process in which the heart as pump is unable to meet the metabolic requirements of the tissue for oxygen and substrates despite the venous return to the heart is either normal or increased.

Heart failure occurs when either side of heart cannot keep up with the flow of blood left or right side of the heart or both, but usually the left side is affected first.
Manifested by:
nadequate cardiac output.

Build-up of blood in veins behind left heart or right heart (increased venous pressure).

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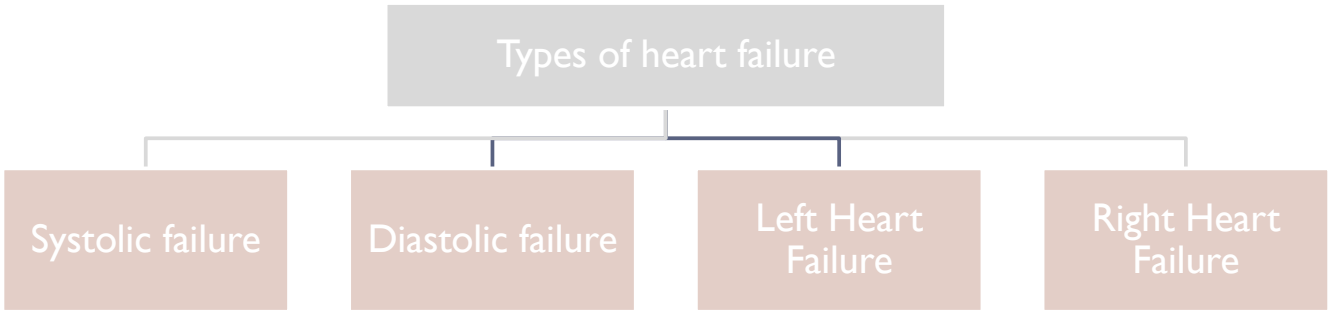


The heart looses it's ability to contract or pump blood into the circulation.

The heart looses it's ability to relax because it becomes stiff. Heart cannot fill properly between each beat.

Systolic and diastolic heart failure are treated with different type of medication .
blood pumped normally to the lungs by the RV
blood accumulates in pulmonary circulation increasing the pulmonary capillary pressure → serious filtration of fluid in the lung interstitial space and alveoli (pulmonary edema).
Fluid may also build up in tissues throughout the body (edema)

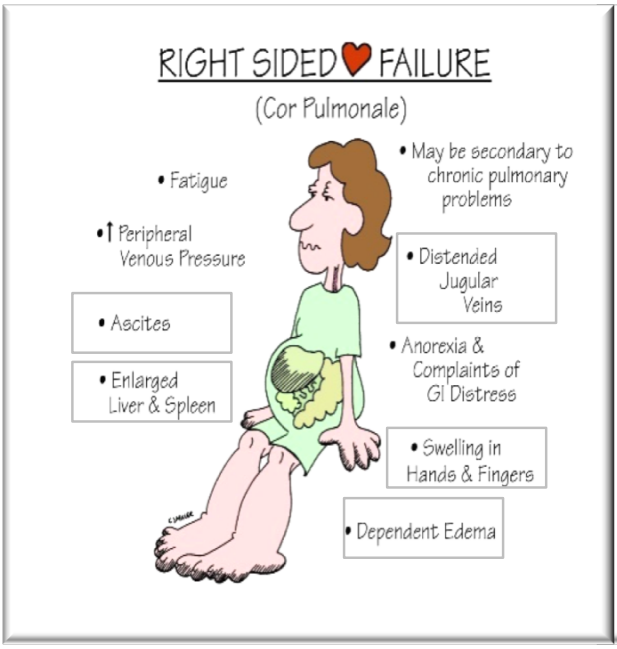
Usually occurs as result of left heart failure.
Occasionally isolated right heart failure can occur due to lung disease or blood clots to the lung (pulmonary embolism).
blood pumped normally to the systemic circulation by the LV
blood accumulates in systemic circulation increasing the systemic capillary pressure → filtration of fluid in the body tissues (systemic edema)

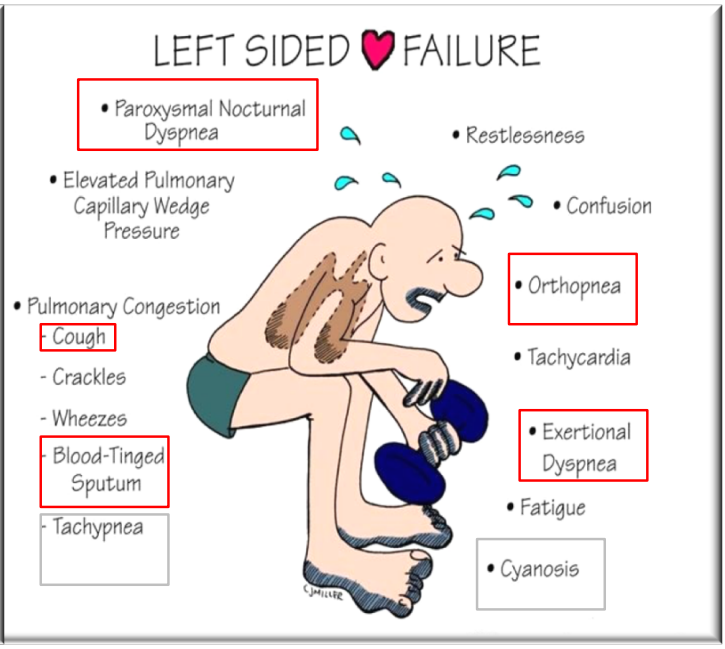
Acute vs. Chronic Heart Failure (very IMP)

Acute (hours-days)	Chronic (months-years)
Caused by: Sudden serious abnormalities of the heart (e.g., massive infarction, arrhythmias, valve rupture; acute infection (sepsis))	Long-term condition
Heart does not have time to undergo compensatory adaptations.	Associated with the heart undergoing adaptive responses (e.g., dilation, hypertrophy).#previous slide
Sudden reduction in CO and blood pressure →decreased perfusion to vital organs	These adaptive responses, however, can be deleterious
Usually left-sided (more serious)	-
Cardiogenic shock may develop if the heart became unable to pump enough to even keep tissues alive	-

Cont.

Right Heart Failure	Left Ventricular Failure
Signs and Symptoms	
• Fatigue • ascites • Distended jugular vein • Weakness • Lethargy • Weight gain, including abdominal girth • Anorexia • Elevated neck veins • Hepatomegaly	• Dyspnea • Orthopnea and paroxysmal nocturnal dyspnea* • Cheyne Stokes breathing • fatigue • Anxiety • Rales (crackles) • pallor, cyanosis (late sign of extremely severe pulmonary edema) • Increased HR and BP • Lateral displacement of apex beat • Gallop rhythm • Tachypnea





Lecture #11 shock

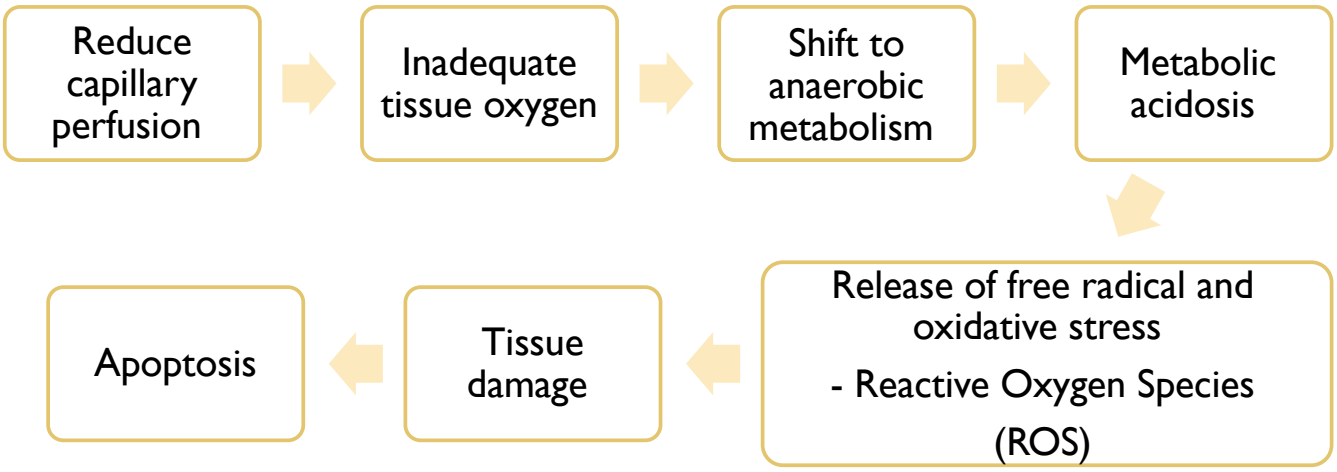
The cell is the basic unit of life and it needs oxygen to produce energy.
No oxygen → No energy → No life

Circulatory shock: When the circulatory system is unable to provide adequate circulation & tissue perfusion → decreased availability of oxygen and nutrients → failure to deliver oxygen to the tissues & vital body organs relative to its metabolic requirement → cellular hypoxia and energy deficit .

Result: organ dysfunction and cellular damage.

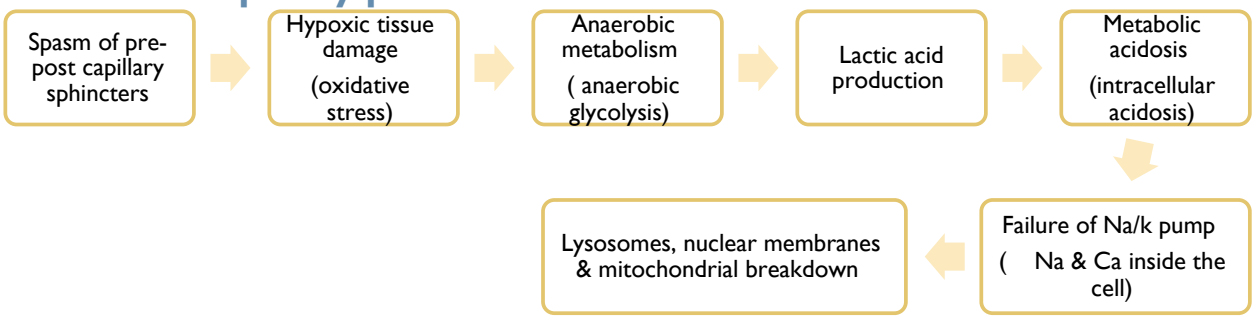
If not quickly corrected: whole body failure → leads to irreversible shock and death.

Pathophysiology of Shock

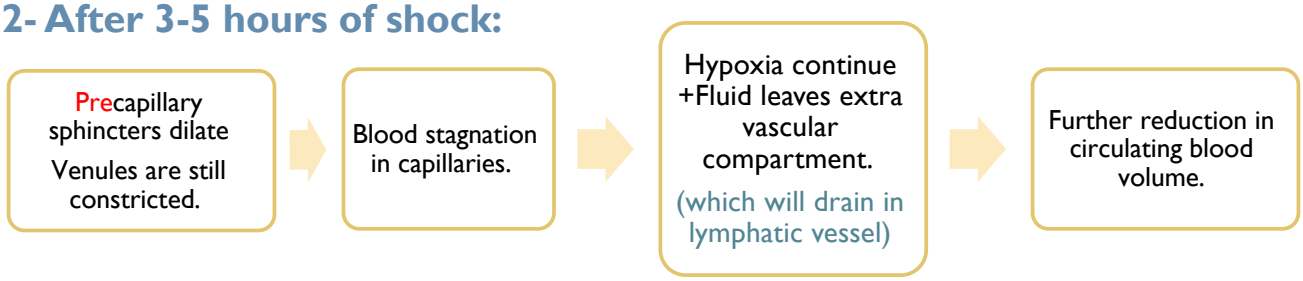


Metabolic Changes & Cellular Response to Shock

1- Reduced capillary perfusion:



2- After 3-5 hours of shock:



3- granulocytes accumulation at injured vessels: (Free radical release and further tissue damage).

4- damage in GIT mucosa : allows bacteria into circulation.

5- cerebral ischemia

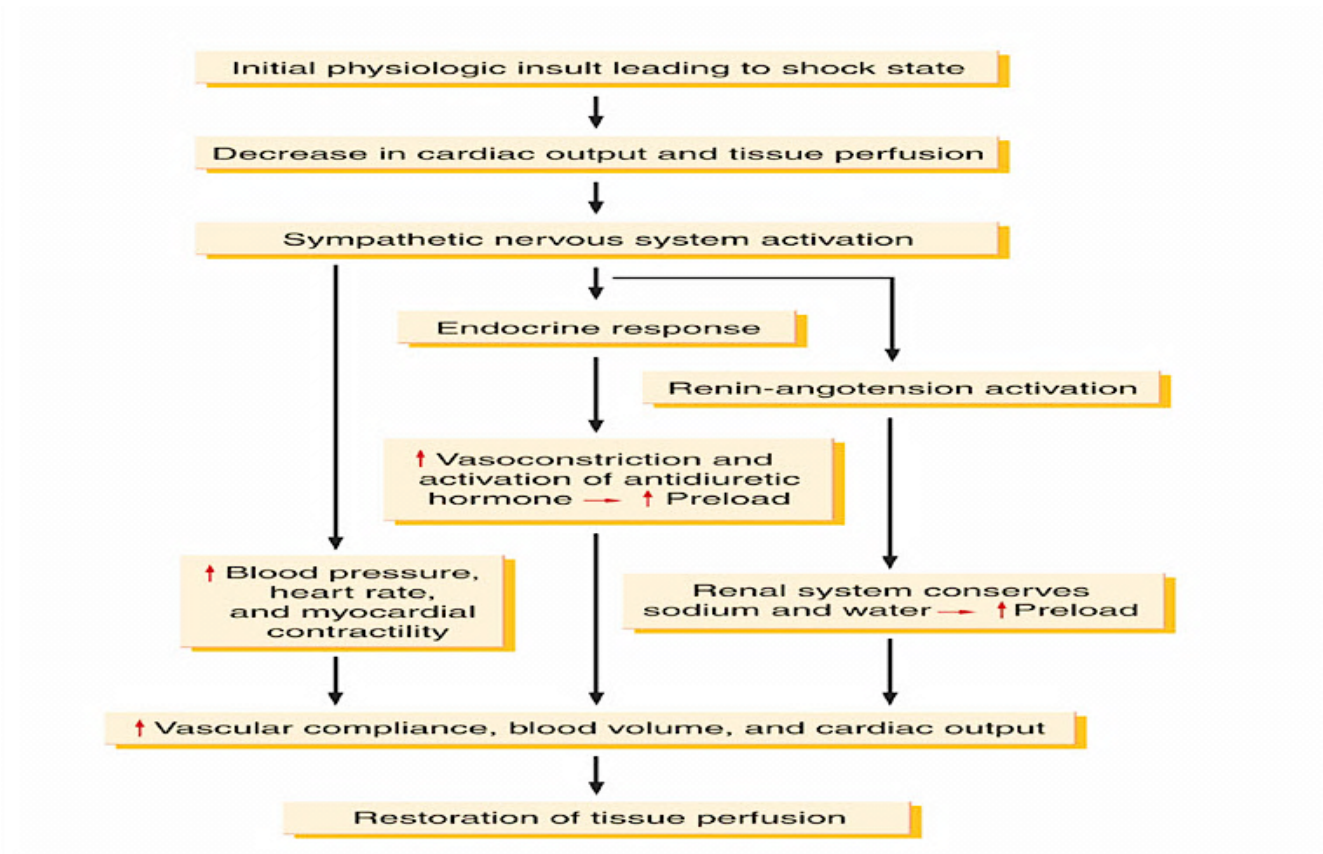
6- Myocardial ischemia (depressed contractility+ myocardial damage(more shock and acidosis).)

7- respiratory distress syndrome occurs : due to damage of capillary endothelial cells & alveolar epithelial cells with release of cytokines.

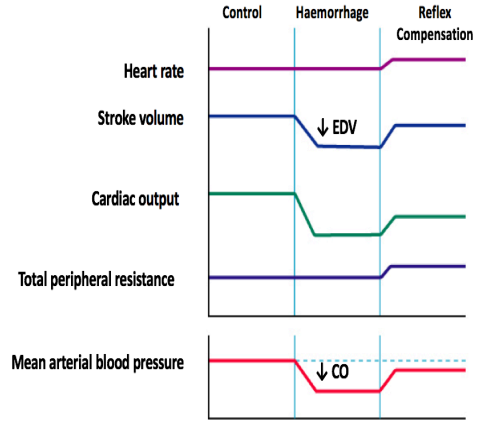
8- multiple organ failure and death.

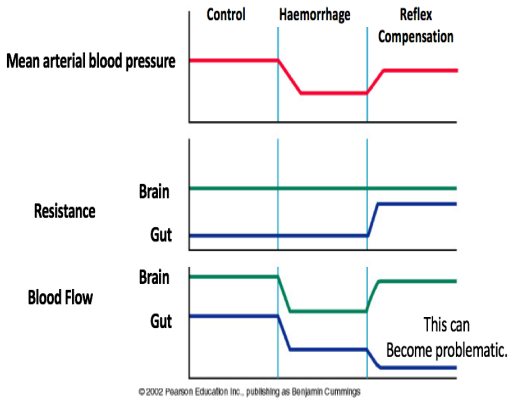
Compensatory Mechanisms

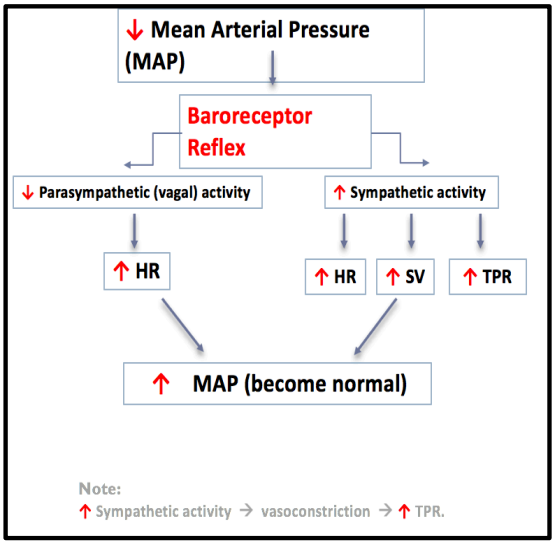
- Compensatory mechanism
  - Sympathetic stimulation
    - Baroreceptor reflex by decreased blood pressure
    - Chemoreceptors reflex by acidosis
  - Renin-Angiotensin mechanism stimulation
    - Angiotensin II +III: powerful vasoconstrictors
    - Aldosterone: Na & water retention
  - Release of antidiuretic hormone (vasopressin)
    - Water retention
    - Vasoconstriction and thirst stimulation
  - Plasma protein synthesis
  - Fluid shift mechanism

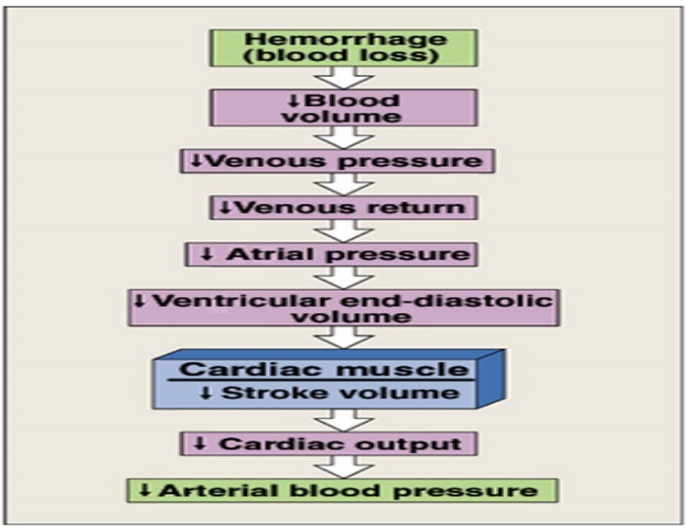


Short-Term Compensatory Mechanisms:
1- Arterial Baroreceptor Reflex









Short Term Compensatory Mechanisms:
2- Arterial Chemoreceptor Reflex

- Reductions in mean arterial blood pressure (MAP) below 60:
  1. do not evoke any additional responses through the baroreceptor reflex.
  2. stimulates peripheral chemoreceptors (aortic bodies, carotid bodies, heart) that sense changes in pO2, pCO2, and pH through tissue hypoxia and lactacidosis.
- This results in:
  - Enhancement of the existing tachycardia and vasoconstriction
  - Respiratory stimulation → tachypnea

Causes and Classification of Shock

TYPE	CAUSES	SYMPTOMS AND SIGNS
Hypovolemic shock (most common)	• Bleeding/ Hemorrhage (internal/external) (Most Common) • dehydration (sever vomiting, sever diarrhea, excess sweating) • plasma loss (as in burns , trauma) → low blood volume Lead to: Reduced venous return (preload)→ loss of 15-25% of CO / 1-2 L→ hypotension	1. Hypotension (≤ 85/40mmHg) ; weak but rapid pulse . 2. Tachycardia (Compensation for↓ MAP sensed by Baroreceptors) Rapid, weak, & thready pulse (140/min). 3. Cool, clammy skin 4. Tachypnea "rapid respiration" (Compensation for hypoxia sensed by Chemoreceptors) shallow breathing , anxiety 5. Restlessness due to hypo-perfusion. 6. Altered mental state 7. Oliguria (low urine output)/ 8. Anuria (no urine output). 9. Blood test: Lactic acidosis.
Cardiogenic shock	Heart problems (e.g., myocardial infarction(Most common), heart failure , cardiac dysrhythmias) → despite adequate ventricular filling pressure →↓ contractility →↓in stroke volume →↓cardiac output → hypotension Myocarditis, cardiomyopathy, cardiac tamponade, congestive heart failure Acute valvular dysfunction (e.g., rapture of papillary muscles post MI) Sustained arrhythmias (e.g. heart block, ventricular tachycardia) pulmonary embolism Is associated with loss of > 40% of LV myocardial function, mortality rate is high 60-90%	1. Just like symptoms of a hypovolemic shock + 2. Distended jugular veins 3. Cardiomegaly 4. Congestion of lungs & viscera: Chest X-ray (CXR): 5. Interstitial pulmonary / Alveolar edema . 6. May be absent pulse
Obstructive shock	• Obstruction of venous return: like Vena Cava syndrome (usually neoplasms) • Compression of heart: like hemorrhagic pericarditis > cardiac tamponade • Obstruction of outflow: like aortic dissection*, massive pulmonary embolism, pneumothorax. • Circulatory obstruction (e.g., constrictive pericarditis) Lead to : reduced blood flow to lungs →↓ cardiac output → hypotension	1. Just like symptoms of a hypovolemic shock + 2. Distended jugular veins 3. Pulses paradoxes (in cardiac tamponade).

Cont.

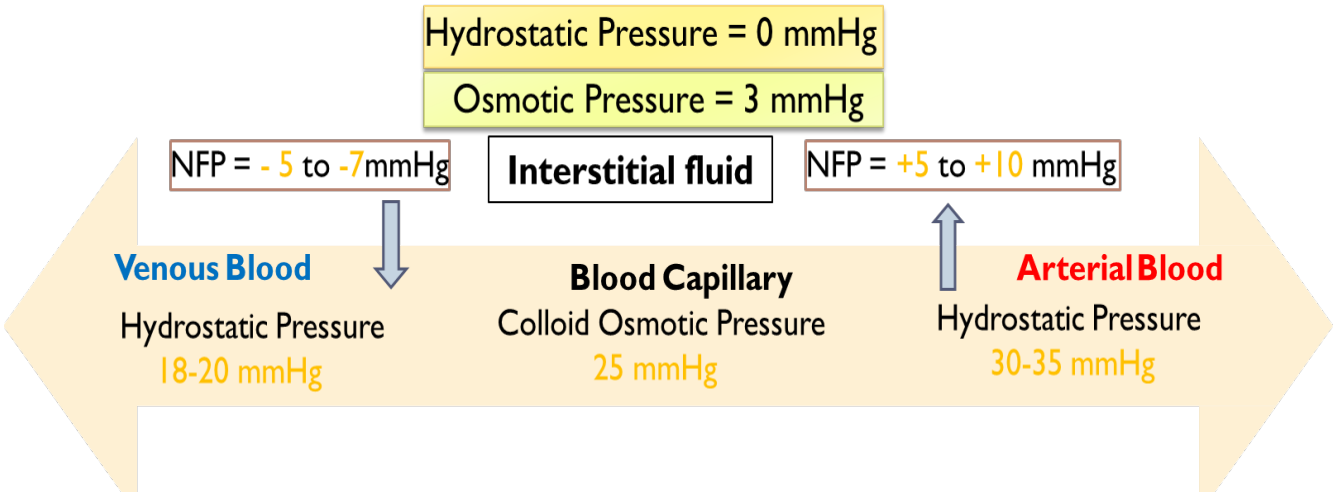
High/Normal Cardiac Output Shock (Distributive)

MAP = CO X PR

(the problem is in **vascular/peripheral resistance**)

TYPE	CAUSES	SYMPTOMS AND SIGNS
Distributive shock 1- Vasogenic (Valvular Obstruction) 2- Low-resistance shock	❑ Septic shock: infection → release of bacterial toxins → activation of NOS in macrophages → production of NO → vasodilation + endothelial injury → decreased vascular resistance→ hypotension ❑ Anaphylactic shock: allergy (release of histamine) → IgE Mediated hypersensitivity (histamine triggers peripheral vasodilation and an increase in capillary permeability → decreased vascular resistance→ hypotension ❑ Neurogenic shock: / Spinal Shock (venous pooling): spinal injury →↓ peripheral vasomotor tone → loss of autonomic and motor reflexes → vasodilation → Blood volume remains normal →↓in peripheral vascular resistance →↓ cardiac output as blood is pooled in peripheral veins → ↑ Capacity of blood →↓ Venous return → hypotension (Behaves like hypovolemic shock) ❑ Psychogenic shock : stress, pain, or fright → ↓ HR & vessels dilate → Brain becomes hypo perfused → Loss of consciousness.	❑ Septic shock: Patient flushed & warm due to his hyperdynamic state fever – warm- sweaty skin and hypotension ❑ Anaphylatic shock: hypotension- skin eruptions- breathlessness- coughing - localized edema- weak - rapid pulse ❑ Neurogenic shock: as for hypovolemic except warm, dry skin ❑ Psychogenic shock : Simple fainting (syncope)

In Normal Microcirculation



- At **arterial** end: Water moves out of the capillary with a NFP of +5 to +10 mmHg Hydrostatic pressure dominates at the arterial end & net fluid flows out of the circulation.
- At **venous** end: Water moves into the capillary with a NFP of -5 to -7 mmHg. Oncotic pressure dominates at the venous end & net fluid will flow into the bloodstream.

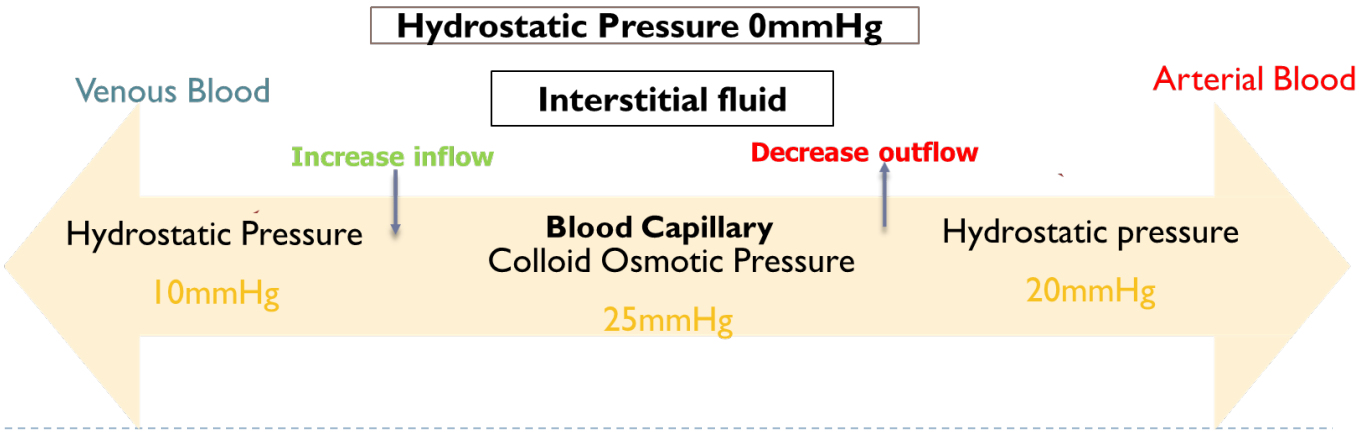
Fluid-Shift Mechanism

In shock, the hydrostatic pressure decreases & oncotic pressure is constant, **as a result:**

- The fluid exchange from the capillary to the extracellular space decreases.
- The fluid return from the extracellular space to the capillary increases.

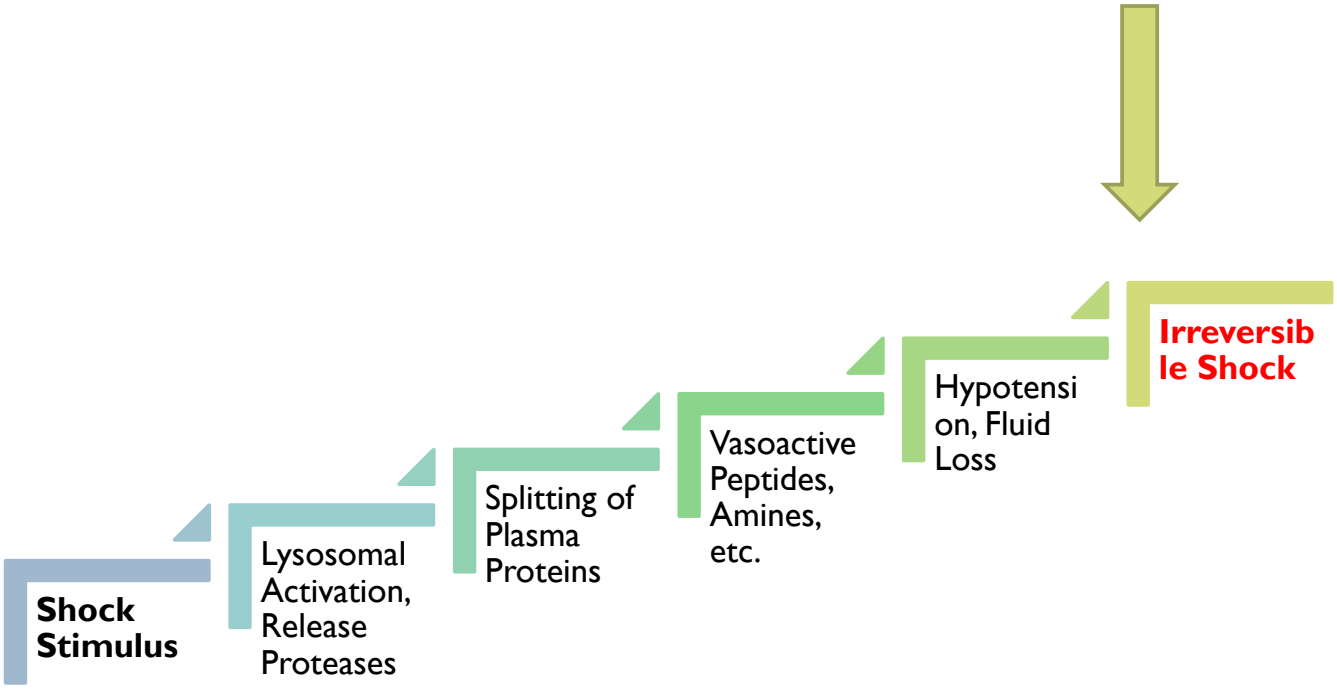
That will increase the blood volume & will increase BP helping to compensate shock.

Fluid-Shift Mechanism in Shock



Stages of Shock

Reversible shock: (Compensated)	Progressive	Irreversible shock:
• Changes can be reversed by compensatory mechanism • (neurohormonal activation) or by treatment. • Defense mechanisms are successful in maintaining perfusion. • Non-progressive	• Defense mechanisms begin to fall. • Multi-organ failure.	• Complete failure of compensatory mechanisms. • Can lead to death.



Lecture #12&13 Arterial Blood Pressure and Regulation of Blood Pressure

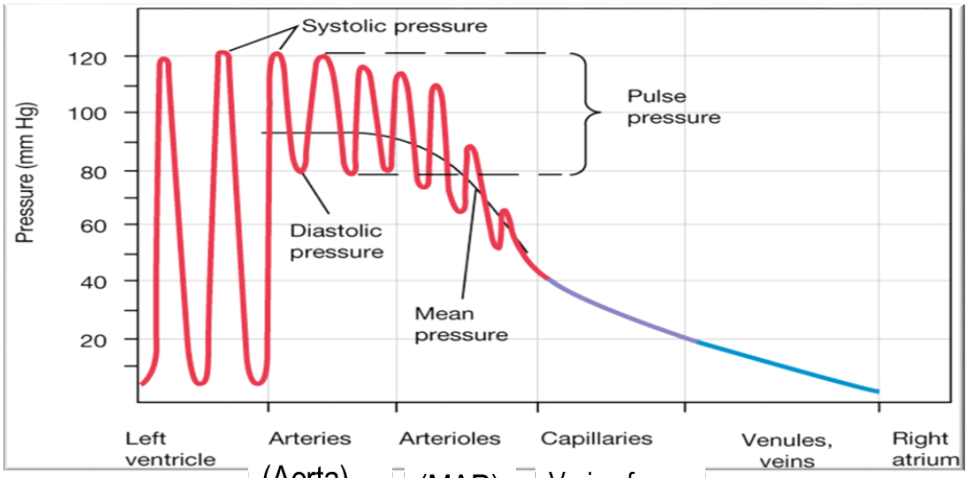
What is meant by Arterial Blood Pressure?

Lateral pressure created by the heart as it pumps blood, against any unit area of the vessel wall.

In normal adult $\approx \frac{120\ mmHg}{80\ mmHg} = \frac{\text{systolic (pressure while heart is beating)}}{\text{diastolic (pressure while heart is relaxing)}}$

(Systole reaches during rapid ejection phase and diastole is reached during isovolumetric contraction phase)

- Blood flows down a pressure gradient. (Highest at the heart.)
- ↓ over distance. ↓ 90% from aorta to vena cava.
- Greatest drop in pressure occurs in arterioles. No large fluctuations in capillaries & veins.



This is the systemic circulation pressure. If we divide it by 6 we get the pulmonary circulation, because the left ventricle generates a pressure six times more than right ventricle.

Mean Arterial Pressure (MAP)

MAP is the average pressure responsible for driving blood into the tissues throughout the cardiac cycle.

MAP = DP + 1/3 PP

Pulse Pressure (PP)

Is the difference between the systolic and diastolic blood pressure values. It is determined by (1) change in volume and (2) compliance.

PP = SP – DP = 120 – 80

PP = 40 mmHg

Factors Affecting ABP

Age Old > young	**Emotions** ↑ BP	**Exercise** ↑ BP	**Pregnancy** ↑ BP	**Hormones** (AD, NA)
Sex M > F	**Gravity** LL > UL	**Sleep** ↓ BP	**Race**	**Temperature** ↓ BP (hot) & ↑ BP (cold)

BP range: 90-140/60-90 mmHg.

Factors Determining ABP

- Cardiac output (Flow).
- Peripheral Resistance.
- Blood volume.

Blood Pressure(MABP) = Cardiac Output (CO) X Peripheral Resistance(PR)

(1) **Cardiac Output**:

Is the amount of blood pumped by ventricles (output) per minute.

CO= Stroke Volume X Heart Rate

Output of ventricles / beat ≈ 70 ml/beat

Beats/ minute ≈ 70-75 beats/min

CO = 70 x 70 = 4900 ml/min ≈ 5 L/min

- All of the CO flows through the systemic circulation. (Amount of blood moving through a vessel in a given time period) Therefore, CO = Flow.
- Pressure is directly proportional to Flow as blood flows down a pressure gradient.
- Absolute value of pressure is not important to flow, but the difference in pressure (DP or gradient) is important to determining flow.

$$\text{Blood Flow (Q)} = \frac{\text{Change in pressure } (\Delta P)}{\text{Resistance (R)}} \qquad Q = \frac{\Delta P}{R}$$

$$\text{Cardiac Output} = \frac{\text{Mean Arterial Pressure (MAP)}}{\text{Total Peripheral Resistance (TPR)}} \qquad C.O. = \frac{MAP}{TPR}$$

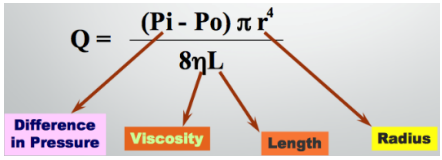
Factors Determining ABP

(2) **Peripheral Resistance**: Doctor said this is very important!

- Resistance is tendency of vascular system to oppose flow. Flow = $\frac{1}{R}$
- Flow decreases (↓) when resistance increases.
- Flow resistance decreases (↓) when vessel diameter increases.
- Resistance if influenced by:
- Length of the vessel(L), radius of the vessel(r), & viscosity of the blood(η) .

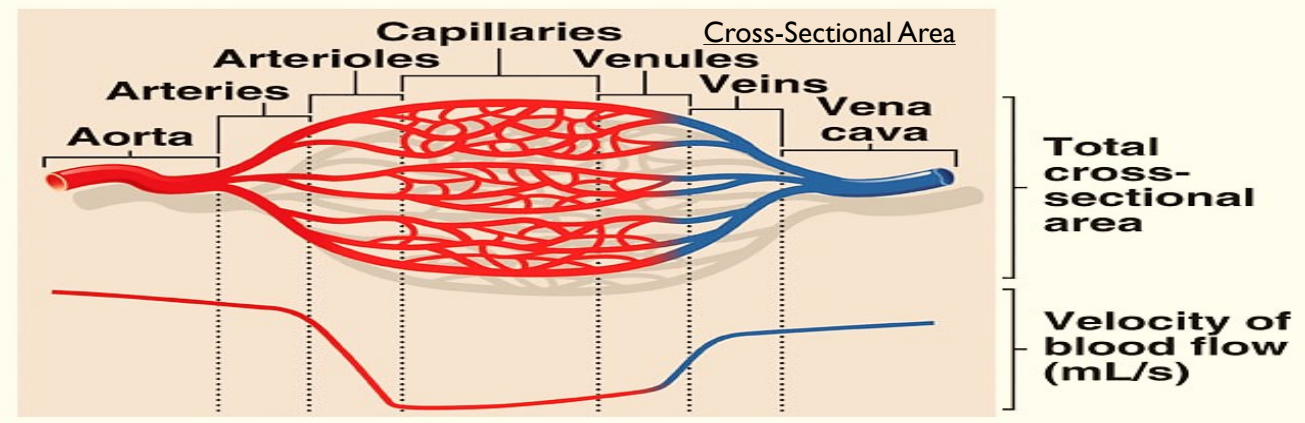
Poiseuille's law: $R = \frac{8L\eta}{\pi r^4}$

$$\text{Flow } (Q) = \frac{\Delta P}{R} \rightarrow Q = \frac{\Delta P}{\frac{8L\eta}{\pi r^4}} \rightarrow Q = \frac{\Delta P\, \pi r^4}{8L\eta} \rightarrow$$



'Systemic circulation has higher resistance than pulmonary circulation, due to the higher pressure difference in systemic circulation'

Resistance is higher in series, and arterioles have the highest resistance.



Cross Sectional Area

As diameter of vessels ↓, the total cross-sectional area ↑ & velocity of blood flow ↓

Capillaries have the highest surface area, and therefore the slowest velocity.

Note: Flow depends on difference of pressure but velocity depends on surface area.

Compliance of Blood Vessels

- Compliance is the **volume** of blood that the vessel can hold at a given **pressure**.
- Compliance = distensibility. $\text{Compliance (C)} = \frac{\text{Volume (V)}}{\text{Pressure (P)}}$
- Venous system has a large compliance & acts as a blood reservoir (high volume & low pressure).

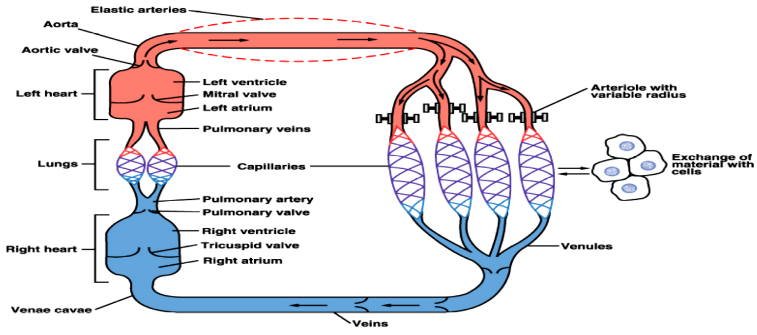
Vascular System Possesses Different Mechanisms for Promoting Continuous Flow of Blood to the Capillaries

1)Elastic recoil (Arteries)

2)Smooth muscle regulation of diameter (arterioles)

3)Sphincters (capillaries)

4)Valves (veins and the heart)



Laminar and Turbulent Flow/BP

Laminar flow

- Stream-lined
- Outermost layer moving slowest & center moving fastest

Turbulent flow

- Interrupted
- Fluid passes a constriction, sharp turn, rough surface
- Rate of flow exceeds critical velocity

BP is measured by listening for Korotkoff sounds produced by turbulent flow in arteries:
Systolic pressure: when 1st sound is heard.
Diastolic pressure: when last sound is heard.

Other Factors Determining Blood Pressure

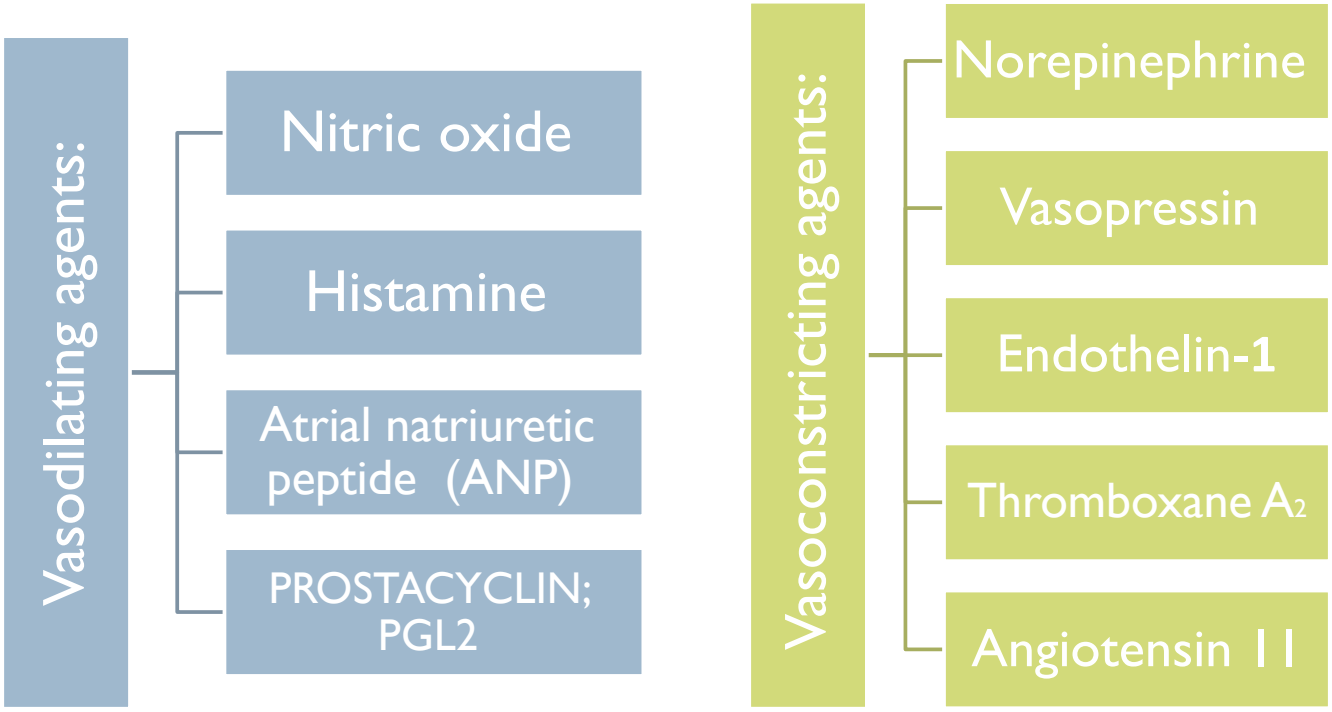
(3) **Blood volume:**

- An increase in blood volume → ↑cardiac output (CO) → ↑arterial blood pressure (ABP).
- A decrease in blood volume as in hemorrhage, dehydration → ↓venous return (VR) → ↓ cardiac output (CO) → ↓ arterial blood pressure(ABP).

(4) **Elasticity of blood vessels:**

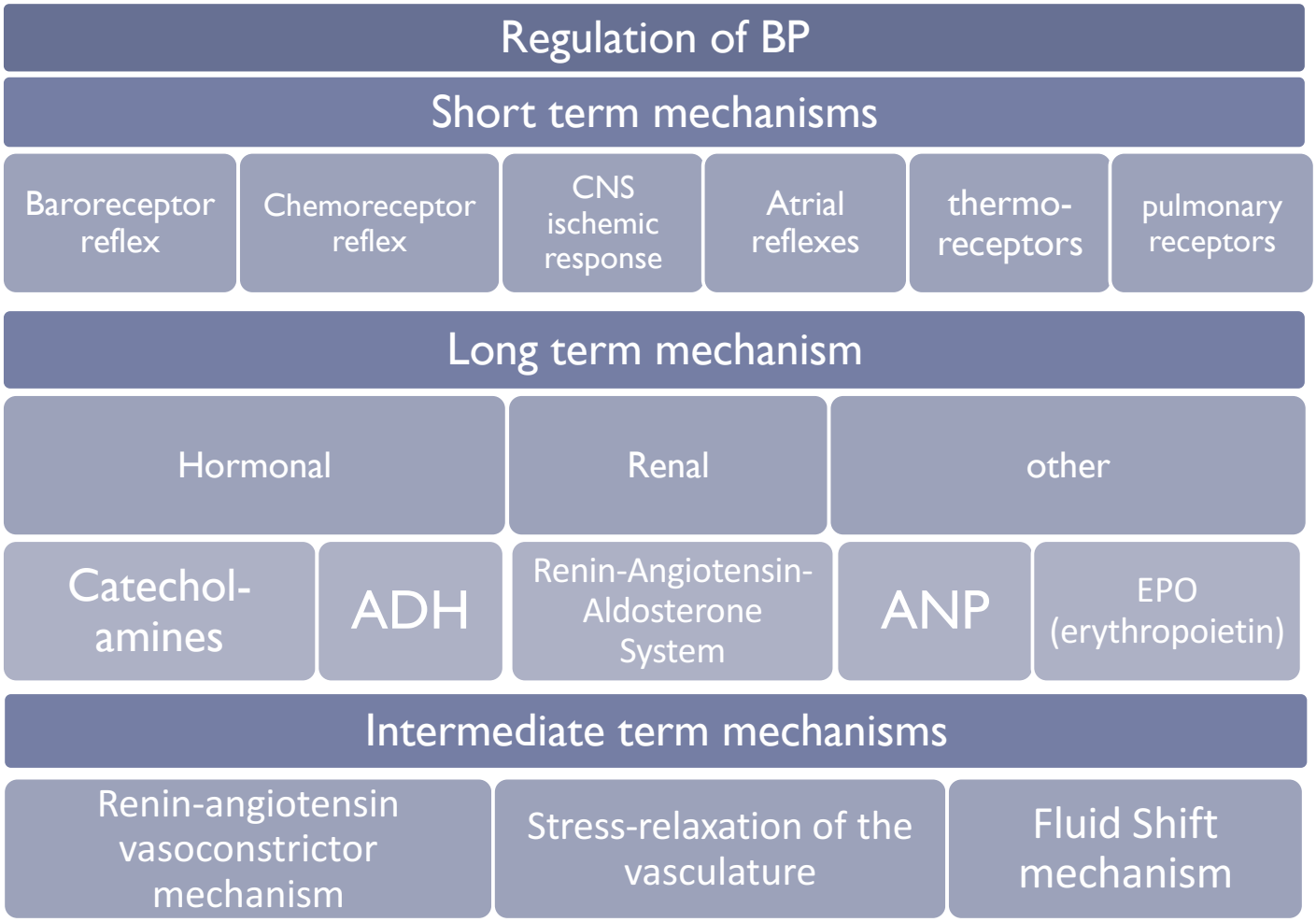
- Changes in the elasticity of great vessels affects ABP.
- In atherosclerosis, there is decrease in arterial compliance ("hardening of the arteries"). This makes arteries like a tube, so during systole, as blood is ejected into the arteries, they don't distend as normal and pressure increases significantly → ↑ PP.

Factors Affecting Vessels Diameter



Regulation of Blood Pressure

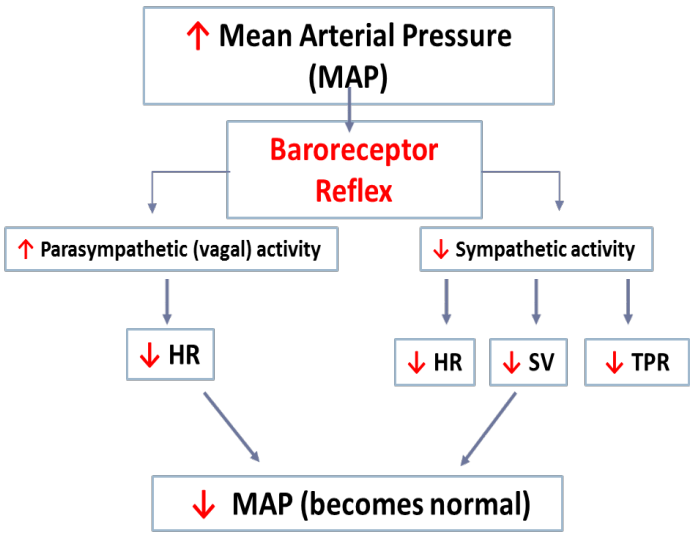
- Blood pressure is well regulated due to various reasons: most importantly to provide organs (especially the brain) with adequate perfusion pressure.
- Inability to regulate blood pressure can contribute to diseases.
- In order to regulate blood pressure, the determining factors have to be regulated: (1) Cardiac Output (2) Peripheral Resistance (3) Blood Volume.
- **Short term mechanisms** (seconds to minutes): are largely neural. They regulate **cardiac function** (output) and **arteriolar diameter** (resistance).
- **Intermediate** and **long term mechanisms** (minutes to days): are largely renal and hormonal. They regulate **blood volume**.



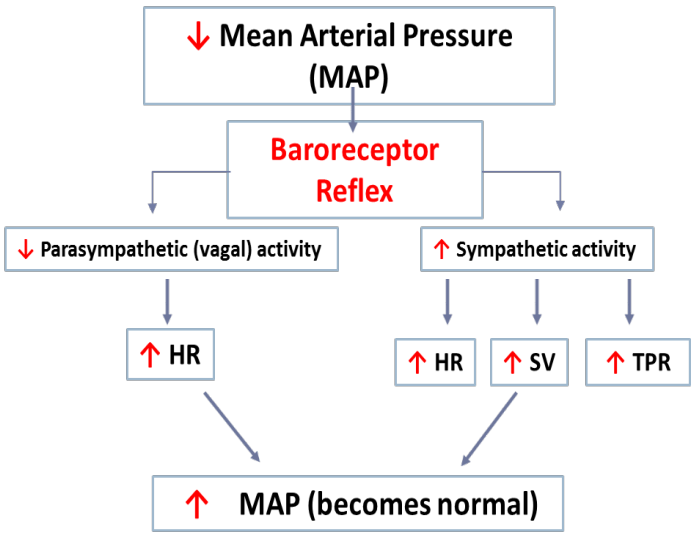
Short Term Mechanism

(I) Arterial Baroreceptors Reflex

- Changes in MAP are detected by baroreceptors (mechano-stretch receptors) located in the right and left carotid sinuses and in the aortic arch.
- These receptors provide information to the cardiovascular centers in the medulla oblongata (Vasomotor center and cardiac inhibitory center) about the degree of stretch because of pressure changes.
- Provide powerful moment-to-moment control of arterial blood pressure.



Note:
↓ Sympathetic activity → vasodilatation → ↓ TPR.



Note:
↑ Sympathetic activity → vasoconstriction → ↑ TPR.

Baroreceptors Reflex Mechanism During:

(A) Hemorrhage: causes the arterial blood pressure (MAP) to decrease.

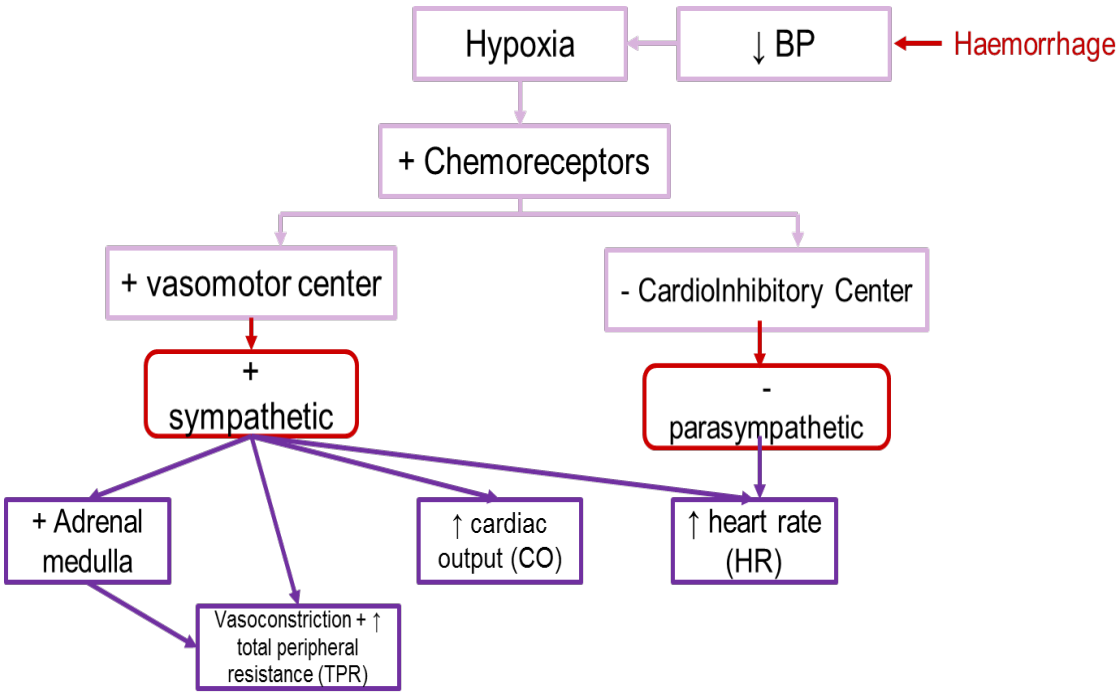
(B) Postural change: On standing, MAP in the head & upper part of the body drops. The baroreceptor reflex is activated → strong sympathetic impulses → vasoconstriction. This minimizes the drop in MAP.

Short Term Mechanism

(2) Arterial Chemoreceptor Reflex

- Chemoreceptor reflex operates in much the same way as the baroreceptor reflex, EXCEPT that chemoreceptors are chemo-sensitive cells instead of stretch receptors.
- Also unlink baroreceptors which both increase and decrease BP, chemoreceptors only increase BP.
- Chemoreceptors are stimulated when the MAP is lower than 60 mmHg.

Peripheral Chemoreceptors	Central Chemoreceptors
Sensory receptors located in carotid & aortic bodies.	Sensory receptors located in the medulla itself.
Sensitive to O2 lack , CO2 (decrease or increase) & pH (decrease or increase)	Very sensitive to CO2 excess increase & decrease pH in medulla.



Short Term Mechanism

(3) CNS Ischemic Response; Cushing Reaction

- It is not a normal mechanisms for regulating ABP; it operates as an emergency arterial pressure control system that acts rapidly and powerfully to prevent further decrease in MAP whenever blood flow to the brain decreases to lethal levels.
- It is one of the most powerful activators of the sympathetic vasoconstrictor system.
- When MAP < 20 mmHg → cerebral ischemia of vasomotor center → strong excitation of vasomotor center (due to accumulation of CO2, lactic acid,….) → strong vasoconstriction of blood vessels including the kidney arterioles.

Other Vasomotor Reflexes

(4) Atrial stretch receptor reflex:

- increase in venous return stimulates atrial stretch receptors which in turn produces reflex vasodilatation & decrease in ABP.

(5) Thermo-receptors (in skin / hypothalamus):

- Exposure to heat > vasodilatation.
- Exposure to cold > vasoconstriction.

(6) Pulmonary receptors:

- Lung inflation > vasoconstriction.

Long Term Mechanism

Hormonal Regulation

(1) Catecholamine's (AD & NA)

- Adrenaline released from the adrenal medulla circulates in the blood and can bind to both α and β adrenoceptors.
- Noradrenaline released from the sympathetic nerves binds primarily to α adrenoceptors.
- α-adrenoceptor stimulation promotes vasoconstriction
- β-adrenoceptor stimulation promotes vasodilation

(2) Vasopressin (Antidiuretic hormone; ADH)

- ADH (vasopressin) is synthesized in the Paraventricular nucleus of the hypothalamus, then it is stored in the posterior pituitary.
- It has two major functions which will lead to Increase in BP:

  1- Vasoconstriction, in order to ↑ ABP.

  2- Promotion of water retention by the kidney (at kidney tubules to ↑ blood volume.

- How is it secreted?

1- Increased Osmolarity.	2- Osmoreceptor Stimulation.	3- ADH release.
This happens with dehydration, salt intake, or hypovolemia.	Receptors in the hypothalamus sense the increased osmolarity in the blood.	The pituitary gland releases ADH. Usually, when it is secreted aldosterone is secreted.

Long Term Mechanism

Renal Regulation

(3) Renin Angiotensin Aldosterone System

- Blood volume is controlled by the kidney which has sensors called Juxtaglomerular cells that secrete Renin with decreased blood flow to them.

Decreased renal blood flow to decrease in sodium activates Juxta-glomerular apparatus of kidneys (volume receptors)

→

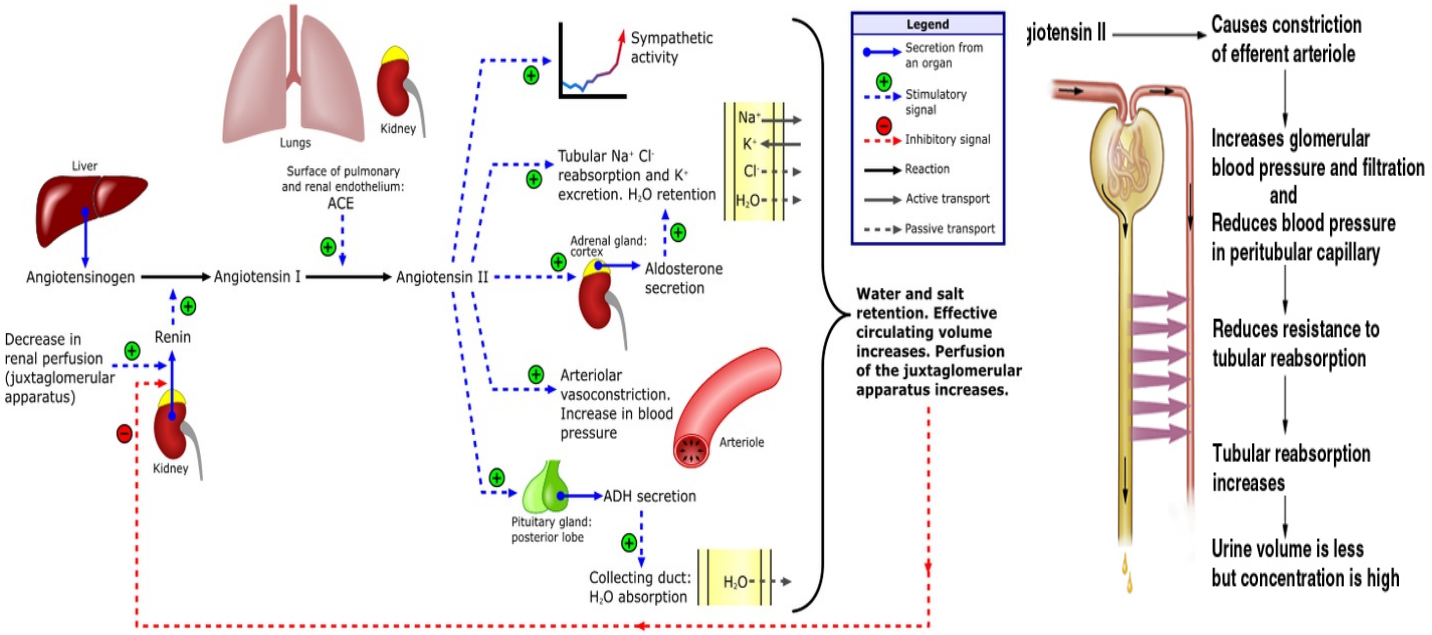
Renin system is activated and converts angiotensin (plasma protein) to angiotensin I (lungs)

→

Through converting enzymes Angiotensin I is converted to Ag II (vasoconstricto r) to Ag III

→

In adrenal cortex corticosterone is converted to aldosterone which promotes Na retention



Long Term Mechanism

Other

(4) Atrial Natriuretic Peptide (ANP) hormone:

- Hormone released from cardiac muscle cells (wall of right atrium) as a response to an increase in ABP.
- Simulates an ↑ in urinary production, causing a ↓ in blood volume & blood pressure.

(5) Erythropoietin (EPO)

- Secreted by kidney when blood volume is too low.
- Leads to RBC formation which increases blood volume.

Intermediate Term Mechanism

(activated within 30 mins to several hrs)

(1) Renin-Angiotensin vasoconstrictor mechanism

(2) Fluid shift mechanism:

- Movement of fluid from interstitial spaces into capillaries in response to ↓ BP to maintain blood volume.
- Conversely, when capillary pressure too high, fluid is lost out of circulation into the tissues, reducing blood volume as well as all pressures throughout circulation.

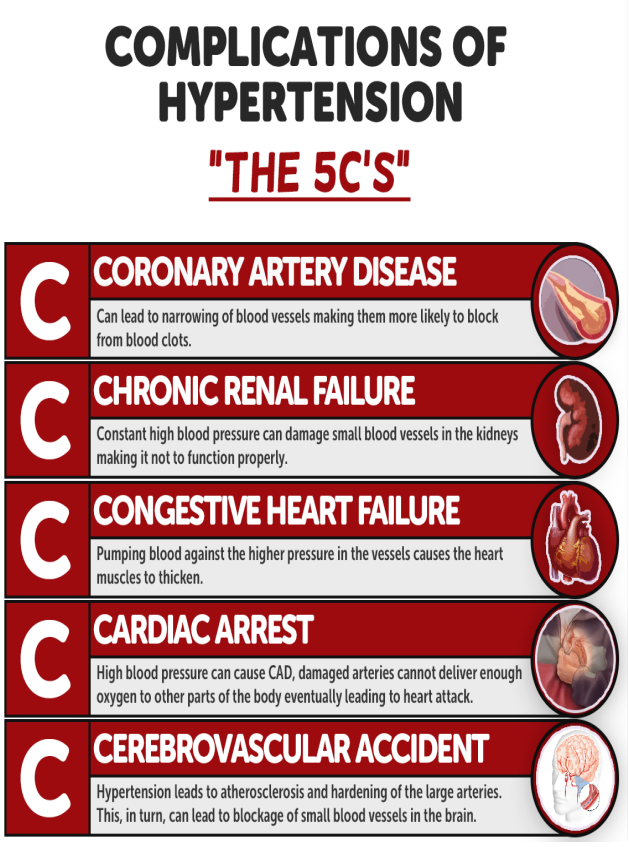
(3) Stress Relaxation mechanism:

- When pressure in blood vessels becomes too high, they become stretched & keep on stretching more & more for minutes or hours; resulting in fall of pressure in the vessels toward normal.
- This continuing to stretch of the vessels can serve as an intermediate-term pressure "buffer."

Hypertension

- Blood pressure may be:
  - Below normal: hypotension if below 100/60 mmHg
  - Above normal: hypertension if above 140/90 mmHg
- Hypertension could result from increase in:
  - Cardiac Output
  - Total peripheral resistance
  - Both
- Hypertension is either:
  - Primary (essential/idiopathic) = 90%
  - Secondary = 10%

1-Drugs
2-Coarctation of the aorta
3- Pregnancy
4-Renal diseases
account for over 80% of the case of secondary hypertension.
5-Endocrine causes
••Conn's syndrome. ••Adrenal hyperplasia. ••Phaeochromocytoma. ••Cushing's syndrome. ••Acromegaly.



Lecture #14 capillary circulation

Capillary

Capillary Bed

Capillary Bed : Arterioles

Arterioles :are resistance blood vessels which may restrict flow to capillaries or allow greater flow.

- Arteriolar diameter is generally 5 – 100 micrometers.
- They have a thick smooth muscle layer and endothelial lining.
- They have precapillary sphincters

Capillary Bed : Metarterioles and A-V Shunt

- They arise from arterioles and give rise to capillaries.
- They can connect with venules and/ or supply capillaries.
- They have pre-capillary sphincters

An A-V shunt is a small vessel with direct connection between an arteriole and a venule.

Capillary beds consist of two types of vessels:
Vascular shunt: directly connects an arteriole to a venule .
True capillaries: exchange vessels.
• Oxygen & nutrients cross to cells.
• Carbon dioxide & metabolic waste products cross into blood.

Capillary Network

Blood flows from arterioles through metarterioles*, then through capillary network Venules drain network.

What regulates the blood flow?

1. Smooth muscle in arterioles.
2. Metarterioles.
3. Precapillary sphincters.

Types

They are classified by diameter/permeability:

1. Continuous: Do not have fenestrae (for gas exchange)
2. Fenestrated: Have pores (for normal molecules)
3. Sinusoidal: Large diameter with large fenestrae (for large molecules)

Characteristics

Smallest blood vessels.
One endothelial cell thickness and no smooth muscles.
They are called exchange vessels.
Why?
Because:
-They provide direct access to cells.
-Most permeable.
-Permits exchange of nutrients & wastes.

Continuous Capillaries: These capillaries are present in most body tissues, e.g., muscle, lung, and adipose tissue.

Fenestrated and Sinusoidal Capillaries:

- Fenestrated capillaries are found in the kidney glomeruli, small intestine, and endocrine glands
- Some endothelial cells have wide pores (fenestrations).
- They are very permeable: they allow even large substances to pass but not plasma proteins.

Cross-Sectional Area

As diameter of vessels decreases, the total cross-sectional area increases & velocity of blood flow decreases.
Much like a stream that flows rapidly through a narrow gorge but flows slowly through a broad plane.

Regulation of Flow in Capillary Beds and Mechanisms of Capillary Exchange

Regulation of flow in capillary beds

The arterioles and the precapillary sphincters function as control valves in the tissue they feed:

- During the "fight or flight" response, flow to non-essential organs (kidney, skin, etc.) is clamped off → increased flow to skeletal muscle.
- Metabolic waste products act as vasodilators to relax precapillary sphincters.
- Vasomotion: intermittent flow through capillary, in response to altering metabolic needs.

Mechanisms of capillary exchange.

Transport of substances across the capillary wall occurs by 3 major mechanisms:
1- Diffusion (according to concertation gradient)
2- Filtration (according to concertation gradient)
3- Transcytosis (vesicular transport)
Keep in mind that capillary permeability is not the same in all tissue.
It is specialized for different tissues:

- Liver sinusoids have discontinuous endothelium → ↑ permeability → allows exchange of **solutes** and **proteins**.
- Blood brain barrier capillaries have tight junctions = low permeability.
- Kidney and intestinal capillaries contain fenestrations (pores) → ↑ permeability.

Diffusion:It is a major process by which most nutritional substances and waste products move between the blood and the interstitium across the capillary wall according to the concentration gradients.
Transcytosis (Vesicular Transport): This is an active process by which large molecules can be transported across the capillary membrane
Filtration: is the process by which plasma and its dissolved crystalloids (electrolytes and glucose) can filter across the capillary according to **pressure** gradient.

Exchange of Fluid Between Capillaries and Tissues

Capillary exchange and interstitial fluid volume regulation:
What affects the movement of fluid from capillaries?
Blood pressure, capillary permeability & osmosis:
A net movement of fluid occurs from blood into tissues.
Fluid gained by tissues is removed by lymphatic system.

Diffusion at Capillary Beds (Fluid Balance)

Outward Forces:
1. Capillary blood pressure (Pc = 30-35 to 10-15 mmHg)
2. Interstitial fluid pressure (PIF = 0 mmHg)
3. Interstitial fluid colloidal osmotic pressure (μIF = 3 mmHg)

TOTAL = 38 to 18 mmHg
Inward Force:
1. Plasma colloidal osmotic pressure (μC = 25- 28 mmHg)

Lymphatic System and Lymph Circulation

Lymphatic System

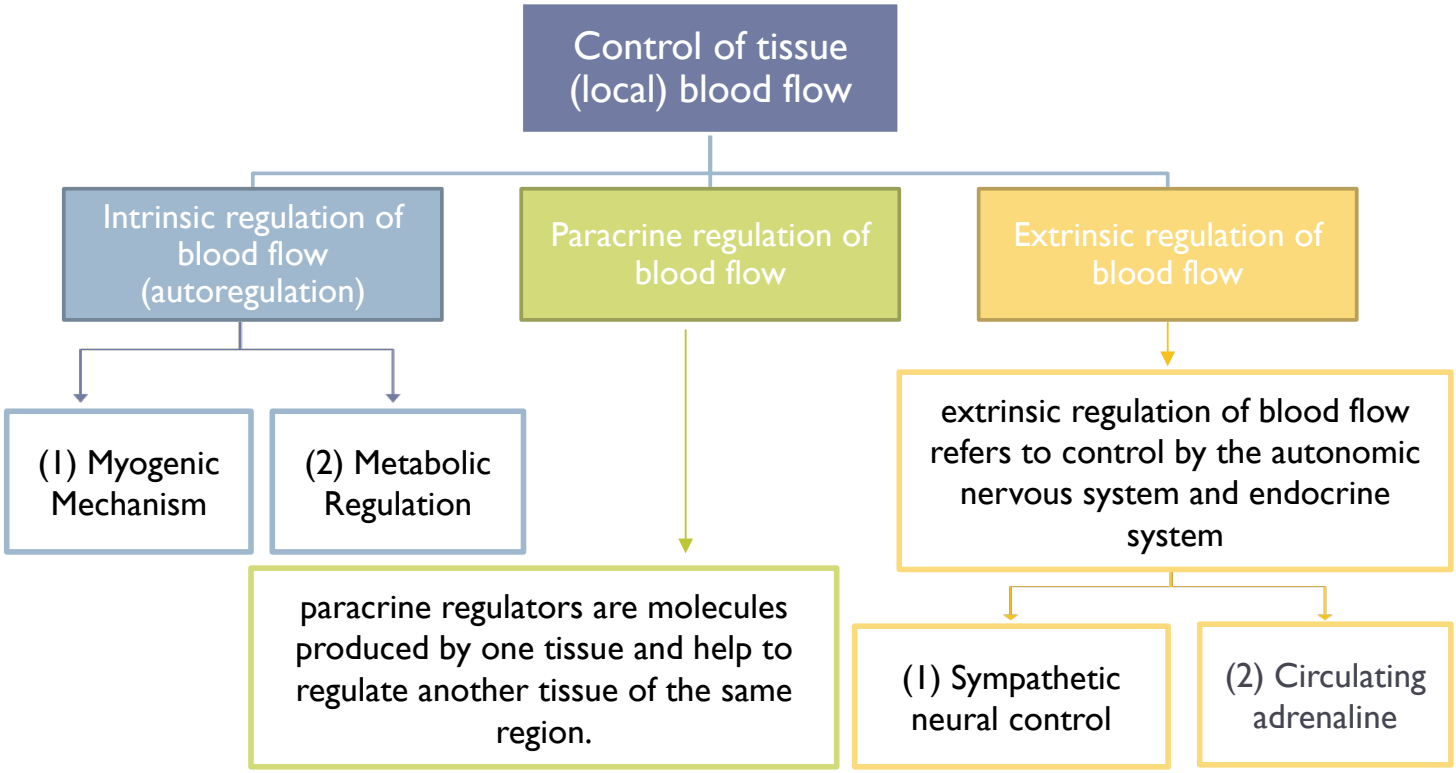
Lymphatic vessels present between capillaries.

3 basic functions:

- Drain excess interstitial (tissue) fluid back to the blood, in order to maintain original blood volume.
- Transports absorbed fat from small intestine to the blood.
- Helps provide immunological defenses against pathogens.

Numbers in this slides are not important since they vary from one tissue to another.

Lecture #15 Coronary Circulation



Intrinsic Regulation of Blood Flow; (Autoregulation)

- Intrinsic mechanisms of control of tissue blood flow are "built-in" mechanisms within individual organs that provide a localized regulation for vascular resistance and blood flow.
- The brain and kidneys in particular, utilize these intrinsic mechanisms to maintain relatively constant flow despite fluctuations in blood pressure.

(1) **Myogenic Mechanism**:

- This is a direct response of vascular smooth muscle to changes in pressure and can occur in the absence of neural or hormonal influences.
- This action is purely myogenic, no mediators required.
- This involves stretch sensitive ion channels on the cell membrane.

Extrinsic Control of Tissue Blood Flow

(1) **Sympathetic neural control**

- Most vascular beads are under resting sympathetic constrictor tone.
- ↑ sympathetic tone constricts vascular smooth muscle.
- ↓ sympathetic tone ↓ vascular smooth muscle constriction.
- Stimulation of a1-receptors by noradrenalin produces vasoconstriction.

(2) **Circulating Adrenaline**

- Adrenaline stimulating a1-receptors contracts vascular smooth muscle.
- Blood vessels also contain β2-receptors which produce vasodilatation when activated.
- The blood vessels in most tissues have more a1-receptors than β2-receptors so adrenaline (and NA) contracts vascular smooth muscle.

Cont..

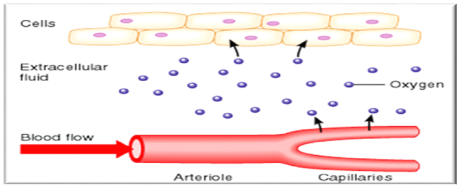
(2) Metabolic Regulation (Metabolic Mediators)

Reduced blood flow or increased metabolic rate (MR), allows metabolic products to accumulate → One or more of the accumulated metabolic products acts as a vasodilator. → Vasodilatation increases local blood flow

Oxygen may act in the opposite manner, i.e. oxygen acts as a vasoconstrictor → Reduced blood flow or increased metabolism reduces oxygen concentration. → Reduced oxygen concentration inhibits oxygen mediated vasoconstriction.

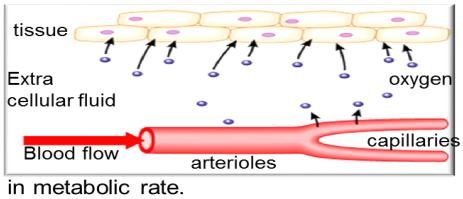
Metabolic Regulation: Effects of Oxygen

1



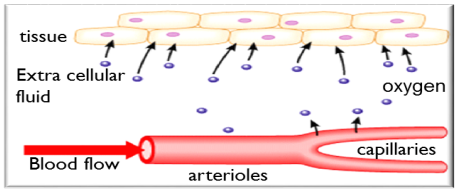
1. Under resting conditions, O2 delivered to a tissue by blood is matched by removal to the metabolizing tissue (Steady state O2 delivery to the tissues)

2



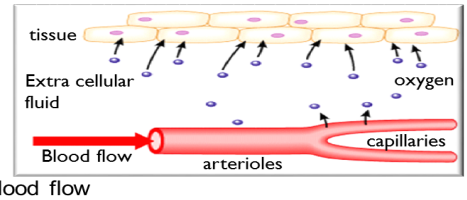
2. Increase in metabolic rate.
3. O2 consumption by the tissues increases.

3



4. O2 levels in the ECF decrease
5. ↓ [O2] causes vascular smooth muscle to relax: vasodilation

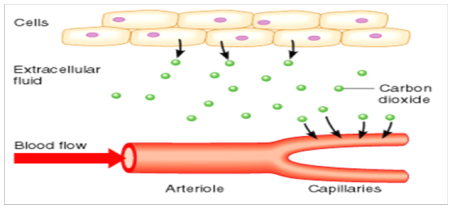
4



6. Increased blood flow
7. Increased O2 delivery

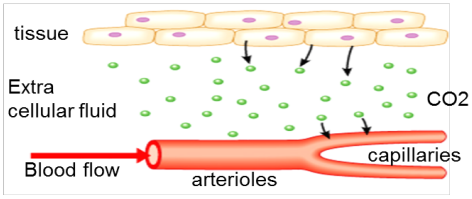
Metabolic Regulation: Effects of CO2

1



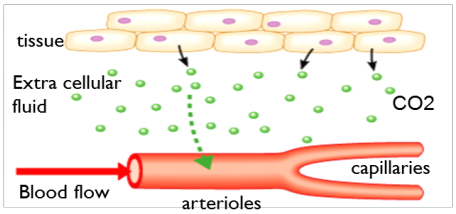
Steady State:
CO2 production = CO2 removal

2



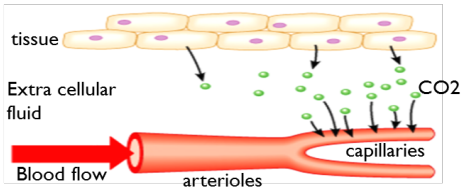
Increased metabolic rate or ↓ Blood Flow:
CO2 production > CO2 removal

3



↑[CO2]: Vasodilation
↓ pH; ↑ K+; ↑ lactic acid → vasodilation

4



Increased Blood Flow:
CO2 removal increases to match CO2 production.

Coronary Arteries

- The coronary arteries supply blood to the heart. They are 2:
  - Right Coronary: smaller, arises from right coronary sinus.
  - Left Coronary: larger, arises from left coronary sinus
  - Both terminate by anastomosing with each other.

	Branches	Distribution
Right Coronary	Right Marginal Artery (RMA)	RV, except the area adjoining the anterior inter ventricular (IV) groove.
	SA nodal Artery	The SA- node Surrounding Right atrium.
	AV nodal artery	The AV- node Surrounding right atrium
	Posterior descending branch (PDA)	Posterior 1/3rd of the inter-ventricular (IV) septum. Inferior part of Left ventricle adjoining the posterior inter ventricular groove.
Left Coronary	Left anterior descending (LAD)	Anterior & apical parts of the heart: LV & the TV area adjoining the anterior inter ventricular groove. Anterior 2/3rd of the inter ventricular septum.
	Circumflex artery (CX)	- Lateral & posterior surfaces of the heart: LV & SA-node
	Left marginal artery (LMA)	
	SA nodal artery	

Coronary Arteries

Phasic Changes in Coronary Blood Flow During Systole & Diastole

- Blood flow through the coronary arteries is greatest during diastole.
- Blood flow to the subendocardial portion of Lt ventricle occurs during diastole only, and is not there during systole thus the subendocardial region of Lt ventricle is prone to ischemic damage and is the most common site of (MI)
- In systole, blood is moving forward too rapidly to provide greatest flow.

Cardiac anastomosis:

- The two coronary arteries anastomose in the myocardium .
- Extra cardiac anastomosis: Vasa vasorum of the aorta.
  - Vasa vasorum of pulmonary arteries.
  - Internal thoracic arteries.
  - The bronchial arteries.
  - Phrenic arteries.

Extra cardiac channels open up in case of emergencies, when the coronary arteries are blocked.

Venous Drainage

- Coronary Sinus
- Anterior, middle & small cardiac veins
- Venae cordis minimae

Lymphatic Drainage

- Right trunk (ends in brachiocephalic node)
- Left trunk (ends into the trachea-bronchial lymph nodes)

Coronary Blood Flow

Coronary blood flow at rest in humans = 250 ml/min (5% of C.O.).

Control of coronary blood flow (CBF)

Autoregulation

Physical factors

Aortic pressure and direction of blood flow influence the perfusion pressure feeding the coronary arteries.

In systole the aortic pressure is highest but the direction and velocity of blood flow limit the coronary perfusion pressure. In diastole the aortic pressure is lower than in systole. However, the perfusion pressure is greatest.

Myogenic mechanisms

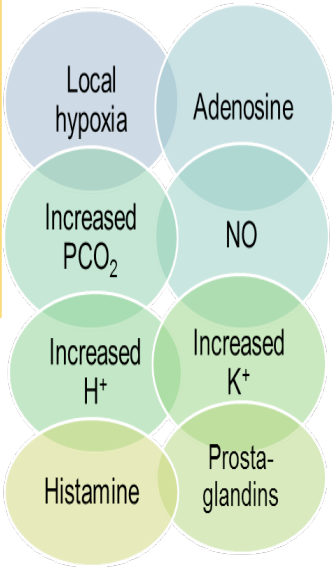
Coronary blood flow is maintained nearly constant over a range of mean MAP, usually 60 to 140 mm Hg.

Above or below these limits autoregulation fails and coronary blood flow increases or decreases in a linear fashion with corresponding increases or decreases in aortic pressure.

Systolic Crunch
70% of CBF occurs during diastole and 30% during systole

Metabolic control

Myocardial oxygen requirement is the single most important factor in determining coronary blood flow.
Coronary vasodilators during increased activity are:



Nervous control

Coronary arteries have both α1-(vasoconstriction) and β2-(vasodilation receptors.

Direct stimulation of the cardiac sympathetic fibers causes coronary vasoconstriction, (α>β)

Sympathetic activation to the heart results in coronary vasodilation and increased coronary flow due to increased metabolic activity (increased heart rate, contractility).
Parasympathetic activation of the heart results in decrease in myocardial oxygen demand due to a reduction in heart rate, and so ↓ coronary blood flow.

YOU ARE DONE!

اللهم إنّي استودعتك ماحفظت وماقرأت وماتعلمت فردّه لي وقت حاجتي إليه، أنك على كل شيء قدير.

تفائل بالله خيراً، فـ «كل متوقَّعٍ آت»

Good luck our DOCTORS!

Physiology Team436