Cardiovascular physiology

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Cardiovascular system (CVS)consists of:

✓ Heart

Is the pump which circulates the blood round the body.

✓ Blood vessels

Flow blood from the heart to cells & back to the heart.

Functions Cardiovascular system:

I -primary main functions of the heart:

- Acts as a muscular pump:

In order to maintain adequate level of blood flow throughout CVS by pumping blood under pressure into vascular system.

- responsible for the mass movement of fluid in body.

II -Secondary functions:

I – Transportation:

- delivers O2 to tissues & brings back CO2 to lungs.
- carries absorbed digestion products to liver & tissues.
- Carries metabolic wastes to kidneys to be excreted.
- Distribution of body fluid.

2-Regulation:

- carries hormones to target tissues to produce their effects.
- carries antibodies, leukocytes(WBC),cytokines& complement to aid body defense mechanism against pathogens.
- carries platelets & clotting factors to aid protection of body in blood clotting mechanism.
- helps in regulation of body temperature

Anatomy of the heart

Right Side of the heart
Left side of the heart

Consists of 2 separated pumps that maintain unidirectional flow of blood: the left & right hearts

- ✓ Lt heart pumps oxygenated blood from the lung to the tissues- Systemic circulation
- ✓ Rt heart pumps deoxygenated blood which has returned from the tissues to the lungs- Pulmonary circulation

The heart contains 4 chambers, each pump contains 2 chambers: an atrium & a ventricle.

Chambers of the heart

2 Atria:

The upper two chambers of the heart (atria) are thin-walled chambers, are divided by a wall-like structure called the interatrial septum.

receive blood returning back to the heart.

2 Ventricles:

The lower two chambers of the heart (ventricles), are thicker, muscular walls.

Pump blood from heart.

Each has same capacity & pumps same volume of blood in a given period of time. Atria & ventricles are separated into 2 functional units by a sheet of fibrous connective tissue, which gives attachment to the valves.

Valves of the heart

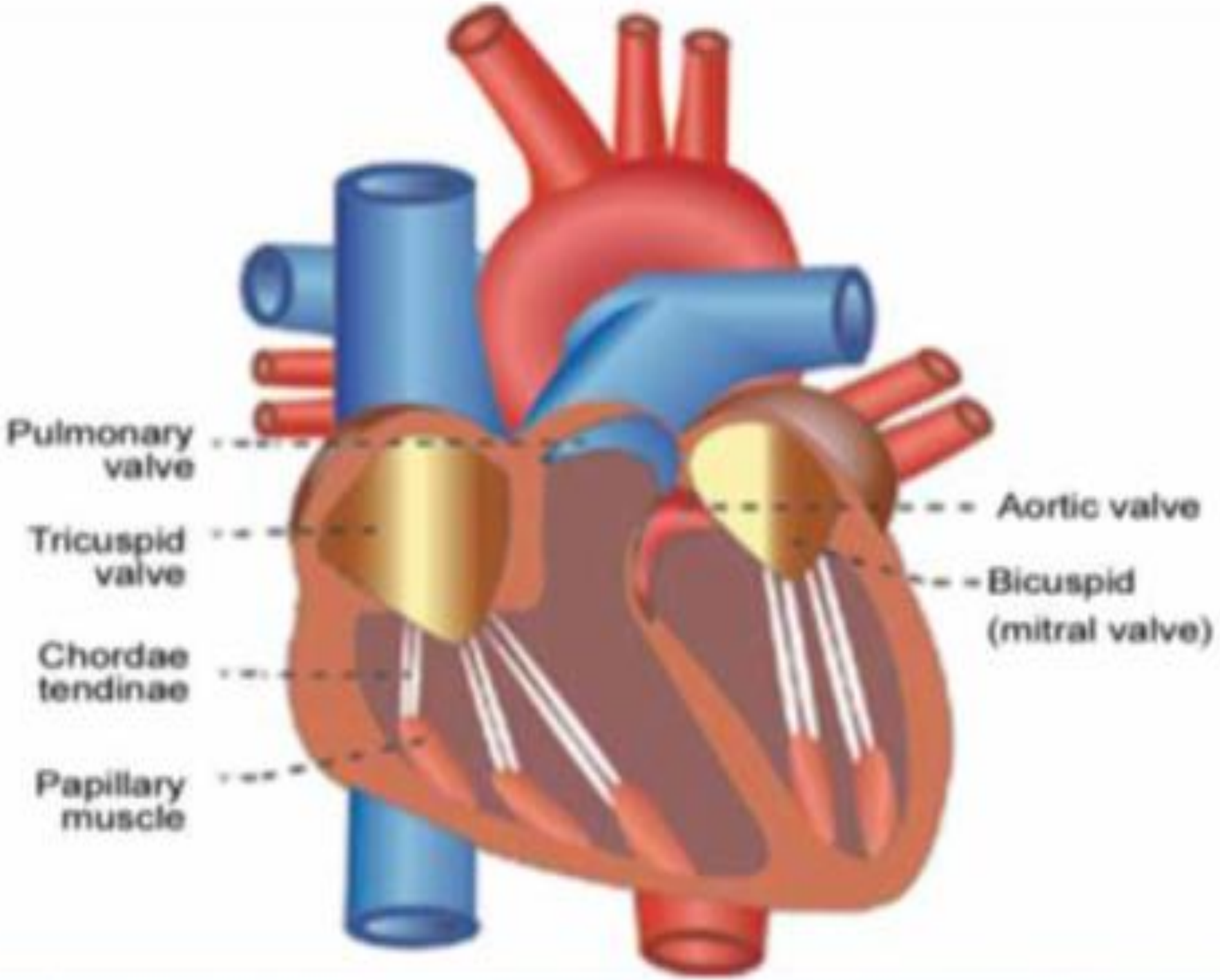
are structures which allow the blood to flow in one direction only, they do not contain any muscle tissue.

- ❑ Each ventricle has a valve at its inlet & valve at its outlet:
- ✓ The inlet valves are termed= atrioventricular (AV)valves, allow blood to flow from atria into ventricles.
  - on the left side it is known as the Mitral valve.
  - On right side it is known as the Tricuspid valve.

- ✓ The outlet valves are known as = the Semilunar valves. At origin of pulmonary artery & aorta.

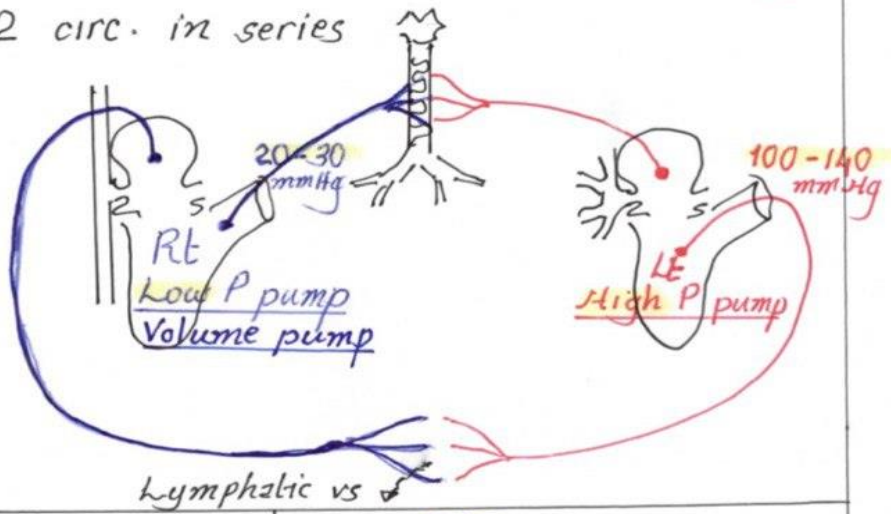
The valve on left side of the heart is known as aortic valve, on the right side it is also known as pulmonary valve.

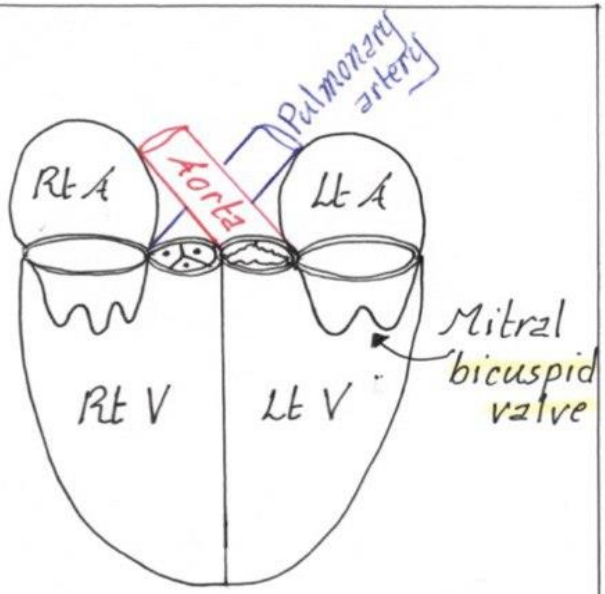
Two of the valves are in between the atria and the ventricles called atrioventricular valves. The other two are the semilunar valves, placed at the opening of the blood vessels arising from the ventricles, i.e. systemic aorta and pulmonary artery. The valves of the heart permit the flow of blood through the heart in only one direction


Pulmonary valve
Tricuspid valve
Chordae tendinae
Papillary muscle
Aortic valve
Bicuspid (mitral valve)

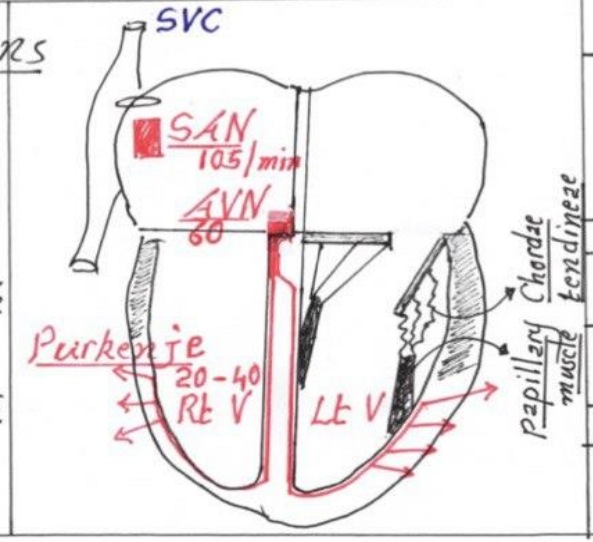
CVS = Heart + bl vessels 2

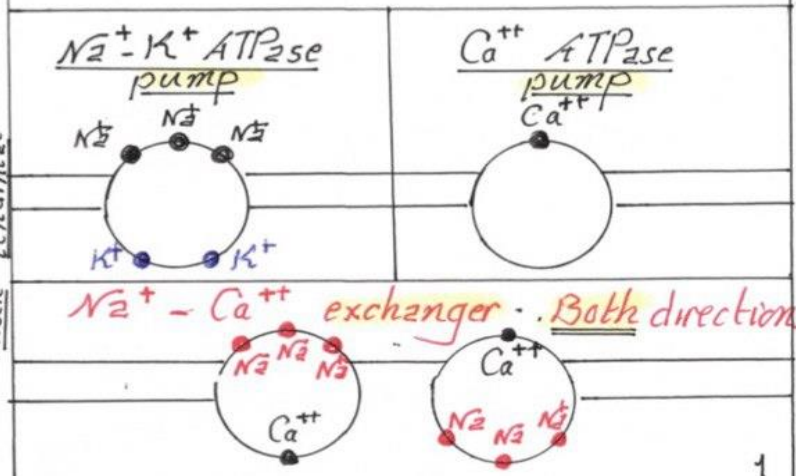
2 circ. in series





2 circulations
2 Hearts
2 Chambers
2 Types of valves
2 Types of m. fibres
2 Syncitia





Layers of Wall of the heart

Pericardium: outer covering of the heart.

Myocardium:: is the middle layer of the wall of the heart, formed by cardiac muscle fibers. it is responsible for the pumping action of the heart. is formed by three types of cardiac muscle fibers:

i. **muscle Fibers which Form the Contractile Unit of the Heart:**

These cardiac muscle fibers are striated fibers , similar to the skeletal muscles in structure. But, unlike the skeletal muscle fibers,
(involuntary in nature).
The cardiac muscle fiber is covered by sarcolemma. has a centrally placed nucleus. The myofibrils are embedded in the sarcoplasm.

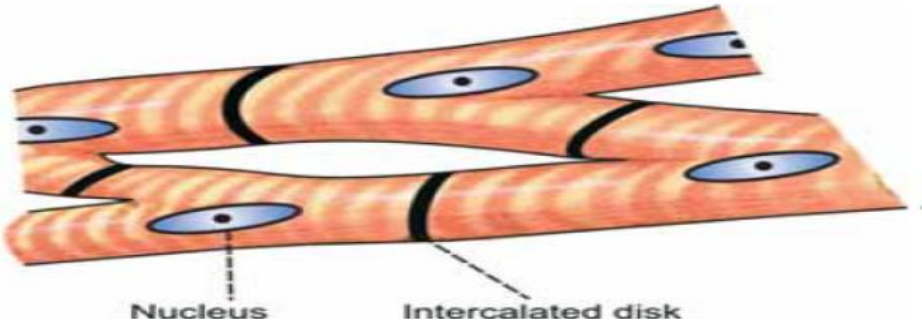
The sarcomere of the cardiac muscle has muscle proteins namely, actin, myosin, troponin and tropomyosin.

The cardiac muscle also have sarcotubular system like that of skeletal muscle.
The important difference between skeletal muscle and cardiac muscle is that the cardiac muscle fiber is branched .

Intercalated disk

is a tough double membranous structure situated at the junction between the branches of neighboring cardiac muscle fibers.

- form adherens junctions which play an important role in contraction of the muscle as a single unit .



Syncytium

The structure of cardiac muscle is considered as a syncytium.

the adjacent muscle fibers fuse together to form gap junctions which facilitates the rapid conduction of electrical activity from one fiber to another.
This makes the cardiac muscle fibers act like a single unit referred as physiological syncytium.

The syncytium in human heart has two portions, atrial syncytium and ventricular syncytium which are connected by atrioventricular ring.

ii. . Muscle Fibers which Form the Pacemaker:

Some of the muscle fibers of the heart are modified into a specialized structure known as pacemaker.

The muscle fibers forming pacemaker have less striation.

Pacemaker:

is structure in the heart that generates the impulses for heart beat. It is formed by the pacemaker cells called P cells. Sinoatrial(SA) node forms the pacemaker in human heart.

iii. Muscle Fibers which Form the Conductive System

The conductive system of the heart is formed by the modified cardiac muscle fibers. The impulses from SA node are transmitted to the atria directly, the impulses are transmitted to the ventricles, through various components of conducting system

ENDOCARDIUM

is the inner layer of the heart wall. It is formed by a single layer of endothelial cells lining the inner surface of the heart. Endocardium continues as endothelium of the blood vessels.

BLOOD VESSELS

The vessels of circulatory system divided into arterial and venous systems.

- Arterial System: comprises the aorta, arteries and arterioles

The arterioles are continued as capillaries which are small, thin walled vessels having a(5 to 8 μ.)

The capillaries are functionally very important because, the exchange of materials between the blood and the tissues occurs through these vessels.

VENOUS SYSTEM

From the capillaries venous system starts and it includes the venules, veins and vena cavae.

The venules are smaller vessels with thin muscular wall than the arterioles.

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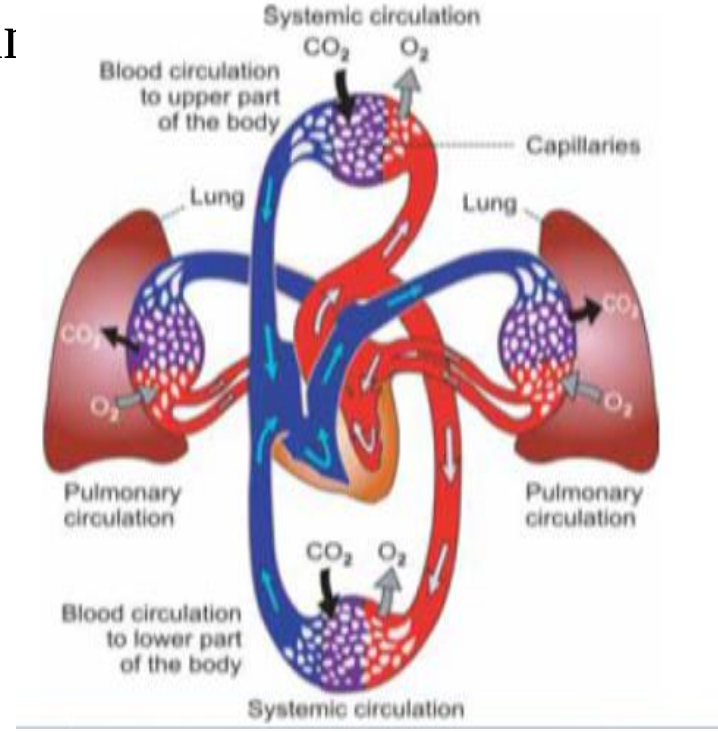
Pulmonary and Systemic Circulations--DIVISIONS OF CIRCULATION

Blood flows through two divisions of circulatir

1. Systemic circulation
2. Pulmonary circulation.



Pulmonary circulation: blood pumped from RV through lungs & back to the heart

Systemic circulation: oxygen- rich blood pumped by the LV to all organ systems to supply nutrients.

Rate of blood flow through systemic circulation= flow rate through pulmonary circulation.

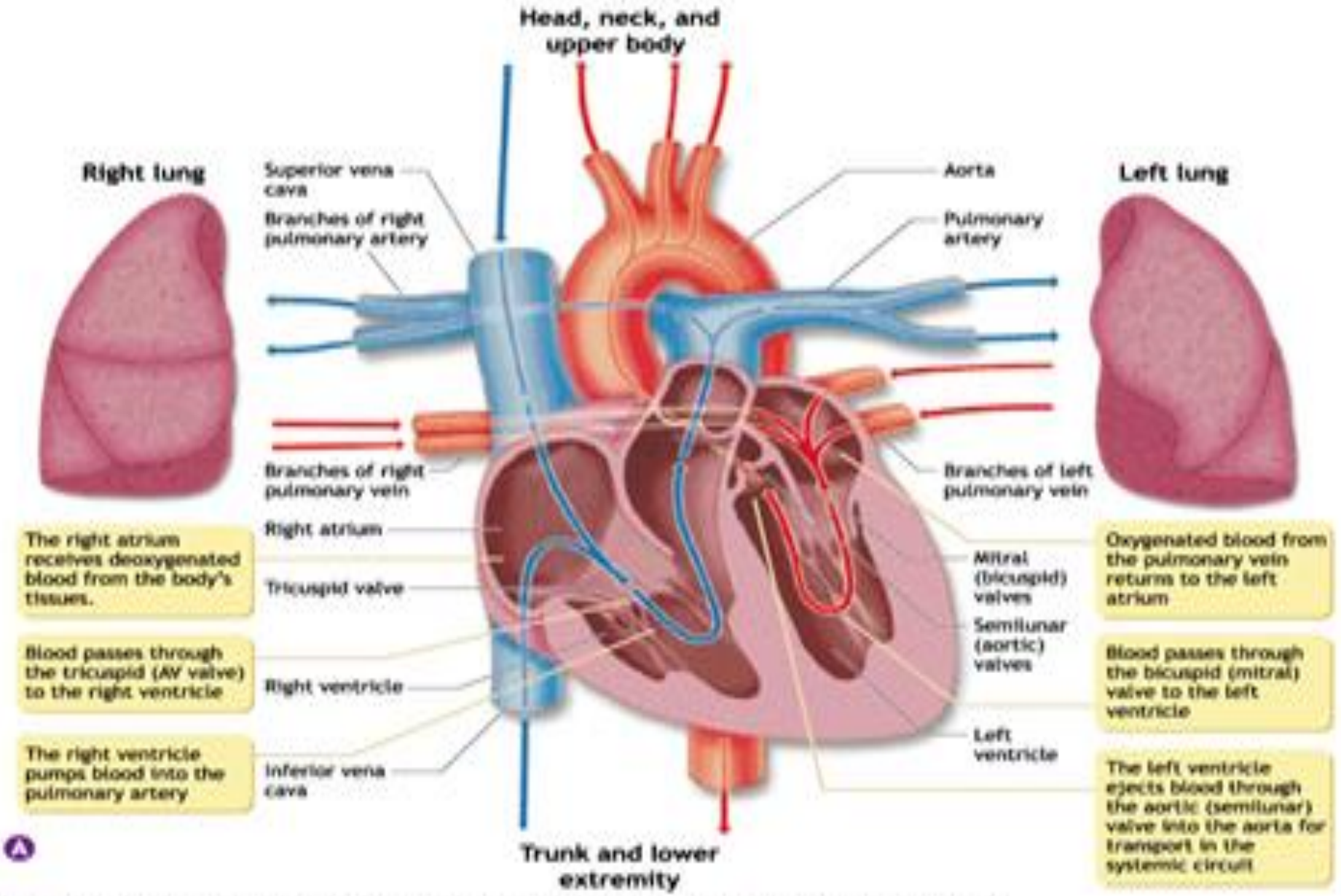


Figure 15.3. A. The heart, its great vessels, and the action of its valves. The valves provide for the one-way flow of blood as indicated by the *arrows*.

Properties of Cardiac Muscle

Physiology of cardiac muscle:

The heart is composed of 2 major types of cardiac muscle:

I- Contractile tissue ordinary muscle (compsed of 2 types of muscles: atrial& ventricular muscles) contract when stimulated, in same way as skeletal muscles except for longer duration.

- ✓ **Autorhythmic** (or automatic) tissue. (pacemaker)

- specialized or modified cardiac tissues, that contract only feebly as they contain few contractile fibrils.
- self stimulating with/out any external stimulation.
- initiate repetitive action potentials, that exhibit ''Pacemaker'' potentials, rhythmicity & varying rates of conduction.
- provide an excitatory system for the heart.

There are four properties to cardiac muscle

1) EXCITABILITY

is defined as the ability of a living tissue to give response to a stimulus. In all the tissues, the initial response to a stimulus is the electrical activity in the form of action potential. It is followed by mechanical activity in the form of contraction, secretion

Excitability

A potential of atrial or ventricular muscle fibres

Fast response AP

nonpace maker AP

0 **Rapid Dep**

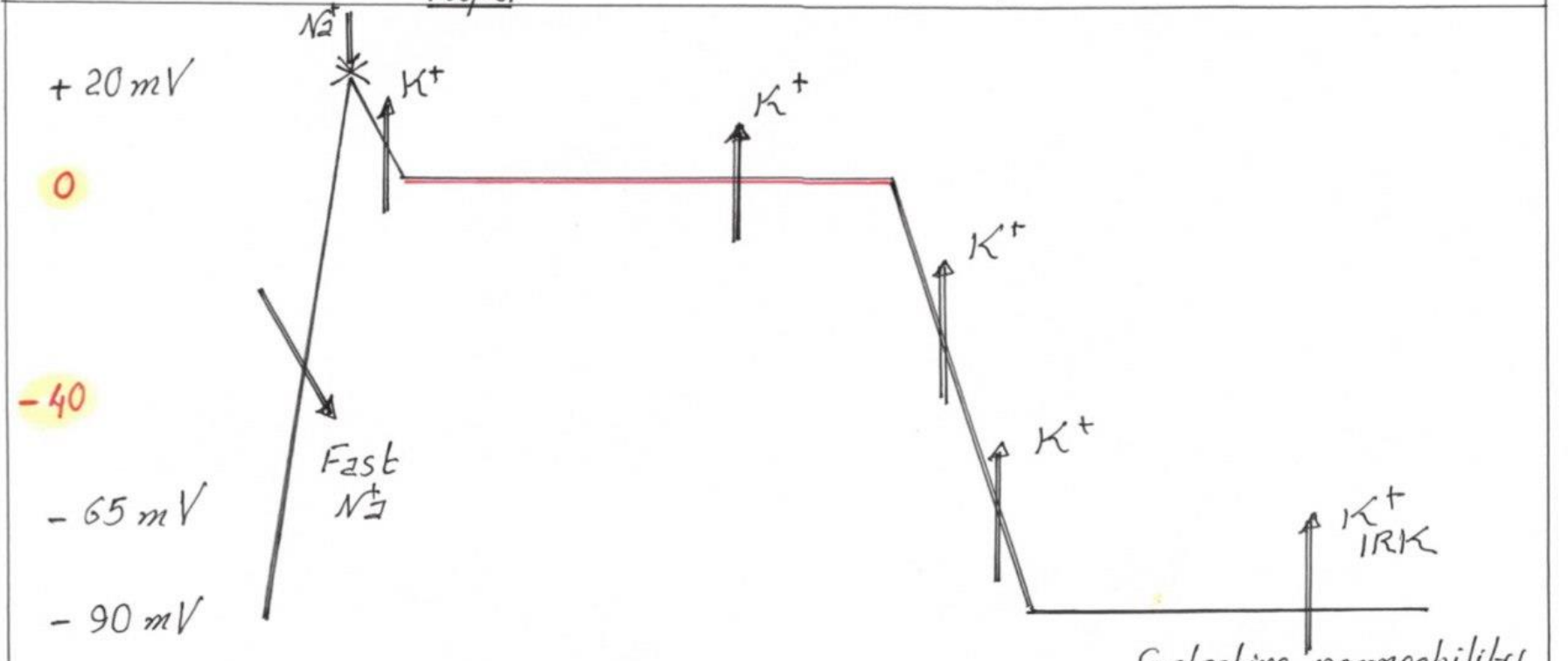
1 rapid small initial Repol

2 **Plateau**

3 rapid large Repol

4 **RMP**

no Hyperpolar



Selective permeability

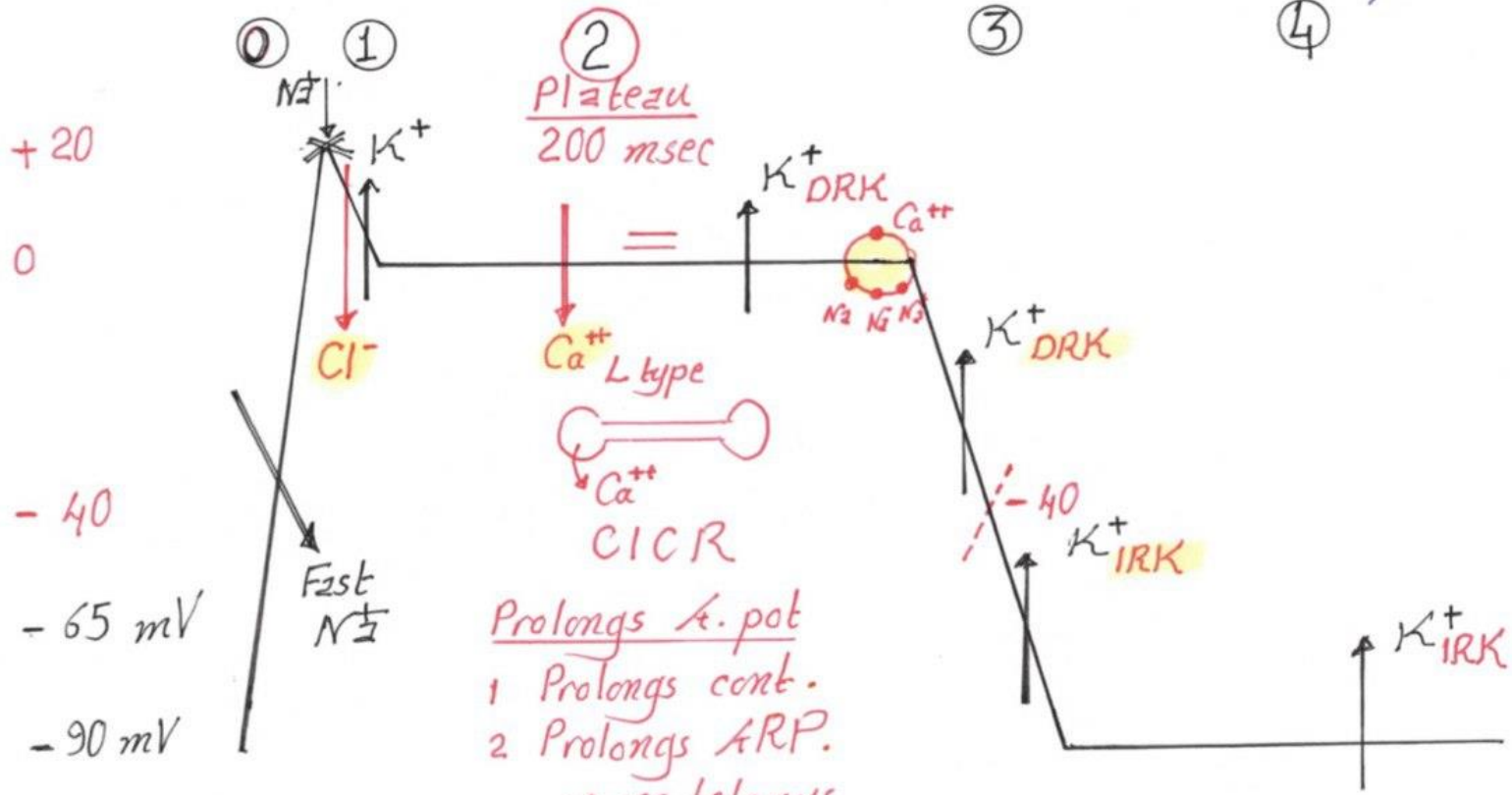
$Na^+ - K^+$ pump 3

E_K -94 E_{Na} +61

Excitability

A Potential of atrial or ventricular muscle fibres

Fast response A pot



Prolongs A. pot

1 Prolongs cont.

2 Prolongs ARP.

i.e no tetanus

Ca^{++} L type

starts phase 0 -40 mV

Fully active phase 2

inactivated at end of phase 2

Selective permeability

$Na^+ - K^+$ pump

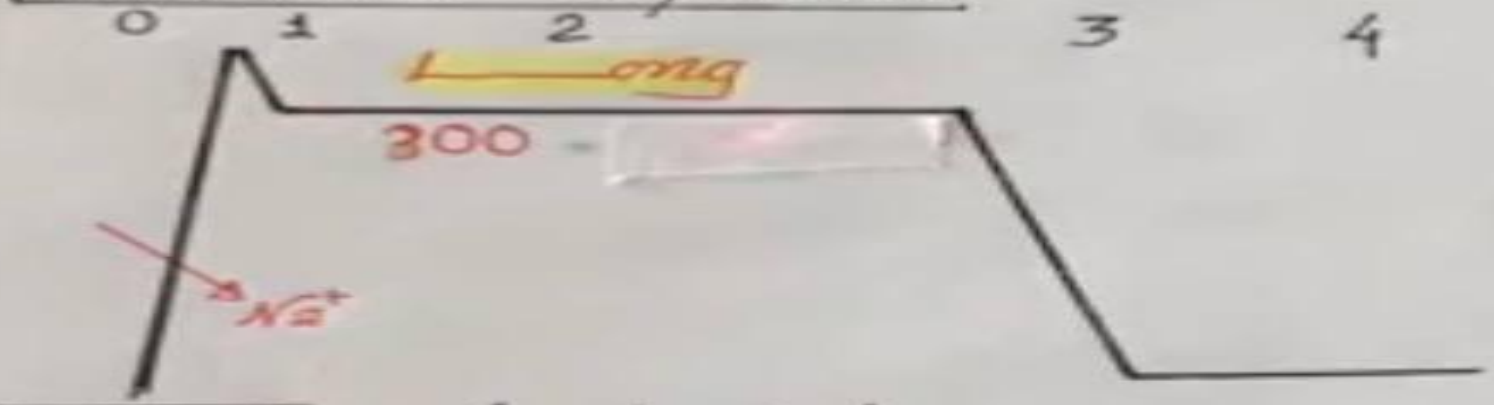
E_K - 94 mV

E_{Na} + 61 mV

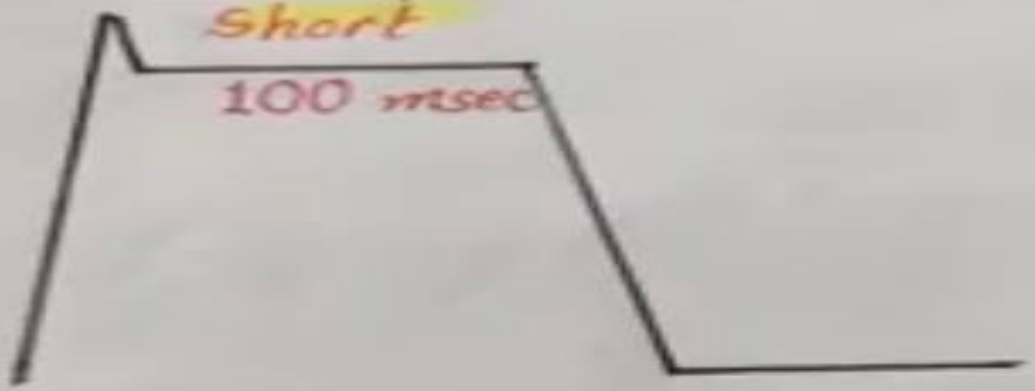
Non pacemaker (Atrial & Vent) A potent.

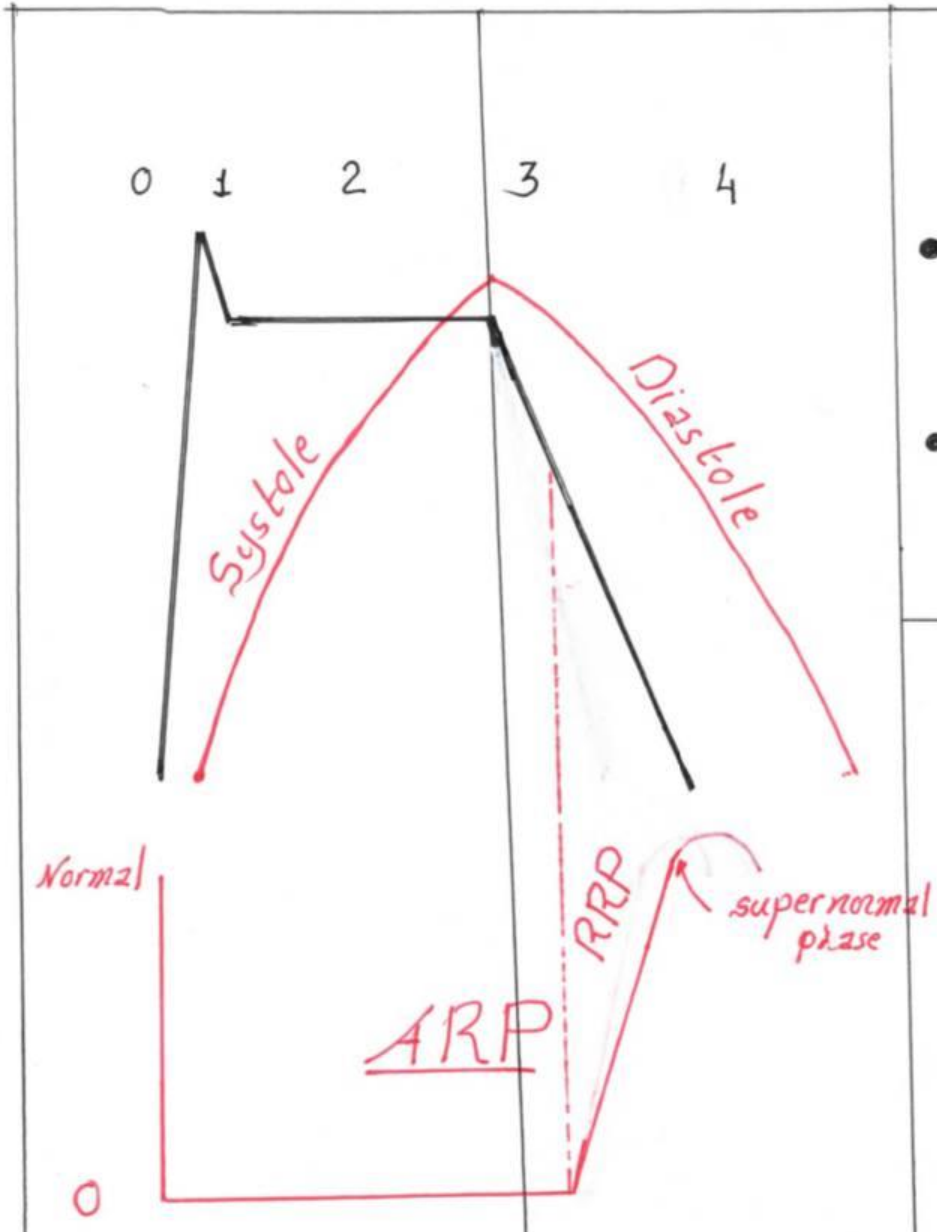
Fast Na^+ response A pot.

Ventricular A potential



Atrial A potential





Mechanical changes

- **Systole**
  - begins immediately after depol
  - ends by end of plateau
- **Diastole** double time of 3rd phase

Mechanical 1½ time Electrical (AP)

Excitability changes

- **ARP** excitability = 0
  - coincides 0, 1, 2 early part 3
  - i.e covers whole period of Systole + early diastole
  - This prevents tetanus
- **RRP** excitability below normal (allows filling)
  - coincides with rest of phase 3
- **Supernormal phase of excitability**
  - vulnerable phase
  - Late part of phase 3

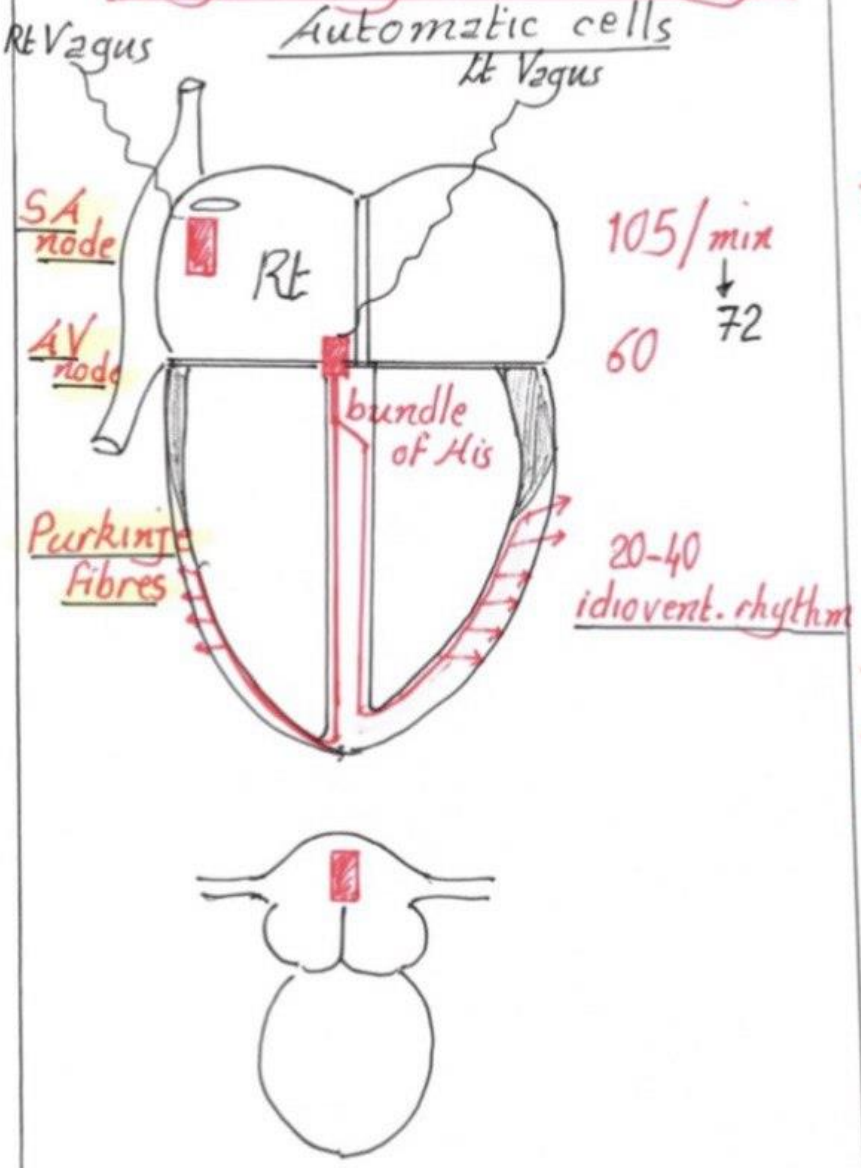
2) RHYTHMICITY

is the ability of a tissue to produce its own impulses regularly. It is more appropriately named as autorhythmicity. It is also called self excitation.
The property of rhythmicity is present in all the tissues of the heart. However, heart has a specialized excitatory structure from which the discharge of impulses is rapid. This specialized structure is called pacemaker. From this, the impulses spread to other parts through the specialized conductive system.

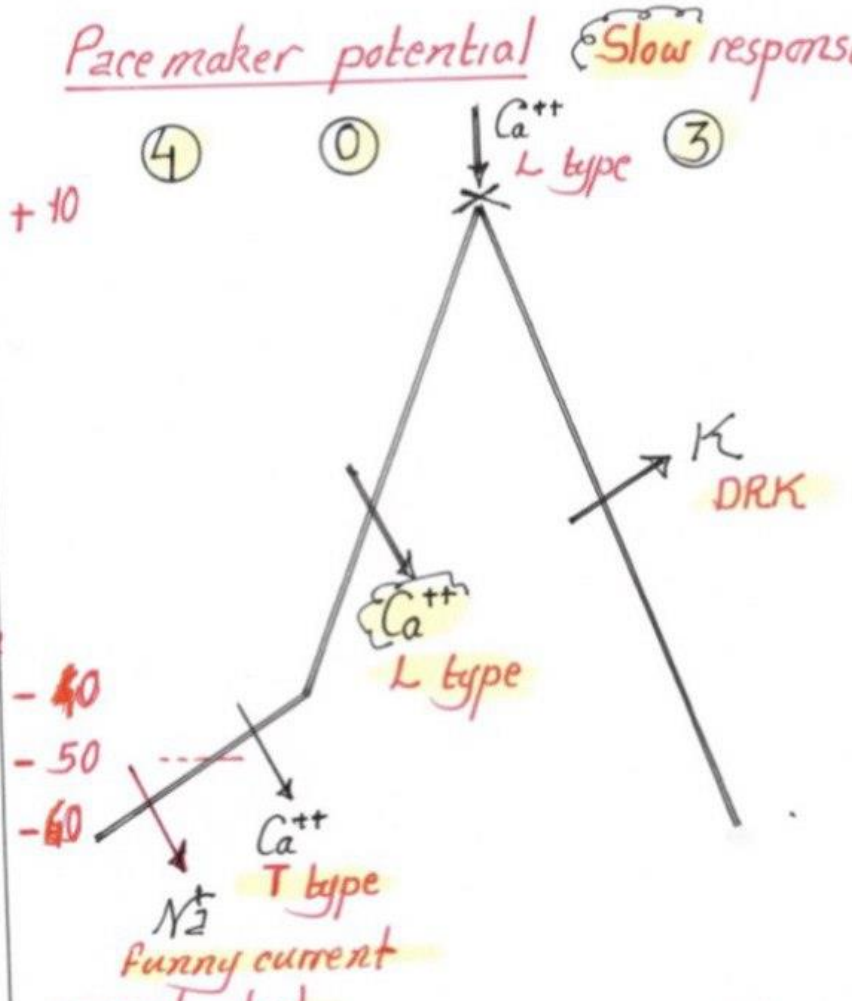
PACEMAKER

Though the SA node is the pacemaker in mammalian heart.

Rhythmicity (Automaticity)



Pace maker potential — Slow response Apot



prepotential

Spontaneous gradual depol

Spontaneous slow DIASTOLIC depol

notes stable
No SRMP
No Plateau

Non pacemaker (Atrial & Vent) A potent.

Fast response A pot.

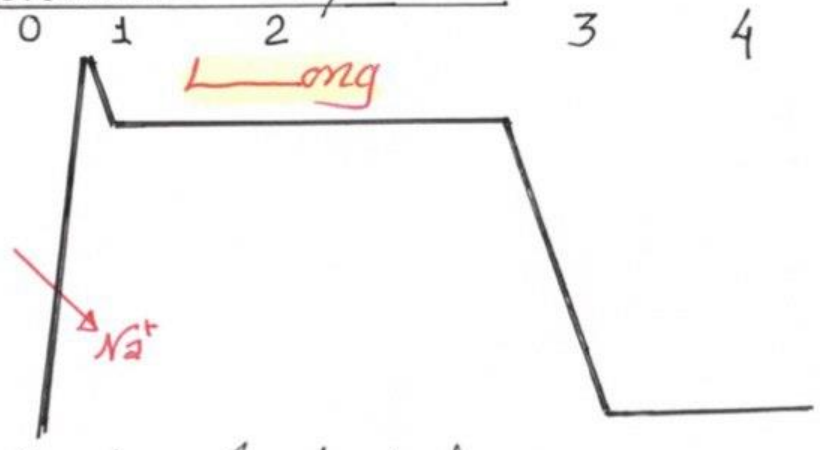
Na^+

Pace maker (SAN & AVN) A. potent

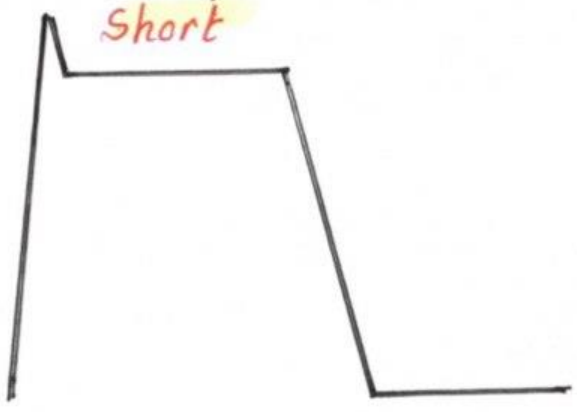
Slow response A pot.

Ca^{++}

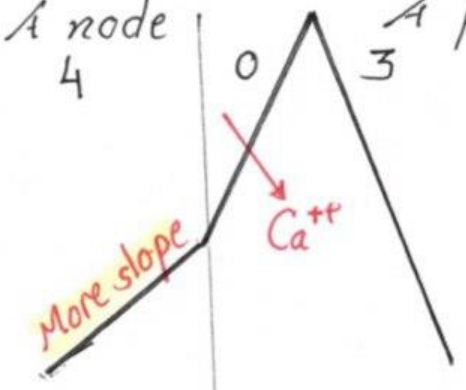
Ventricular A potential



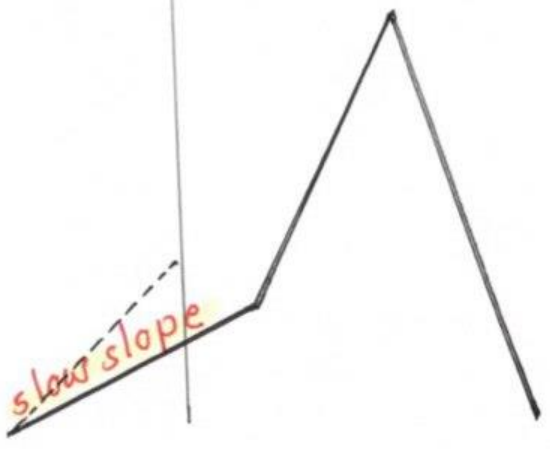
Atrial A potential



SA node A potential



AV node A potential.



Factors affecting rate of discharge of SAN (rhythmicity or HR):

① Autonomic nerves

Sympathetic ⟶ ++ i.e tachycardia
+ve chronotropy

Mech Noradrenaline (Norepinephrine)
β_1 ⟶ ++ cAMP
++ funny current
++ slope of phase 4
reach threshold " 0
in a shorter time.

Parasympathetic ⟶ -- i.e bradycardia
-ve chronotropy

Mech Acetylcholine
a Muscarinic R ⟶ -- cAMP
b Activates K_{ACh} channels
++ K efflux
Antagonises funny current
-- slope of phase 4

② Catecholamines = Symp. n.s

③ Body temp
1 °C ⟶ 10 beats/min

④ Extracell K
a ↓ K^+ ⟶ ↑ HR ++ slope phase 4
by -- K^+ conductance in SAN
b ↑ K^+ ⟶ ↓ HR

⑤ Calcium channel blocking drugs
↓ HR & ↓ contractility
by inactivating Ca^{++} L type.

Factors affecting the rhythmicity of the cardiac muscle :

Factors that increase the rate (positive chronotropic factors) :

1. sympathetic stimulation : as its neurotransmitter norepinephrine increases the membrane permeability to sodium and calcium.

2. moderate warming : moderate warming increases temperature by 10 beats for

each 1 Fahrenheit degree increase in body temperature, this due to decrease in permeability to potassium ions in pacemaker membrane by moderate increase in temperature.

3. Catecholaminic drugs have positive chronotropic effect.

4. Thyroid hormones : have positive chronotropic effect , due to the fact that these drugs increase the sensitivity of adrenergic receptors to adrenaline and noreadrenaline .

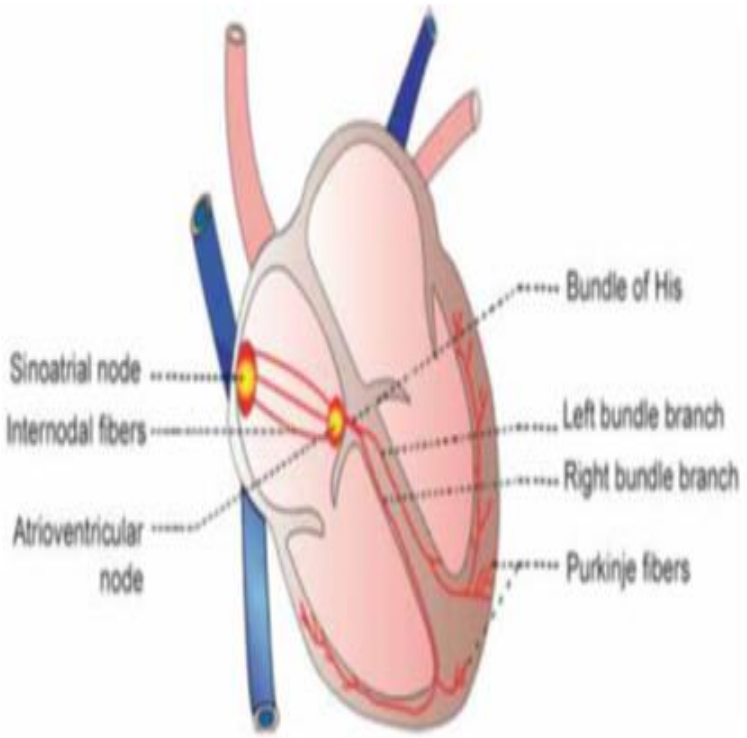
3)Conductivity : the ability of the heart to propagate Action potential

Human heart has a specialized conductive system through which the impulses from SA node are transmitted to all other parts of the heart

CONDUCTIVE SYSTEM IN HUMAN HEART

The conductive system of the heart is formed by the modified cardiac muscle fibers. The conductive tissues of the heart are also called the junctional tissues. The conductive syste

1. SA node (Sinoatrial node)
2. AV node (Atrioventricle node)
3. Bundle of His: Right and left bundle branches
4. Purkinje fibers.



Conductivity

Velocity of conduction depends on :

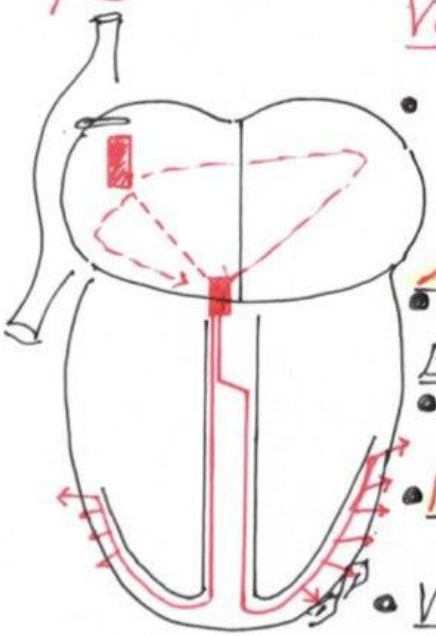
1. **Number of Gap junctions**
   - **Note** Ability to allow current flow
   - is decreased by ↓O_2 & ↑Ca^{++} in myocytes
2. **Amplitude & speed of upstroke** of A potential

Factors affecting velocity of conduction

1. **Autonomic nerves**
   - **Sympathetic**
     - **Norepinephrine** β_1
     - ++ rate of conduction
     - **Mech** Faster upstroke
   - **Parasymp**
     - **Acetylcholine** Muscarinic R
     - -- rate of conduction
     - **Mech** Slower upstroke
2. **Drugs** **Digitalis** stimulates parasymp.

Propagation of Cardiac impulse

Velocity in meter/sec



- **Atrial myocytes** 0.5
- **Internodal bundles** 1
- **AV node** (Slowest) 0.05
- **Bundle of His.** & Rt & Lt bundles 2
- **Purkinje F** (Fastest) 4
- **Vent myocytes** 0.5

AV node		Purkinje Fibres
SLOWES		FASTEST
Few	**Gap junctions**	Many
Slow	**Upstroke of AP**	Rapid

1. **Delays vent. cont** till end of A emptying
2. **Protects vent.** against High path. A rhythms

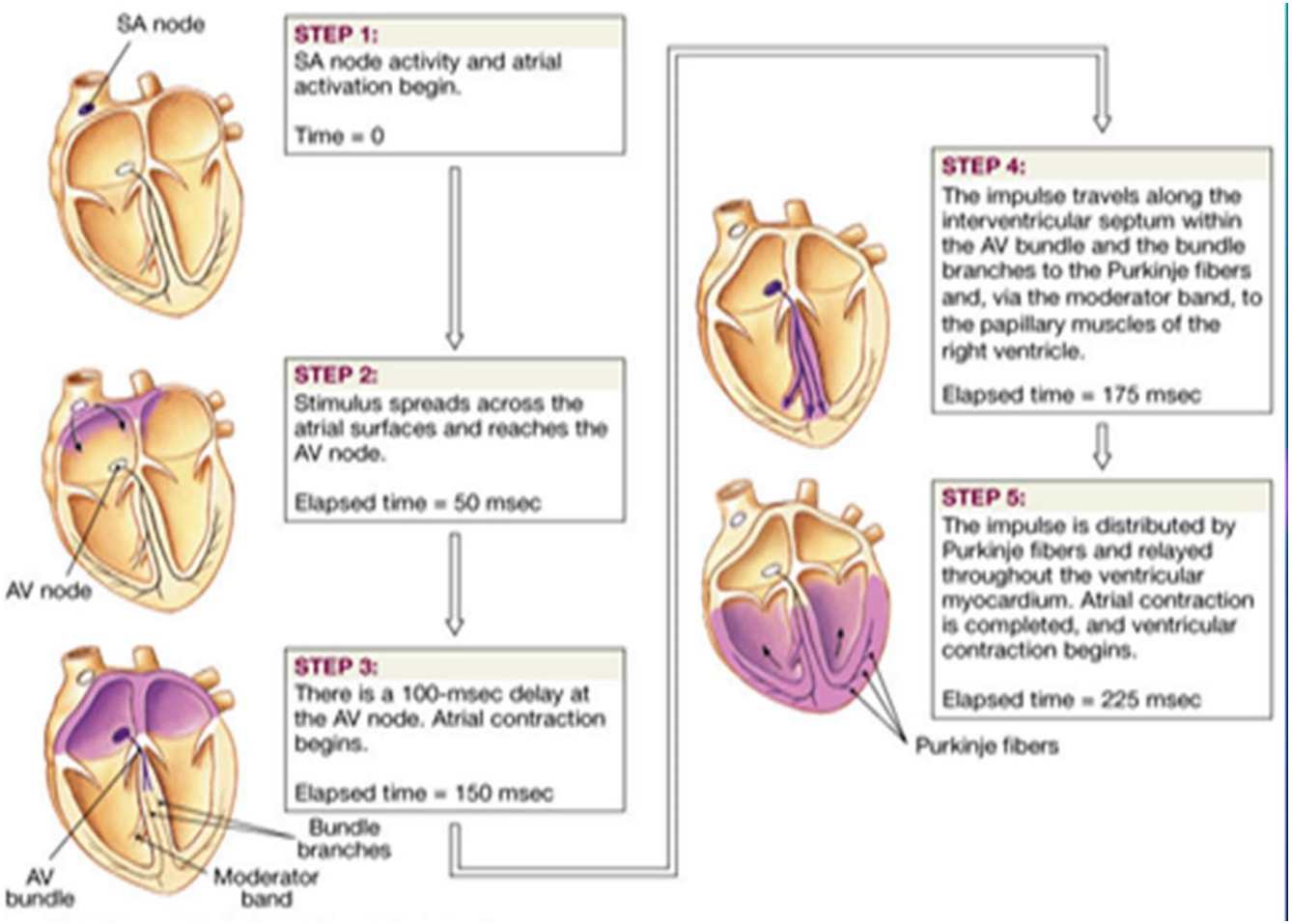
Importance To excite all vent fibres at one time & as one unit → forcible cont

Impulse Conduction through the heart

- ✓ SA node begins the action potential
- ✓ Stimulus spreads to the AV node
- ✓ Impulse is delayed at AV node
- ✓ Impulse then travels through ventricular conducting cells
- ✓ Then distributed by Purkinje fibers

The impulses from SA node are conducted throughout right and left atria. The impulses also reach the AV node via some specialized fibers called internodal fibers.
There are three types of intermodal fibers, All these fibers from SA node converge on AV node and interdigitate with fibers of Av node.
From AV node, the bundle of His arises. It divides into right and left bundle branche switch run on either side of the interventricular septum. From each branch of Bundle of His

Propagation of cardiac impulse velocity in meter/second



4) Contractility is ability of the tissue to shorten in length (contraction) after receiving a stimulus.

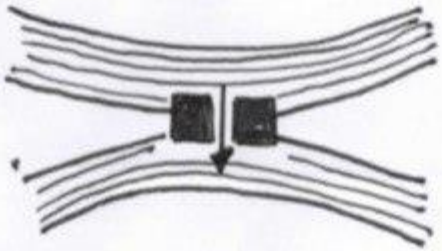
There are two type of muscle contraction:

Isometric: A muscular contraction in which the length of the muscle does not change.

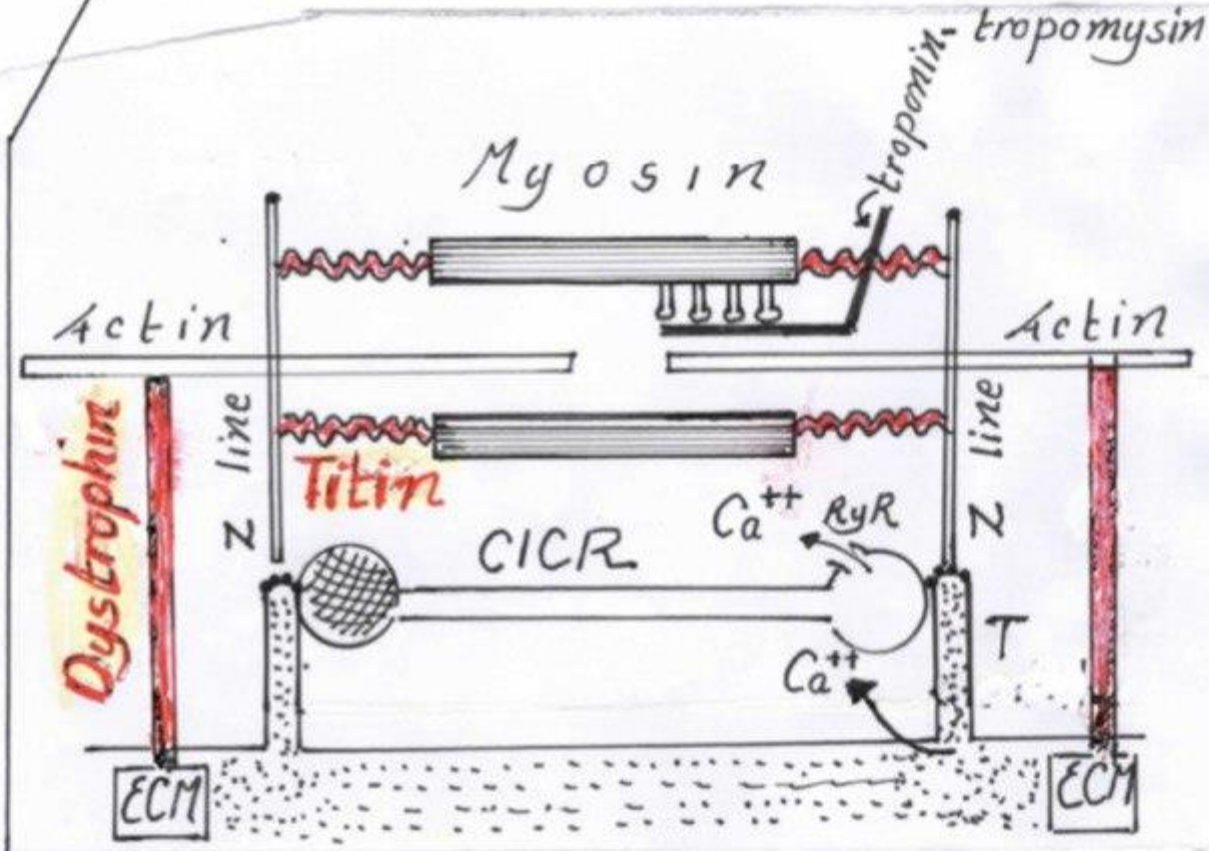
isotonic: A muscular contraction in which the length of the muscle changes
Various factors affect the contractile properties of the cardiac muscle.

Smooth muscle
Syncitium

Skeletal muscle
Straited



Intercalated disc
Gap junction



2 functional syncitia

- T tubule at Z line

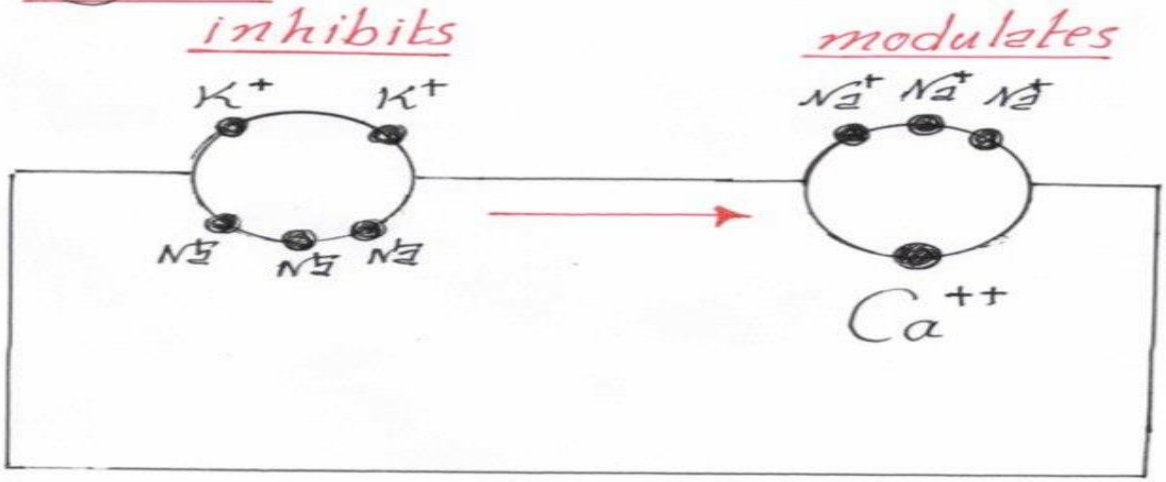
(connectin)

- Titin Giant filamentous elastic ptn

c AMP → Activate → ptn kinase A → phosphorylation

- L type Ca^{++} ch. → Open longer time
- Certain site in SR → Release more Ca^{++}

Digitalis



REFRACTORY PERIOD

is the period in which the muscle does not show any response to a stimulus. It is of two types:

1. Absolute refractory period

Absolute refractory period is the period during which the muscle does not show any response at all, whatever may be the strength of the stimulus. It include phase 0,1,2,and part of phase 3

2. Relative Refractory Period

The relative refractory period is the period during which the muscle shows response if the strength of stimulus is increased to maximum. It is the stage at which the muscle is in repolarizing state.

Refractory Period in Cardiac Muscle

Cardiac muscle has a long refractory period compared to that of skeletal muscle.

Electrocardiogram (ECG)

Electrocardiography

is the technique by which the electrical activities of the heart are studied.

Electrocardiograph

is the instrument (ECG machine) by which the electrical activities of the heart are recorded.

USES OF ECG- is useful in determining and diagnosing the following:

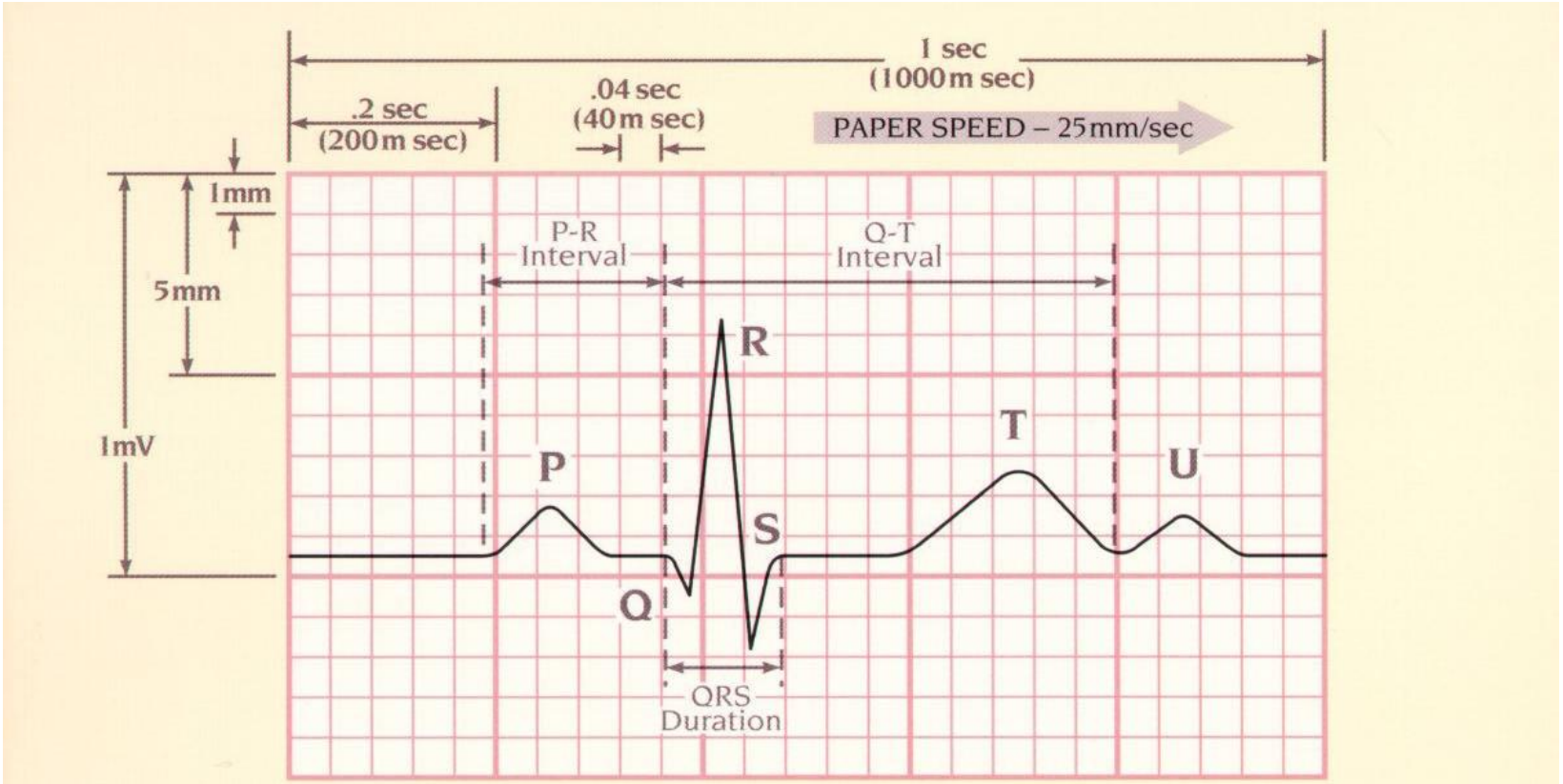
1. Heart rate
2. Heart rhythm noitcudnoc lacirtcele lamronbA .3
4. Ischemia
5. Heart attack
6. Coronary artery disease
7. Hypertrophy of heart chambers.

ELECTROCARDIOGRAPHIC

The paper that is used for recording ECG is called ECG paper.

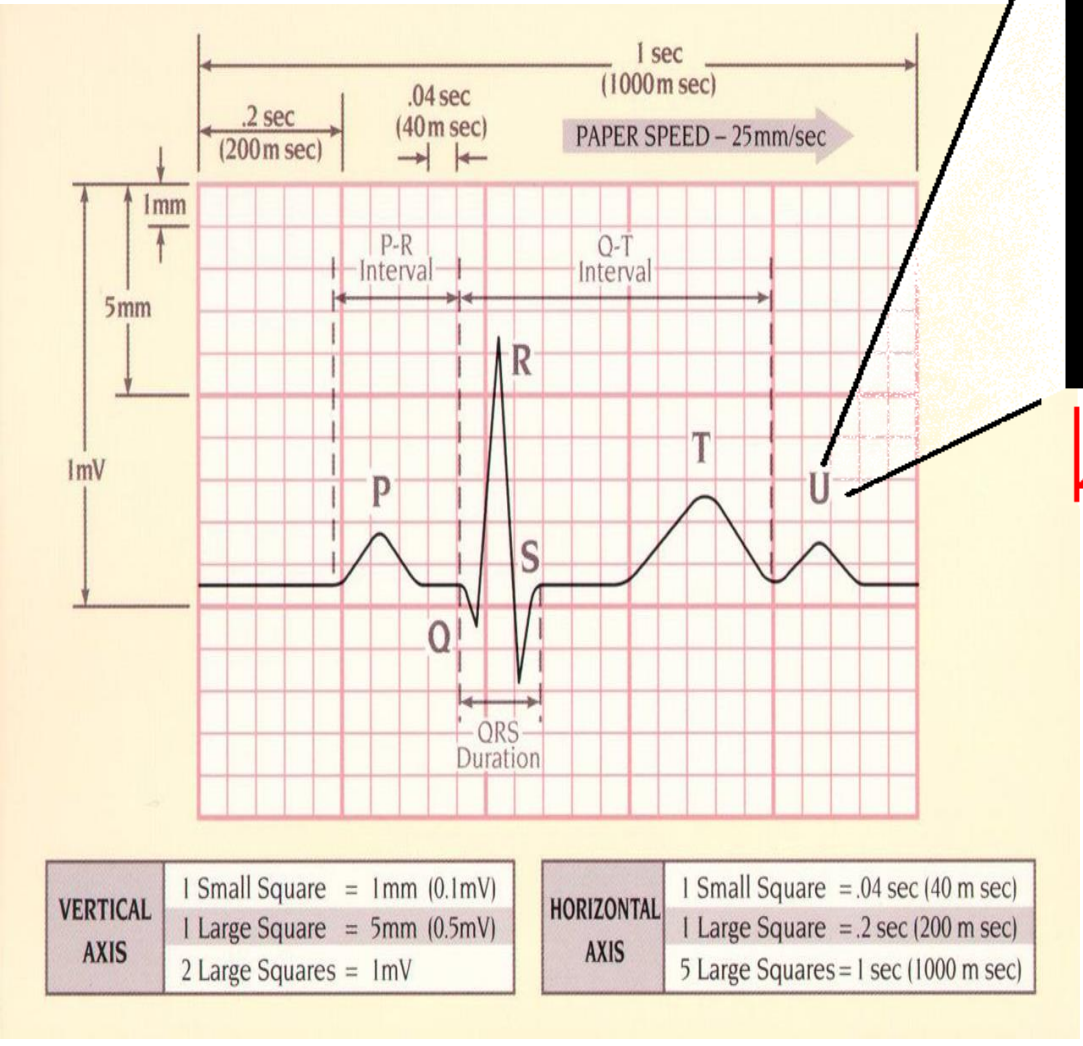
ECG grid refers to the markings (lines)on ECG paper, has horizontal & vertical lines at regular intervals of 1 mm.

Large square (5 mm) = 0.2 second small square (1 mm) = 0.04 second.



VERTICAL AXIS	1 Small Square	= 1mm	(0.1mV)
	1 Large Square	= 5mm	(0.5mV)
	2 Large Squares	= 1mV	

HORIZONTAL AXIS	1 Small Square	= .04 sec (40 m sec)
	1 Large Square	= .2 sec (200 m sec)
	5 Large Squares	= 1 sec (1000 m sec)



VERTICAL AXIS	
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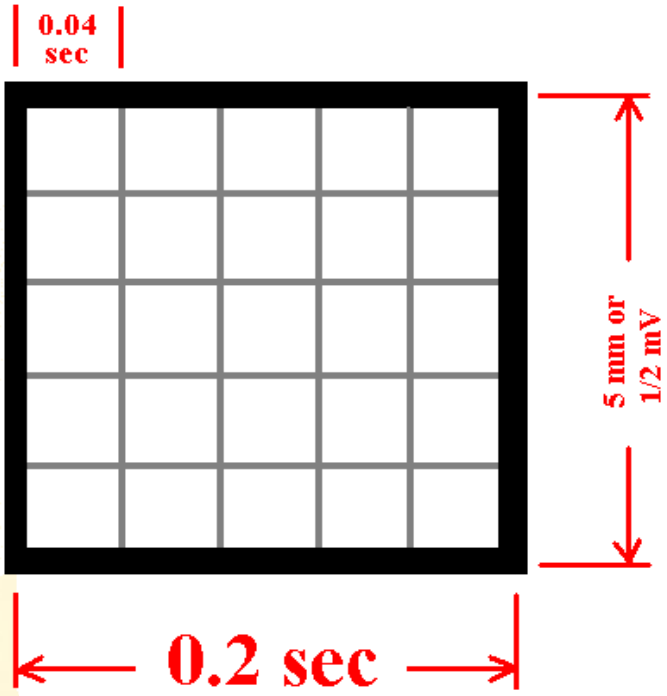
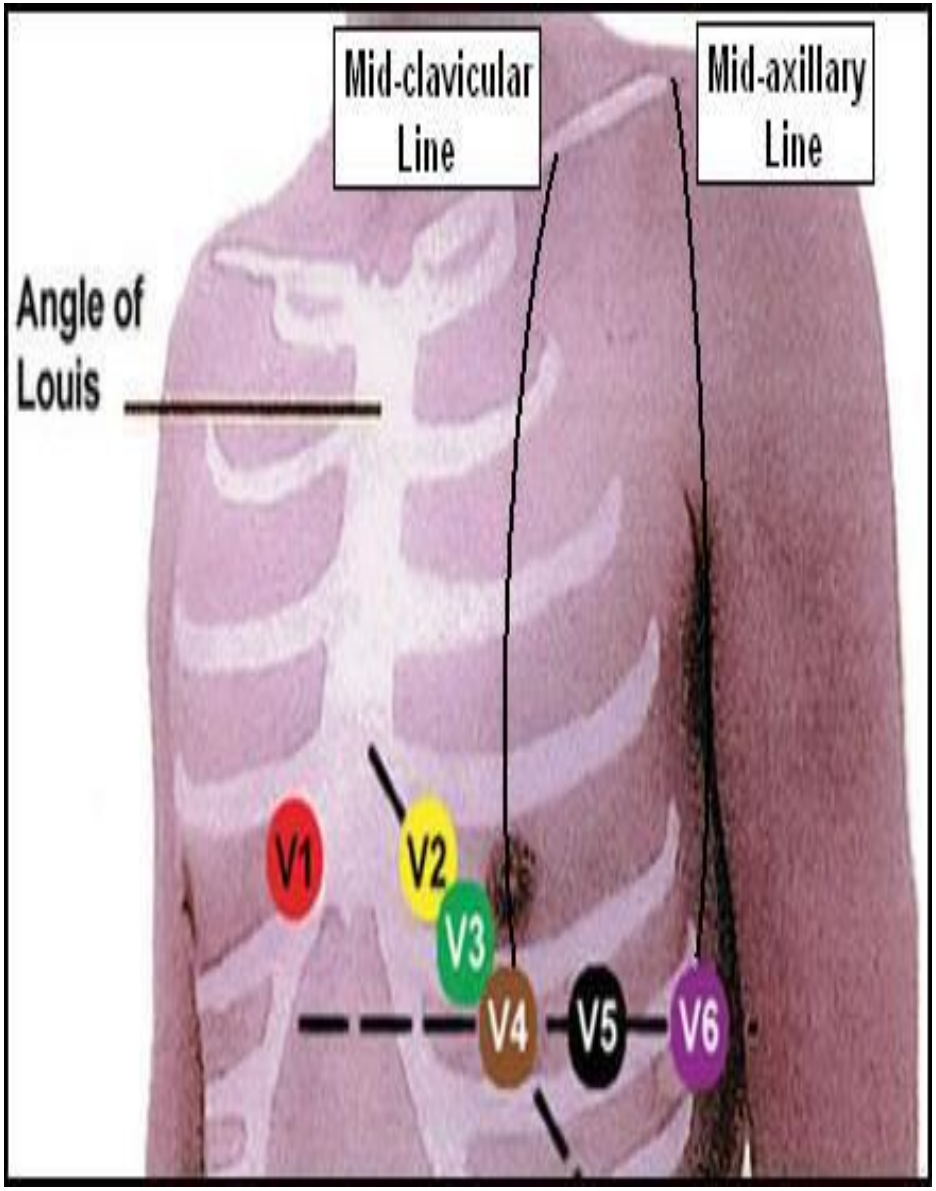
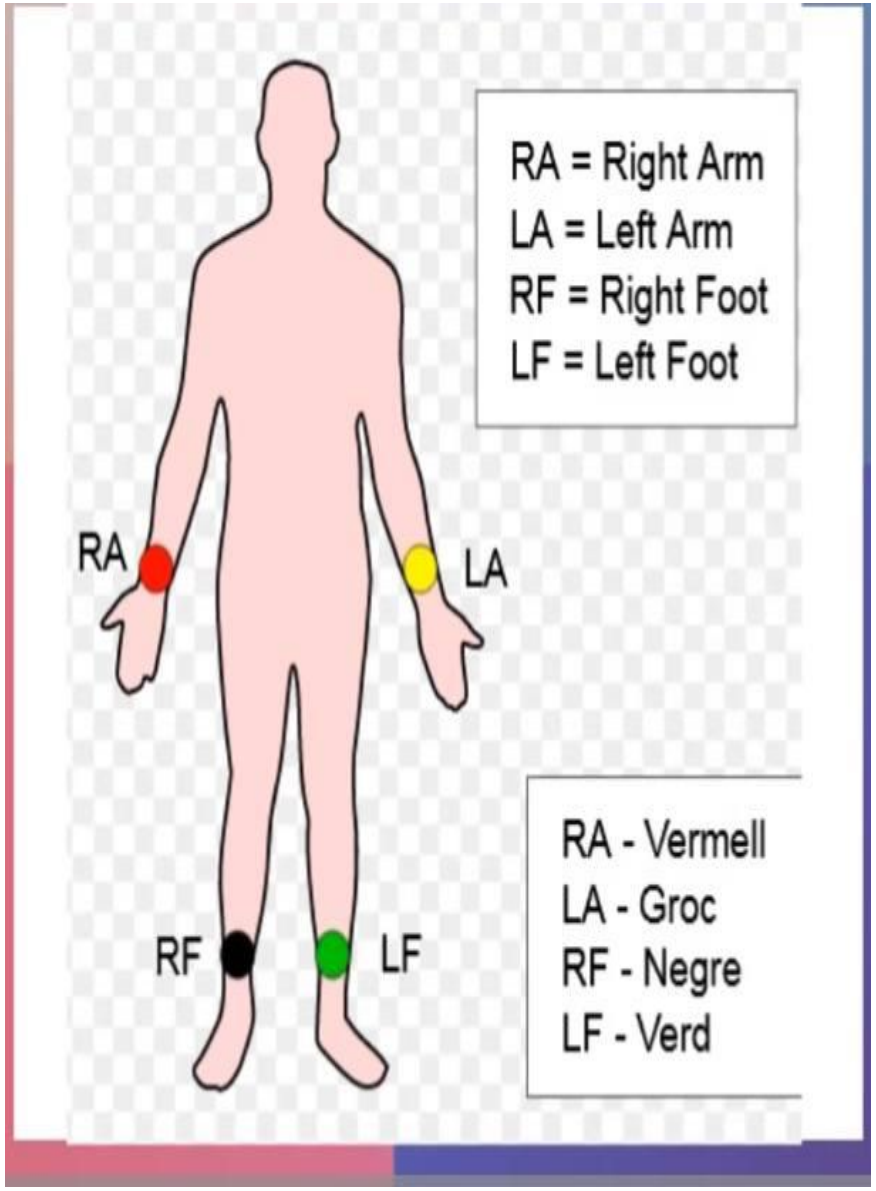
	1 Large Square = .2 sec (200 m sec)
	5 Large Squares = 1 sec (1000 m sec)




Mid-clavicular Line
Mid-axillary Line
Angle of Louis
V1
V2
V3
V4
V5
V6


RA = Right Arm
LA = Left Arm
RF = Right Foot
LF = Left Foot
RA
LA
RF
LF
RA - Vermell
LA - Groc
RF - Negre
LF - Verd

ECG LEADS

ECG is recorded by placing series of electrodes on the surface of body. These electrodes
are= ECG leads & are connected to the ECG machine.

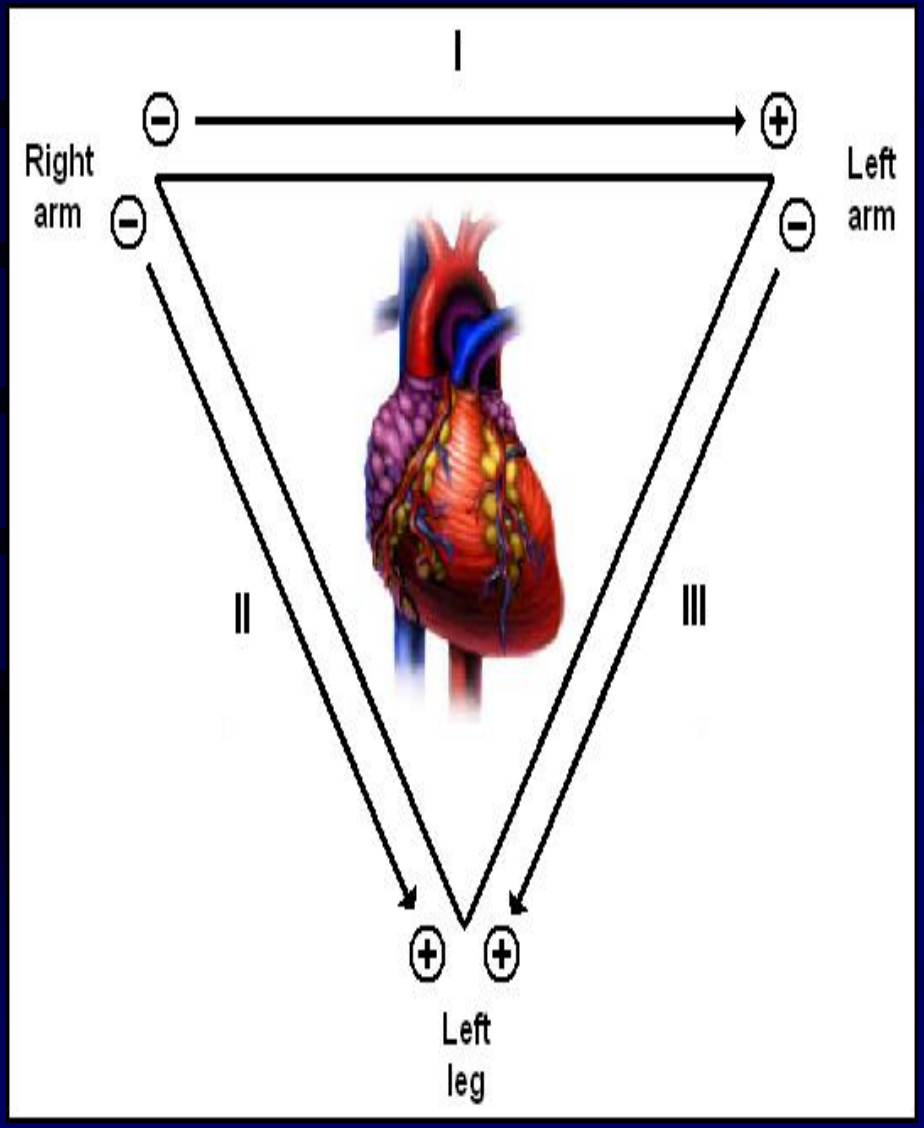
The electrodes are fixed on the limbs. The heart is said to be in the center of an imaginary equilateral triangle drawn by connecting the roots of these three limbs. This triangle is = Einthoven's triangle. The electrical potential generated from the heart appears simultaneously on the roots of these three limbs.

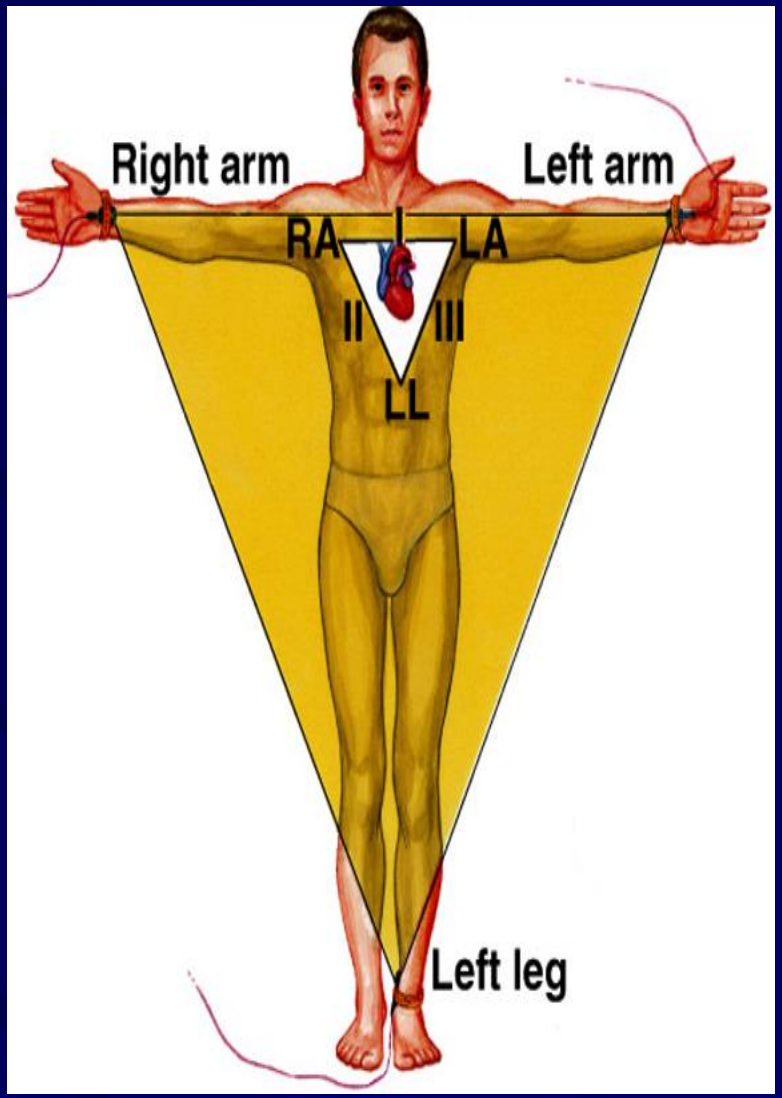
ECG is recorded in 12 leads which are generally classified into two categories.

A. Bipolar leads I , II , III

B. Unipolar leads AVR, AVL, AVF

STANDARD LIMB LEADS





Lead I

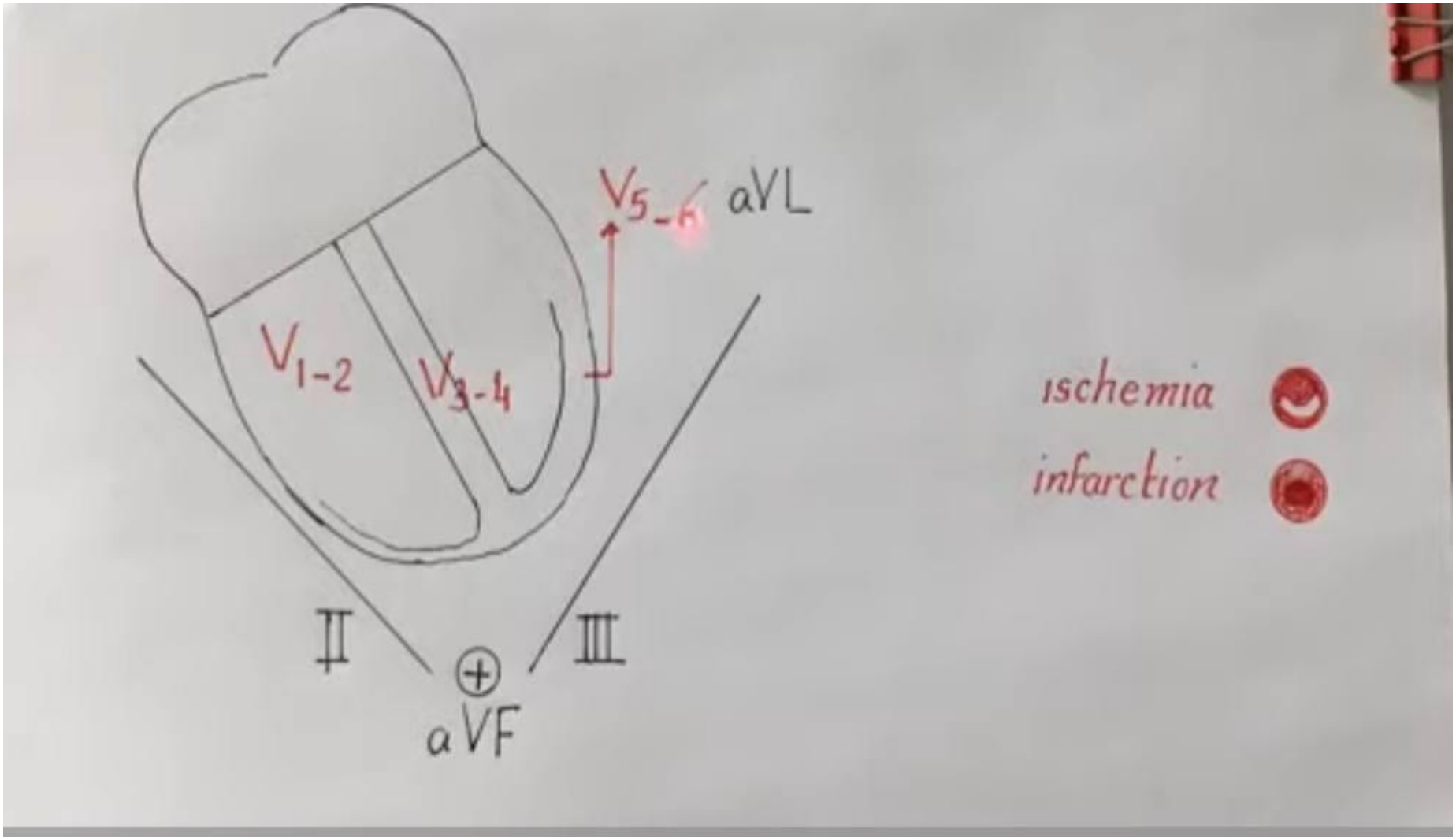
Lead I is obtained by connecting right arm and left arm. The right arm is connected to the negative terminal of the instrument and the left arm is connected to the positive terminal.

Lead II

Lead II is obtained by connecting right arm and left leg. The right arm is connected to the negative terminal of the instrument and the left leg is connected to the positive termina-l.

Lead III

Lead III is obtained by connecting left arm and left leg. The left arm is connected to the negative terminal of the instrument and the left leg is connected to the positive terminal.


V5-6
aVL
V1-2
V3-4
II
III
aVF
ischemia
infarction

UNIPOLAR LEADS

Here, one electrode is active electrode is positive and the other one is an indifferent electrode-is serving as a composite negative electrode. The unipolar leads are 2 types:

1. Unipolar limb leads

also called augmented limb leads..

Unipolar limb leads are of 3 types:

i. aVR lead in which the active

electrode is from right arm

ii.aVL lead in which the active

electrode is from left arm

iii.aVF lead in which the active

electrode is from left leg (foot)

2. Unipolar chest leads. V1, V2,V3, V4,V5,V6

Limb Leads

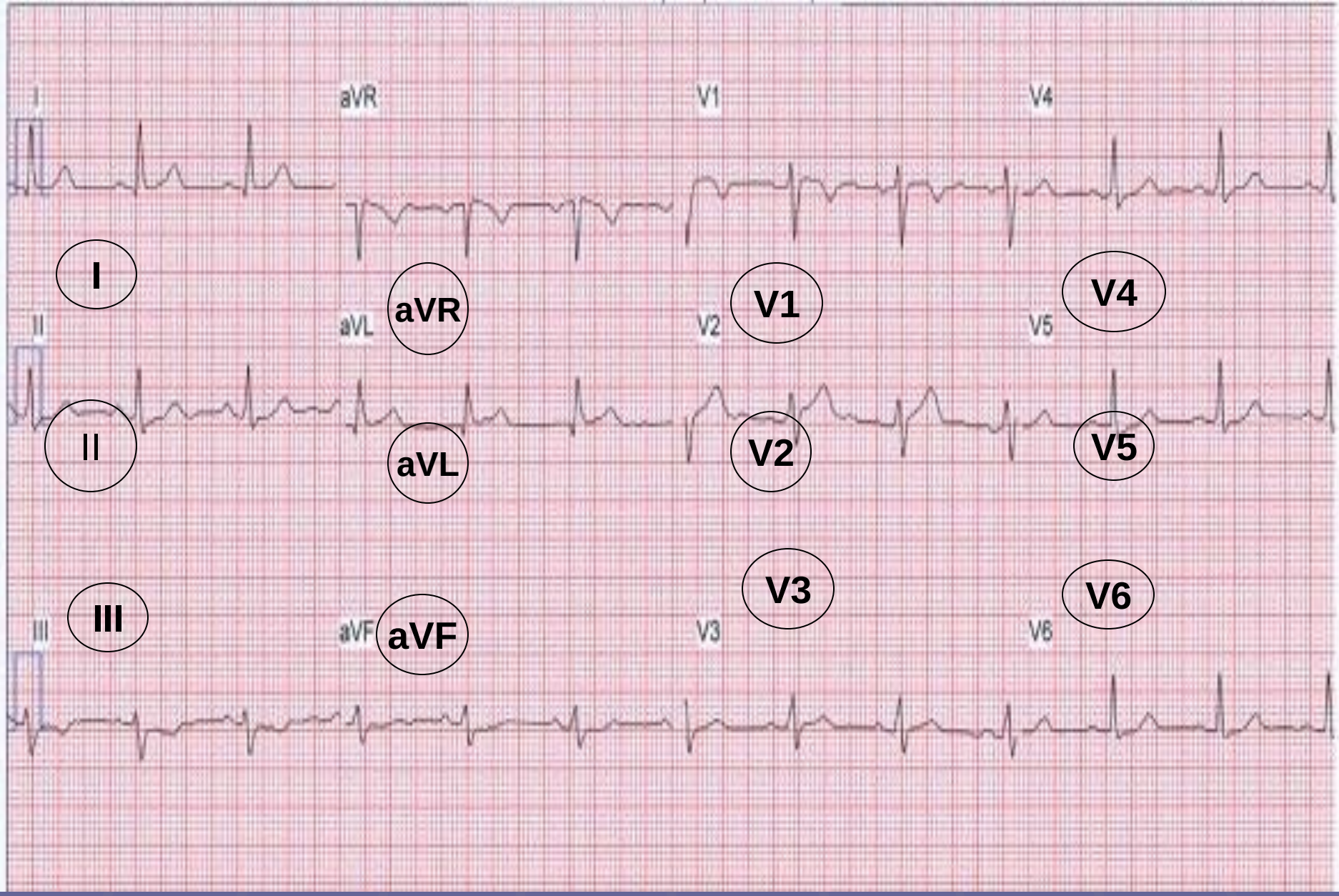
Bipolar I, II, III

Unipolar aVR, aVL, aVF

chest Leads (unipolar) V_1, V_2, V_3, V_4, V_5, V_6

ARRANGEMENT OF LEADS ON THE ECG

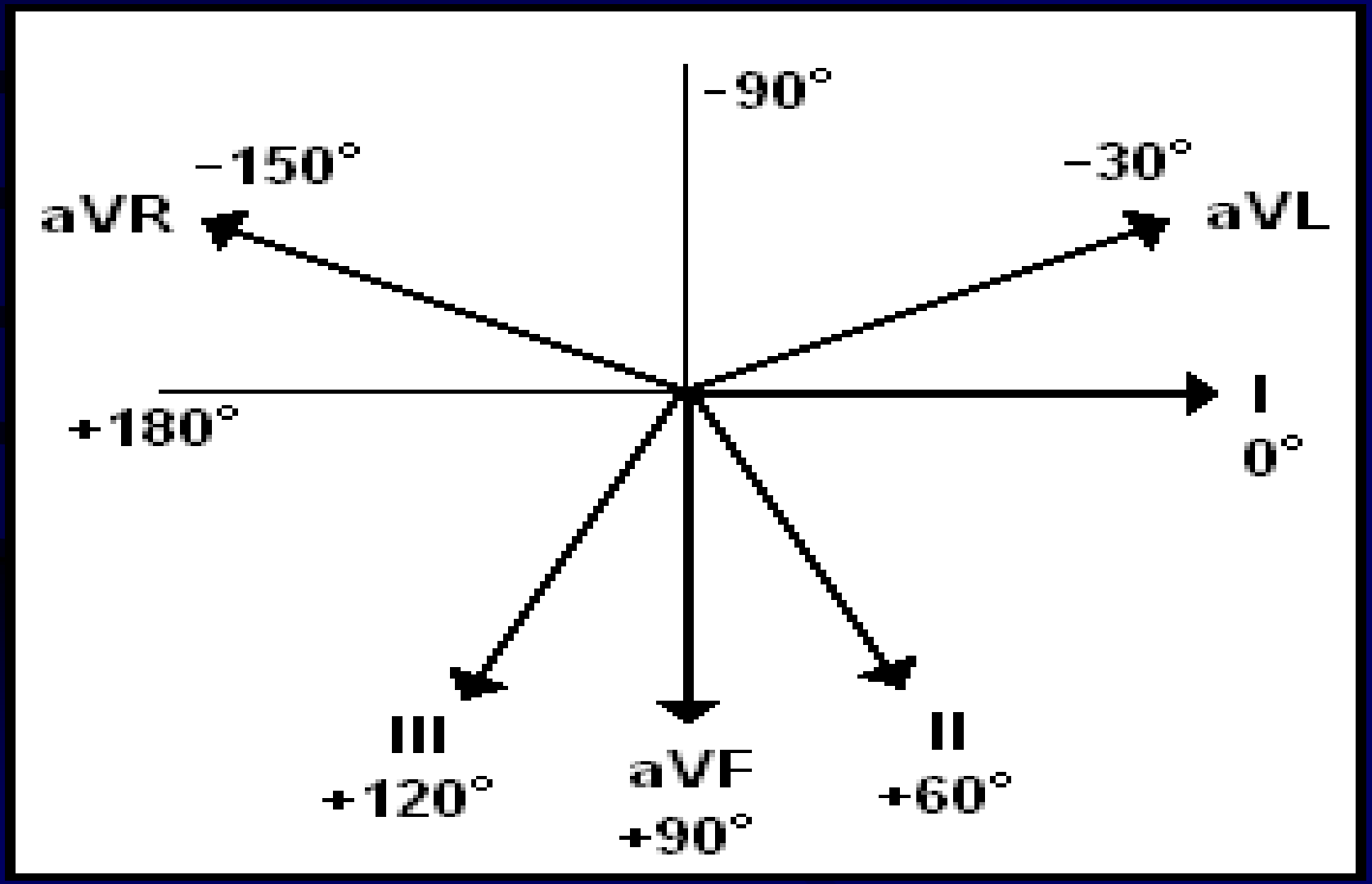
I	aVR	V_1	V_4
II	aVL	V_2	V_5
III	aVF	V_3	V_6


I
aVR
V1
V4
II
aVL
V2
V5
III
aVF
V3
V6

ANATOMICAL PRESENTATION
(SUMMARY)

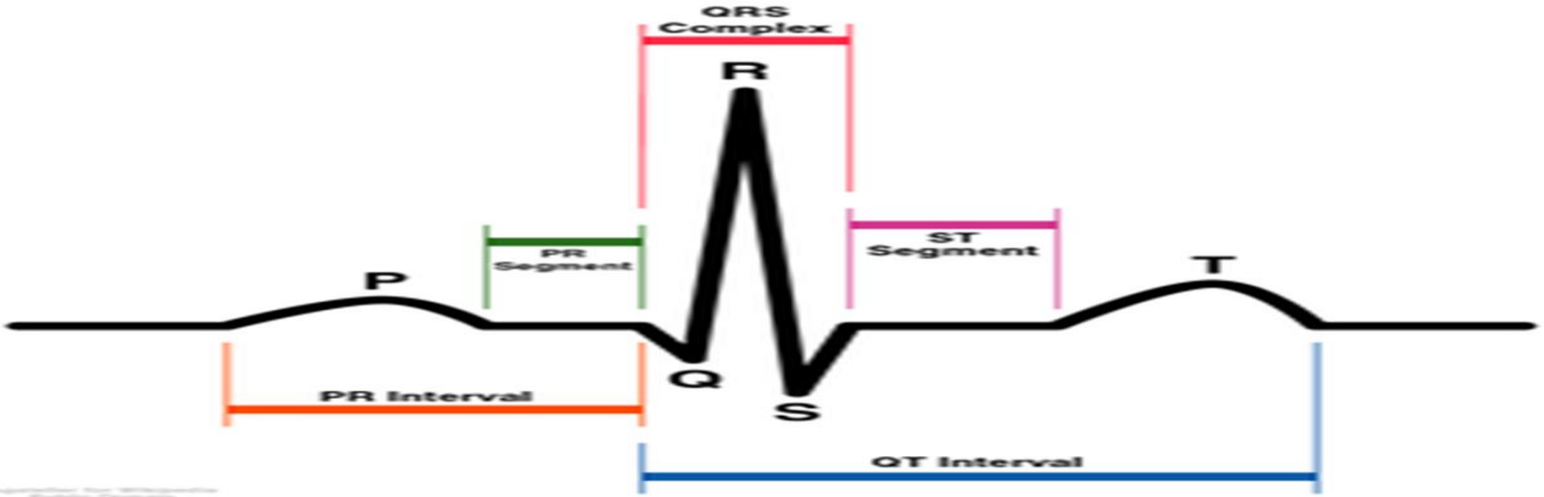
I Lateral	aVR None	V_1 Septal	V_4 Anterior
II Inferior	aVL Lateral	V_2 Septal	V_5 Lateral
III Inferior	aVF Inferior	V_3 Anterior	V_6 Lateral

ALL LIMB LEADS



WAVES OF NORMAL ELECTROCARDIOGRAM

A normal ECG consists of waves, complexes, intervals and segments, has the waves namely P, Q, R, S & T.)



The major complexes in ECG are:

1. 'P' wave, the atrial wave produced due to the depolarization of atrial musculature.

Atrial repolarization is not recorded as a separate wave in ECG because it merges with QRS complex.

2. '. 'QRS' complex is due to depolarization of ventricular musculature.

3. 'T' wave : a positive wave, due to the repolarization of ventricular musculature

4. 'U' WAVE: is not always seen. It is supposed to be due to repolarization of papillary muscle.

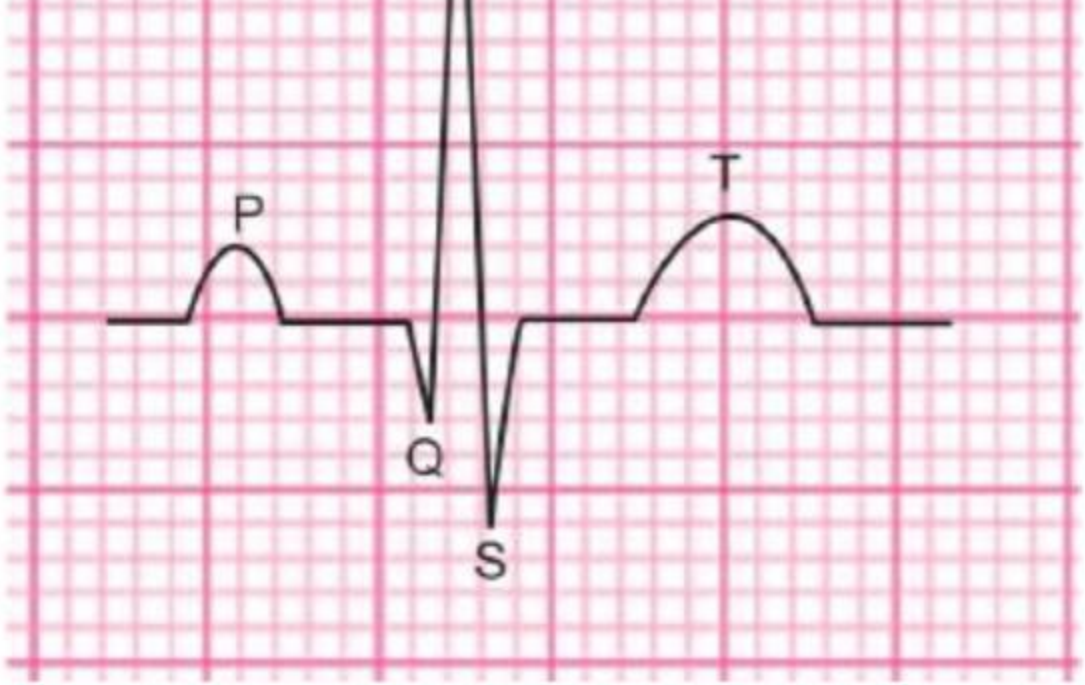


Fig. 6.3: ECG wave morphology

e-atrial depolarization

omplex-ventricular depolarization

gment, T wave-ventricular repolarization

tter understanding:

mm = 0.04 sec

mm = 0.08 sec

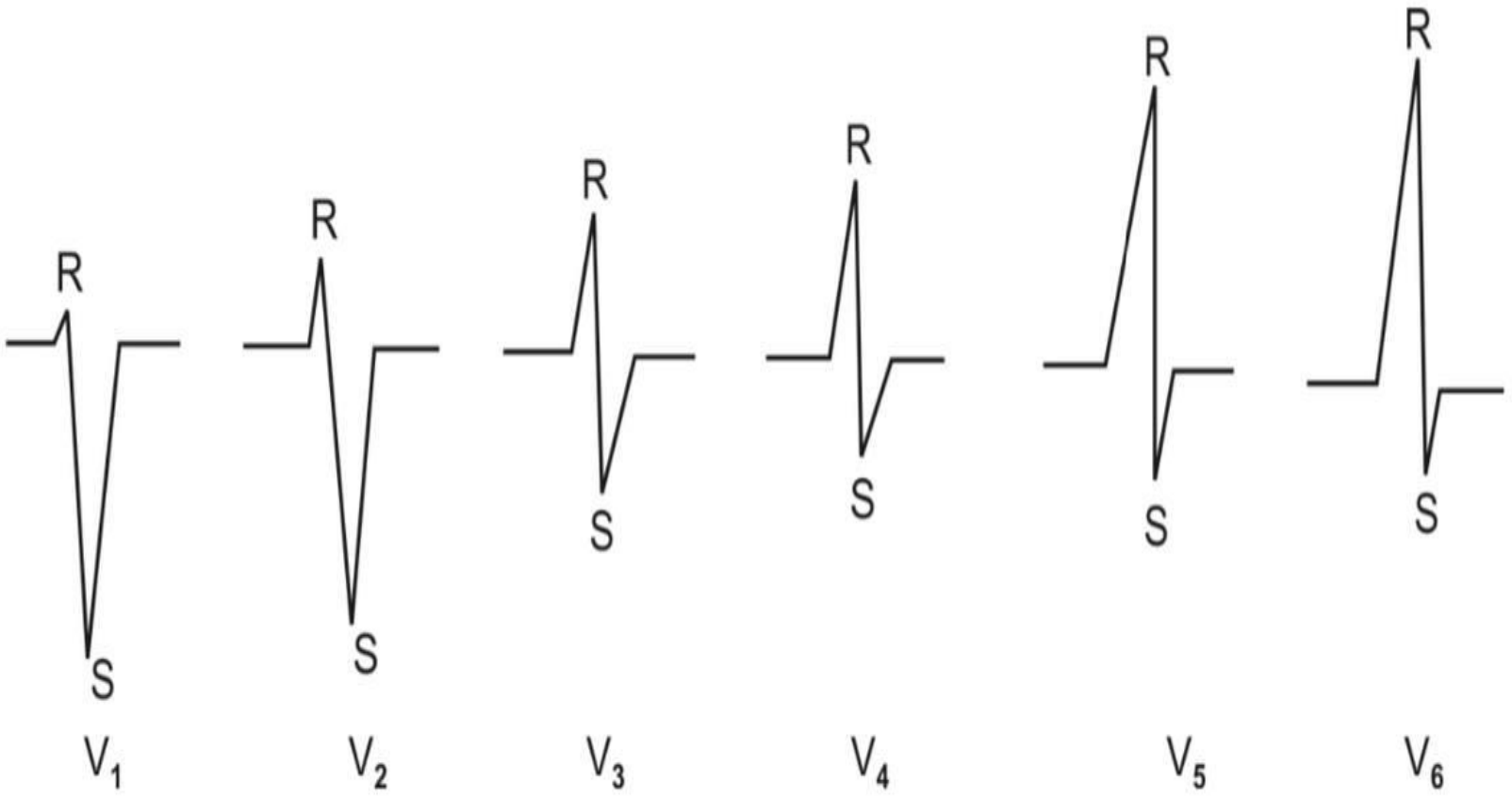


Fig. 6.7: Normal R wave progression in chest leads

What are the steps to read an ECG?

1. Look for Standardization and Lead aVR

At the end of each ECG strip, a standardization box is present which should be 10 mm in height 0.20 second in width (5 mm).

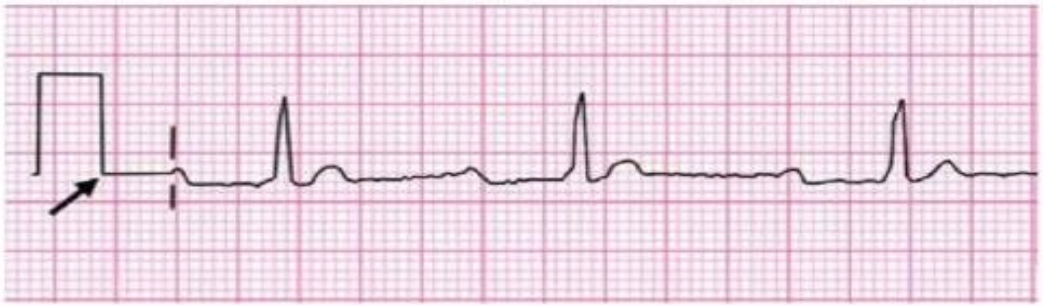


Fig. 7.1: Standardization mark

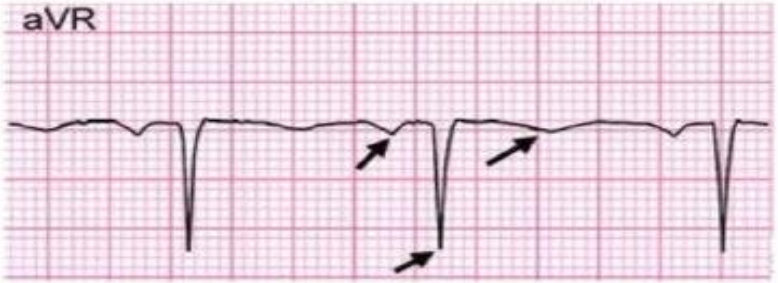


Fig. 7.2: Lead aVR showing inverted P, QRS & T

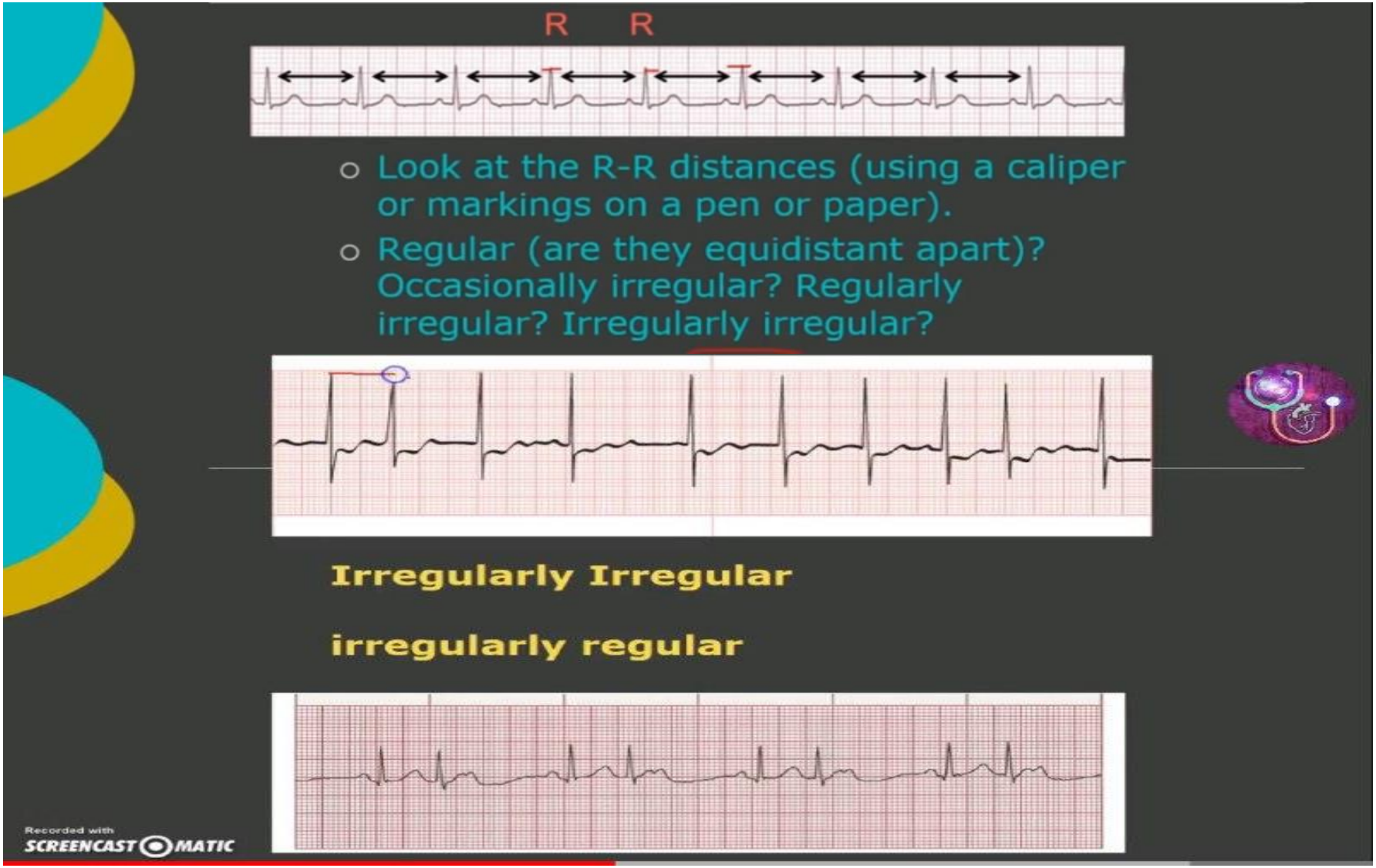
All waves should be inverted in lead aVR unless the limb leads are wrongly connected except in dextrocardia.

2. Determin regularty:

Rhythm

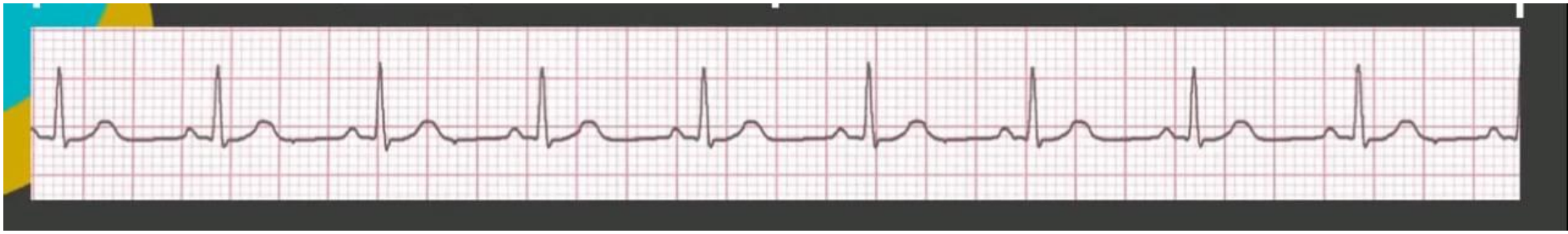
Regular : each R-R interval will be the same distance.

Irregular each R-R interval will be different.



3. Calculate rate

If Rhythm is regular
300/ R_R



300/3= 100

If the rhythm is irregular each R-R interval will be different, in that case the number of R waves in the 30 large squares (6 seconds) should be counted and multiply the number by 10 to get an approximate heart rate per minute.

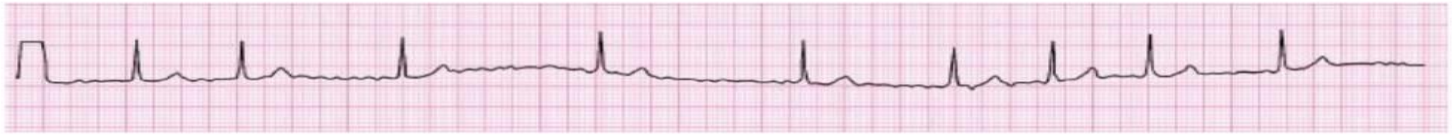


Fig. 7.5: Irregular R-R interval

9*10=90

4. Axis

Look at Lead I and Lead aVF for electrical axis of the heart. In both these leads, normally, QRS complex is upwards.

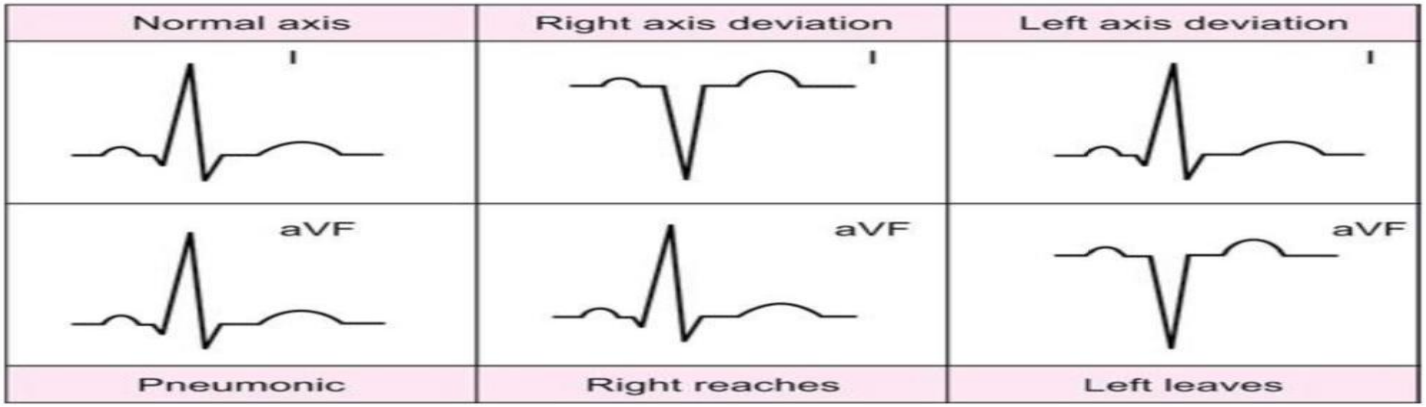


Fig. 7.6: Comparison of lead I with aVF to get the axis

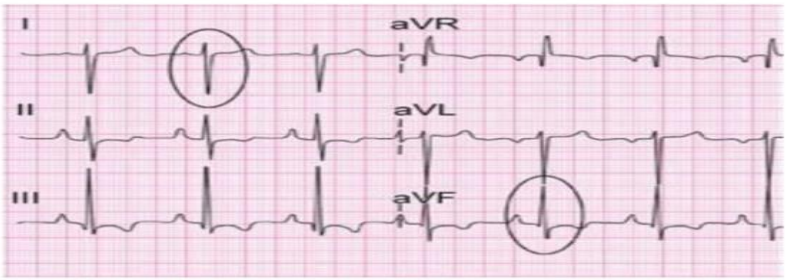


Fig. 7.7: Right axis deviation

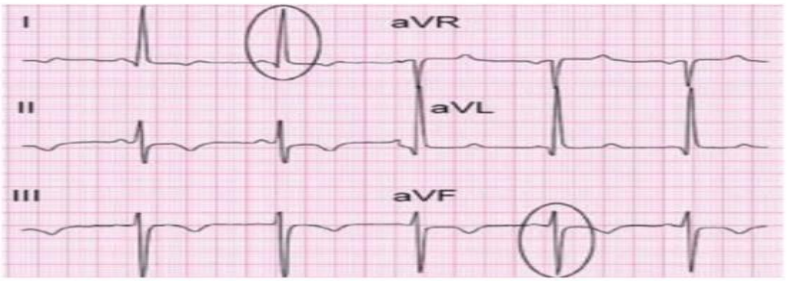


Fig. 7.8: Left axis deviation

Causes

Right axis deviation	*Left axis deviation*
Right ventricular hypertrophy	Left ventricular hypertrophy
Right bundle branch block	Left bundle branch block

5.

P wave : clinical importance

absent replaced by F wave (saw teeth) Atrial fibrillation

Small multiple Atrial flutter

Large Atrial enlagment

Inverted AV nodal pacemaker

PR segment and ST segment

Flat isoelectric

Elevated ischemia

Depressing myocardial infarction (MI)

QRS complex

Very tall ventricular enlargement

Very short pericardial effusion

Bizarre MI or bundle branch block BBB

T wave

Invered in ischemia

Peaked increase K

Flat decrease K

INTERVALS AND SEGMENTS OF ECG

‘P-R’ INTERVAL

It is the interval between the onset of ‘P’ wave & the onset of ‘Q’ wave.

it signifies the atrial depolarization & conduction of impulses through AV node. It shows the duration of conduction of the impulses from the SA node to ventricles through atrial muscle and AV node.

It is represented by the short isoelectric (zero voltage) period after the end of ‘P’ wave & onset of ‘Q’ wave. It denotes the time taken for the passage of depolarization within AV node.

The normal duration is 0.18 second & varies between 0.12 - 0.2 sec. If it is more than 0.2 second, signifies the delay in the conduction of impulse from SA node to the ventricles. Usually, the delay occurs in the AV node. So it is called= the AV nodal delay.

‘Q-T’ INTERVAL

the interval between the onset of ‘Q’ wave and the end of ‘T’ wave.

indicates the ventricular depolarization & ventricular repolarization, i.e. it signifies the electrical activity in ventricles. Duration--Between 0.4 and 0.42 second.

‘S-T’ SEGMENT

The time interval between the end of ‘S’ wave and the onset of ‘T’ wave is called ‘S-T’ segment. It is an isoelectric period.

Duration of ‘S-T’ Segment 0.08 second.

J Point

The point where ‘S-T’ segment starts is called ‘J’ point. It is the junction between the QRS complex and ‘S-T’ segment.

‘R-R’ INTERVAL

‘R-R’ interval is the time interval between two consecutive ‘R’ waves. signifies the duration of one cardiac cycle.

The normal duration of ‘R-R’ interval is 0.8 second.

Cardiovascular Adjustments during Exercise

واجب بيتي للمناقشة مع الطلبة

Cardiac cycle &
Cardiac output
Arterial blood pressure

Cardiac cycle

the sequence of events in heart which are repeated during every heartbeat in a cyclic manner. Each heartbeat consists of 2 major periods- systole & diastole. Systole is contraction of cardiac muscle & diastole is relaxation of cardiac muscle. The events of cardiac cycle are classified into 2 divisions:

1. Atrial events which constitute atrial systole & atrial diastole
2. Ventricular events - constitute ventricular systole &ventricular diastole.

Each cycle is initiated by depolarization of the SA node, followed by atrial systole (0.1 sec) →

ventricular systole (0.3 sec) → diastole of whole heart (0.5 sec).

Events:

Mechanical events: pressure, volume, and sound changes

Electrical events (ECG): action potentials

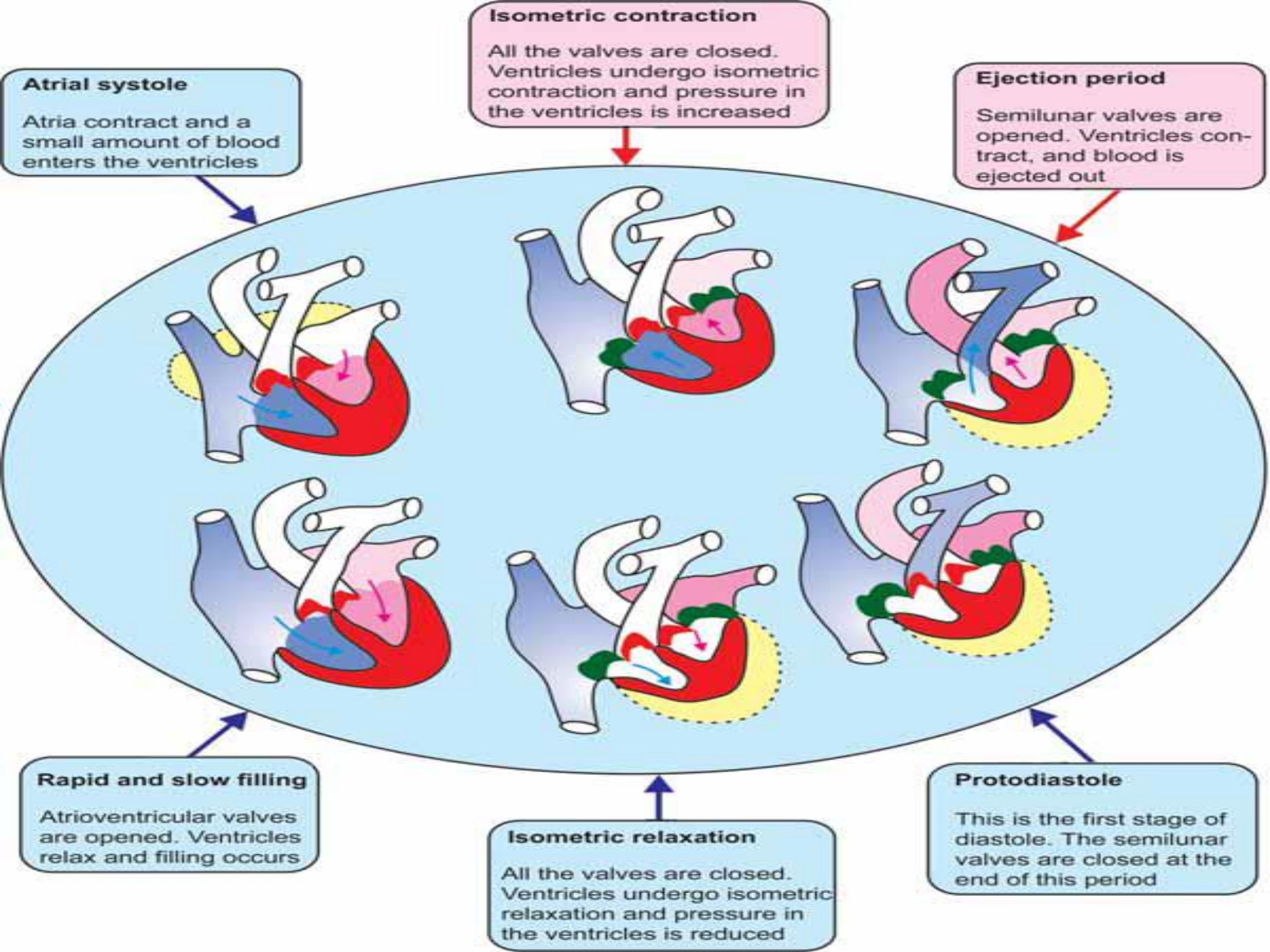
Cardiac cycle time:60/75 = 0.8 s Duration is inversely proportional to the Heart rate

Atrial Events	
Systole 0.1 s	Diastole 0.7 s
Ventricular Events	
Systole 0.3 s After exercise: Systole 0.14	Diastole 0.5 s After exercise: Diastole 0.16

The total time for the cardiac cycle (HR = 75 bpm)
0.8 seconds

Ventricular diastole is **long** for **three** important reasons:

1- Coronary blood flow
2 Ventricular filling
3 Rest


Isometric contraction
All the valves are closed. Ventricles undergo isometric contraction and pressure in the ventricles is increased
Atrial systole
Atria contract and a small amount of blood enters the ventricles
Ejection period
Semilunar valves are opened. Ventricles contract, and blood is ejected out
Rapid and slow filling
Atrioventricular valves are opened. Ventricles relax and filling occurs
Isometric relaxation
All the valves are closed. Ventricles undergo isometric relaxation and pressure in the ventricles is reduced
Protodiastole
This is the first stage of diastole. The semilunar valves are closed at the end of this period

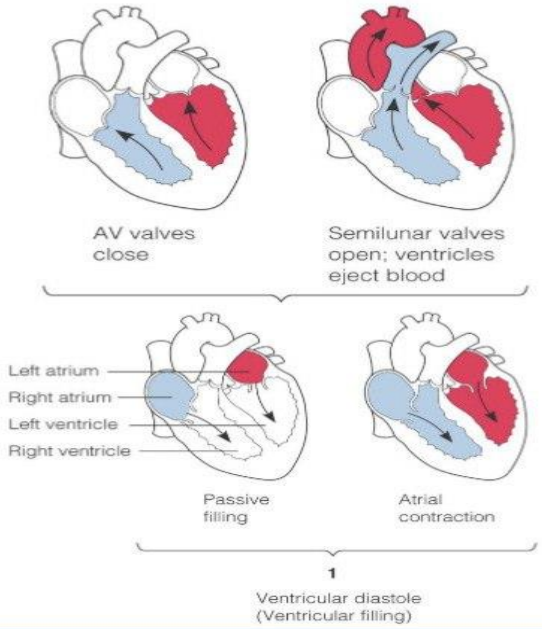
Phases of the Cardiac Cycle

Ventricular systole
(0.3 seconds)

1- Isovolumetric contraction
(Early systole)

2- Rapid Ejection
(Late systole)

3- Reduced Ejection
(Late systole)



Ventricular diastole
(0.5 seconds)

4- Isovolumetric relaxation
(Early diastole)

5- Rapid filling
(Late diastole)

6- Slow filling
(Late diastole)

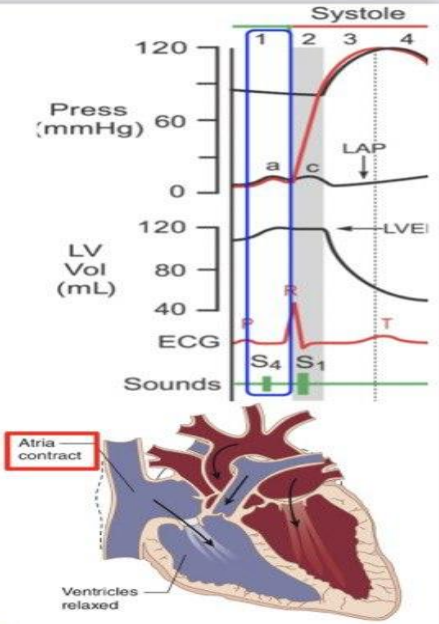
7- Atrial systole

Volume Changes

ESV End-systolic volume	Volume of blood left in a ventricle at the end of systole **(40–60 ml)**
EDV End-diastolic volume	Volume of blood in a ventricle at the end of diastole **(120–130 ml)** **MAX**
SV Stroke volume	Volume of blood ejected by a ventricle during systole **(~70 ml)** (Per beat)

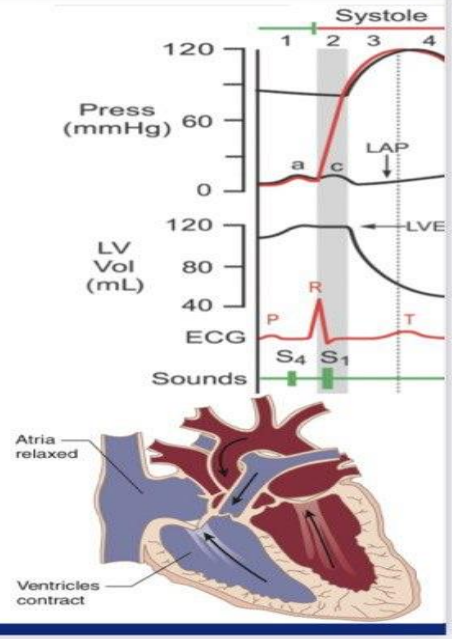
Atrial Systole

Description	The atria contract, pushing the last 25% of blood to the ventricles.			
Duration	0.11 seconds			
Valves	**AV**	Open		
	Semilunar	Closed		
Ventricular volume	Ventricular volume rise to EDV (120–130 ml) at the end of this phase			
Ventricular pressure	First a slight ↑ (blood entry) Then slight ↓ (ventricular dilation)		**Atrial pressure**	First ↑ (by systole) Then ↓ (blood exit)
Sounds	**4th** heart sound (S4)			



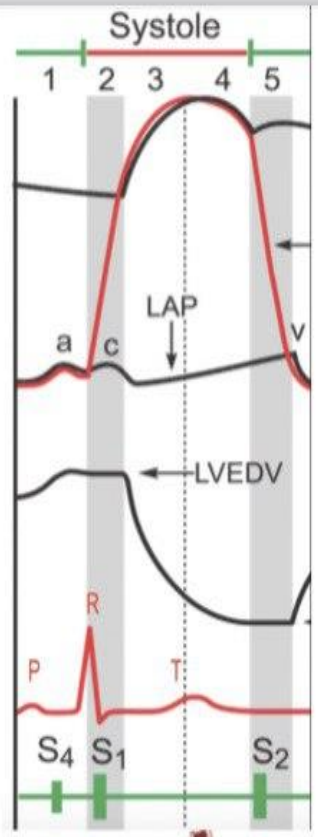
Isovolumetric contraction (AKA Isometric contraction)

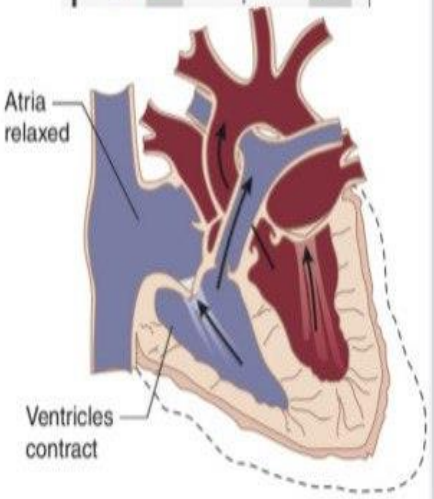
Description	The ventricle builds up tension <u>without</u> changing its length to open the semilunar valves It occurs at the beginning of ventricular systole			
Duration	0.05 seconds			
Valves	**AV**	Closed		
	Semilunar	Closed		
Ventricular volume	Maximum EDV = 120–130 ml			
Ventricular pressure	<u>Sudden</u> rise up to 80 mmHg which will open the aortic valve		**Atrial pressure**	↑ Due to doming of closed A-V cusps into atria
Sounds	**1st** heart sound (S1) **(AV valve closure)**			



Ejection (Rapid & Reduced)

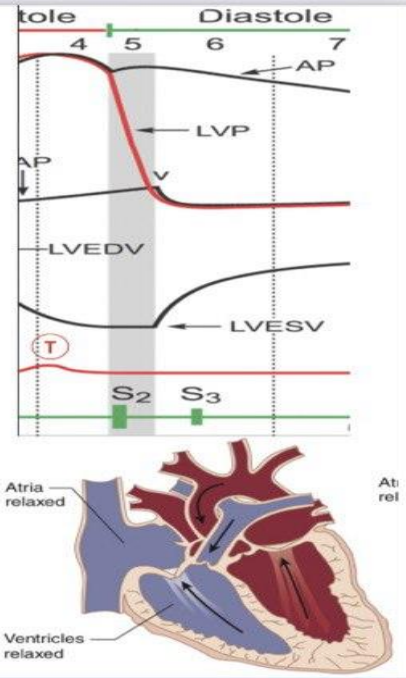
Description	The ventricle shortens its wall (isotonically) ejecting blood through the aorta and pulmonary artery in two phases, marking the end of systole: **Rapid (ejecting 70%) & Reduced (ejecting 30%)**			
Duration	Rapid: 0.10 seconds Reduced: 0.15 seconds			
Valves	**AV**	Closed		
	Semilunar	Open		
Ventricular volume	Decrease to ESV = 50 ml			
Ventricular pressure	Rapid: increase to 120 mmHg Reduced: decrease		**Atrial pressure**	First ↓ because when ventricles contract, they pull the AV fibrous ring & valves down then increase.
Sounds	None			





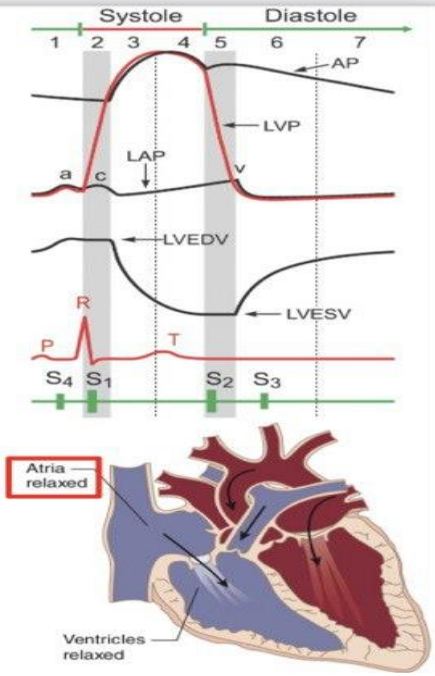
Isovolumetric relaxation

Description	The ventricles relax, causing a drop in pressure which leads to backflow of blood from the aorta (closing the valves)			
Duration	0.06 –0.04 seconds			
Valves	**AV**	Closed		
	Semilunar	Closed		
Ventricular volume	Volume does not change ESV= 50 ml			
Ventricular pressure	Decreases rapidly to diastolic levels (2–10 mmHg) because the valves are closed & the relaxation is isometric		**Atrial pressure**	Increases gradually due to accumulation of venous blood
Sounds	**2nd** heart sound (S2) **(Sudden Aortic valve closure)**			



Filling phase (Rapid & Slow)

Description	The AV opens, filling the ventricle in 3 phases: Rapid (70%) & Slow/Diastasis (5%) & Atrial systole (25%)			
Duration	Rapid: 0.11 seconds		Slow (diastasis): 0.22 seconds	
Valves	**AV**	Open		
	Semilunar	Closed		
Ventricular volume	Volume is increased in ventricles and decreased in atria			
Ventricular pressure	↑ slightly due to increase in volume, but is still **less** than atrial pressure		**Atrial pressure**	First sudden ↓ due to rush of blood into ventricles. Then ↑ due to venous blood entry.
Sounds	**3rd** heart sound (S3) during **rapid filling** phase (rush of blood and vibrations in ventricular wall)			

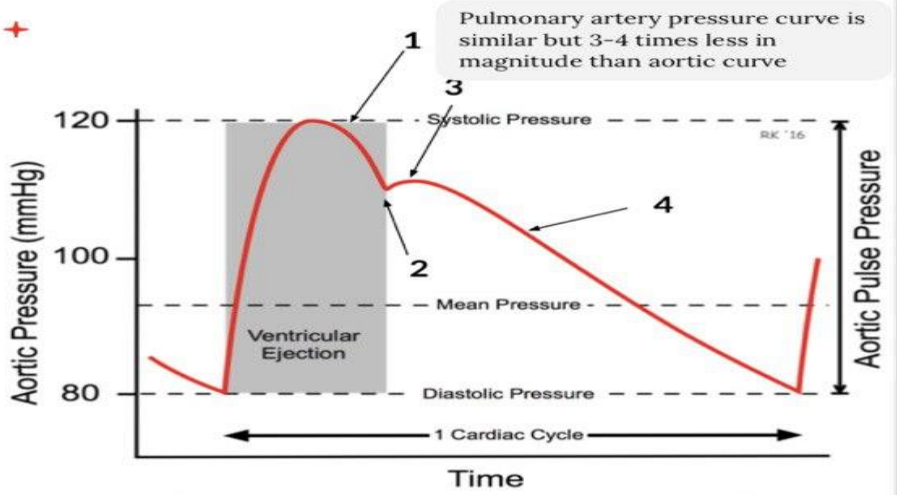


Aortic pressure curve

1- **Ascending phase (anacrotic limb):**
Aortic pressure increases to 120 mmHg, coincides with rapid ejection.

2- **Descending phase (catacrotic limb):** Can be split into 4 stages:

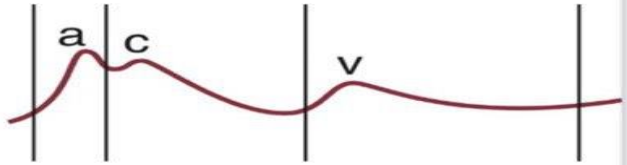
1. **Decrease in aortic pressure**
   Coincides with reduced ejection (blood entering aorta is less than blood leaving it)
2. **Dicrotic notch (incisura)**
   Sudden drop in pressure caused by closure of aortic valve at the end of ventricular systole.
3. **Dicrotic wave**
   Slight increase in aortic pressure caused by the aortic elastic recoil
4. **Slow aortic pressure decrease**
   Down to 80 mmhg due to continuous blood flow in systemic arteries.



Arterial curve is similar to aortic, but **sharper**.
- **systolic peak pressure** of 110-130 mmHg.
- **diastolic pressure** of 70-85 mmHg.

Atrial pressure waves

1. **"a" wave (atrial systole):**
   increase due to atrial contraction
   decrease due to blood passing into ventricles
2. **"c" wave (ventricular systole):**
   Increase due to bulging of AV valve in isometric contraction
   decrease due the downward pulling of AV valve during ventricular rapid ejection
3. **"x" descent:**
   decrease due continued pulling of AV valve during ventricular reduced ejection
4. **"v" wave (atrial diastole):**
   Increase due to venous return
   decrease due to blood entry into the ventricles during rapid filling phase
5. **"y" descent:**
   Decrease due to continued blood flow during reduced filling phase.



In Jugular venous pulse(JVP), the same waves can be seen but are delayed

Atrial pressure waves

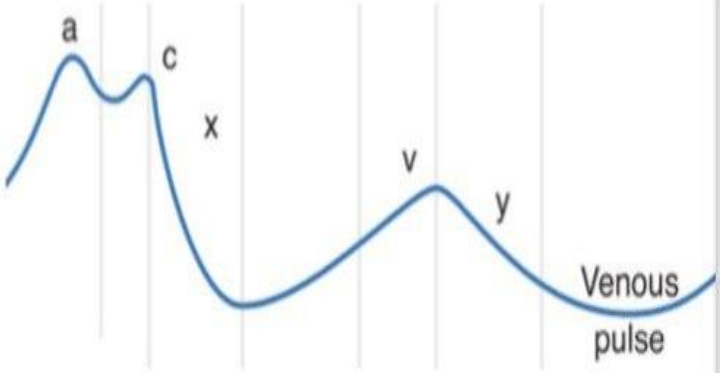
1. **"a" wave (atrial systole):**
   increase due to atrial contraction
   decrease due to blood passing into ventricles

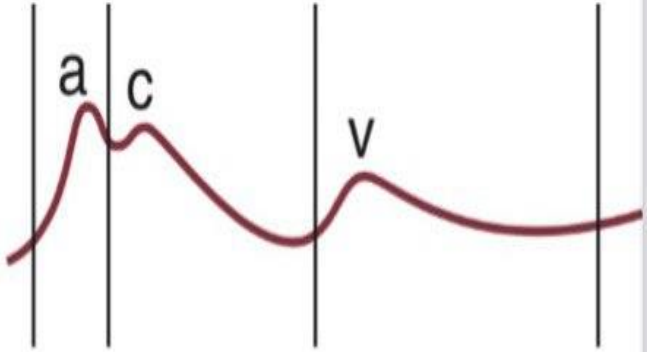
2. **"c" wave (ventricular systole):**
   Increase due to bulging of AV valve in isometric contraction
   decrease due the downward pulling of AV valve during ventricular rapid ejection

3. **"x" descent:**
   decrease due continued pulling of AV valve during ventricular reduced ejection

4. **"v" wave (atrial diastole):**
   Increase due to venous return
   decrease due to blood entry into the ventricles during rapid filling phase

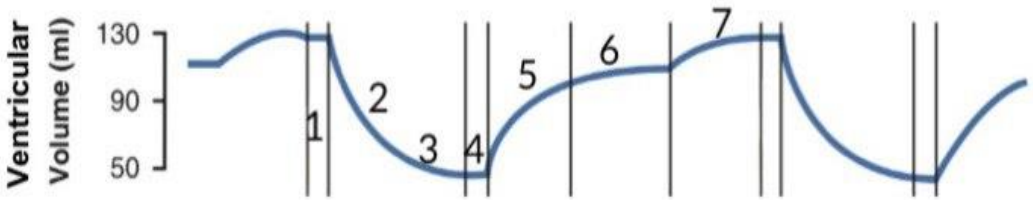
5. **"y" descent:**
   Decrease due to continued blood flow during reduced filling phase.





In Jugular venous pulse(JVP), the same waves can be seen but are delayed

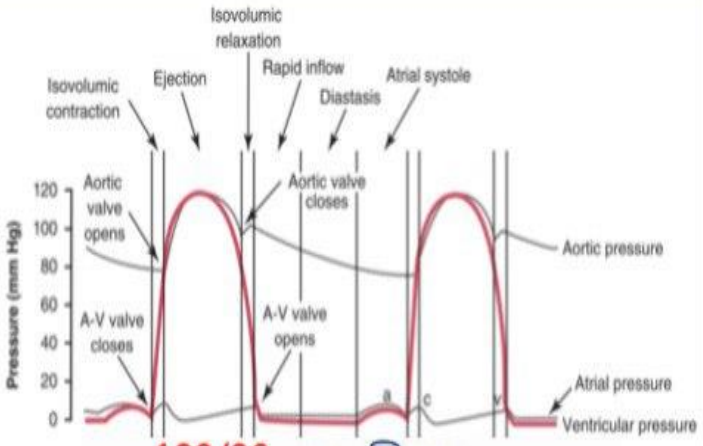
Volume changes

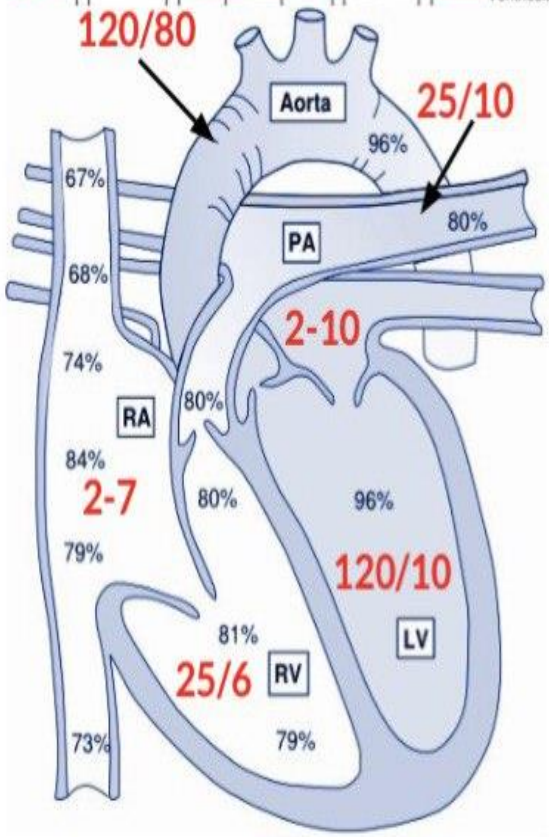


#	Phases	Ventricular Volume	Atria Volume
1	**Isometric Contraction**	Constant (EDV)	Increase
2	**Rapid Ejection**	Decrease rapidly	Increase
3	**Reduced Ejection**	Decrease slowly	Increase
4	**Isometric Relaxation**	Constant (ESV)	Increase
5	**Rapid Filling**	Increase rapidly	Decrease
6	**Reduced Filling**	Increase slightly	Decrease
7	**Atrial Systole**	Increase moderately	Decrease

Pressure changes

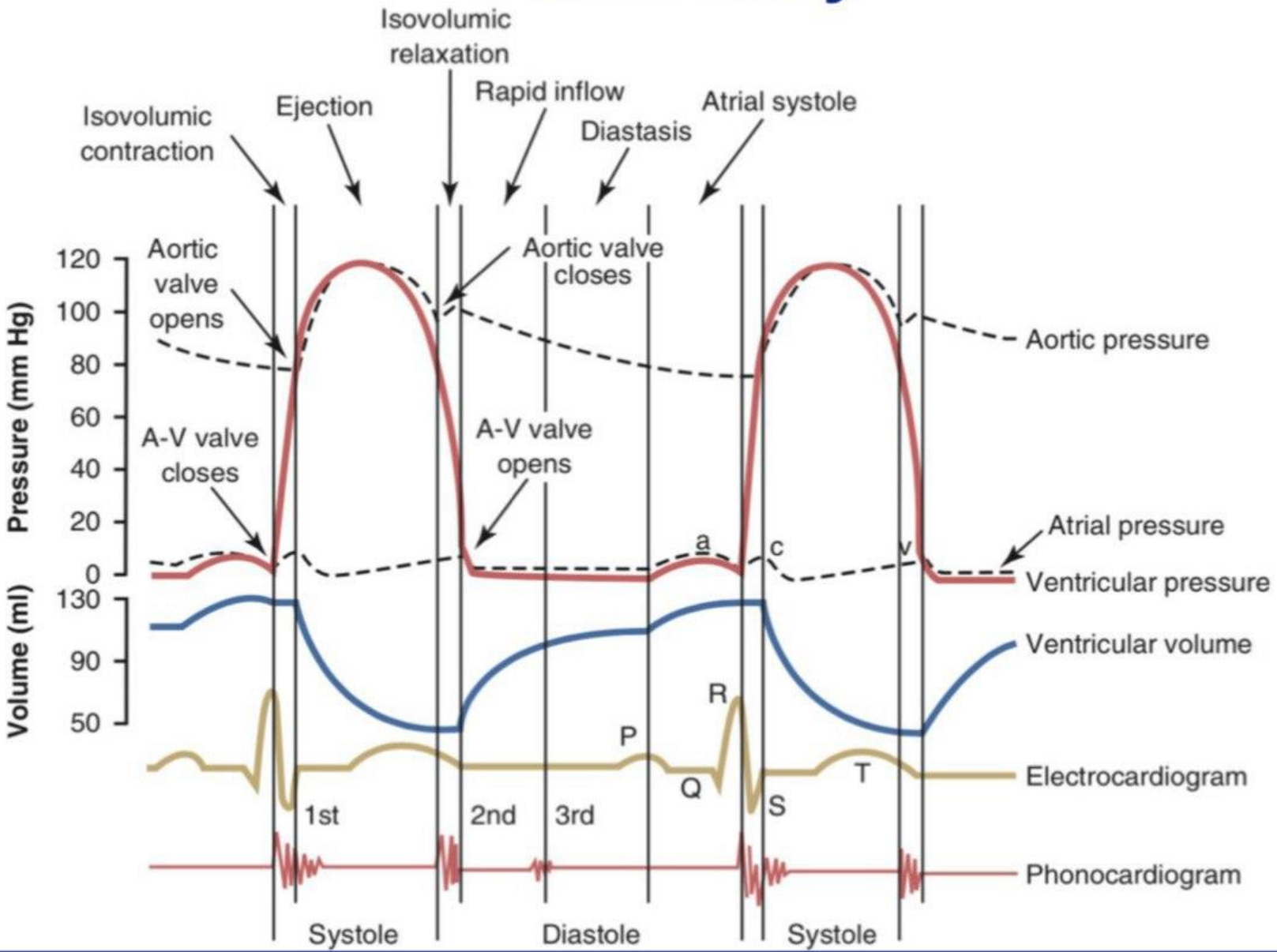
#	Phases	Ventricular Pressure
1	**Isovolumetric Contraction**	Increase suddenly (80mmHg)
2	**Rapid Ejection**	Increase rapidly (120mmHg)
3	**Reduced Ejection**	Decrease slowly
4	**Isovolumetric Relaxation**	Decrease rapidly
5	**Rapid Filling**	Increase slightly
6	**Reduced Filling**	Increase gradually
7	**Atrial Systole**	Increase slightly then decrease





Different pressures in the chambers of the heart

Summary


Isovolumic relaxation
Isovolumic contraction
Ejection
Rapid inflow
Diastasis
Atrial systole
Aortic valve opens
Aortic valve closes
A-V valve closes
A-V valve opens
Pressure (mm Hg)
120
100
80
60
40
20
0
Volume (ml)
130
90
50
Aortic pressure
Atrial pressure
Ventricular pressure
Ventricular volume
Electrocardiogram
Phonocardiogram
a
c
v
R
P
Q
S
T
1st
2nd
3rd
Systole
Diastole
Systole

Heart sounds

are the sounds produced by mechanical activities of heart during each cardiac cycle. Generally, heart sounds are produced by:

1. Flow of blood through the chambers of the heart
2. Contraction of cardiac muscle
3. Closure of valves of the heart.

heart sounds are heard by placing ear over the chest or by using a stethoscope or microphone & also recorded graphically.

Four heart sounds are produced during each cardiac cycle.

The first & second heart sounds= called classical heart sounds. These sounds are more prominent and resemble the spoken words ‘LUB’ (or LUBB) and ‘DUB’ (or DUP) respectively. These two heart sounds are heard by using the stethoscope.

IMPORTANCE OF HEART SOUNDS

heart sounds has important diagnostic value in clinical practice because the alteration- indicates cardiac diseases involving the valves of heart.

The first heart sound is a long, soft & low pitched sound. It resembles the spoken word ‘LUBB’. The duration of this sound is 0.10 to 0.17 second. Its frequency is 25 to 45 cycles/second.

The second heart sound

is a short, sharp and high pitched sound. It resembles the spoken word ‘DUBB’ (or DUP).

THIRD HEART SOUND

The third heart sound is a low pitched. Usually, the third heart sound is inaudible by stethoscope and it can be heard only by using microphone.

Third heart sound is a short and low pitched sound. Third heart sound can be heard by stethoscope in children and athletes. Pathological conditions when third heart sound becomes loud and audible by stethoscope are aortic regurgitation, cardiac failure and cardiomyopathy with dilated ventricles.

When third heart sound is heard by stethoscope the condition is called triple heart sound.

FOURTH HEART SOUND

Normally is an inaudible sound, audible only in pathological conditions. It is studied only by graphical recording that is by phonocardiography.

Fourth heart sound is a short and low pitched sound. Ventricular stiffness occurs in conditions like ventricular hypertrophy, long standing hypertension & aortic stenosis. To overcome the ventricular stiffness, the atria contract forcefully producing audible fourth heart sound.

METHODS OF STUDY OF HEART SOUNDS

Heart sounds are studied by three methods:

1. By using stethoscope
2. By using microphone
3. By phonocardiogram.

CARDIAC MURMUR

is the abnormal or unusual heart sound heard by stethoscope along with normal heart sounds-- also called abnormal heart sound or cardiac bruit. The abnormal sound is produced because of the change in the pattern of blood flow.

cardiac murmur is heard by placing the chest piece of the stethoscope over the auscultatory areas. The murmur due to disease of a particular valve is heard well over the auscultatory area of that valve.

Valvular diseases that cause murmur are of two types:

1. Stenosis or narrowing of the heart valve.
2. valve regurgitation : When the valve becomes weak, it cannot close properly. It causes back flow of blood resulting in turbulence.

CLASSIFICATION OF MURMUR

Cardiac murmur is classified into three types:

1. Systolic murmur produced during systole of the heart
2. Diastolic murmur produced during diastole of the heart
3. Continuous murmur produced continuously.

Cardiac output (MINUTE VOLUME)

is the amount of blood pumped out by each ventricle in one minute. It is the product of stroke volume and heart rate:

Cardiac output = Stroke volume × Heart rate

Normal value: 5 liters/ ventricle/ minute.

cardiac output is **expressed** in three ways:

1. STROKE VOLUME

It is the amount of blood pumped out by each ventricle during each beat. Normal value: 70 mL (60 to 80 mL) when the heart rate is normal (72/minute).

2. MINUTE VOLUME

is the amount of blood pumped out by each ventricle in one minute. It is the product of stroke volume and heart rate: Minute volume = Stroke volume × Heart rate

Normal value: 5 liters/ ventricle/ minute.

3. CARDIAC INDEX

is the minute volume expressed in relation to square meter of body surface area. It is defined as the amount of blood pumped out per ventricle/minute/ square meter of the body surface area. Normal value: Cardiac index = 2.8 ± 0.3 liters/ square meter of body surface area/ minute.

(In an adult, the average body surface area is 1.734 square meter and normal minute volume is 5 liters/minute).

HEART RATE

Normal heart rate is 72/minute. It ranges = 60 & 80 per minute.

TACHYCARDIA

is the increase in the heart rate above 100/minute.

Physiological conditions when tachycardia occurs are:

1. Childhood 2. Exercise 3. Pregnancy 4. Emotional conditions(anxiety)

Pathological conditions when tachycardia occurs are:

1. Fever 2. Anemia 3. Hypoxia4. Hyperthyroidism
5. Hypersecretion of catecholamines 6. Cardiomyopathy
7. Valvular heart diseases.

BRADYCARDIA

is the decrease in the heart rate below 60/minute.

Physiological conditions when bradycardia occurs are:

1. Sleep 2. Athletic heart.

Pathological conditions when bradycardia occurs are:

1. Hypothermia 2. Hypothyroidism 3. Heart attack 4. Congenital heart disease 5. Degenerative process of aging 6. Obstructive jaundice

Arterial blood pressure

is the lateral pressure exerted by the column of blood on the wall of arteries. is expressed in four different terms:

1. Systolic blood pressure
2. Diastolic blood pressure
3. Pulse pressure
4. Mean arterial blood pressure.

Systolic blood pressure (systolic pressure) is the maximum pressure exerted in the arteries during systole of the heart. The normal systolic pressure is 120 mm Hg. It ranges = 110 & 140 mm Hg.

Diastolic blood pressure (diastolic pressure) is the minimum pressure in the arteries during diastole of the heart. The normal diastolic pressure is 80 mm Hg. It varies between 60 and 80 mm Hg.

Pulse pressure is the difference between systolic pressure and diastolic pressure. Normally, it is 40 mm Hg (120 to 80).

PHYSIOLOGICAL VARIATIONS

1. Age
2. Sex
3. Body Built: The pressure is more in obese persons than in lean persons.
4. Diurnal Variation
5. After Meals
6. During Sleep

Usually, the pressure is reduced up to 15 to 20 mm Hg during deep sleep. However, it increases slightly during sleep associated with dreams.

7. Emotional Conditions
8. After Exercise systolic pressure increased and diastolic pressure decrease.

DETERMINANTS OF ARTERIAL BLOOD PRESSURE – FACTORS MAINTAINING ARTERIAL BLOOD PRESSURE

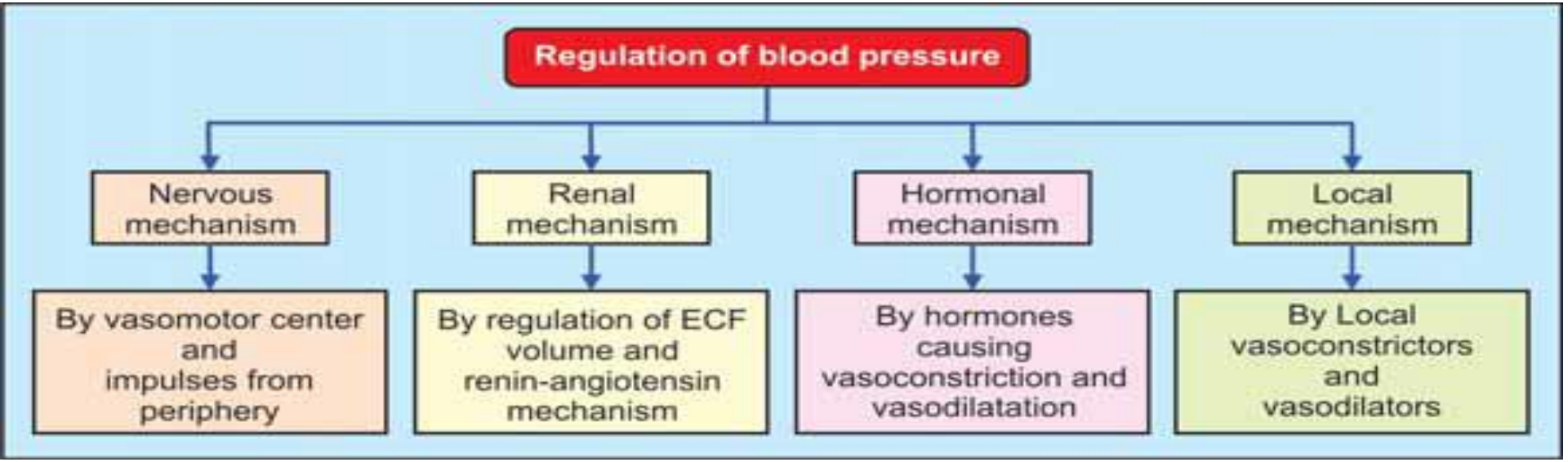
Some factors are necessary for maintenance of normal blood pressure. These factors are divided into 2 types: p = Cardiac output * TPR

I. Central factors -:(Cardiac output& Heart rate).

II. Peripheral factors-- pertaining to blood and blood vessels:

1. Peripheral resistance
2. Blood volume
3. Venous return
4. Elasticity of blood vessels
5. Velocity of blood flow
6. Diameter of blood vessels
7. Viscosity of blood.

REGULATION OF ARTERIAL BLOOD PRESSURE

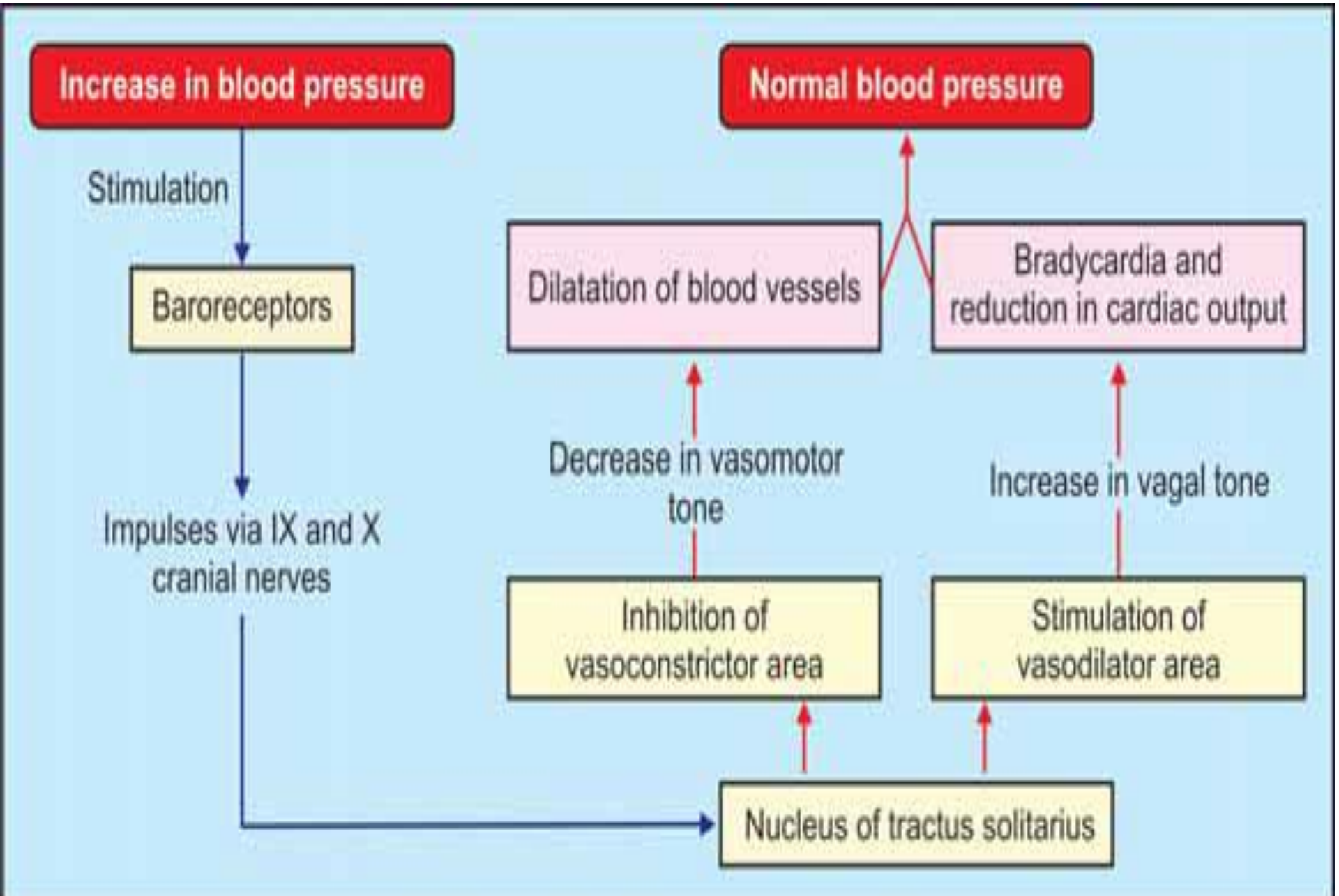


The nervous regulation is rapid among all the mechanisms involved in regulation of ABP. When BP alters, nervous system brings the pressure back to normal within few minutes. Although nervous mechanism is quick in action, it operates only for a short period & then it adapts to the new pressure= called short-term regulation. The nervous mechanism regulating ABP operates through the vasomotor system. The vasomotor system includes three components:

1. Vasomotor center 2. Vasoconstrictor fibers 3. Vasodilator fibers.

The vasomotor center regulates ABP by causing vasoconstriction or vasodilatation, its actions depend upon the impulses it receives from other structures such as baroreceptors, chemoreceptors, higher centers and respiratory centers. --baroreceptors and chemoreceptors play a major role in the short-term regulation of blood pressure.

Regulation of blood pressure by baroreceptor mechanism



2. Chemoreceptor Mechanism

Chemoreceptors are receptors giving response to change in chemical constituents of blood. Peripheral chemoreceptors influence the vasomotor center.

Peripheral chemoreceptors are sensitive to lack of oxygen, excess of carbon dioxide and hydrogen ion concentration in blood. Whenever

blood pressure decreases, the blood flow decreases resulting in decreased oxygen content and excess of carbon dioxide and hydrogen ion.

These factors stimulate the chemoreceptors, which send impulses to stimulate the vasoconstrictor center. The blood pressure rises and blood flow increases.

Chemoreceptors play a major role in maintaining respiration rather than blood pressure.

Sinoaortic mechanism

Mechanism of action of baroreceptors and chemoreceptors in carotid and aortic region. The nerves from the baroreceptors and chemoreceptors are called buffer nerves because these nerves regulate the heart rate, blood pressure and respiration.

RENAL MECHANISM FOR REGULATION OF B P – LONG-TERM REGULATION

kidneys play an important role in the long term regulation of ABP. by 2 ways:

1. By regulation of ECF volume
2. Through renin-angiotensin mechanism.

BY REGULATION OF EXTRACELLULAR FLUID VOLUME

When the BP increases, kidneys excrete large amounts of water & salt, particularly sodium by means of pressure diuresis & pressure natriuresis. Pressure diuresis is the excretion of large quantity of water in urine because of increased BP

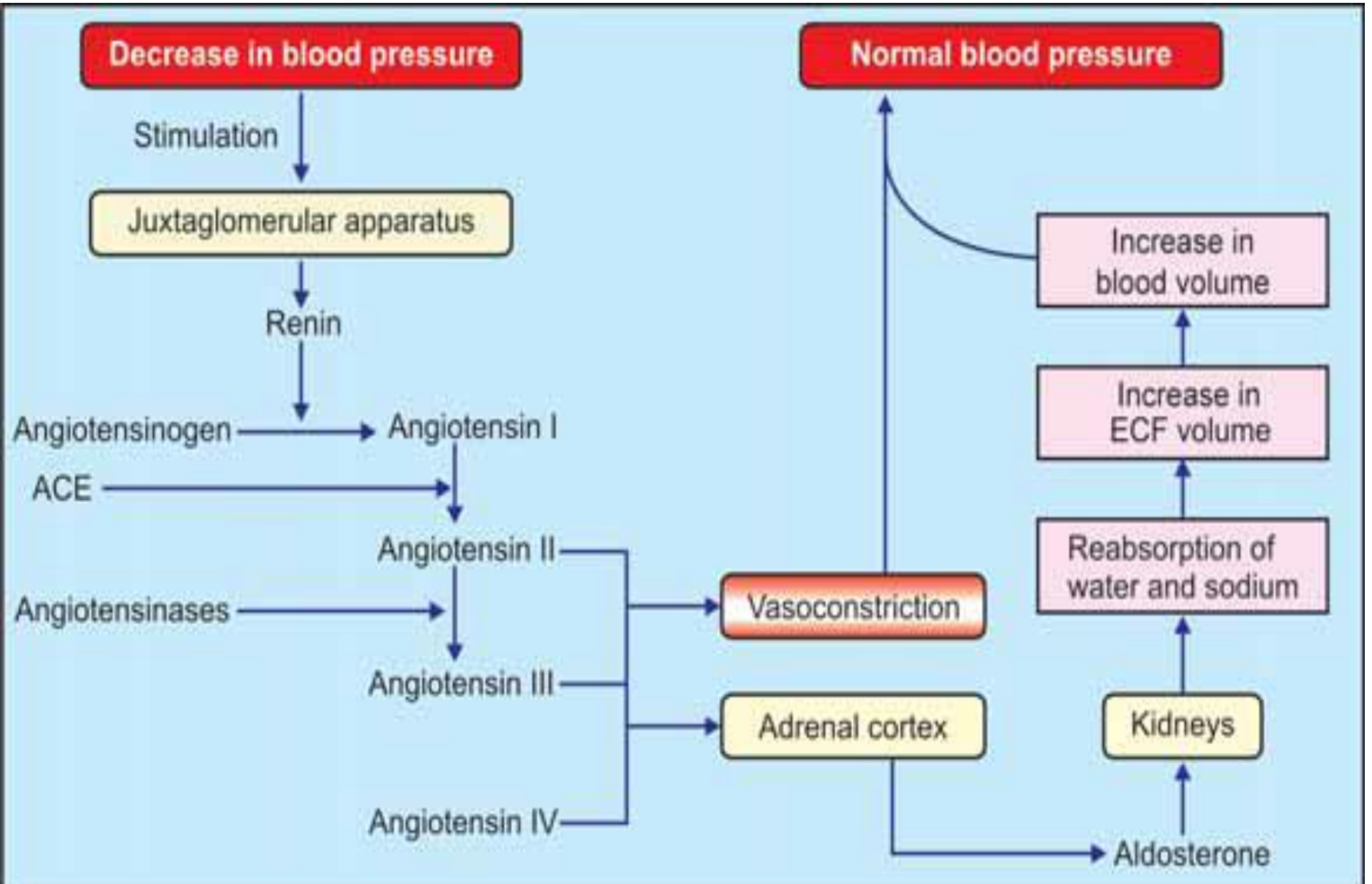
Even a slight increase in BP doubles the water excretion.

Pressure natriuresis is the excretion of large quantity of sodium in urine.

Because of diuresis & natriuresis, there is decrease in the ECF volume &blood volume, which in turn brings the ABP back to normal level.

When blood pressure decreases, the reabsorption of water from renal tubules is increased. This in turn, increases ECF volume, blood volume & cardiac output resulting in restoration of BP.

Regulation of blood pressure by renin-angiotensin mechanism.
ACE = Angiotensin converting enzyme



HORMONAL MECHANISM FOR REGULATION Of BP

Hormones which Increase the Blood Pressure

1. Adrenaline
2. Noradrenaline
3. Thyroxine
4. Aldosterone
5. Vasopressin
6. Angiotensin
7. Serotonin.

Hormones which Decrease the Blood Pressure

1. Vasoactive intestinal polypeptide (VIP)
2. Bradykinin
3. Prostaglandin
4. Histamine
5. Acetylcholine
6. Atrial natriuretic peptide
7. Brain natriuretic peptide
8. C-type natriuretic peptide.

LOCAL MECHANISM FOR REGULATION OF BP

some local substances also regulate the BP. The local substances regulate the blood pressure by vasoconstriction or vasodilatation.

LOCAL VASOCONSTRICTORS

The local vasoconstrictor substances are of vascular endothelial origin and are known as endothelins (ET). Endothelins are produced by stretching of blood vessels. These peptides act by activating phospholipase, which in turn activates the prostacyclin and thromboxane A2. These two substances cause constriction of blood vessels and increase in blood pressure.

LOCAL VASODILATORS

The local vasodilators are of two types:

1. Vasodilators of metabolic origin such as carbon dioxide, lactate, hydrogen ions and adenosine
2. Vasodilators of endothelial origin such as nitric oxide (NO).

HYPERTENSION

the persistent high blood pressure. Clinically, systolic pressure remains elevated above 150 mm Hg & diastolic pressure remains elevated above 90 mm Hg, it is considered as hypertension. If there is increase only in systolic pressure, it is called systolic hypertension.

Types of Hypertension

1. Primary hypertension or essential hypertension

Primary hypertension is the elevated blood pressure in the absence of any underlying disease- called essential hypertension.

The arterial blood pressure is increased because of increased peripheral resistance, which occurs due to some unknown cause.

2. Secondary hypertension

Secondary hypertension is the high blood pressure due to some underlying disorders. The different forms of secondary hypertension are:

i. Cardiovascular hypertension that is produced due to the cardiovascular disorders such as atherosclerosis(hardening of blood vessels by fat deposition) and coarctation (narrowing) of aorta

ii. Endocrine hypertension which is due to hyperactivity of some endocrine glands such as pheochromocytoma, hyperaldosteronism and Cushing's syndrome

iii. Renal hypertension that is caused by renal diseases like glomerulonephritis and stenosis of renal arteries

iv. Neurogenic hypertension which is developed by nervous disorders such as increased intracranial pressure and lesion in tractus solitarius

v. Hypertension during pregnancy which is due to toxemia of pregnancy.

HYPOTENSION

is the low BP. When the systolic pressure is less than 90 mm Hg, considered as hypotension. Types

1. Primary hypotension

is the low BP that develops in the absence of any underlying disease and develops due to some unknown cause. It is also called essential hypotension. Frequent fatigue and weakness are the common symptoms of this condition. However, the persons with primary hypotension are not easily susceptible to heart or renal disorders.

2. Secondary hypotension It is the hypotension that occurs due to some underlying diseases. The diseases which cause hypotension are:

i. Myocardial infarction

ii. Hypoactivity of pituitary gland

iii. Hypoactivity of adrenal glands

iv. Tuberculosis

v. Nervous disorders.

Lec. 19, 20

The Reproductive System

- Sexual reproduction produces new individuals
  - Gametes (sperm & egg) formed by testes and ovaries
  - Fertilization produces one cell (a zygote) with one set of chromosomes from each parent
  - Creates genetic variation
- Gonads produce gametes & secrete sex hormones
- Reproductive systems

Gonads, ducts, glands & supporting structures

Male reproductive system

The **male reproductive system** consists of a number of sex organs that play a role in the process of human reproduction. These organs are located on the outside of the body and within the pelvis.

The main male sex organs are the penis and the testicles which produce semen and sperm, which, as part of sexual intercourse, fertilize an ovum in the female's body; the fertilized ovum (zygote) develops into a fetus, which is later born as an infant.

External genital organs include the penis and scrotum

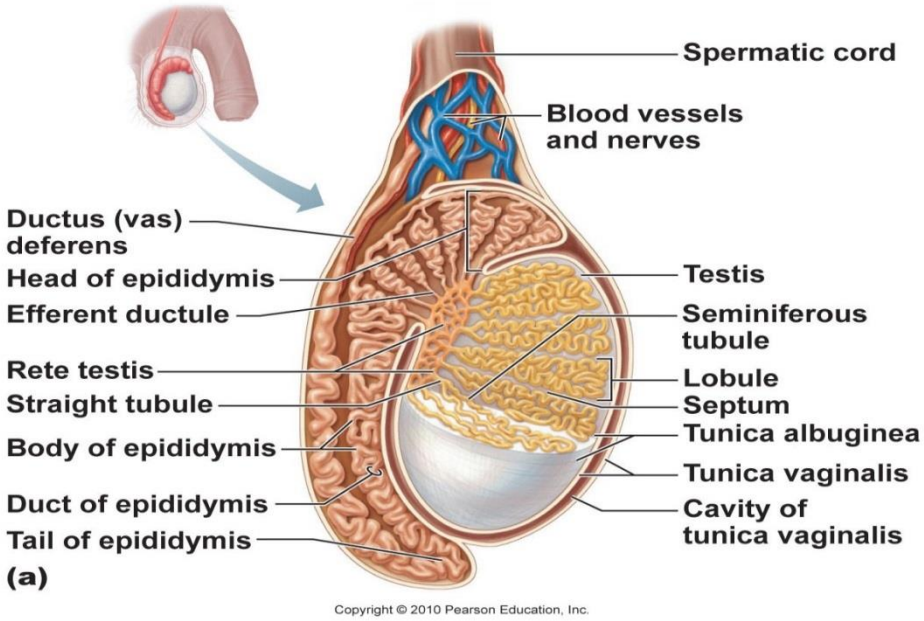
Scrotum: Sac of loose skin, fascia & smooth muscle divided into

- two pouches by a septum
- Temperature regulation of testes
  - Sperm survival requires 2-3 degrees lower temperature than core body temperature
  - Muscle in scrotum
    - Elevates testes on exposure to cold & during arousal
    - Warmth reverses the process

Internal genital organs include:

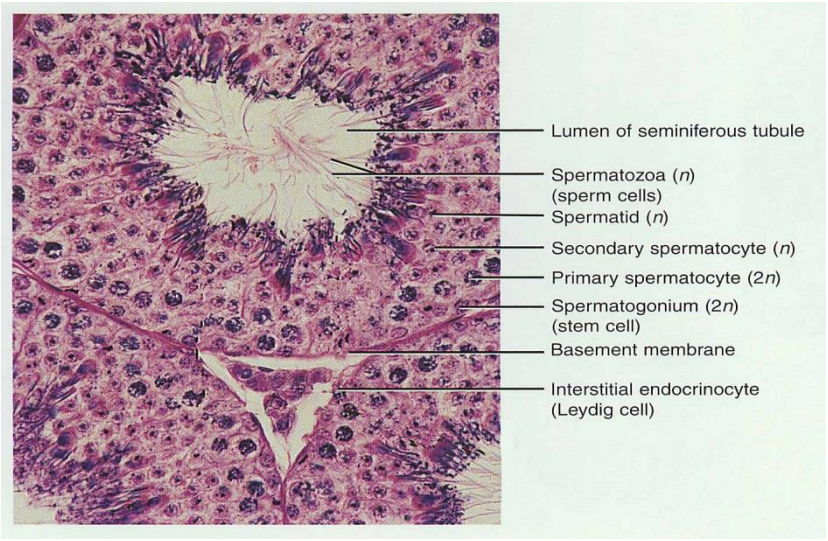
1. The epididymis, a whitish mass of tightly coiled tubes cupped against the testicles, acts as a maturation and storage for sperm before they pass into the vas deferens, that carry sperm to the ampullary gland and prostatic ducts.
2. The vas deferens, also known as the sperm duct, is a thin tube approximately 30 centimeters long that starts from the epididymis to the pelvic cavity. It carries the spermatozoa from the epididymis to ejaculatory duct.

3. Three accessory glands provide fluids that lubricate the duct system and nourish the sperm cells. They are the seminal vesicles, the prostate gland, and the bulbourethral glands (Cowper glands).
   Testes: Paired oval glands surrounded by dense white capsule
   – Septa form 200 - 300 compartments called lobules
- Each is filled with seminiferous tubules where sperm are formed.

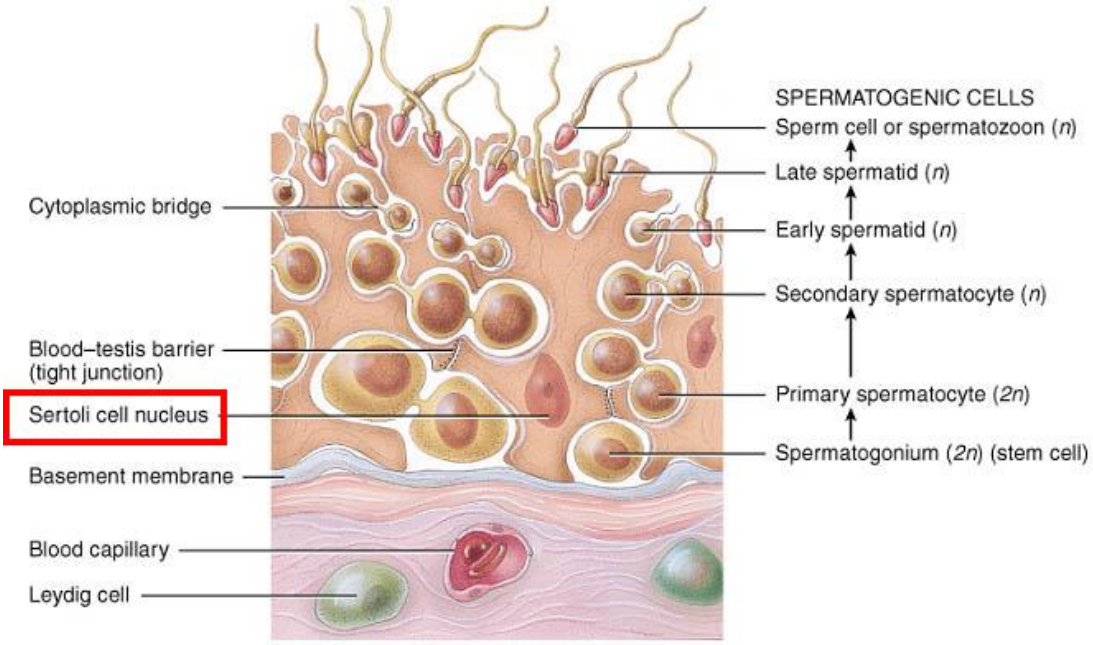


Seminiferous Tubules

- Seminiferous tubules contain
  – Sperm forming cells
  – Sertoli cells (supporting cells)
- Interstitial cells in between tubules secrete testosterone



Sertoli Cells and Sperm Cells
Sertoli cells -- extend from basement membrane to lumen
-form blood-testis barrier
-support developing sperm cells
-produce fluid & control release of sperm into lumen
-secrete inhibin which slows sperm production

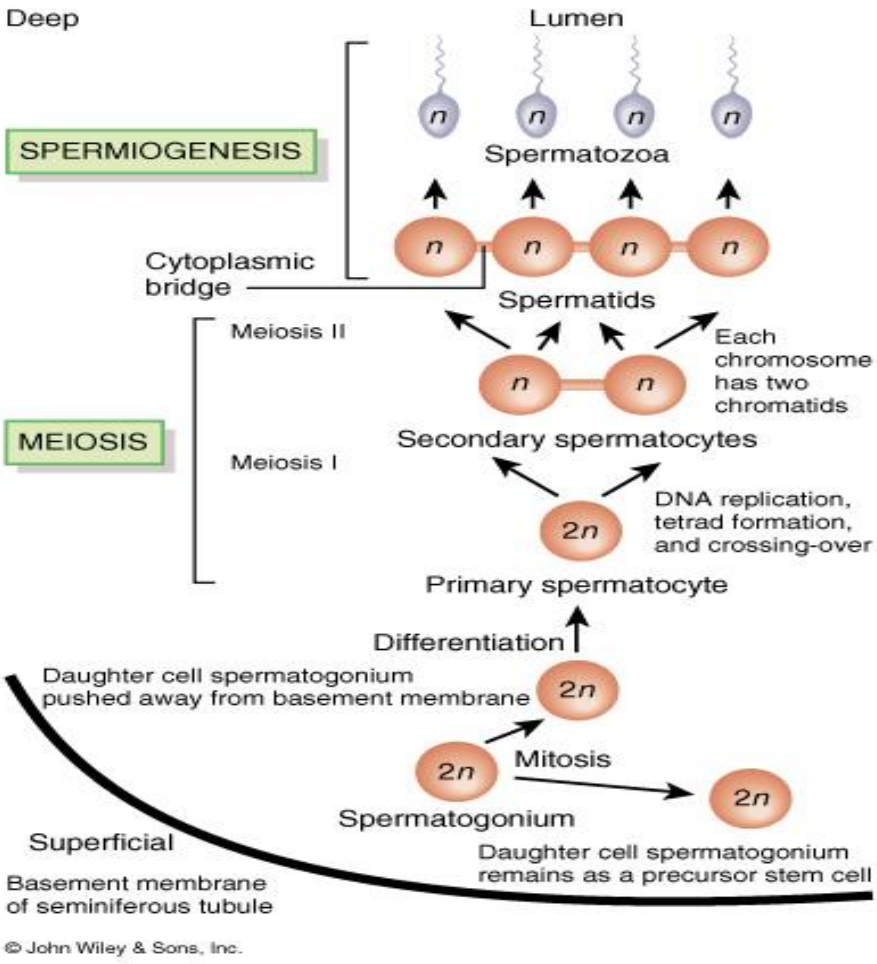


Spermatogenesis

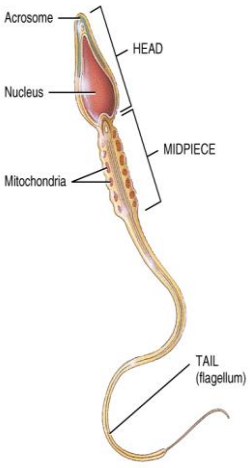
Sperm forming cells go through two meiotic divisions

- Each of four spermatids develop into a sperm
- Second meiosis division give four spermatids,each with 23 single stranded chromosomes
- First meiosis division give two secondary spermatocytes, each with 23 chromosomes that become double stranded.
- Primary spermatocyte with 2n=46 chromosomes

Spermatogonium with 2n=46 chromosomes multiply by mitosis



- **Sperm Morphology**
- Adapted for reaching and fertilizing the egg
- Head contains DNA and the acrosome with enzymes for penetrating the egg
- Midpiece contains mitochondria to form ATP for energy
- Tail is flagellum used for locomotion



Hormonal Control of Male Physiology

- Hypothalamus secretes gonadotropin releasing hormone (GnRH)
- Anterior pituitary secretes FSH and LH
- FSH causes Sertoli cells to secrete ABP and inhibin
- LH causes interstitial cells to secrete testosterone
- ABP and testosterone stimulate spermatogenesis
- Control is Negative FB by ↑testosterone and inhibin

Semen

- Mixture of sperms and seminal fluid
- 60% from seminal vesicles, 30% from prostate
- Slightly alkaline, milky appearance and sticky
- Contains nutrients, clotting proteins & an antibiotic to protect the sperms
- Typical ejaculate is 2.5 to 5 ml in volume
- Normal sperm count is 50 to 150 millions/mL
  - Actions of many sperm are needed for one to enter
  - If less than 20 millions/mL sterile

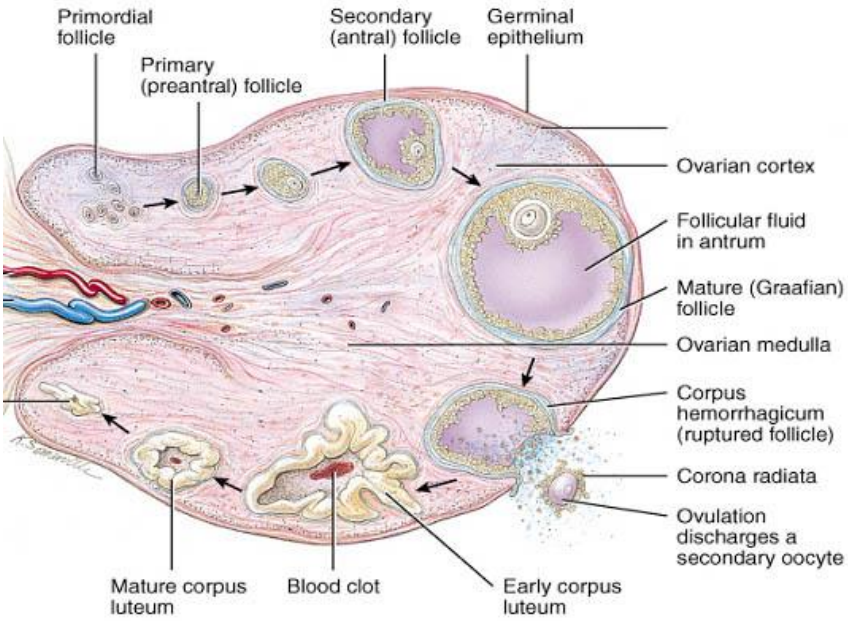
Female Reproductive System

- Ovaries produce eggs (oöcytes) & hormones
- Uterine tubes transport the eggs
- Uterus where fetal development occurs
- Vagina or birth canal
- External genitalia constitute the vulva
- Mammary glands produce milk

The Ovary

- Pair of organs, size of unshelled almonds in upper pelvic region
- Histology
  - Capsule of dense CT
  - Cortex just deep to capsule contains follicles with egg cells (oöcytes)
  - Medulla is middle region composed of connective tissue, blood vessels & lymphatics

Germinal epithelium is peritoneal membrane covering the ovary



Ovarian Follicles

- Ovarian Follicles
  - Contain oöcytes (egg cells) in various stages of development
  - Secrete estrogens that function for:-
    - Growth and repair of uterine lining
    - Regulation of monthly female cycle
    - Female sexual characteristics
    - Maintenance of bone and muscle
  - Mature (Graafian) follicle releases an oöcyte each month during ovulation

    Oöcytes (egg cells) develop within follicles

    Stages of follicular development

    Primordial follicle

    Single layer of squamous cells around the oöcyte

    Primary follicle

    Layers of cuboidal granulosa cells around the oöcyte

    Granulosa cells secrete estrogens
  - Secondary follicle
    - Antral cavity forms
  - Graafian follicle
- Follicle mature ready to ovulate oöcyte
- Ovulation
    - Follicle ruptures releasing oöcyte

Corpus Luteum

- After ovulation, empty follicle becomes a corpus luteum
  - Corpus Luteum secretes:-
    - Progesterone – completes the preparation of uterine lining
    - Estrogens – work with progesterone
    - Relaxin – relaxes uterine muscles and pubic symphysis
    - Inhibin – decreases secretion of FSH and LH
- Corpus albicans is a white scar tissue left after the corpus luteum dies.

Oögenesis – Oögonia to Oöcytes

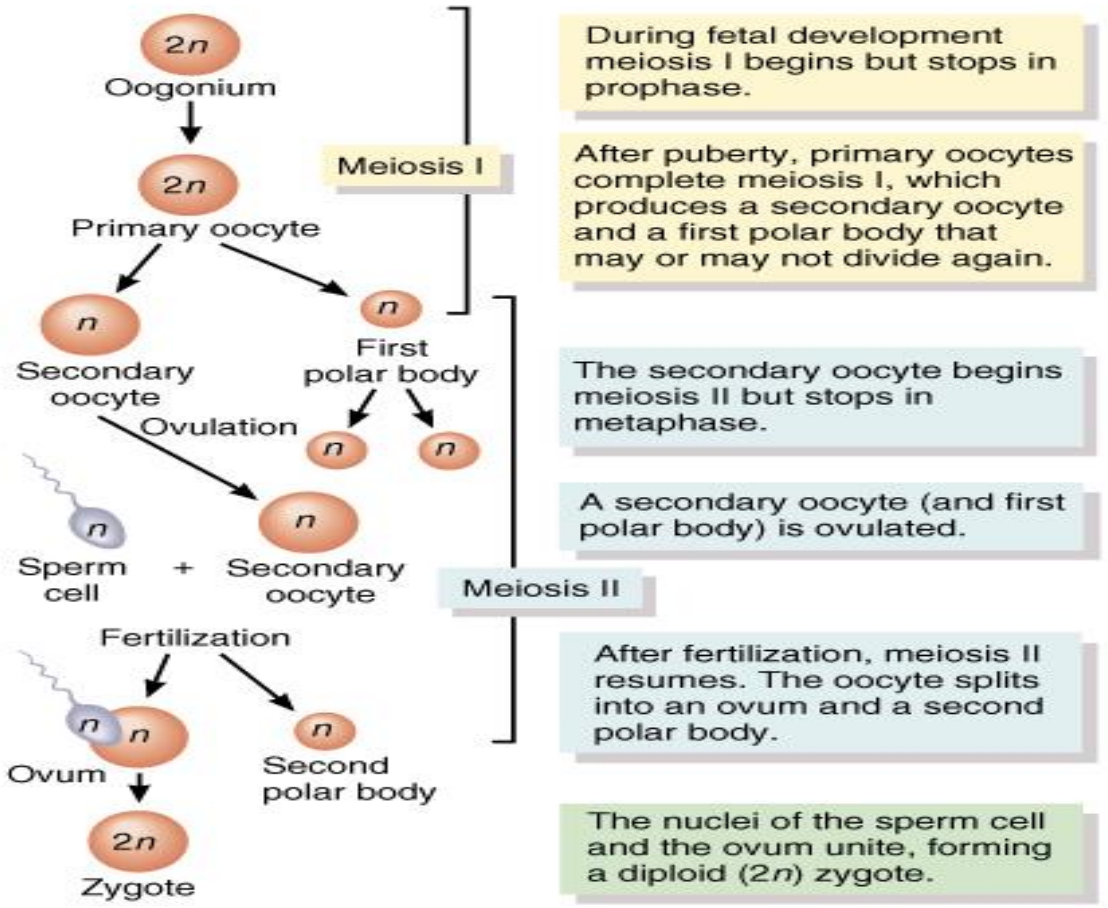
- Germ cells from yolk sac migrate to ovary and become potential egg cells called oögonia
- In fetus, millions of oögonia produced by mitosis but most of them degenerate (atresia)
- Some develop into immature egg cells called primary oöcytes during fetal development
  - 200,000 to 2 millions present at birth
  - 40,000 remain at puberty but only 400 mature during a woman's reproductive life
- Each month about 20 primary oöcytes become secondary oöcytes but usually only one survives to be ovulated from Graffian follicle

Egg forming cells (oöcytes) go through two divisions

1º = primary

2º = secondary

- Starts with a 2n=46 1ºoöcyte that divides, resulting in two n=23 cells, but one is a large 2º oöcyte and one is a small 1st polar body that may itself divide
- Second division only occurs if 2º oöcyte is fertilized. Results in one large n=23 ovum (egg) and one small n=23 2nd polar body
- Thus oögenesis results in one large fertilized egg (zygote) and possibly three small polar bodies

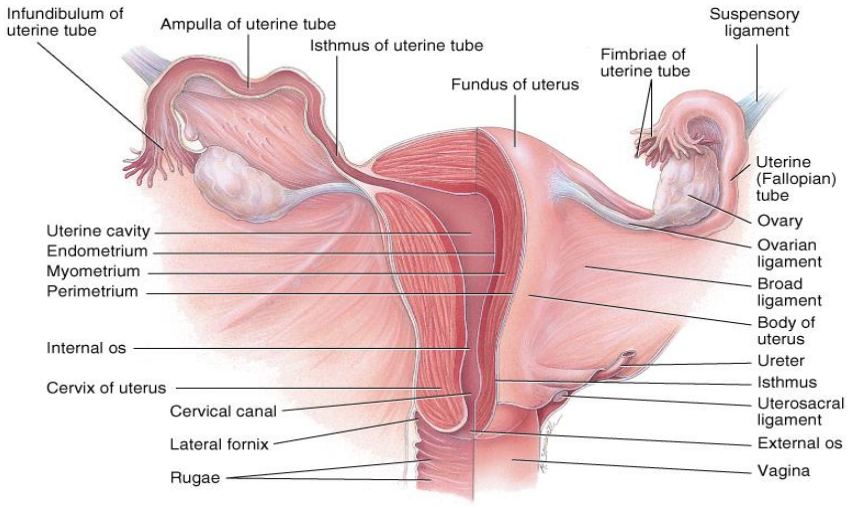


Uterine or Fallopian Tubes

- Narrow, 4 inch tube that extends from the ovary to uterus
  - Infundibulum is open, funnel-shaped portion near the ovary
  - Fimbriae are moving finger-like processes
  - Ampulla is central region of tube
  - Isthmus is narrowest portion joins uterus

  Functions -- events occurring in the uterine tube
  - fimbriae sweep oöcyte into tube
  - Cilia and peristalsis move it along
  - Sperm reaches oöcyte in ampulla
  - Fertilization occurs within 24 hours after ovulation
  - Zygote reaches uterus about 7 days after ovulation
- Site of menstruation
  & development of fetus
- Description
  - 3 inches long by 2 in.
    Wide and 1 in. Thick

- Subdivided into fundus, body & cervix
- Interiorly contains uterine cavity accessed by cervical canal

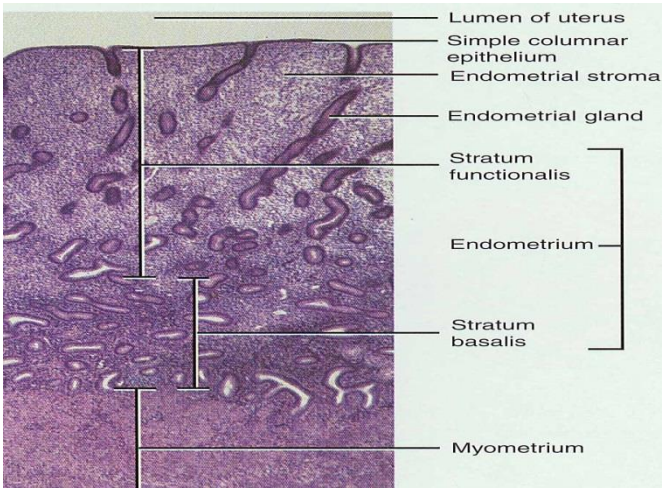


Histology of the Uterus

- Endometrium
  - Simple columnar epithelium
  - Stroma of connective tissue and endometrial glands
    - Functional layer
      - Shed during menstruation

Basal layer
Replaces functional layer each month

- Myometrium
  - 3 layers of smooth muscle
- Perimetrium
  - Visceral peritoneum



Mammary Glands

- Modified sweat glands that produce milk (lactation)
  - Amount of adipose tissue determines size of breast
  - Milk-secreting mammary glands alveoli open by lactiferous ducts at the nipple
  - Areola is pigmented area around nipple

- Suspensory (Cooper's) ligaments suspend breast from deep fascia of pectoral muscles

Physiology of the Breast

- Milk production and secretion
  - Estrogens develop the ducts system in the breasts
  - Progestrone develop the milk-secreting glands which are called alveoli
  - Prolactin stimulate milk synthesis in the alveoli
  - Oxytocin stimulate milk ejection from the alveoli
- Milk ejection (release from glands)
  - Nursing stimulates the hypothalamus to produce oxytocin
  - Oxytocin secreted from the posterior pituitary
  - Oxytocin causes smooth muscles around alveoli to contract and squeeze milk into lactiferous ducts, lactiferous sinuses and into the nipple
  - Operated by positive feedback

Female Reproductive Cycle

- Controlled by monthly hormonal cycle from the hypothalamus, anterior pituitary and ovary
- Monthly cycle of changes in ovary and uterus
- Ovarian cycle
  - Changes in ovary during and after maturation of the follicle and oocyte
- Uterine cycle (menstrual cycle)
  - Preparation of the uterus to receive fertilized ovum
  - If implantation does not occur, the functional layer of endometrium is shed during menstruation

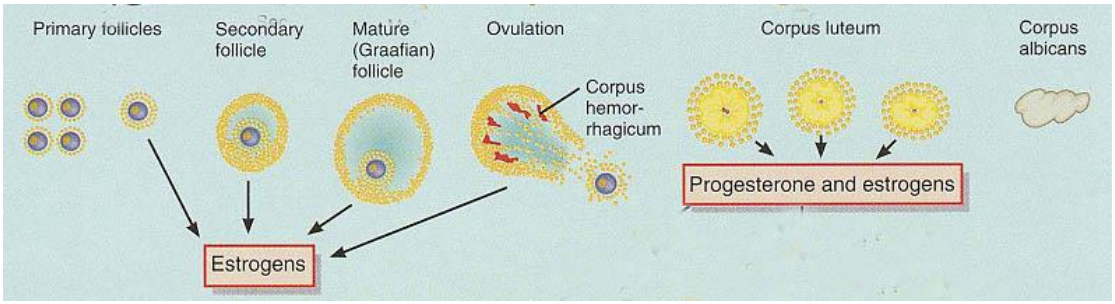
Hormonal Regulation of Reproductive Cycle

- Gonadotropin Releasing Hormone (GnRH), secreted by the hypothalamus, controls the female reproductive cycle
  - Stimulates anterior pituitary to secrete Follicle Stimulating Hormone (FSH) & Luteinizing Hormone (LH)
- FSH & LH target the ovaries and drive the ovarian cycle (monthly changes in the ovary)
- Estrogens and progesterone from the ovaries drive the uterine cycle (monthly changes in the uterus)

Phases of Ovarian Cycle

- Follicular Phase
  - FSH from anterior pituitary stimulates follicle growth
  - Follicles grow into Graafian (mature) follicle
  - Granulosa cells of follicle secrete estrogens and inhibin
  - Increasing levels of estrogens and inhibin inhibit FSH

- Increasing estrogens also stimulates secretion of LH
- Ovulation
  - LH stimulates rupture of the Graafian follicle and release of oöcyte from ovary into the pelvic cavity
  - Fimbriae of Fallopian tube picks up the ovulated oöcyte
- Luteal phase (postovulatory phase)
  - LH stimulates development of Corpus luteum from ovulated or ruptured follicle
  - Corpus luteum secretes mostly progesterone & some estrogens
  - Progesterone prepares endometrium for possible pregnancy

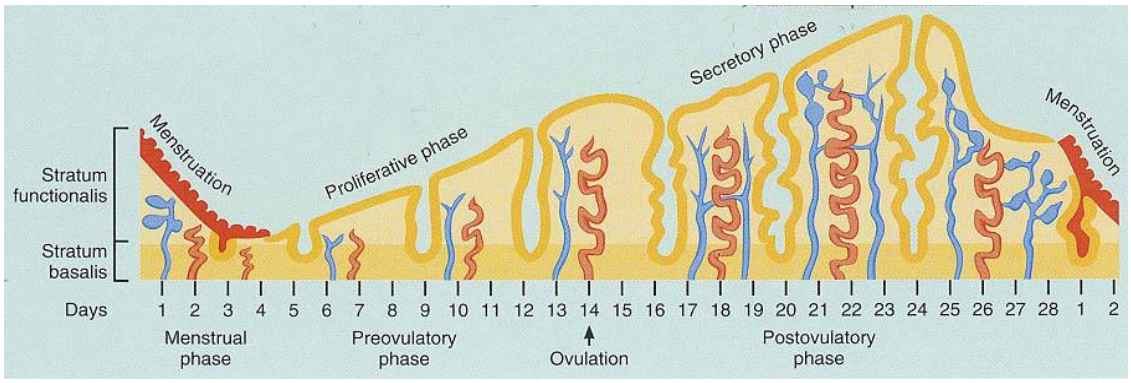


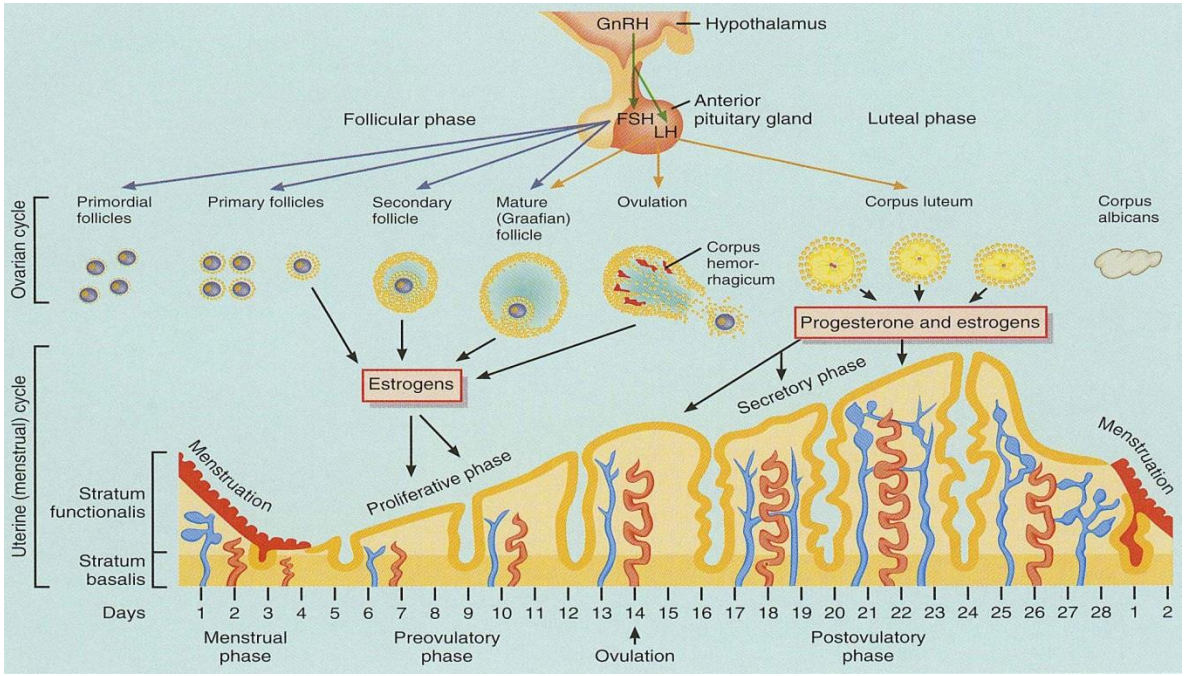
Follicular Phase Ovulation Luteal Phase

Phases of Uterine Cycle

- Proliferative phase
  - Rising estrogen levels from the growing follicle stimulates growth of the functional layer of endometrium to 4-10 mm thickness
- Secretory phase
  - Corpus luteum of ovary secretes progesterone
  - Progesterone stimulates
    - Increased thickening of the functional layer of endometrium to 12-18 mm
    - Increased blood supply into the endometrium
    - Growth of endometrial glands and secretion of uterine milk
- Menstruation phase (menses)
  - Decline in progesterone levels causes functional layer of endometrium to discharge resulting in vaginal bleeding called menstruation

Mark the beginning of the next cycle





Negative Feedback Controls Cycle

- If no pregnancy
  - Increasing levels of progesterone cause negative feedback that inhibits LH secretion
  - After about two weeks corpus luteum atrophies to corpus albicans (white body)
  - Progesterone and estrogen levels decline
  - Functional layer of endometrium discharged into first five days of next cycle
- Starting the next cycle

  - With the decline in progesterone, estrogens and inhibin secretion:-
    - Inhibition of GnRH, FSH and LH stops
    - Renewed secretion of these hormones starts a new cycle of growth and preparation in ovaries and uterus
- If fertilization occurs:-
  - Embryo implants in endometrium
  - Must maintain levels of progesterone to maintain the endometrium and pregnancy
  - Since corpus luteum secretes progesterone, it must be maintained
  - LH normally maintains the corpus luteum, but LH is inhibited by high progesterone levels
  - What maintains the corpus luteum during pregnancy?
- The outer part of blastocyst (the chorion) secretes the hormone human chorionic gonadotropin (hCG)
- hCG takes the place of LH and maintains the corpus luteum
- After about 3-4 months of pregnancy, corpus luteum degenerates
  - Placenta now produces its estrogen and progesterone and maintains endometrium

Respiratory system

Every cell in the body needs oxygen to survive. The respiratory system provides a way for oxygen (O_2) to enter the body. It also provides a way for carbon dioxide (Co_2), the waste product of cells, to leave the body.

The respiratory system is made up of 2 sections:

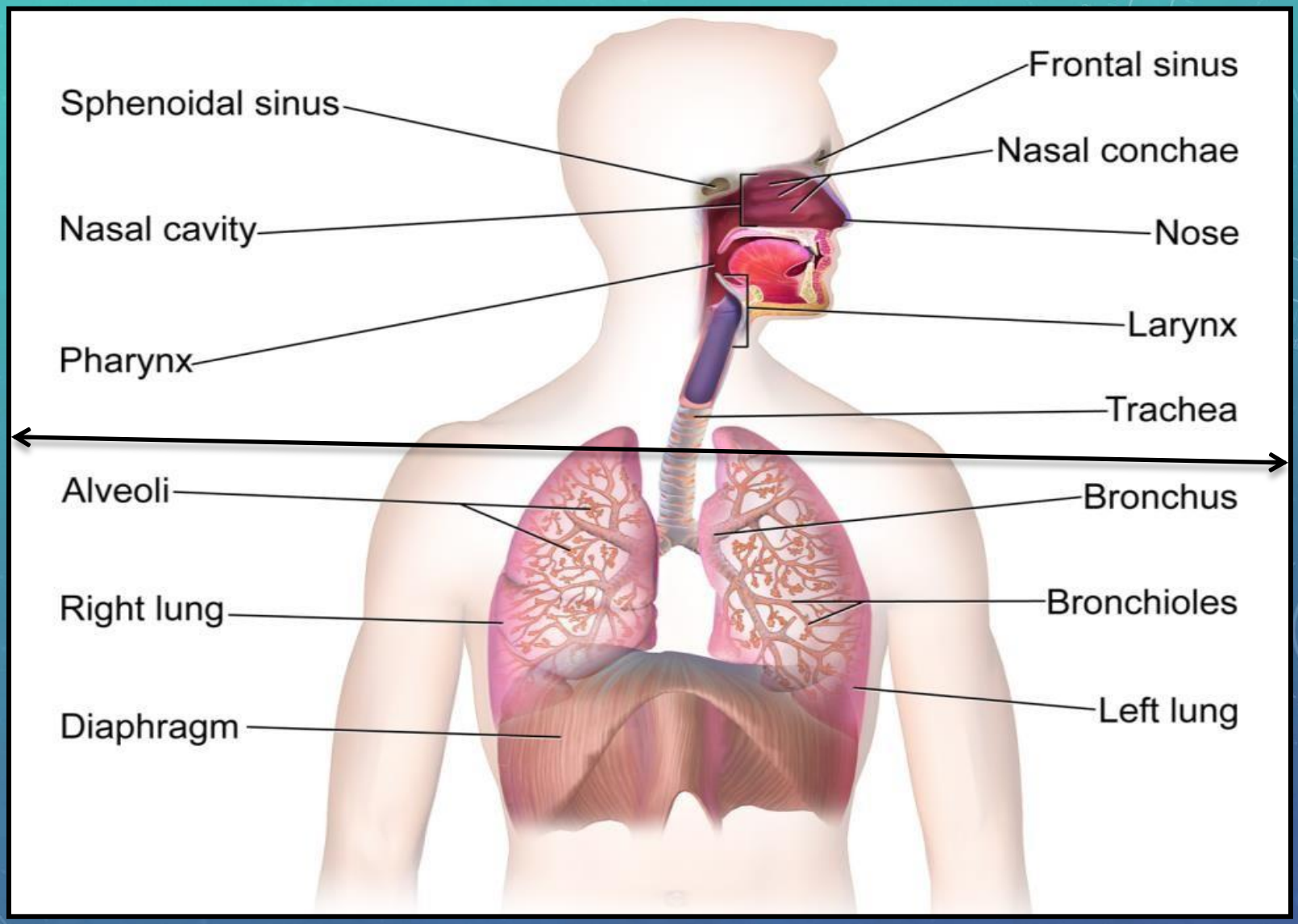
1) The upper respiratory tract
2) The lower respiratory tract

RESPIRATORY TRACT

Respiratory tract is the anatomical structure through which air moves in and out.

The organs of the *respiratory tract can* be divided **"STRUCTURALLY"** into 2 groups:

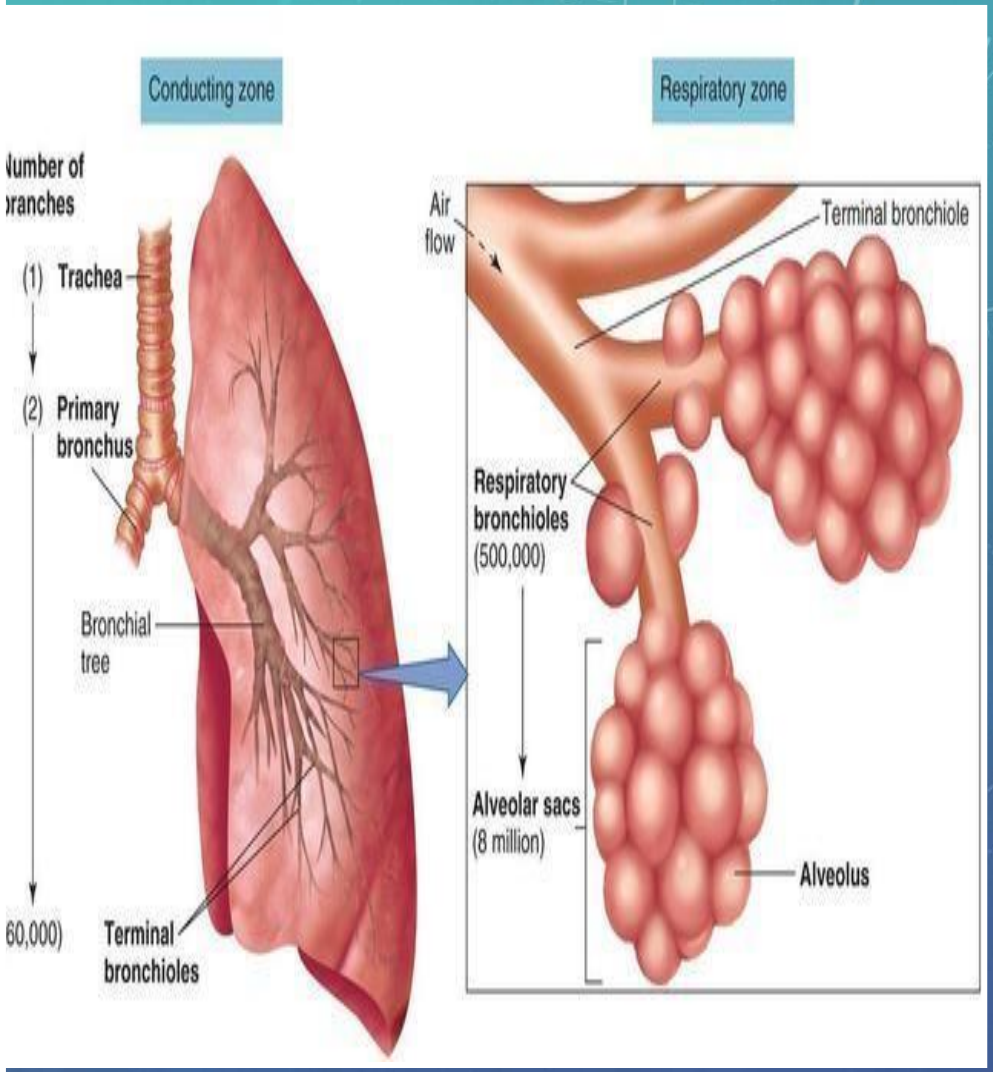
The Upper Respiratory Tract	The Lower Respiratory Tract
* Nose * Nasal cavity * Sinuses * Pharynx * Larynx	* Trachea * Bronchial Tree * Lungs


Sphenoidal sinus
Frontal sinus
Nasal conchae
Nasal cavity
Nose
Pharynx
Larynx
Trachea
Alveoli
Bronchus
Right lung
Bronchioles
Diaphragm
Left lung

The organs of the "Respiratory Tract" can be divided into two groups "FUNCTIONALLY"

The Conducting Portion	The Respiratory Portion
system of interconnecting cavities and tubes that conduct air into the lungs	system where the exchange of respiratory gases occurs
* Nose * Pharynx * Larynx * Trachea * Bronchi * Terminal Bronchioles	* Respiratory Bronchioles * Alveolar Ducts * Alveoli

	Name of branches	Number of tubes in branch
Conducting zone	Trachea	1
	Bronchi	2
		4
		8
	Bronchioles	16
		32
	Terminal bronchioles	6×10^4
Respiratory zone	Respiratory bronchioles	5×10^5
	Alveolar ducts	
	Alveolar sacs	8×10^6



Non respiratory functions of respiratory tract

Besides the primary function of gaseous exchange, the respiratory tract is involved in several non-respiratory functions of the body:

1. **Olfaction**
2. **Vocalization**
3. **Prevention of dust particles**

4. Defense mechanism

5. Maintenance of water balance
6. Regulation of body temperature
7. Regulation of acid- base balance
8. Anticoagulant function
9. Secretion of angiotensin converting enzyme

Respiration

Respiration is the movement of oxygen (O_2) from the outside environment to the cells within tissues, and the transport of carbon dioxide (Co_2) in the opposite direction. Or, it is the exchange of gases between the atmosphere, lungs, blood, and tissues; where the O_2 is taken in and Co_2 is given out.

Types of Respiration

Respiration is often classified into two types:

1. External respiration
2. Internal respiration

Stages of Respiration

- Respiration occurs in two stages:

1. ***Inspiration*** during the air enters the lungs from atmosphere
2. ***Expiration*** during the air leaves the lungs.

The term respiration includes 4 basic separate process:

1. **<u>Pulmonary ventilation</u>**="breathing"

   -Is the inhalation (inflow) & exhalation (outflow) of air.

   -***involve the exchange of air between the atmosphere and lungs alveoli (in and out).***

2. **<u>External respiration</u>**= within the lungs.

   -exchange of gases between lung's alveoli & blood in pulmonary capillaries which gains O_2 and loses Co_2.

3. **<u>Transport of respiratory gases</u>**=via the blood.

-O_2 and Co_2 transported to and from the lungs and tissue cells of the body via the bloodstream.

4. **<u>Internal respiration</u>**= within the tissues. (cellular respiration)

-O_2 utilization: Exchange of gases between blood in systemic capillary & tissue cells.

The lung

It is the main and primary organ of the respiratory system. The paired soft, spongy, cone-shaped lungs separated medially and are enclosed by the diaphragm and thoracic cage. Each lung is enclosed by a bilayered serous membrane called **pleura or pleural sac**, the **visceral (inner) layer** and the **parietal (outer) layer**. The narrow space in between the two layers of pleura is called **intrapleural space or pleural cavity**. Its space contains a thin film of pleural fluid which is involved in the creating the negative pressure called **intrapleural pressure** within **intrapleural space**.

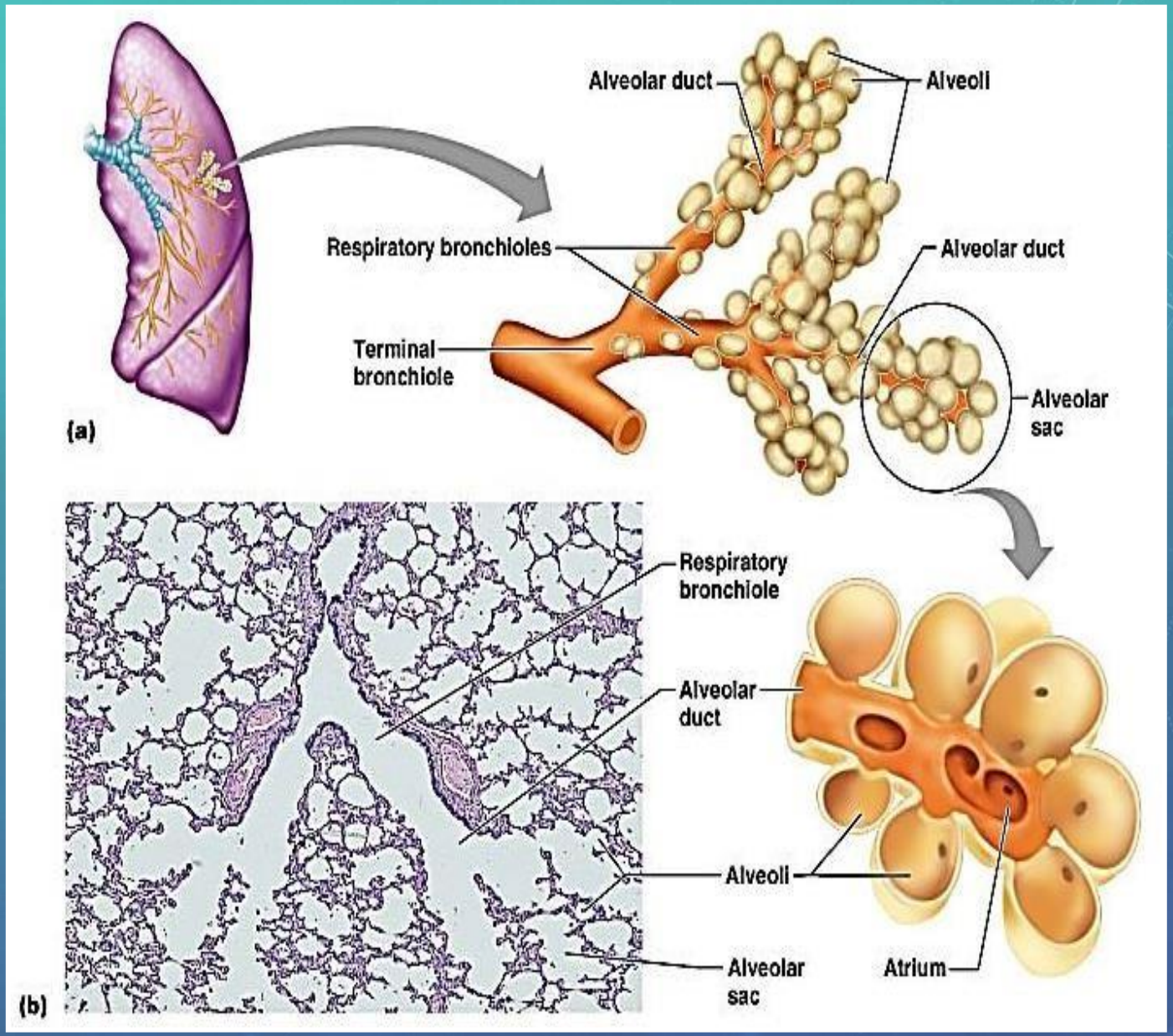
Tracheobronchial Tree

The trachea and bronchi are together called **tracheobronchial tree**. It forms a part of air passage.

The trachea bifurcates into two main or primary bronchi called right and left bronchi. Each **primary bronchus** enters the lungs and divides into **secondary bronchi**, these divided into **tertiary bronchi**. The tertiary bronchi divide several times and the latest called **terminal bronchiole**. Terminal bronchiole continues or divides into **respiratory bronchiole**.

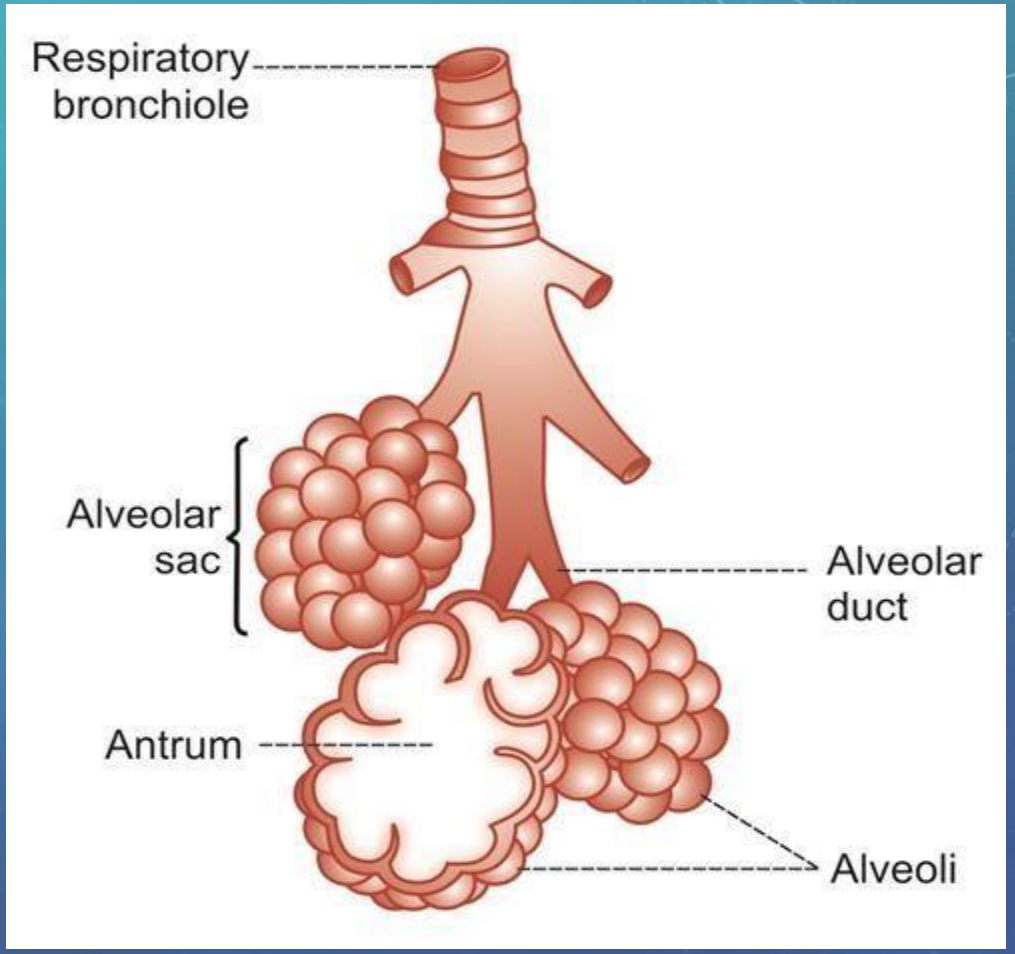
Respiratory unit

- Respiratory unit is defined as the structural and functional unit of lung. The exchange of gases occurs only in this part of the respiratory tract.
- The respiratory unit starts from the respiratory bronchioles. Each respiratory bronchiole divides into alveolar ducts. Each alveolar duct enters an enlarged structure called the alveolar sac. The space inside the alveolar sac is called antrum. Alveolar sac consists of a cluster of alveoli. Few alveoli are present in the wall of alveolar duct also.


Alveolar duct
Alveoli
Respiratory bronchioles
Alveolar duct
Terminal bronchiole
Alveolar sac
(a)
Respiratory bronchiole
Alveolar duct
Alveoli
Alveolar sac
Atrium
(b)

- **Thus, Respiratory unit includes:**

1. Respiratory bronchioles.
2. Alveolar ducts.
3. Alveolar sacs.
4. Antrum.
5. Alveoli.



Mechanics of Pulmonary Ventilation:

The lungs can be expanded and contracted in two ways:

1. By downward and upward movement of diaphragm to lengthen or shorten the chest cavity.
2. By elevation and depression of ribs to increase and decrease the anteroposterior diameter of chest cavity.

Inhalation (inspiration):

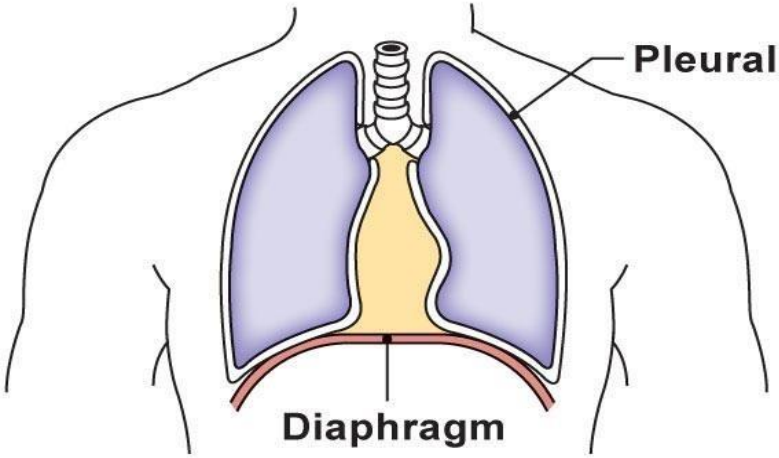
Stages involved during inhalation (active process) are:

1. External intercostal muscle contract and internal intercostal muscle relax, expanding rib cage (increased thoracic volume laterally).
2. Rib cage moves upward and forward.
3. Diaphragm contracts and flattens; increased thoracic volume vertically.
4. Intrapulmonary pressure decreases.
5. Air pushes in.

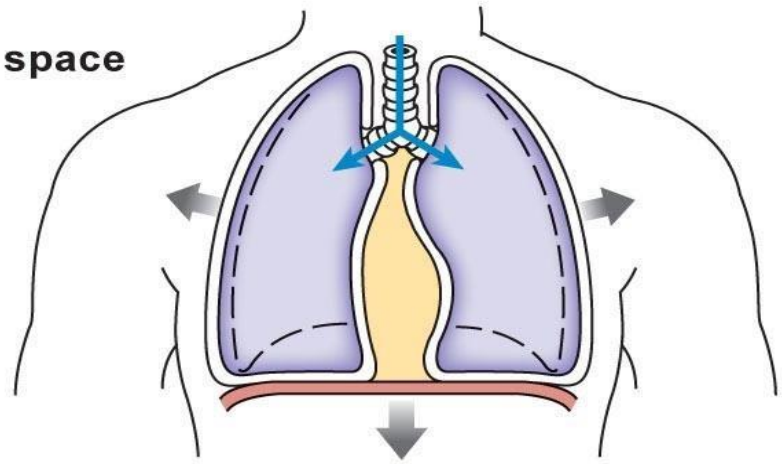
Exhalation (expiration):

Stages involved during exhalation (passive process) are:

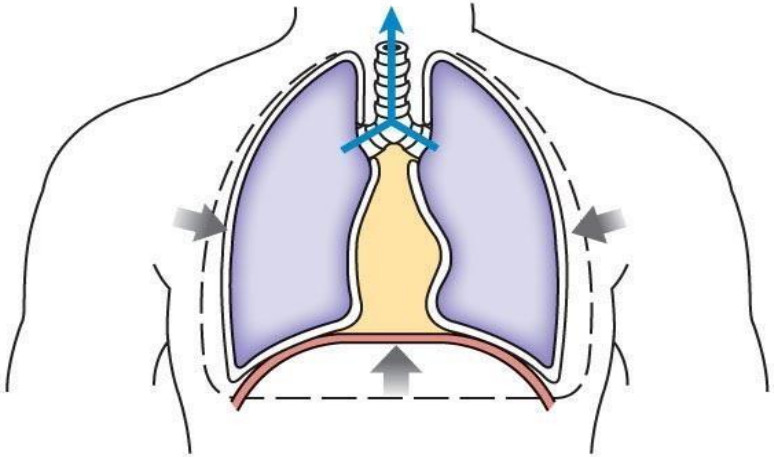
1. External intercostal muscles relax and internal intercostal muscle contract, reducing rib cage - (decreased thoracic volume laterally).
2. Rib cage moves downward and backward.
3. Diaphragm relaxes; decreased thoracic volume vertically.
4. Intrapulmonary pressure increases.
5. Air moves out



(a) At rest, diaphragm is relaxed.



(b) Diaphragm contracts, thoracic volume increases.



(c) Diaphragm relaxes, thoracic volume decreases.

Respiratory pressures

Two types of pressures are exerted in the thoracic cavity and the lungs during the process of respiration:

1. Intrapleural pressure or intrathoracic pressure.
2. Intra-alveolar pressure or intrapulmonary pressure.

Intrapleural pressure

It is the pressure existing in pleural cavity, that is, in between the visceral and parietal layers of pleura. It is exerted by the suction of the fluid that lines the pleural cavity. It is also called intrathoracic pressure since it is exerted in the whole of thoracic cavity. Intrapleural pressure is always negative.

- ***Importance of Intrapleural Pressure*:**
  1) Throughout the respiratory cycle intrapleural pressure remains lower than intra-alveolar pressure; this keeps the lungs always inflated.
  2) It prevents the collapsing tendency of lungs.
  3) It causes dilatation of vena cava and larger veins in thorax.

Intra-alveolar pressure

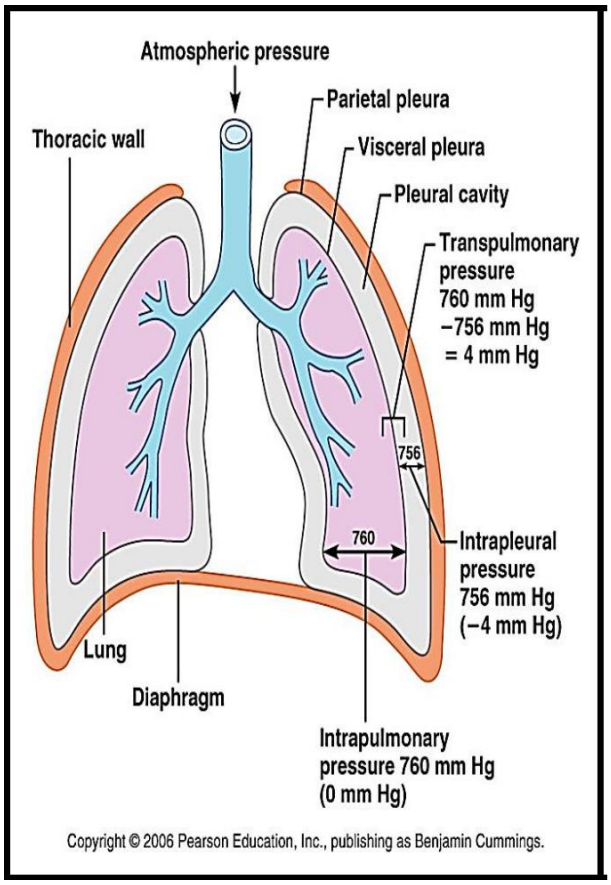
It is the pressure existing in the alveoli of the lungs. Normally, intra-alveolar pressure becomes negative during inspiration and positive during expiration.

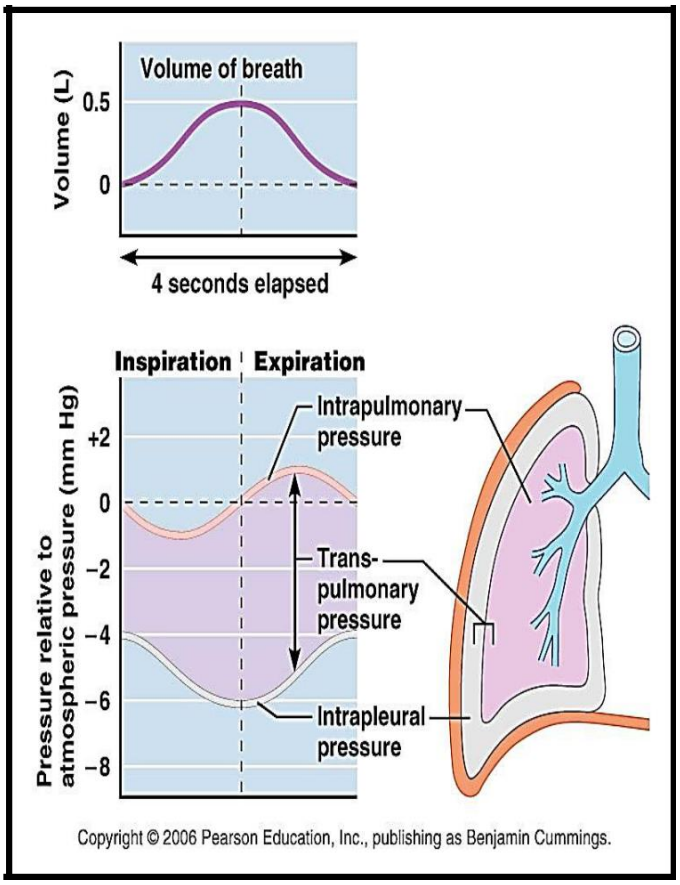
- ***Importance of Intra-alveolar Pressure***
  1) It causes flow of air in and out of alveoli. During inspiration, the intra-alveolar pressure becomes negative, so the atmospheric air enters the alveoli. And, during expiration, the air is expelled out of alveoli
  2) It also helps in the exchange of gases between the alveolar air and the blood.

1- Transpulmonary Pressure

It is the difference between intra-alveolar pressure and intrapleural pressure.

Changes in respiratory pressures during inspiration and expiration '0' indicate the normal atmospheric pressure (760 mm Hg).





Factors causing collapsing tendency of lungs

Two factors are responsible for the collapsing tendency of lungs

1. Elastic property of lung tissues which show constant recoiling tendency and try to collapse the lungs.
2. Surface tension exerted on the surface of the alveolar membrane by the fluid secreted from alveolar epithelium.

Fortunately, there are some factors which save the lungs from collapsing.

Factors preventing collapsing tendency of lungs

Two factors preventing collapsing tendency of lungs. In spite of the elastic property of the lungs and the surface tension in the alveoli of lungs, the collapsing tendency of lungs is prevented by two factors:

1. Intrapleural pressure which is always negative. Because of negativity, it keeps the lungs expanded and prevents the collapsing tendency of lungs produced by the elastic tissues.
2. Surfactant secreted in alveolar epithelium. It is surface acting materials that decrease surface tension on the alveolar membrane and prevents the collapsing tendency produced by surface tension.

Compliance

Compliance is the ability of the lungs and thorax to expand. It is defined as the change in volume per unit change in the respiratory pressure. Determination of compliance is useful as it is the measure of stiffness of lungs. Stiffer the lungs, less is the compliance.

If lungs are removed from thorax, the expansibility (compliance) of lungs alone is doubled. It is because of the absence of the inactivity and the restriction exerted by the structures of thoracic cage, which interfere with expansion of lungs.

Variation in Compliance

Compliance decreases in pathological conditions such as:

1. Deformities of thorax.
2. Paralysis of respiratory muscles.
3. Pleural effusion.
4. Fibrosis
5. Abnormal thorax.

Compliance increases in physiological and pathological conditions.

1. In old age, lung compliance increases due to loss of elastic property of lung tissues.
2. In emphysema, lung compliance increases because of damage of alveolar membrane.

The work of breathing

It is the work done by the respiratory muscles during breathing to overcome the resistance in the thorax and respiratory tract.

During the respiratory processes, inspiration is active process and the expiration is a passive process. So, during quiet breathing, the respiratory muscles perform the work only during inspiration and not during expiration.

During normal quiet breathing, all respiratory muscle contraction occurs during inspiration; expiration is almost entirely a passive process caused by elastic recoil of the lungs and chest cage. Thus, under resting conditions, the respiratory muscles normally perform "work" to cause inspiration but not to cause expiration.

The resistance and work of breathing

The energy obtained during the work of breathing is utilized to overcome three types of resistance:

1. **Airway resistance (airway resistance work)**

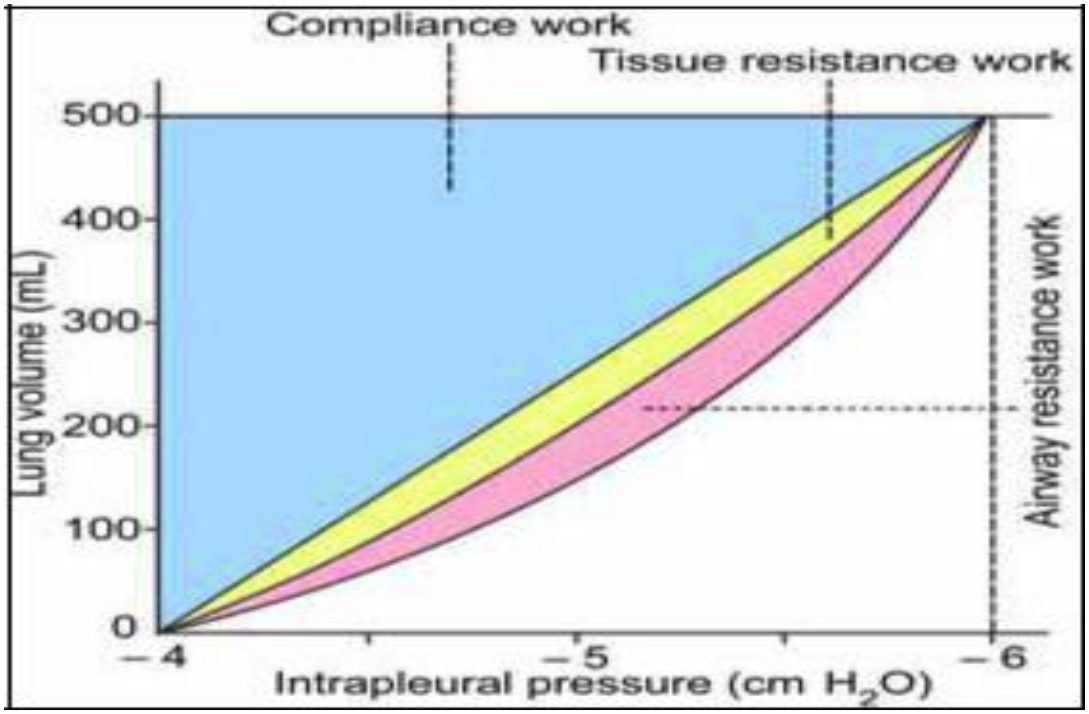
   Airway resistance is the resistance offered to the passage of air through respiratory tract. Resistance increases during bronchiolar constriction, which increases the work done by the muscles during breathing. Work done to overcome the airway resistance is called airway resistance work.

2. **Elastic resistance of lungs and thorax (compliance work).**

   Energy is required to expand lungs and thorax against the elastic force. Work done to overcome this elastic resistance is called compliance work.

3. **Non-elastic viscous resistance (tissue resistance work).**

   Energy is also required to overcome the viscosity of lung tissues and tissues of thoracic cage. Work done to overcome this viscous resistance is called tissue resistance work.



Work of breathing

Dead space

Dead space is defined as the part of the respiratory tract, where gaseous exchange does not take place. The air present in the dead space is called dead space air.

Dead space is of two types:

I. Anatomical dead space.

II. Physiological dead space.

Physiological Dead Space

Physiological dead space includes anatomical dead space plus two additional volumes:

1. The air in the alveoli, which are nonfunctioning. In some of the respiratory diseases, alveoli do not function because of dysfunction or destruction of alveolar membrane
2. The air in the alveoli, which do not receive adequate blood flow. Gaseous exchange does not take place during inadequate blood supply.

Normal value and measurement of dead space

Under normal conditions, the physiological dead space is equal to anatomical dead space. It is because, all the alveoli are functioning and all alveoli receive adequate blood flow in normal conditions. *The volume of normal dead space is 150 ml.*

In respiratory disorders, which affect the pulmonary blood flow or the alveoli, the dead space increases. It is associated with reduction in alveolar ventilation. *The dead space is measured by single breath nitrogen washout method.*

Respiratory Protective Reflexes

Respiratory protective reflexes are the reflexes that protect the lungs and air passage from foreign particles. The respiratory protective reflexes are:

1- Cough Reflex

Cough is a modified respiratory process characterized by forced expiration. It is the protective reflex that occurs because of irritation of respiratory tract and some other areas such as external auditory canal. Cough begins with deep inspiration followed by forced expiration with closed glottis. This increases the intrapleural pressure above 100 mm Hg. Then, glottis opens suddenly with explosive outflow of air.

2- Sneezing Reflex

Sneezing is also a modified respiratory process characterized by forced expiration. It is the protective reflex caused by irritation of nasal mucous membrane. This irritation occurs because of dust particles, debris, mechanical obstruction of the airway, and excess fluid accumulation in the nasal passages. Sneezing starts with deep inspiration, followed by forceful expiratory effort with opened glottis resulting in exclusion of irritant agents out of respiratory tract.

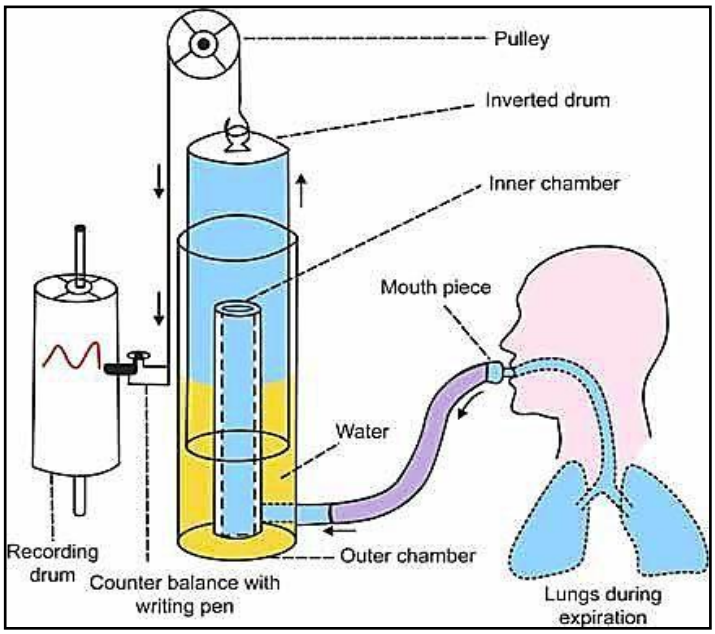
3- Swallowing Reflex (Deglutition)

Swallowing is a respiratory protective reflex that prevents entrance of food particles into the air passage during swallowing. While swallowing of the food, the respiration is arrested for a while. The temporary arrest of respiration is called apnea. The arrest of breathing during swallowing is called swallowing apnea or deglutition apnea.

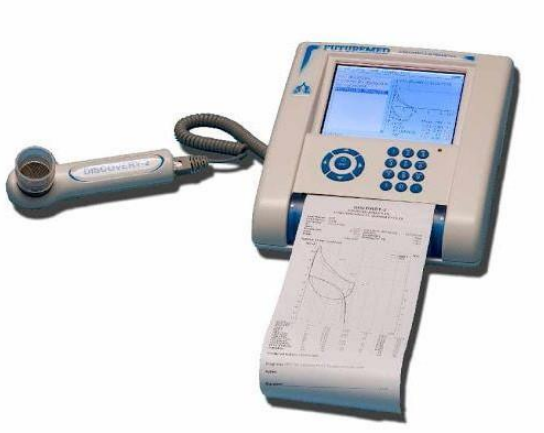
Lung volumes and capacities

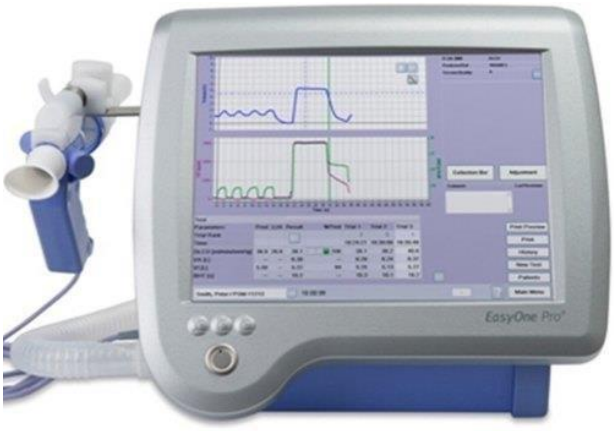
Pulmonary function tests

Pulmonary or lung function tests are useful in assessing the functional status of the respiratory system. These tests involve measurement of lung volumes and capacities. Pulmonary ventilation can be studied by recording the volume movement of air into and out of the lungs, a method called ***spirometry***. Pulmonary function tests are carried out mostly by using spirometer. The graphical recording of lung volumes and capacities is called ***spirogram***.



Spirometer: During expiration, the air enters the spirometer from lungs. The inverted drum moves up and the pen draws a downward curve on the recording drum.





The air in lung is classified into two divisions:

1. Lung volumes. 2. Lung capacities.

Lung volume

Lung volumes are the static volumes of air breathed by an individual. The lung volumes are of four types:

1. **Tidal volume (TV)**

   Tidal volume is the volume of air breathed in and out of lungs in a single normal quiet respiration. Tidal volume signifies the normal depth of breathing.

   Normal value = 500 mL (0.5 L).

2. **Inspiratory reserve volume (IRV)**

   Inspiratory reserve volume is an additional volume of air that can be inspired forcefully after the end of normal inspiration.

   Normal value = 3300 mL (3.3 L).

3. **Expiratory reserve volume (ERV)**

   Expiratory reserve volume is the additional volume of air that can be expired out forcefully, after normal expiration.

   Normal value = 1000 mL (1 L).

4. **Residual volume (RV)**

   Residual volume is the volume of air remaining in the lungs even after forced expiration. Normally, lungs cannot be emptied completely even by forceful expiration. Some quantity of air always remains in the lungs even after the forced expiration. Normal value = 1200 mL (1.2 L).

Lung capacity

Lung capacities are the combination of two or more lung volumes. Lung capacities are of four types:

1. Inspiratory capacity (IC)

Inspiratory capacity is the maximum volume of air that is inspired after normal expiration. It includes tidal volume and inspiratory reserve volume.

IC = TV + IRV = 500 + 3300 = 3800 mL.

2. Vital capacity (VC)

It is the maximum volume of air that can be expelled out forcefully after a deep (maximal) inspiration. Vital capacity includes tidal volume, inspiratory reserve volume and expiratory reserve volume.

VC = TV + IRV + ERV = 500 + 3300 + 1000 = 4800 mL.

3. Functional residual capacity (FRC)

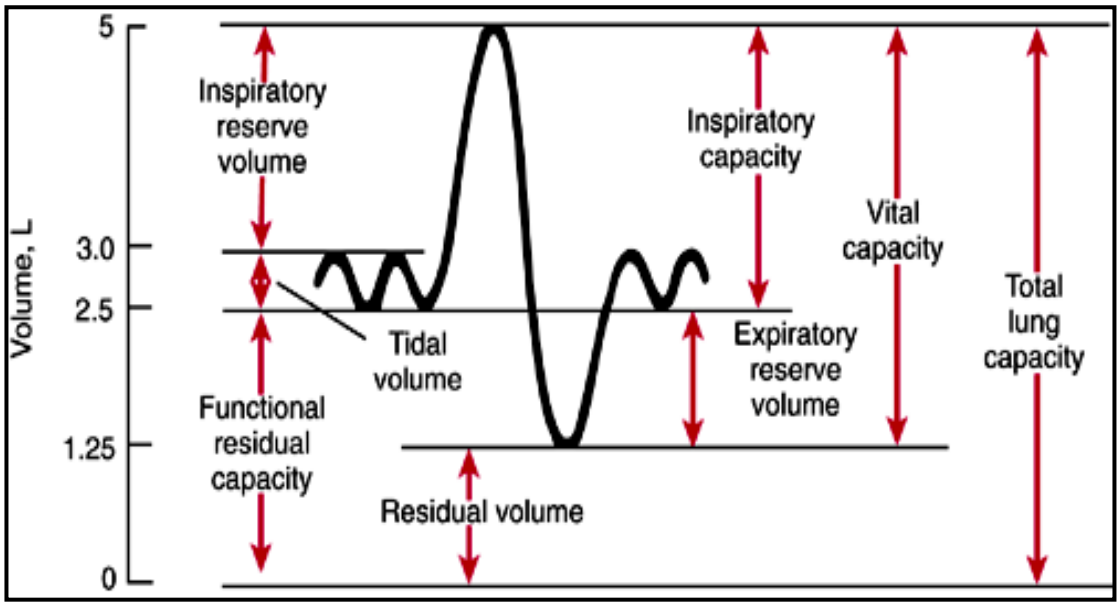
It is the volume of air remaining in the lungs after normal expiration (after normal tidal expiration). Functional residual capacity includes expiratory reserve volume and residual volume.

FRC = ERV + RV = 1000 + 1200 = 2200 mL.

4. Total lung capacity (TLC)

Total lung capacity is the volume of air present in the lungs after a deep (maximal) inspiration. It includes all the volumes.

TLC = IRV + TV + ERV + RV = 3300 + 500 + 1000 + 1200 = 6000 mL.



Respiratory volume and capacity

Ventilation

Pulmonary ventilation

It is the volume of air moving in and out of lungs per minute in quiet breathing. It is also called *respiratory minute volume (RMV).*

Normal value and calculation

Normal value of pulmonary ventilation is 6 L/minute. It is the product of tidal volume (TV) and the rate of respiration (RR). It is calculated by the formula:

Pulmonary ventilation = Tidal volume × Respiratory rate

= 500 mL × 12/minute

= 6,000 mL = 6 L/minute.

Factors affecting pulmonary ventilation:

1. Surface tension of alveolar fluid (Surfactant)
2. Lung compliance:
    a. Elasticity.
    b. Surface tension
3. Airway resistance.

Alveolar ventilation

Alveolar ventilation is the amount of air utilized for gaseous exchange every minute.

Alveolar ventilation is different from pulmonary ventilation. In pulmonary ventilation, six (6) L of air moves in and out of lungs in every minute. But the whole volume of air is not utilized for exchange of gases. *The volume of air subjected for exchange of gases is the alveolar ventilation*. The air trapped in the respiratory passage (dead space) does not take part in gaseous exchange. Normal value of alveolar ventilation is 4,200 mL (4.2 L)/ minute.

Regulation of Respiration

Respiration is a reflex process. But it can be controlled voluntarily also. Voluntary arrest of respiration (voluntary apnea) is possible only for a short period of about 40 seconds. However, by practice, breathing can be withheld for a long period. At the end of that period, the person is forced to breathe. Though, normally, the quiet regular breathing takes place because of regulatory mechanisms.

Respiration is regulated by two mechanisms:

A. ***Nervous or neural mechanism:*** Nervous mechanism that regulates respiration includes respiratory centers, afferent nerves and efferent nerves. The nervous system normally adjusts the rate of alveolar ventilation almost exactly to the demands of the body, even during heavy exercise and most other types of respiratory stress.

Respiratory center

Respiratory centers are group of neurons, which control the rate, rhythm and force of respiration. These centers are bilaterally situated in reticular formation of brainstem, receive afferent impulses from different parts of the body and, modulate the movements of thoracic cage and lungs accordingly through efferent nerve fibers.

The respiratory center is composed of several groups of neurons. It is divided into three major collections of neurons:

1. **A dorsal respiratory group**, located in the dorsal portion of the medulla, which mainly causes inspiration. Its control inspiration and respiratory rhythm
2. **A ventral respiratory group,** located in the ventrolateral part of the medulla, which mainly causes expiration. Functions in both inspiration and expiration. The function of this neuronal group differs from that of the dorsal respiratory group in several important ways.
3. **The pneumotaxic center**, located dorsally in the superior portion of the pons, which mainly controls rate and depth of breathing. The function of this center is primarily to limit inspiration. This has a secondary effect of increasing the rate of breathing because limitation of inspiration also shortens expiration and the entire period of each respiration.

B. Chemical mechanism:

The chemical mechanism of respiratory regulation is operated through the chemoreceptors which give response to chemical changes in blood such as:

1. Hypoxia {decreased partial pressure of O_2 in blood (PO_2)}
2. Hypercapnea {increased partial pressure of CO_2 in blood (PCO_2)}
3. Increased hydrogen ion concentration.

Types of Chemoreceptors

Chemoreceptors are classified into two groups:

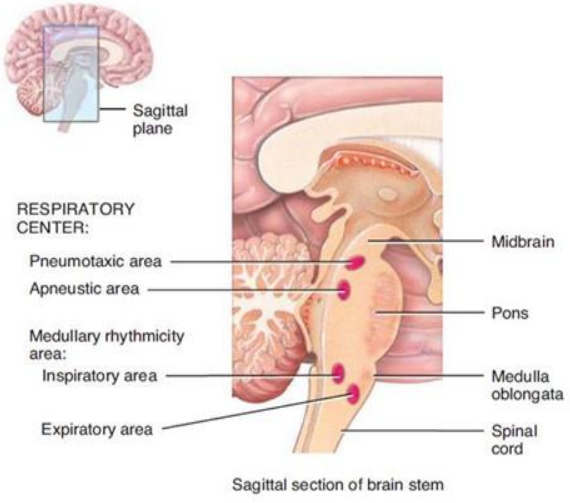
1. **Central chemoreceptors:** The chemoreceptors are present in the brain, situated in medulla oblongata, close to dorsal respiratory group of neurons. The main stimulant for the central chemoreceptors is the increased hydrogen ion concentration.

If hydrogen ion concentration increases in the blood, it cannot stimulate the central chemoreceptors because, the hydrogen ions from blood cannot cross the blood-brain barrier and blood cerebrospinal fluid barrier.

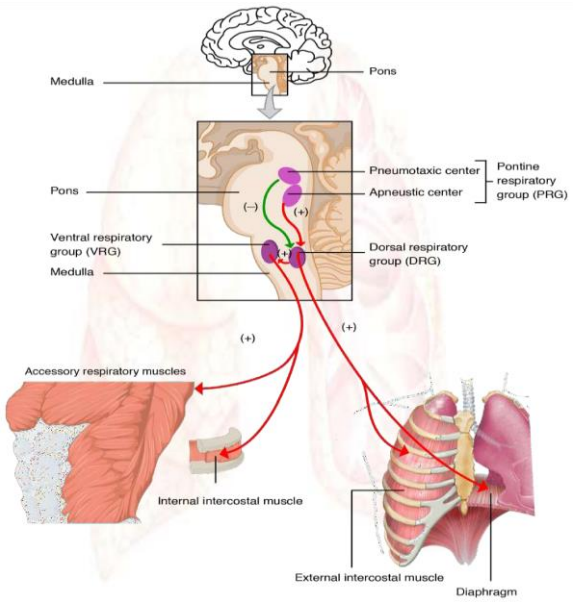
On the other hand, if carbon dioxide increases in the blood, it can easily cross the blood-brain barrier and blood cerebrospinal fluid barrier and enter the interstitial fluid of brain or the cerebrospinal fluid. There, the carbon dioxide combines with water to form carbonic acid. Since carbonic acid is unstable, it immediately dissociates into hydrogen ion and bicarbonate ion.

The hydrogen ions stimulate the central chemoreceptors. Chemoreceptors in turn send stimulatory impulses to dorsal respiratory group of neurons causing increased ventilation (increased rate and force of breathing). Because of this, the excess carbon dioxide is washed out and the respiration is brought back to normal.

2. **Peripheral chemoreceptors:** Chemoreceptors present in the carotid and aortic region of brain are called peripheral chemoreceptors. Reduction in PO_2 is the most potent stimulant for the peripheral chemoreceptors; but these receptors are mildly sensitive to the increased PCO_2 and increased hydrogen ion concentration.



Sagittal section of brain stem



Oxygen Transport

Oxygen does not dissolve easily in water, so only about 1.5% of inhaled O2 is dissolved in blood plasma, which is mostly water. About 98.5% of blood O2 is bound to hemoglobin in red blood Cells. Each 100 mL of oxygenated blood contains the equivalent of 20 mL of gaseous O2.

The heme portion of hemoglobin contains four atoms of iron, each capable of binding to a molecule of O2. The 98.5% of the O2 that is bound to hemoglobin. Oxygen and hemoglobin bind in an easily reversible reaction to form oxyhemoglobin. O2 +Hgb = 4HgbO2

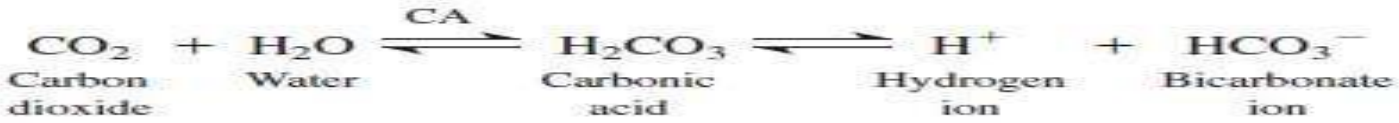
As blood flows through tissue capillaries, the iron–oxygen reaction reverses. Hemoglobin releases oxygen, which diffuses first into the interstitial fluid and then into cells

Factors Affecting the Affinity of Hemoglobin for Oxygen

Although PO2 is the most important factor that determines the percent O2 saturation of hemoglobin. The following four factors affect the affinity of hemoglobin for O2 :

1. Acidity pH: As acidity increases (pH decreases), the affinity of hemoglobin for O_2 decreases ,and O_2dissociates more readily from hemoglobin.When ions bind to aminoacids in Hemoglobin, they alter its structure slightly, decreasing its oxygen-carrying capacity. Thus, lowered pH drives O2 off hemoglobin, making more O2 available for tissue cells.

2. Partial pressure of carbon dioxide: CO2 enters the blood it is temporarily converted to carbonic acid H2CO3 It dissociates and form hydrogen ions and bicarbonate ions. So in red blood cells the H+ concentration increases, pH decreases. Thus, an increased



3. Temperature: Heat is a by-product of the metabolic reactions of all cells, and the heat released by contracting muscle fibers tends to raise body temperature. Metabolically active cells require more O2 and liberate more acids and heat.
4. **2,3-bisphosphoglycerate (BPG):** BPG is formed in red blood cells when they break down glucose to produce ATP in a process called glycolysis. When BPG combines with hemoglobin, it unloads or decreases the bonding with oxygen.

CO2 Transportation

Normal resting conditions, each 100 mL of deoxygenated blood contains the equivalent of 53 mL of gaseous CO2, which is transported in the blood in three main forms

a. Dissolved CO2. The smallest percentage— about 7%—is dissolved in blood plasma. On reaching the lungs, it diffuses into alveolar air and is exhaled.

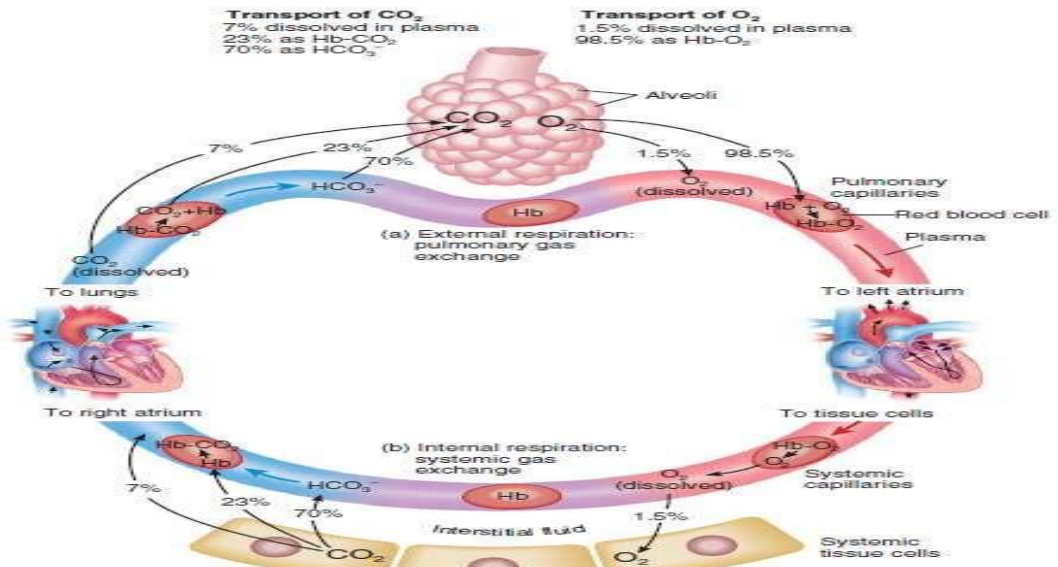
b. Carbamino compounds:- About 23% of CO2, combines with the amino groups of amino acids and proteins in blood to form carbamino compounds. The main CO2 binding sites are the terminal amino acids in the two alpha and two beta globin chains. Hemoglobin that has bound CO2 is termed carbaminohemoglobin (Hb—CO2):

$$\underset{\text{Hemoglobin}}{Hb} + \underset{\text{Carbon dioxide}}{CO_2} \rightleftharpoons \underset{\text{Carbaminohemoglobin}}{Hb{-}CO_2}$$

c. Bicarbonate ions. The greatest percentage of CO2 about 70%—is transported in blood plasma as bicarbonate ions HCO3

CO2 diffuses into systemic capillaries and enters red blood cells, it reacts with water in the presence of the enzyme carbonic anhydrase CA to form carbonic acid, which dissociates into H+ and HCO3-

$$\underset{\text{Carbon dioxide}}{CO_2} + \underset{\text{Water}}{H_2O} \xrightleftharpoons{CA} \underset{\text{Carbonic acid}}{H_2CO_3} \rightleftharpoons \underset{\text{Hydrogen ion}}{H^+} + \underset{\text{Bicarbonate ion}}{HCO_3^-}$$



The relationship between oral health and respiratory disease

- The relationship between oral health and systemic conditions, including the association between poor oral hygiene, periodontal disease, and respiratory disease, has been increasingly debated over recent decades. Oral bacteria and, especially, periodontal pathogens have been implicated as important agents with regard to causing other illnesses including respiratory diseases

- Four possible mechanisms to explain the biological plausibility of an association between oral conditions and nosocomial respiratory infections have been described:

1. Oral pathogens directly aspirated into the lungs.

The most common respiratory pathogens are found within the dental plaque inside the oral cavity. These bacteria, once established in the mouth, can be aspirated into the lungs and cause infection.

2. Salivary enzymes associated with periodontal disease modify respiratory tract mucosal surfaces and promote adhesion and colonization by respiratory pathogens, with consequent aspiration into the lungs thereby causing infection.

3. Hydrolytic enzymes from periodontopathic bacteria may destroy the salivary film that protects against pathogenic bacteria. This may reduce the ability of mucins to adhere to pathogens, thus leaving them free to adhere to mucosal receptors in the respiratory tract.

4. The presence of a large variety of cytokines and other biologically active molecules continually released from periodontal tissues and peripheral mononuclear cells, in case of untreated periodontitis, may alter the respiratory epithelium and promote colonization by respiratory pathogens, thereby resulting in infection.

Respiratory System Terminologies

- **Apnea :**temporary cessation of breathing
- **Tachypnea :**abnormally rapid respirations
- **Bradypnea** :abnormally slow respiration
- **Dyspnea :**labored breathing or shortness of breath
- **Hypoxemia :**decrease in arterial oxygen tension in

the blood

- **Hypoxia :**decrease in oxygen supply to the tissues and cells
- **Hypercapnia:** an increase in the partial pressure of carbon dioxide in the blood.
- **Hypocapnia :**a decreased amount of carbon dioxide in the blood.
- **Physiologic dead space :**portion of the tracheobronchial tree that does not participate in gas exchange.
- **Central cyanosis :**bluish discoloration of the skin or mucous membranes due to hemoglobin carrying reduced amounts of oxygen.
- **Intrapleural (intrathoracic (pressure :**pressure between the two pleural layers in the pleural cavity.

Assist. prof. Dr. Takea Sh Ahmed Lec. 1
Collage of dentistry - 2nd class
Tikrit university
Suggested books and resources:
Medical Physiology 12th edition (Guyton and Hall)
Essential of physiology for dental students (K Sembulingam &prema sembulingam

General Physiology

Physiology: The science that is concerned with the function of the living organism and its component parts, includes all its chemical and physical processes.

The goal of physiology is to explain the physical and chemical factors that are responsible for the origin development and progression of life.

In human physiology we attempt to explain the specific characteristics and mechanisms of the human body that make it living being.

Basic properties of life

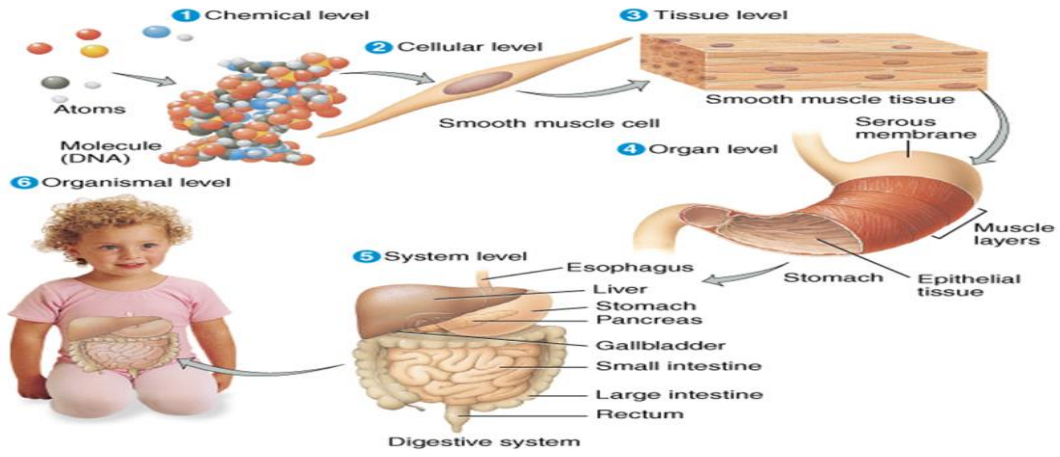
The seven properties of life: 1) Cellular organization, 2) Reproduction, 3) Metabolism, 4) Homeostasis, 5) Heredity, 6) Responsiveness, 7) Growth and development.

Function organization of the human body

The basic living unit of the body is the cell. All cells use oxygen as one of the major substances from which energy is divided; the oxygen combines with carbohydrates, fat or protein to release the energy required for cell function.

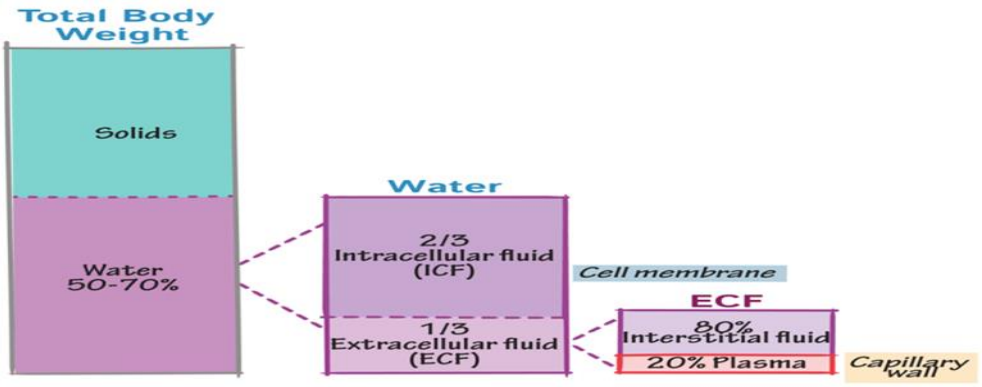
Levels of Organization

Atoms → molecules → macromolecules → organelles → cells → tissues→ organs → organ systems



Body fluids: About 60% of the adult human body is fluid, most of this fluid is inside the cells and is called intracellular fluid, about one-third of it is in the spaces outside the cells and is called extracellular fluid. This E.C.F is in constant motion throughout the body. It is rapidly mixed by the blood and the tissue fluids, and E.C.F are the ions and nutrients needed by the cells for maintenance of cellular function. Therefore all cells live in essentially the

same environment, that is the E.C.F, and for this reason is often called the internal environment of the body.



Although there is a constant change between E.C.F. and I.C.F., but there is a significant difference between the constituents of the two fluids.

The E.C.F. contains large amounts of sodium, chloride and bicarbonate ions, plus nutrients for cells, such as oxygen, glucose, fatty acids and amino acids …etc.

The I.C.F. differs significantly from the E.C.F. particularly, it contains large amount of potassium, magnesium and phosphate ions instead of the sodium and chloride found in E.C.F.

No		ICF	ECF
1	volume	40% 2:	20% 1
2	Chief kation	Potasium K^{+} Po4- Pln	Sodium Na^{++} Cl^{-} $HCO3^{-}$
3	PH	More acidic	Less acidic
4	Osmotic conc.	290mosm	290mosm

Homeostasis:

The term of homeostasis mean maintenance of state or constant conditions in the internal environment. Essentially all of the organs and tissues of the body perform functions. That helps to maintain constant conditions.

The process of homeostasis can be understood through the followings:

1. The E.C.F. is transported through all parts of the body in two different stages. The first entails movement of blood around the circulatory system & the second , movement of fluid between the blood capillaries and the cells. All the blood in the circulation transverses the entire of the circulation in an average once each minute when the body is at rest and as six times during activity. In general , no cell is located more than 25- 50 micrometers from a capillary.

2. Origin of nutrients in the E.C.F. :
   a. Respiratory system: the blood passes through the body and also flows through the lungs. The blood picks up oxygen in the alveoli, thus acquiring the oxygen needed by the cells.

   The membrane between the alveoli and the lumen of the pulmonary capillaries is only 0.4-2.0 micrometers in thickness.

   b. Gastrointestinal track: here, different dissolved nutrients including carbohydrates, fatty acids, amino acids and others are absorbed into the E.C.F.

      The liver changes the chemical composition of many of these to more usable forms.

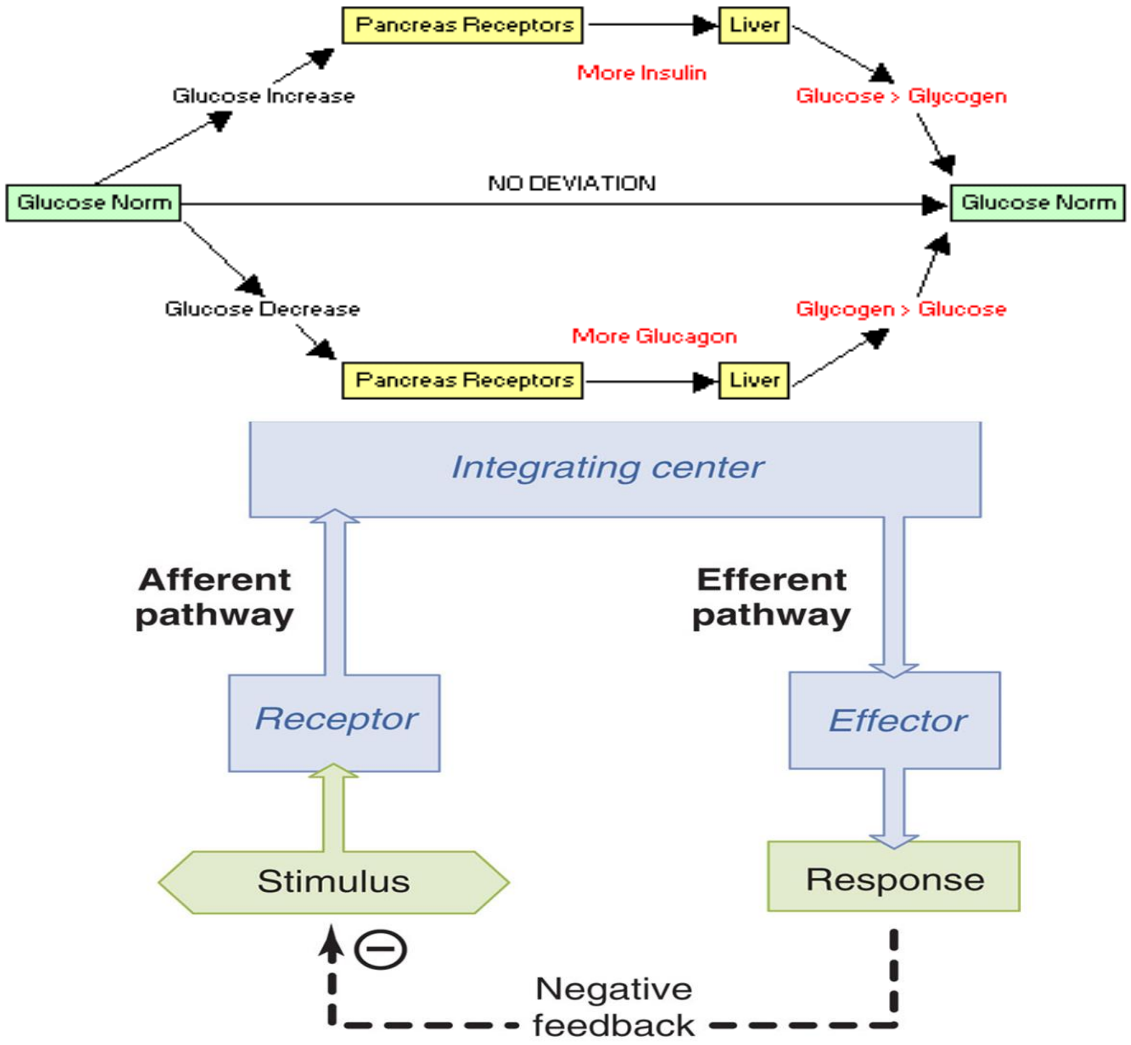
   c. The muscloskeletal provides motility and energy.

3. Removal of metabolic end products:
   a. Removal of carbon dioxide by the lungs.
   b. Kidney, regulation of blood fluid and excretion of excess substances.

4. Regulation of body functions:
   a. Nervous system: The nervous system is composed of three major parts:
      i. Sensory input portion.
      ii. Central nerve system.
      iii. Motor output portion.
   b. Hormonal system: Located in the body, are eight major endocrine glands that secrete chemical substances called hormones. Hormones are transported in the E.C.F. to all parts of the body to help regulate cellular function.
   c. Reproduction: Help to maintain static condition by generating new beings to take the phase of those that are dying.

Homeostasis: in a general sense refers to stability, balance or equilibrium. It is the body's attempt to maintain a constant internal environment. Maintaining a stable internal environment requires constant monitoring and adjustments as conditions change. This adjusting of physiological systems within the body is called homeostatic regulation.

Homeostatic regulation involves three parts or mechanisms: 1) the receptor, 2) the control center and 3) the effector. The receptor receives information that something in the environment is changing. The control center or integration center receives and processes information from the receptor. And lastly, the effector responds to the commands of the control center by either opposing or enhancing the stimulus. This is an ongoing process that continually works to restore and maintain homeostasis. For example, A) in regulating body temperature there are temperature receptors in the skin, which communicate information to the brain, which is the control center, and the effector is our blood vessels and sweat glands. Because the internal and external environment of the body are constantly changing and adjustments must be made continuously to stay at or near the set point, homeostasis can be thought of as a synthetic equilibrium. B) Glucose levels within the blood are constantly monitored by a sensor, the islets of Langerhans in the pancreas. When levels increase, the islets secrete the hormone insulin, which stimulates the uptake of blood glucose into muscles, liver, and adipose tissue. The islets are, in this case, the sensor and the integrating center. The muscles, liver, and adipose cells are the effectors, taking up glucose to control the levels. The muscles and liver can convert the glucose into the polysaccharide glycogen; adipose cells can convert glucose into fat. These actions lower the blood glucose and help to store energy in forms that the body can use later.



❖In emergencies, adrenaline is released by the body to override the homeostatic control of glucose. This is done to promote the breakdown of glycogen into glucose to be used in the emergency. These emergencies are often known as 'fight or flight reactions'. Adrenaline is secreted by the adrenal glands. The secretion of it leads to increased metabolism, breathing and heart rate. Once the emergency is over, and adrenaline levels drop, the homeostatic controls are once again back in place.

Feedback mechanisms regulate biological systems:

♦**Negative Feedback**: In negative feedback systems, the output shuts off the original stimulus . Most control systems of the body the acting stimulus. examples :

- Increased CO2 causes increased pulmonary ventilation, which decreases CO2.

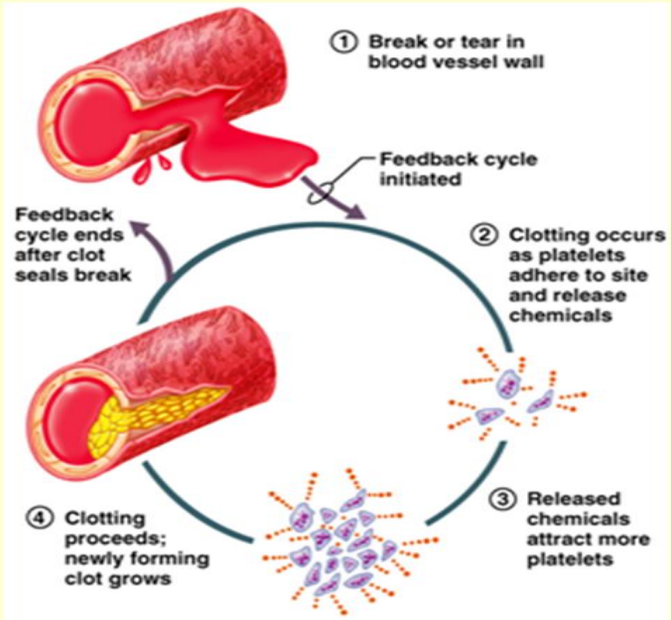
- Decreased arterial pressure activates the baroreceptor system which acts increase heart rate and arterial constriction, which increases arterial pressure
- thyroid stimulating hormone (TSH) released from pituitary gland stimulates thyroid gland which in turn secretes thyroxine. When thyroxin level increases in blood, it inhibits the secretion of TSH from pituitary so that, the secretion of thyroxine from thyroid gland decreases . On the other hand, if thyroxin secretion is less, it induces pituitary gland to release TSH. Now, TSH stimulates thyroid gland to secrete thyroxine
- Regulation of blood glucose levels (explained above)

The negative feedback system acts to maintain homeostasis

♦Positive Feedback : In positive feedback systems, the output enhances or overstates the original stimulus.in a positive feedback control system, a stimulus causes a responses that promotes the stimulus. In general, positive feedback systems lead to instability and therefore are not utilized as often as negative feedback systems. Examples:

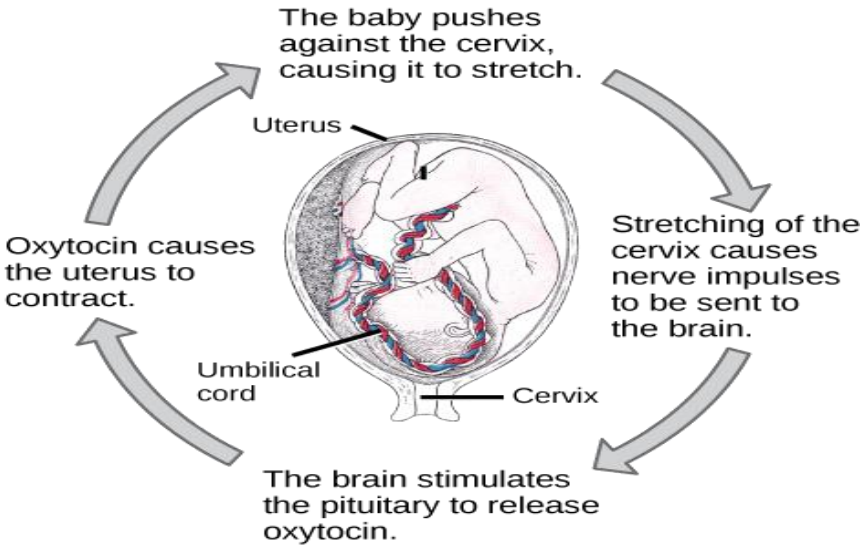
❖Regulation of blood clotting. A rupture in a blood vessel initiates a clot formation, and enzyme activation within the clot causes other enzymes in the blood to clot.

The cycle continues until the vessel in plugged and bleeding stops



❖Positive Feedback during Childbirth

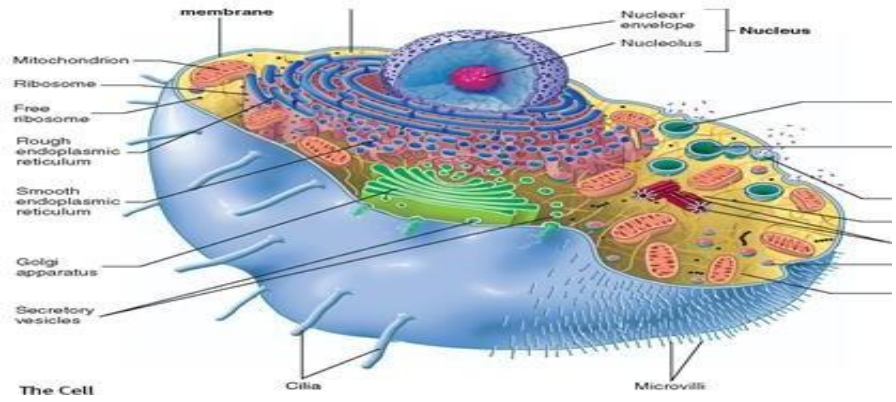
- Stretch receptors in walls of uterus send signals to the brain
- Brain induces release of hormone (oxytocin) into bloodstream
- Uterine smooth muscle contracts more forcefully
- More stretch, more hormone, more contraction etc.
- Cycle ends with birth of the baby & decrease in stretch



Lect. 2

Cell

Cell is the structural and functional unit of the living body because it hasall the characteristics of life



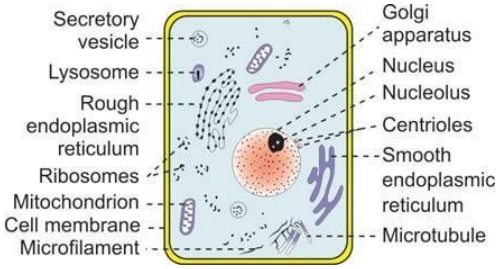
The cell membrane is a protective sheath that envelops the cell body. It separates the fluid outside the cell called extracellular fluid (ECF) and the fluid inside the cell called intracellular fluid (ICF). It is a semipermeable membrane and allows free exchange of certain substances between ECF and ICF

The cell membrane is composed of three types of substances

1. Proteins (55%)
2. Lipids (40%)
3. Carbohydrates (5%).

Each cell is formed by a cell body and a cell membrane or plasma membrane that covers the cell body. The important parts of the cell are

a. Cell membrane
b. Nucleus
c. Cytoplasm with organelles



The cell membrane is a unit membrane having the 'fluid mosaic model' i.e., the membrane is a fluid with mosaic of proteins (mosaic means pattern formed by arrangement of different colored pieces of stone, tile, glass or other such materials , lipids and carbohydrates. The electron microscopic study reveals threelayers in the cell membrane namely, one electron lucent lipid layer in the center and two electron dense layers on either side of the central layer. Carbohydrate molecules are found on the surface of the cell membrane.

FUNCTIONS OF CELL MEMBRANE

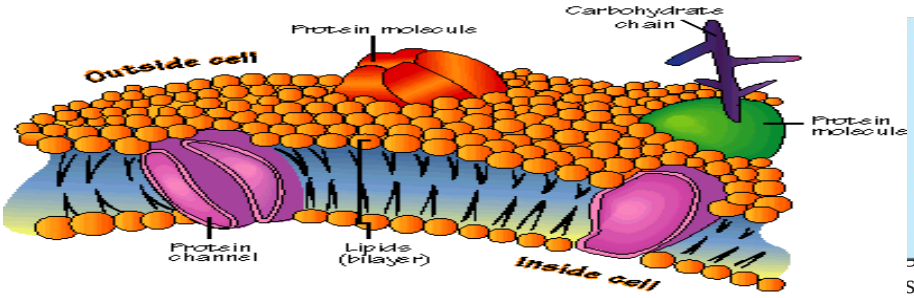
1. Protective function: Cell membrane protects the cytoplasm and the organelles present in the cytoplasm.
2. Selective permeability: Cell membrane acts as a semipermeable membrane which allows only some substances to pass through it and acts as a barrier for other substances.
3. Absorptive function: Nutrients are absorbed into the cell through the cell membrane.
4. Excretory function: Metabolites and other waste products from the cell are excreted out through the cell membrane.
5. Exchange of gases: Oxygen enters the cell from the blood and carbon dioxide leaves the cell and enters the blood through the cell membrane.
6. Maintenance of shape and size of the cell: Cell membrane is responsible for the maintenance of shape and size of the cell.

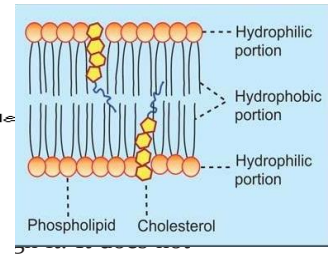
Lipid Layer of Cell Membrane

It is a bilayered structure formed by a thin film of lipids. Lipid bilayer formed by phospholipids that have a polar hydrophilic end formed by the phosphate head and a non - polar hydrophobic end formed by the lipid tail. Within this lipid bilayer are membrane carbohydrates , cholesterol molecules and ,most importantly , membrane proteins.

It is fluid in nature and the portions of the membrane along with the dissolved substances move to all areas of the cell membrane. The major lipids are:

a. Phospholipids
b. Cholesterol





s to pass through

Protein Layers of the Cell Membrane

The protein layers of the cell membrane are the electron dense layers situated on either side of the central lipid layer. The protein substances present in these layers are mostly glycoproteins. These protein molecules are classified into two categories:

a. Integral proteins
b. Peripheral proteins.

Functions of protein layers

Functionally, the proteins in the cell membrane exist in different forms such as integral proteins (channel proteins, carrier proteins) &peripheral protein (recepter,enzym)

1. *Integral proteins* provide structural integrity of the cell membrane
2. *Channel proteins* provide route for diffusion of water soluble substances like glucose and electrolytes
3. *Carrier proteins* help in transport of substances across the cell membrane
4. *Receptor proteins* serve as receptor sites for hormones and neurotransmitters

5. *Enzymes:* some of the protein molecules form the enzymes which control chemical reactions within the cell membrane
6. *Antigens:* Some proteins act as antigens and induce the process of antibody formation.

Carbohydrate of the Cell Membrane

Carbohydrate molecules form a thin loose covering over the entire surface of the cell membrane called glycocalyx. Some carbohydrate molecules are attached with proteins and form glycoproteins and some are attached with lipids and form glycolipids.

Functions of carbohydrates

1. The carbohydrate molecules are negatively charged and do not permit the negatively charged substances to move in and out of the cell.
2. The glycocalyx from the neighboring cells helps in the tight fixation of cells with one another.
3. Some of the carbohydrate molecules form the receptors for some hormones.

CYTOPLASM

The cytoplasm is the fluid present inside the cell. It contains a clear liquid portion called cytosol which contains various substances like proteins, carbohydrates, lipids and electrolytes. Apart from these substances, many organelles are also present in cytoplasm. The cytoplasm is distributed as peripheral ectoplasm just beneath the cell membrane and inner endoplasm between the ectoplasm and the nucleus.

ORGANELLES IN CYTOPLASM

All the cells in the body contain some common structures called organelles in the cytoplasm. Some organelles are bound by limiting membrane and others do not have limiting membrane .

1. ENDOPLASMIC RETICULUM

Endoplasmic reticulum is made up of tubules and microsomal vesicles. These structures form an interconnected network which acts as the link between the organelles and cell membrane.

The endoplasmic reticulum is of two types namely, rough endoplasmic reticulum and smooth endoplasmic reticulum.

Functions of rough endoplasmic reticulum

It is concerned with the protein synthesis in the cell, especially those secreted from the cell such as insulin from cells of islets of Langerhans in pancreas and antibodies in leukocytes.

It also plays an important role in degradation of worn out cytoplasmic organelles like mitochondria. It wraps itself around the worn out organelles and forms a vacuole which is often called the autophagosome. It is digested by lysosomal enzymes

Functions of smooth endoplasmic reticulum

i. It is responsible for synthesis of cholesterol and steroid
ii. It is concerned with various metabolic processes of the cell because of the presence of many enzymes on the outer surface
iii. It is concerned with the storage and metabolism of calcium

IV. It is also concerned with catabolism and detoxification of toxic substances like some drugs and carcinogens (cancer producing substances) in liver.

Rough endoplasmic reticulum and smooth endoplasmic reticulum are interconnected and continuous with one another. Depending upon the activities of the cells, the rough endoplasmic reticulum changes to smooth endoplasmic reticulum and *vice versa*.

GOIGI APPARATUS

The Golgi apparatus is situated near the nucleus. It has two ends or faces namely, *cis* face and *trans* face. The *cis* face is positioned near the endoplasmic reticulum. The reticular vesicles from endoplasmic reticulum enter the Golgi apparatus through *cis* face. The *trans* face is situated near the cell membrane. The processed substances make their exit from Golgi apparatus through *trans* face.

Functions of Golgi Apparatus

i. It is concerned with the processing and delivery of substances like proteins and lipids to different parts of the cell.
ii. It functions like a post office because, it packs the processed materials into the secretory granules, secretory vesicles, and lysosomes
iii. It also functions like a shipping department of the cell because it sorts out and labels the materials for distribution to their proper destinations.

Lysosomes

These are small globular structures filled with enzymes. These enzymes are synthesized in rough endoplasmic reticulum and transported to the Golgi apparatus.

Lysosomes are of two types:

i. Primary lysosome which is pinched off from Golgi apparatus. It is inactive in spite of having the hydrolytic enzymes.
ii. Secondary lysosome which is active lysosome formed by the fusion of a primary lysosome with phagosome or endosome.

Functions of Lysosomes

i. Digestion of unwanted substances

With the help of hydrolytic enzymes like proteases, lipases, amylases and nucleases, lysosome digests and removes the unwanted substances.

ii. Removal of excess secretory products in the cells

Lysosomes in the cells of the secretory glands play an important role in the removal of excess secretory products by degrading the secretory granules.

iii. Secretory function – Secretory lysosomes

Recently, lysosomes having secretory function called secretory lysosomes are found in some of the cells, particularly in the cells of immune system. The conventional lysosomes are modified into secretory lysosomes by combining with secretory granules

Peroxisomes

Peroxisomes are otherwise called as microbodies. These are pinched off from endoplasmic reticulum. Peroxisomes contain some oxidative enzymes such as catalase, urate oxidase and D-amino acid oxidase.

Functions of Peroxisomes

i. Degrade the toxic substances like hydrogen peroxide and other metabolic products by means of detoxification
ii. Form the major site of oxygen utilization in the cells
iii. Break down the excess fatty acids
iv. Accelerate gluconeogenesis from fats
v. Degrade purine to uric acid
vi. Participate in the formation of myelin and bile acids.

Centrosome AND CENTRIOLES

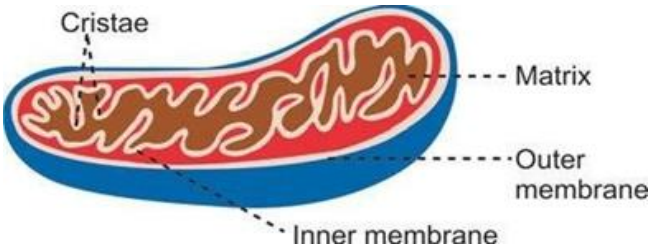
The centrosome is situated near the center of the cell close to the nucleus. It consists of two cylindrical structures called centrioles which are responsible for the movement of chromosomes during cell division.

Secretory VESICLES

The secretory vesicles are globular structures, formed in the endoplasmic reticulum, and processed and packed in Golgi apparatus. When necessary, the secretory vesicles rupture and release the secretory substances into the cytoplasm.

MITOCHONDRION

The mitochondrion is a rod or oval shaped structure with a diameter of 0.5 to 1µ. It is covered by a double layered membrane .



Functions of Mitochondrion

i. The mitochondrion is called the 'power house of the cell' because it produces the energy required for the cellular functions. The energy is produced by oxidation of the food substances like proteins, carbohydrates and lipids by the oxidative enzymes in cristae. During oxidation, water and carbon dioxide are produced with release of energy. The released energy is stored in mitochondria and used later for synthesis of ATP.

ii. The components of respiratory chain in the mitochondrion are responsible for the synthesis of ATP by utilizing the energy through oxidative phosphorylation. The ATP molecules defuse throughout the cell from mitochondrion. Whenever energy is needed for cellular activity, the ATP molecules are broken down

iii. Apoptosis

ORGANELLES WITHOUT LIMITING MEMBRANE

RIBOSOMES

The ribosomes are small granular structures with a diameter of 15 nm. The ribosomes are made up of proteins (35%) and RNA (65%). The RNA present in ribosomes is called ribosomal RNA (rRNA).

Functions of Ribosomes

Ribosomes are called protein factories because of their role in the synthesis of proteins. Messenger RNA (mRNA) passes the genetic code for protein synthesis from nucleus to the ribosomes. The ribosomes, in turn arrange the amino acids into small units of proteins. The ribosomes attached with endoplasmic reticulum are involved in the synthesis of proteins like the enzymatic proteins, hormonal proteins, lysosomal proteins and the proteins of the cell membrane. The free ribosomes are responsible for the synthesis of proteins in hemoglobin, peroxisome and mitochondria.

Cytoskeleton

The cytoskeleton of the cell is a complex network that gives shape, support and stability to the cell. It is also essential for the cellular movements and the response of the cell to external stimuli. The cytoskeleton consists of three majorprotein components viz.

a. Microtubules
b. Intermediate filaments
c. **Microfilaments**

Microtubules

Microtubules are straight and hollow tubular structures formed by bundles of globular protein called □ and □ tubulin

Functions of microtubules

Microtubules:

i. Determine the shape of the cell
ii. Give structural strength to the cell
iii. Responsible for the movements of centrioles and the complex cellular structures likecilia
iv. Act like conveyer belts which allow the movement of granules, vesicles, protein molecules and some organelles like mitochondria to different parts of the cell
v. Form the spindle fibers which separate the chromosomes during mitosis

Intermediate Filaments

The intermediate filaments form a network around the nucleus and extend to the periphery of the cell. These filaments are formed by fibrous proteins and help to maintain the shape of the cell. The adjacent cells are connected by intermediate filaments by desmosomes.

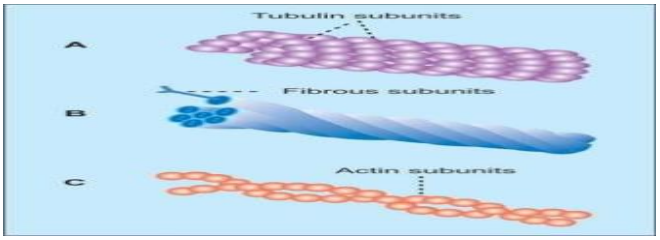
Microfilaments

Microfilaments are long and fine thread like structures which are made up of non tubular contractile proteins called actin and myosin. Actin is more abundant than myosin.

Functions of microfilaments

Microfilaments:

i. Give structural strength to the cell
ii. Provide resistance to the cell against the pulling forces
iii. Responsible for cellular movements like contraction, gliding andcytokinesis(partition of cytoplasm during cell division).



NUCLEUS

Nucleus is present in those cells which divide and produce enzymes. The cells with nucleus are called eukaryotes and those without nucleus are known as

prokaryotes (e.g. red blood cells). Prokaryotes do not divide or synthesize theenzymes.

Most of the cells have only one nucleus (uninucleated). Few types of cells like skeletalmuscle cells have many nuclei (multinucleated). Generally the nucleus is located near thecenter of the cell. It is mostly spherical in shape. However, the shape and situation of nucleus vary in different cells.

Nuclear Membrane

The nucleus is covered by a double layered membrane called nuclear membrane. It encloses the fluid called nucleoplasm. Nuclear membrane is porous and permeable innature and it allows nucleoplasm to communicate with the cytoplasm

Nucleoplasm

It is a gel like ground substance and contains large quantities of the genetic materialin the form of DNA. The DNA is made up of chromatin threads. These chromatin threads become the rod shaped chromosomes just before the cell division.

Nucleoli

One or more nucleoli are present in each nucleus. The nucleolus contains RNA and some proteins, which are similar to those found in ribosomes. The RNA is synthesized by chromosomes and stored in the nucleolus.

FUNCTIONS OF NUCLEUS

1. Controls all the activities of the cell
2. Synthesizes RNA
3. Forms subunits of ribosomes
4. Sends genetic instruction to the cytoplasm for protein synthesis throughmRNA

5. Controls the cell division through genes
6. Stores the hereditary information (in genes) and transforms this informationfrom one generation of the species to the next.

Cell Junctions

The connection between the cells or the contact between the cell and extracellular matrix is called the cell junction. It is also called as membrane junction. It is generally classified into three types:

1. Occluding junction
2. Communicating junction
3. Anchoring junction

OCCLUDING JUNCTION

The junction which prevents the movement of ions and molecules from one cell toanother cell is called the occluding junction.

Tight junctions belong to this category. It is formed by the tight fusion of the cell membranes from the adjacent cells. The area of the fusion is very tight and forms a ridge. This type of junction is present in the apical margins of epithelial cells in intestinal mucosa, wall of renal tubule, capillary wall and choroid plexus.

Functions of Tight Junctions

1. The tight junctions hold the neighboring cells of the tissues firmly and thusprovide strength and stability to the tissues.
2. It provides the barrier or gate function by which the interchange of ions,water and macromolecules between the cells is regulated.
3. It acts like a fence by preventing the lateral movement of integral membraneproteins and lipids from cell membrane
4. By the fencing function, the tight junctions maintains the cell polarity bykeeping the proteins in the apical region of the cell membrane.
5. Tight junctions in the brain capillaries form the blood-brain barrier (BBB) which prevents the entrance of many harmful substances from the blood into the brain tissues

COMMUNICATING JUNCTIONS

The junctions, which permit the movement of ions and molecules from one cell to another cell, are called communicating junctions. Gap junction and chemicalsynapse are the communicating junctions.

GAP JUNCTION OR NEXUS

The gap junction is also called nexus. It is present in heart, basal part of epithelial cells of intestinal mucosa, etc.

Functions of Gap Junction

1. The diameter of the channel in the gap junction is about 1.5 to 3 nm. So, the substances having molecular weight less than 1000 such as glucose also can pass through this junction easily
2. It helps in the exchange of chemical messengers between the cells
3. It helps in rapid propagation of action potential from one cell to another cell

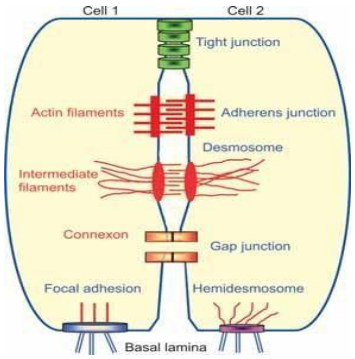
CHEMICAL SYNAPSE

Chemical synapse is the junction between a nerve fiber and a muscle fiber or between two nerve fibers, through which the signals are transmitted by the release of chemical transmitter

ANCHORING JUNCTIONS

Anchoring junctions are the junctions, which provide firm structural attachment between two cells or between a cell and the extracellular matrix. There are four types of anchoring junctions

i. Adherens junctions (cell to cell)
ii. Focal adhesions (cell to matrix)
iii. Desmosomes (cell to cell)
iv. Hemidesmosomes (cell to matrix)



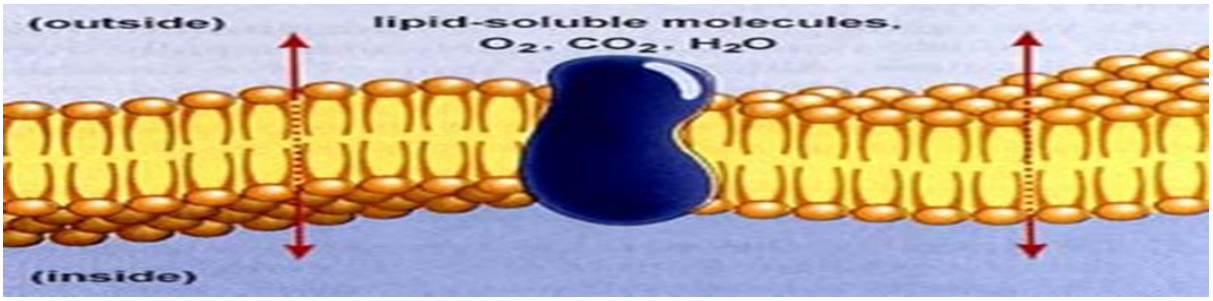
Transport across cell membrane

- **Transport**: is any process in which movement of matter and / or energy occurs from one part of a system to another .If a substance can cross a membrane , the membrane is said to be permeable to that substance , if a substance is unable to pass ,the membrane is impermeable to it.

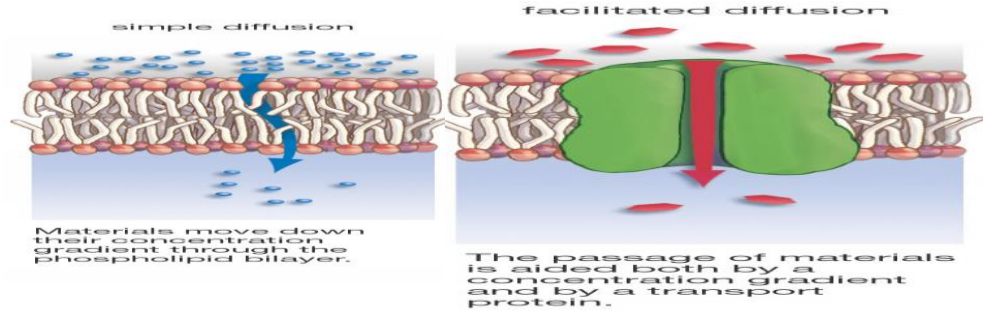
The plasma membrane is selectively permeable in that it permits some particles to pass through while excluding others. substances can pass

- **Passive Transport** is a means of moving biochemical, and other atomic or molecular substances , across membranes. Unlike active transport, this process does not involve chemical energy.

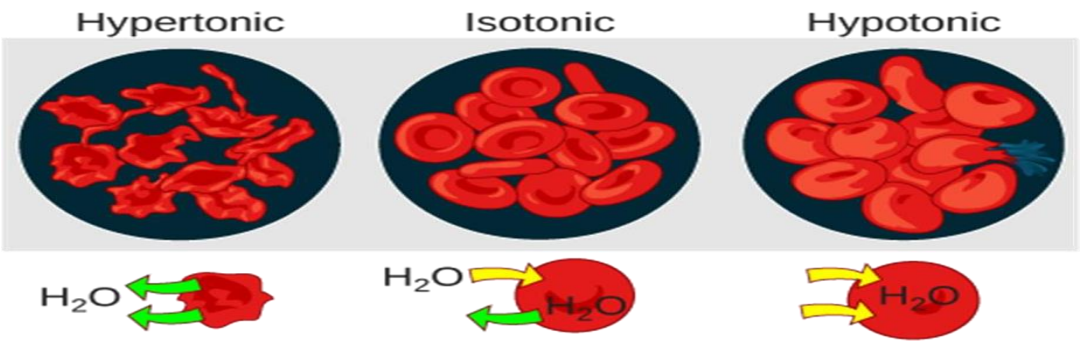
kinds of passive transport are simple diffusion, facilitated diffusion and osmosis.
Diffusion: is the net movement of material from an area of high concentration of that substance to an area with lower concentration of that substance .
Simple Diffusion means that kinetic movement of molecules or ions occurs through a membrane opening or through intermolecular spaces without any interaction with carrier proteins in the membrane . Simple diffusion of lipid soluble substances can take place through the lipid bilayer, its rate dependent on how highly lipid soluble it is (e.g. oxygen, carbon dioxide , nitrogen , alcohol). Water & lipid -insoluble substances simply diffuse through protein channels , the number and size of openings available determining its rate .
The protein channels involved in simple diffusion are distinguished by 2 important characteristics :1. They are often selectively permeable to certain substances .2. Many of the channels can be opened or closed by gates .



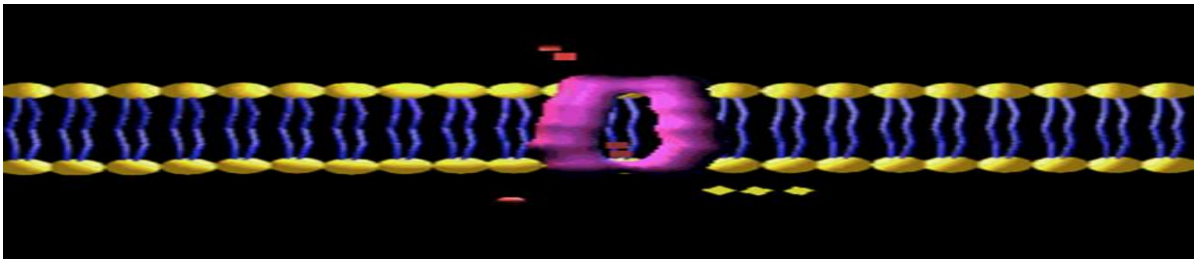
Facilitated Diffusion is also called carrier - mediated diffusion because a substance transported in this manner diffuses through the membrane using a specific carrier protein to help .The carrier protein has a pore large enough to transport a specific molecule partway through . It also has a binding receptor on the inside of the protein carrier to which the molecule binds itself causing conformational or chemical changes in the carrier protein so that the pore now opens up on the opposite side . The molecule is released because the binding force is weak and the thermal motion of the attached molecule causes it to break away .Carrier - Mediated Transport Systems display 3 characteristics determining the kind &amount of substance that will be transferred : 1. Specificity 2. Saturation 3. Competition



Osmosis is the diffusion of a solvent across a membrane to a region of higher solute concentration . In biological processes then , it usually is diffusion of water molecules . It is a physical process in which a solvent moves ,without input of energy , across a semipermeable membrane separating two solutions of different concentrations .The osmotic pressure is defined to be the pressure required to maintain equilibrium , with no net movement of solvent . Osmotic pressure depends on the molar concentration of the solute but not on its identity . It is the exact amount of pressure required to stop osmosis .The tonicity of a solution refers to the effect on cell volume of the concentration of non -penetrating solutes in the solution surrounding the cell .



- **Active Transport** Active Transport (sometimes called active uptake) is the mediated transport of biochemicals, and other molecular substances , across membranes. This process requires the expenditure of cellular energy to move molecules " uphill " against a gradient . It also involves the use of a protein carrier to transfer a specific substance across the membrane , but against its concentration gradient .Primary Active Transport when energy is directly derived from breakdown of ATP to move a substance uphill . Examples: Pumping Na^+ (sodium ions) out and K^+ (potassium ions) in against strong concentration gradients called Na+-K+ Pump.(3 Na+ pumped in for every 2 K+ pumped out; creates a membrane potential).



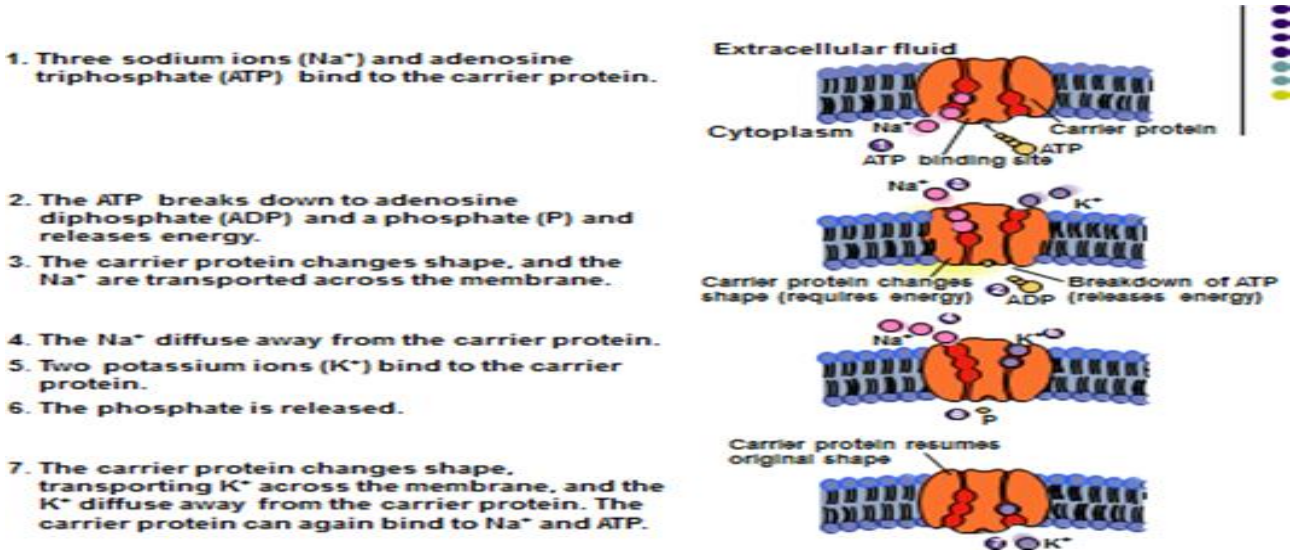
Sodium-Potassium Pump as an example of Primary Active Transport:

The active transport mechanism that has been studied in greatest detail is the **sodium- potassium (Na+-K+) pump**, a transport process that pumps sodium ions outward through the cell membrane of all cells and at the same time pumps potassium ions from the outside to the inside. This pump is responsible for maintaining the sodium and potassium concentration differences across the cell membrane, as well as for establishing a negative electrical voltage inside the cells. This pump is also the basis of nerve function, transmitting nerve signals throughout the nervous system. The carrier protein is a complex of two separate globular proteins: a larger one called the a subunit, and a smaller one called the b subunit, the larger protein has three specific features that are important for the functioning of the pump:

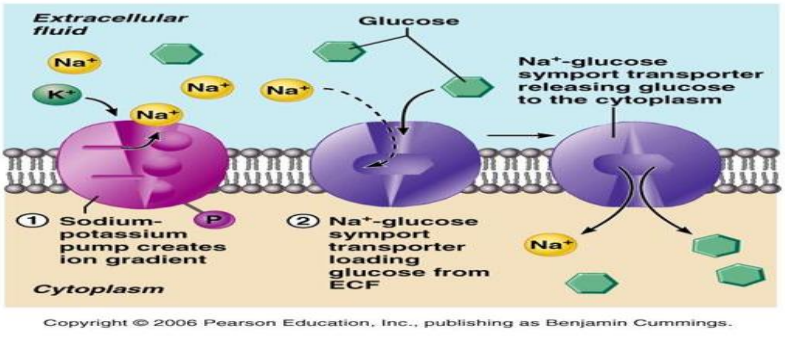
1. It has three **receptor sites for binding sodium ions** on the portion of the protein that protrudes to the inside of the cell.
2. It has two **receptor sites for potassium ions** on the outside.
3. The inside portion of this protein near the sodium binding sites has **ATPase activity**.

When two potassium ions bind on the outside of the carrier protein and three sodium ions bind on the inside, the ATPase function of the protein becomes activated. This then cleaves one molecule of ATP, splitting it to adenosine diphosphate (ADP) and liberating a high-energy phosphate bond of energy. This liberated energy is then believed to cause a chemical and conformational change in the protein carrier molecule, extruding the three sodium ions to the outside and the two potassium ions to the inside. For some cells, such as electrically active nerve cells, 60 to 70

per cent of the cells' energy requirement may be devoted to pumping Na+ out of the cell and K+ into the cell.



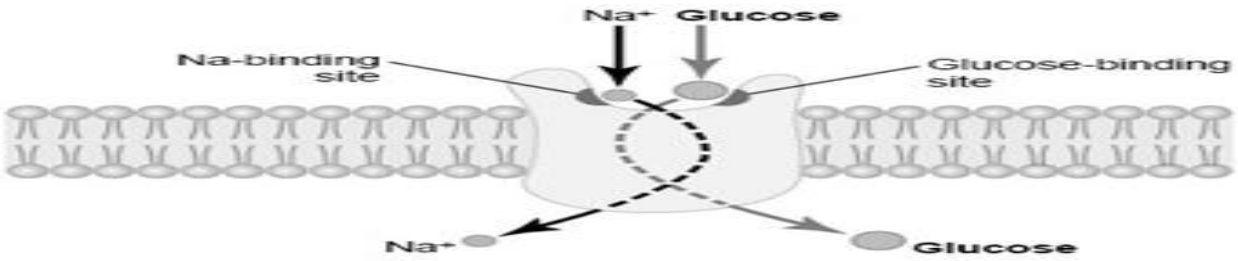
- Secondary Active Transport -when energy is derived secondarily from energy that has been stored in the form of ionic concentration differences of secondary molecular or ionic substances between the two sides of a cell membrane , created originally by primary active transport. In this mode of transport , the transport of two or molecules are coupled either the substances moving together in the same direction through a common carrier (co-transport) or the substances moving in opposite directions using the same carrier (counter transport).



Co-Transport of Glucose and Amino Acids Along with Sodium Ions

Glucose and many amino acids are transported into most cells against large concentration gradients; the mechanism of this is entirely by co-transport. Note that the transport carrier protein has two binding sites on its exterior side, one for sodium and one for glucose. Also, the concentration of sodium ions is very high on the outside and very low inside, which provides energy for the transport. A special property of the transport protein is that a conformational change to allow sodium movement to the interior will not occur until a glucose molecule also attaches. When they both become attached, the conformational change takes place automatically, and the sodium and glucose are transported to the inside of the cell at the same time. Hence, this is a **sodium-glucose co-**

transport mechanism. **Sodium co-transport of the amino acids** occurs in the same manner as for glucose, except that it uses a different set of transport proteins. Five **amino acid transport proteins** have been identified, each of which is responsible for transporting one subset of amino acids with specific molecular characteristics. **Sodium co-transport of glucose and amino acids occurs especially through the epithelial cells of the intestinal tract and the renal tubules of the kidneys to promote absorption of these substances into the blood**. Other important co-transport mechanisms in at least some cells include co-transport of chloride ions, iodine ions, iron ions, and urate ions.



Vesicular Transport

Materials move into or out of the cell by means of vesicles, also called **bulk transport**

1. Endocytosis (Clathrin-mediated)
2. Receptor mediated endocytosis
3. Pinocytosis
4. Phagocytosis
5. Exocytosis

ALL are active processes (require ATP) though they are not usually referred to as "active transport"

ENDOCYTOSIS

Endocytosis is the process in which the substance is trans ported into the cell by unfolding of the cell membrane around the substance and inter nailing it . It is further categorized into three types:

1. Pinocytosis, i.e. cell drinking refers to the process of engulfing liquid substances by the enfolding of cell membrane, e.g. reabsorption by renal tubular epithelial cells.

2. Phagocytosis, i.e. cell eating is the process of engulfing of solid particles, such as bacteria, dead tissue and for engulfing particles by the cells. The process of phagocytosis involves three steps:
   (i) the attachment stage,
   (ii) (ii) the engulfment stage and
   (iii) (iii) killing or degradation stage .
3. Receptor-mediated endocytosis. In this process the substance to be transported binds with the special receptor protein present on the cell surface. The receptor protein–substance complex is then engulfed by the cell membrane by the process of endocytosis. Transport of iron and cholesterol into the cells occurs by receptor mediated

endocytosis

EXOCYTOSIS

Exocytosis is reverse of endocytosis, i.e. by this process the substances are expelled from the cell without passing through the cell membrane. In this process, the substances which are to be extruded are collected in the form of granules or vesicles which move towards the cell membrane. Their membrane then fuses to the cell membrane. The area of fusion breaks down releasing the con tents to the exterior and leaving the cell membrane intact. Release of hormones and enzymes by secretory cells of the body occurs by exocytosis. The process of exocytosis requires Ca2+ and energy along with docking proteins.

TRANSCYTOSIS

Vesicular transport within the cell is called transcytosis or cytopempsis. It is quite similar to exocytosis and endocytosis. Three basic steps involved in this process are: (i) vesicle formation, (ii) vesicle transportation and (iii) docking in the cell.

Renal Physiology

Kidney Functions

- **Regulation of body fluid osmolality & volume**: Excretion of water and NaCl is regulated in conjunction with cardiovascular, endocrine, & central nervous systems
- **Regulation of electrolyte balance**:
    - Daily intake of inorganic ions (Na+, K+, Cl-, HCO3-, H+, Ca2+, Mg+ & PO43-)
    - Should be matched by daily excretion through kidneys.
- **Regulation of acid-base balance**: Kidneys work in concert with lungs to regulate the pH in a narrow limits of buffers within body fluids.

- **Excretion** of metabolic products & foreign substances:
    - **Urea** from amino acid metabolism
    - **Uric acid** from nucleic acids
    - **Creatinine** from muscles
    - **End products** of hemoglobin metabolism
    - Hormone metabolites
    - Foreign substances (e.g., Drugs, pesticides, & other chemicals ingested in the food)

- **Production and secretion of hormones**:
    - **Renin** -activates the renin-angiotensin-aldosterone system, thus regulating blood pressure & Na+,K+ balance
    - **Prostaglandins/kinins** - bradykinin = vasoactive, leading to modulation of renal blood flow & along with angiotensin II affect the systemic blood flow
    - **Erythropoietin** -stimulates red blood cell formation by bone marrow

Renal Anatomy

- Functional unit - **nephron**:
    - **Glomerulus**
        - Bowman's capsule
        - Glomerular capillaries
    - Proximal Convoluted Tubule
    - Loop of Henley
    - Distal Convoluted Tubule
    - Collecting duct
        - Production of filtrate
        - Reabsorption of organic nutrients
        - Reabsorption of water and ions
        - Secretion of waste products into tubular fluid

2 Types of Nephron

Cortical nephrons ~85% of all nephrons, located in the cortex

Juxtamedullary nephrons, closer (juxta = next to) renal medulla, Loops of Henle extend deep into renal pyramids

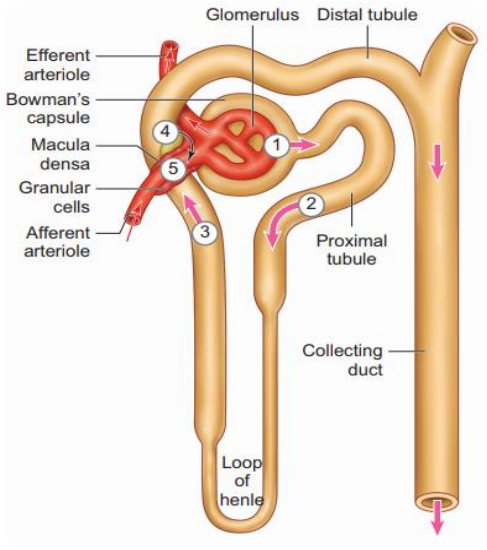
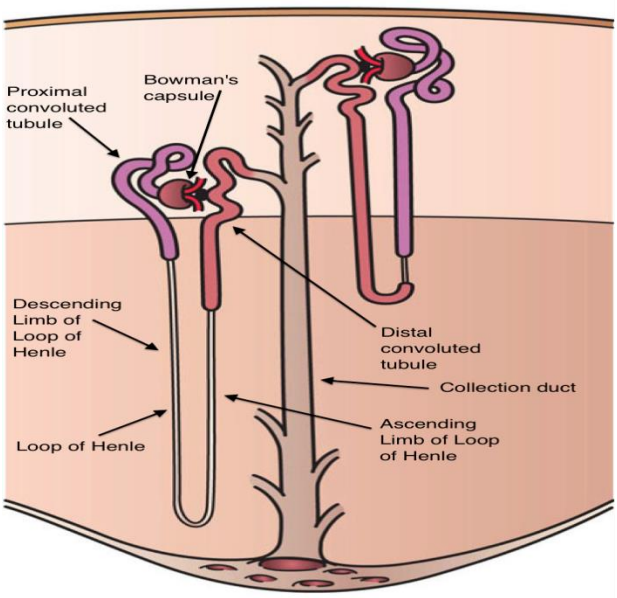
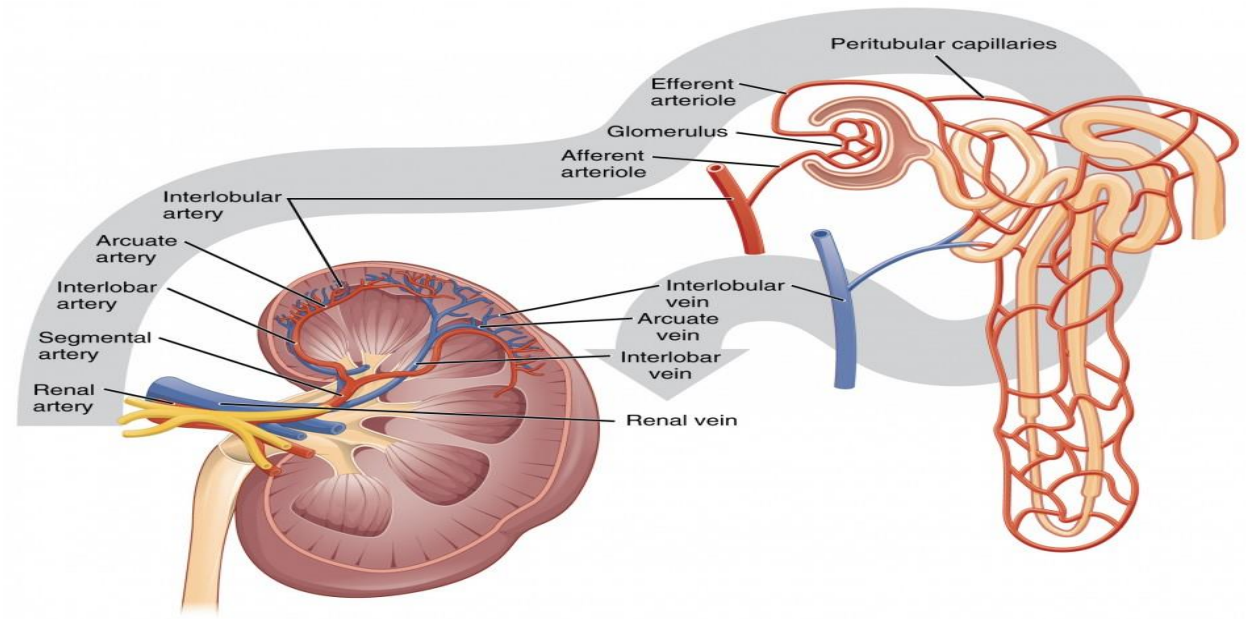


Figure 8.4 Structure of a Nephrons



Blood Supply to the Kidneys

- Blood travels from afferent arteriole to capillaries in the nephron called glomerulus
- Blood leaves the nephron via the efferent arteriole
- Blood travels from efferent arteriole to peritubular capillaries and vasa recta



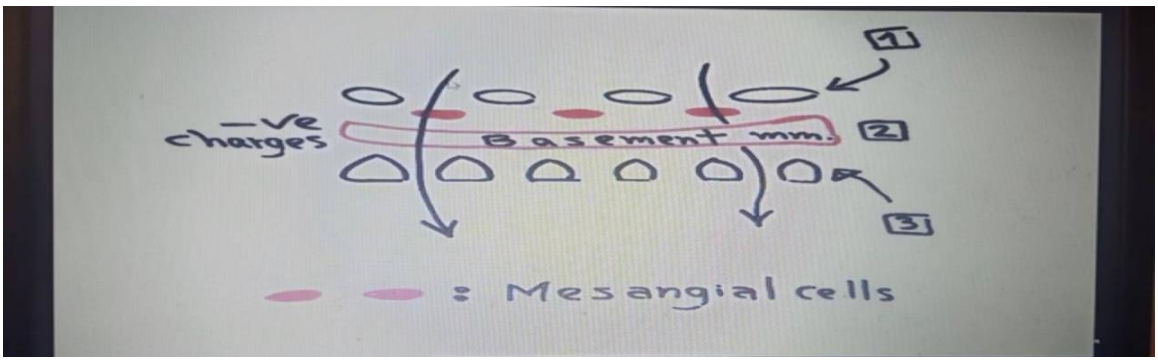
Filtrate Composition

- Glomerular filtrate is produced from blood plasma
- Must pass through:
    - **Pores** between endothelial cells of the glomerular capillary
    - **Basement membrane** - Acellular gelatinous membrane made of collagen and glycoprotein

- **Filtration slits** formed by podocytes
- Filtrate is similar to plasma in terms of concentrations of salts and of organic molecules (e.g., glucose, amino acids) except it is ***essentially protein-free***
- Glomerular filtration barrier restricts the filtration of molecules on the basis of **size and electrical charge**
- Serum albumin is anionic and has a 355 nm radius, only ~7 g is filtered per day (out of ~70 kg/day passing through glomeruli)
- In a number of glomerular diseases, the negative charge on various barriers for filtration is lost due to immunologic damage and inflammation, resulting in **proteinuria** (i.e. increased filtration of serum proteins that are mostly negatively charged).

125 ml/min plasma filtered 20% plasma are filtered

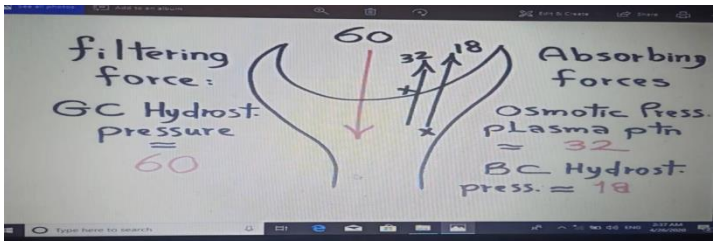
- The glomerulus is more efficient than other capillary beds because:
    - Its filtration membrane is significantly more permeable
    - Glomerular blood pressure is higher
    - It has a higher net filtration pressure
    - Plasma proteins are not filtered and are used to maintain **oncotic (colloid osmotic**) pressure of the blood



Forces Involved in Glomerular Filtration

- **Net Filtration Pressure (NFP)** - pressure responsible for filtrate formation
- NFP equals the glomerular hydrostatic pressure (HPg) (60) + glomerular osmotic pressure (0) minus the osmotic pressure of glomerular blood (OPg) (32)plus capsular hydrostatic pressure (HPc) (18)

NFP = HPg – (OPg + HPc)
NFP = 60- (32+18)
NFP = 60- (50)
NFP = 10



Glomerular Filtration Rate (GFR)

The total amount of filtrate formed per minute by the kidneys

- Filtration rate factors:
    - Total **surface area** available for filtration and membrane permeability (filtration coefficient = Kf)
    - **Net filtration pressure (NFP)**
    - **GFR = Kf x NFP**
- GFR is directly proportional to the NFP
- Changes in GFR normally result from changes in glomerular capillary blood pressure

Decrease in GFR increase creatinin which must be less than 1

Clearance: volume of plasma cleared from substance (ml/min)
Amount of substance in plasma = Amount of substance in urine
GFR= Clearance = 125ml/min use substance inulin (fructose)
C= $\frac{U \times V}{P}$
GFR= $\frac{\text{concentration in urine X volume of urine per unit of time}}{\text{Plasma concentration}}$

- **Detect glomerular damage**
- **Follow the progress of diagnosed renal disease**

Creatinine Clearance: C= $\frac{U \times V}{P}$

- **Creatinine clearance is the amount of creatine in the urine, divided by the concentration in the blood plasma, over time.**
- **Glomerular filtration rate can be calculated by measuring any chemical that has a steady level in the blood, and is filtered but neither actively absorbed or excreted by the kidneys.**
- **Creatinine is used because it fulfills these requirements (though not perfectly), and it is produced naturally by the body.**
- **The result of this test is an important gauge used in assessing excretory function of the kidneys. For example grading of chronic renal insufficiency and dosage of drugs that are primarily excreted via urine are based on GFR**
- **Other methods involve constant infusions of inulin or another compound, to maintain a steady state in the blood.**

Renal function

1. **BUN/ Creatinine Ratio normal range 10:1**
   BUN: blood urea nitrogen
   Abnormal >10:1 example 30:1 mean blood flow slow causes are dehydration or renal artery stenosis.
   <10:1 example 7:1 mean intrinsic damage in kidney
   <1 creatinine normal in old because reduce mass of mascle

2. **Creatinine Clearance = GFR**
   a. **Creatinine Clearance $\frac{\text{U creatinine X Volume of urine}}{\text{P creatinine}}$ normal 80-120 ml/min**
   (in patients 24hr)
   b. **Serum creatinine**

Regulation of Glomerular Filtration

- If the GFR is too high, needed substances cannot be reabsorbed quickly enough and are lost in the urine
- If the GFR is too low - everything is reabsorbed, including wastes that are normally disposed of
- Control of GFR normally result from adjusting glomerular capillary blood pressure
- 3 mechanisms control the GFR

- **Renal autoregulation (intrinsic system**)
- **Neural controls**
- **Hormonal mechanism (the renin-angiotensin system**)

Autoregulation of GFR

- Under normal conditions (Mean Arterial pressure =80-180mmHg) renal autoregulation maintains a nearly constant glomerular filtration rate
- 2 mechanisms are in operation for autoregulation:

Myogenic mechanism:

- Arterial pressure rises, afferent arteriole stretches
- Vascular smooth muscles contract
- Arteriole resistance offsets pressure increase; Renal Blood Flow RBF (& hence GFR) remain constant.

Tubuloglomerular feedback mechanism for autoregulation:

- Feedback loop consists of a flow rate (increased NaCl) sensing mechanism in macula densa of juxtaglomerular apparatus (JGA)
- Increased GFR (& RBF) triggers release of vasoactive signals
- Constricts afferent arteriole leading to a decreased GFR (& RBF)

Extrinsic Controls

When the sympathetic nervous system is at rest:

- Renal blood vessels are maximally dilated
- Autoregulation mechanisms prevail

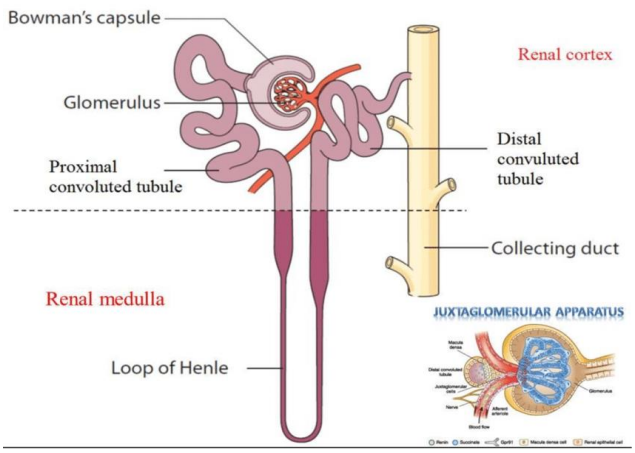
- **Under stress**:
  - **Norepinephrine** is released by the sympathetic nervous system
  - Epinephrine is released by the adrenal medulla
  - **Afferent arterioles constrict and filtration is inhibited**
- The sympathetic nervous system also stimulates the **renin-angiotensin mechanism**
- A drop in filtration pressure stimulates the Juxtaglomerular apparatus (JGA) to release **renin and erythropoietin**

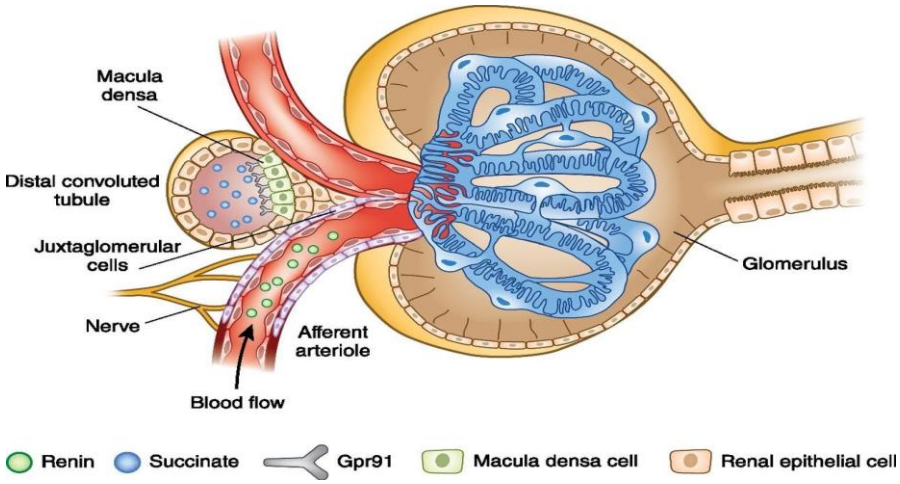
Renin-Angiotensin Mechanism

- The juxtaglomerular apparatus consists of macula densa modified cells of the distal tubule and juxtaglomerular cells in the walls (modified smooth cells) of the afferent and mesengial cells. When blood pressure is decreased, delivery of sodium chloride is decreased to the macula densa cells, which are capable of sensing this change (due to osmoreceptors). The decrease in sodium chloride concentration at the macula densa, in turn, causes two main effects: (1) a decrease in the resistance of the afferent arterioles, which increases glomerular hydrostatic pressure and the GFR toward normal levels, and (2) an increase in renin release from the juxtaglomerular apparatus, which causes increased angiotensin II formation. Angiotensin II then constricts efferent arterioles, increases arterial pressure, and increases glomerular hydrostatic pressure and the GFR toward normal levels.

  Renine----------adrenal gland----------aldosterone----------reabsorbs Na and secret K----blood pressure increase and blood volume increase

  juxtaglomerular apparatus secrete Renin & erythropoietin





Other Factors Affecting Glomerular Filtration

- Prostaglandins (PGE2 and PGI2)
  - Vasodilators produced in response to sympathetic stimulation and angiotensin II
  - Are thought to prevent renal damage when peripheral resistance is increased
- Nitric oxide – vasodilator produced by the vascular endothelium
- Adenosine – vasoconstrictor of renal vasculature
- Endothelin – a powerful vasoconstrictor secreted by tubule cells

Control of Kf

- Mesangial cells have contractile properties, influence capillary filtration by closing some of the capillaries – effects surface area
- **Podocytes change size of filtration slits**

Process of Urine Formation

- Glomerular filtration
- Tubular **reabsorption** of the substance from the tubular fluid into blood
- Tubular **secretion** of the substance from the blood into the tubular fluid
- **Amount Excreted in Urine = Amount Filtered through glomeruli into renal proximal tubule MINUS amount reabsorbed into capillaries PLUS amount secreted into the tubules**

1. **Reabsorption and secretion**
   - Accomplished via
     - **diffusion**
     - **osmosis**
     - **active and facilitated transport**
       - Na active transport
       - Cotransport
         - Glucose
         - Ions
         - Amino acids
       - Proximal tubule, key site

Non-Reabsorbed Substances

- Substances are not reabsorbed if they**:**

- **Lack carriers**
- **Are not lipid soluble**
- **Are too large to pass through membrane pores**

- **Urea, creatine, and uric acid** are the most important nonreabsorbed substances

Sodium Reabsorption:
Primary Active Transport

- **Sodium** reabsorption is almost always by active transport via a Na+-K+ ATPase pump
- Na+ reabsorption provides the energy and the means for reabsorbing most other solutes
    - Water by osmosis
    - Organic nutrients and selected cations by secondary (coupled) active transport

2.Tubular Secretion

- Essentially reabsorption in reverse, where substances move from peritubular capillaries or tubule cells into filtrate
- Tubular secretion is important for:
    - Eliminating undesirable substances such as urea and uric acid
    - Ridding the body of excess potassium ions
    - Controlling blood pH

Reabsorption and secretion at the PCT

- Glomerular filtration produces fluid similar to plasma without proteins
- The **PCT reabsorbs 60-70% of the filtrate produced**
- Sodium, all nutrients, amino acids cations, anions, and water
    - Urea and lipid-soluble solutes
    - Small proteins
- H+ secretion also occurs in the PCT

Reabsorption and secretion at the DCT

DCT performs final adjustment of urine

- Active secretion or absorption
- Absorption of Na+ and Cl-
- Secretion of K+ and H+ based on body pH

- Water is regulated by ADH (vasopressin)
- Na+, K+ regulated by aldosterone

Atrial Natriuretic Peptide Activity

- ANP reduces blood Na+ which:
    - Decreases blood volume
    - Lowers blood pressure
- ANP lowers blood Na+ by:
    - inhibit Na+ reabsorption
    - Counteracting the effects of angiotensin II
    - Antagonistic to aldosterone and angiotensin II.
    - Promotes Na+ and H20 excretion in the urine by the kidney.
    - Indirectly stimulating an increase in GFR reducing water reabsorption

Regulation by ADH

- Released by posterior pituitary when osmoreceptors detect an increase in plasma osmolality.
- Dehydration or excess salt intake:
    - Produces sensation of thirst.
    - Stimulates H_2o reabsorption from urine.

Regulation of Urine Concentration and Volume

- **Osmolality**
- The kidneys keep the solute load of body fluids constant at about 300 mOsm
- This is accomplished by the **countercurrent mechanism**

Countercurrent Mechanism

- Interaction between the flow of filtrate through the loop of Henle (countercurrent multiplier) and the flow of blood through the vasa recta blood vessels (countercurrent exchanger)
- The solute concentration in the loop of Henle ranges from 300 mOsm to 1200 mOsm
- Vasa Recta prevents loss of medullary osmotic gradient equilibrates with the interstitial fluid
    - Maintains the osmotic gradient
    - Delivers blood to the cells in the area

Loop of Henle: Countercurrent Multiplication

- The descending loop: relatively impermeable to solutes, highly permeable to water
- The ascending loop: permeable to solutes, impermeable to water
- Collecting ducts in the deep medullary regions are permeable to urea

Physical Characteristics of Urine

- Color and transparency
- Clear, pale to deep yellow (due to urochrome)
    - Concentrated urine has a deeper yellow color
    - Drugs, vitamin supplements, and diet can change the color of urine
    - Cloudy urine may indicate infection of the urinary tract
- pH
    - Slightly acidic (pH 6) with a range of 4.5 to 8.0
    - Diet can alter pH
- Specific gravity
    - Ranges from 1.001 to 1.035
    - Is dependent on solute concentration

Chemical Composition of Urine

- Urine is 95% water and 5% solutes
- Nitrogenous wastes include urea, uric acid, and creatinine
- Other normal solutes include:
    - Sodium, potassium, phosphate, and sulfate ions
    - Calcium, magnesium, and bicarbonate ions

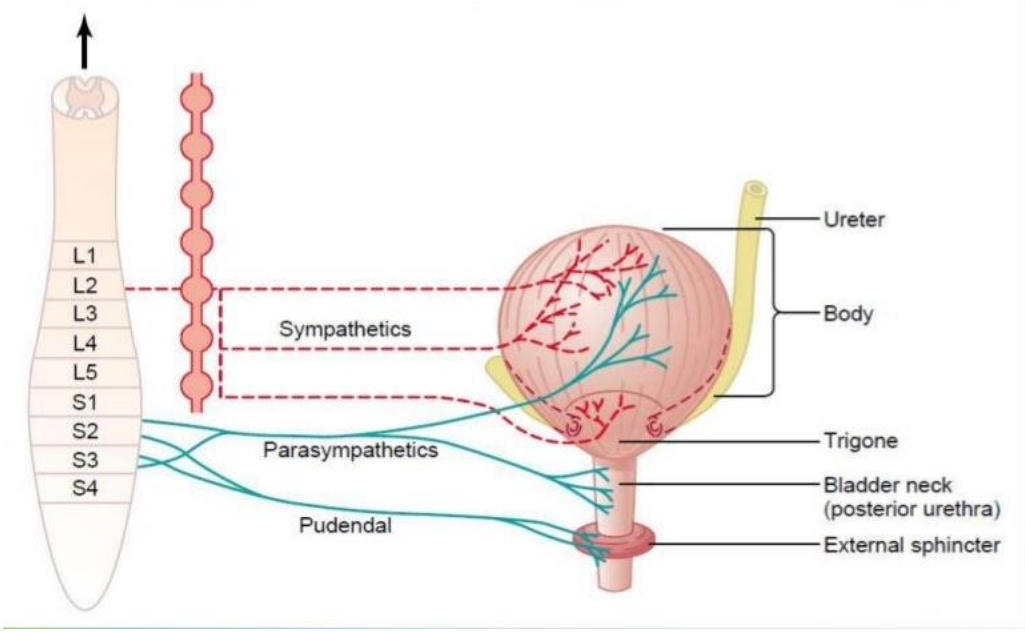
- Abnormally high concentrations of any urinary constituents may indicate pathology

Micturition

- From the kidneys urine flows down the ureters to the bladder propelled by peristaltic contraction of smooth muscle. The bladder is a balloon-like bag of smooth muscle

Bladder can hold 250 - 400ml

S: Stimulus :Bladder fills with urine
R: Receptor: Strech receptors in the bladder wall (mainly neck)
A: Afferent: Sensory signals (pelvic nerve)
C: central: Sacral segments S2.3.4
E: Efferent: parasympathetic motor signals (pelvic nerve)
E: Effector: Detrusor muscle (Bladder muscle)
R: Response: contraction of the bladder Internal sphincter opens
External sphincter relaxes due to inhibition



Resting Membrane Potentials and Action Potentials

. Nerves and muscles are called **excitable tissue because they respond to:**
Chemical.
Mechanical.
Electrical stimuli.
Muscles demonstrate by **contraction,** while nerves by **integration and transmission**.

Electrical signals in neurons:

- Production of signals depend on two basic features of the plasma membrane of excitable cells:

i) Resting membrane potential.

ii)Ion channels.

I) Ion channels:

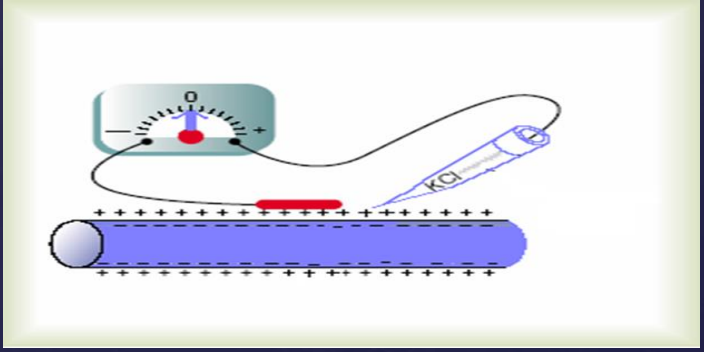
- Ion channels open and close due to **the presence of (gates).**
- ***There are four kinds of ion channels:***

1. **leakage channels:** open and close randomly
2. **Voltage-gated channels:** opens to a change in Membrane Potential (voltage).
3. **Ligand-gated channels:** opens and close in response to chemical stimulus, such as Ach.
4. **mechanical gated channels:** open or close in response to mechanical stimulation, such as touch or tissue stretching.

Resting membrane potential(RMP):

The difference in voltage across the cell membrane when a neuron or muscle cells is not producing an Action Potential.

- A typical value is: **-70 mV(-50 to -90)**
- **A cell that exhibits a membrane potential is said to be *polarized.***



Why RMP is negative inside the cell relative to the outside?

- Because of the following:-

1. the resting membrane is **10-100 times more permeable to K+** than to Na+.
   - **K+ tends to leak out of the cell down its concentration gradient, carrying +ve charge with it, and unable to carry Cl- with it because Cl- has higher concentration outside.**
2. The non-diffusible anion **(protein, sulphate and phosphate ions)** cannot leave the cell.

Forces act on cell membrane at rest:

1. **Diffusion:** is the movement of molecules from a region of higher concentration to a region of lower concentration.
2. **Electrical gradient:** +ve ions move to the –ve area and –ve ions move to +ve area
3. **Active transport:** transport ions against their concentration gradient. Most important example is Na+_K+ pump(need energy); responsible transport of Na+ to the outside and K+ to the inside.

These forces are responsiple for:

i- The maintenance of the RMP

ii- The development of the AP

iii- Bringing the cell back to its resting state after the AP is over.

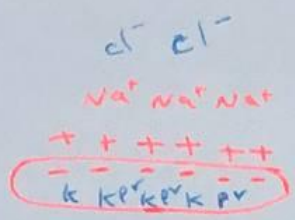
The action potential (AP):

The AP **is a sudden reversal of membrane polarity by a stimulus.**

- **Importance:**

AP occurs in living organism to produce physiological effects such as:

1. **Transmission of impulses along nerve fibers**
2. **Release of neurosecretions or chemical transmitters in synapses.**
3. **Contraction of muscle.**
4. **Activation or inhibition of glandular secretion.**



Stimulus
1- mechanical
2- Electrical
3 - chemical

Na voltage channel

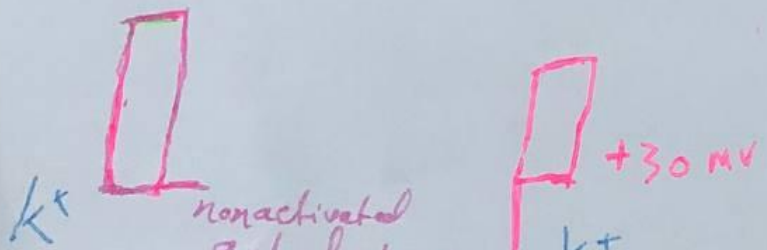
activated

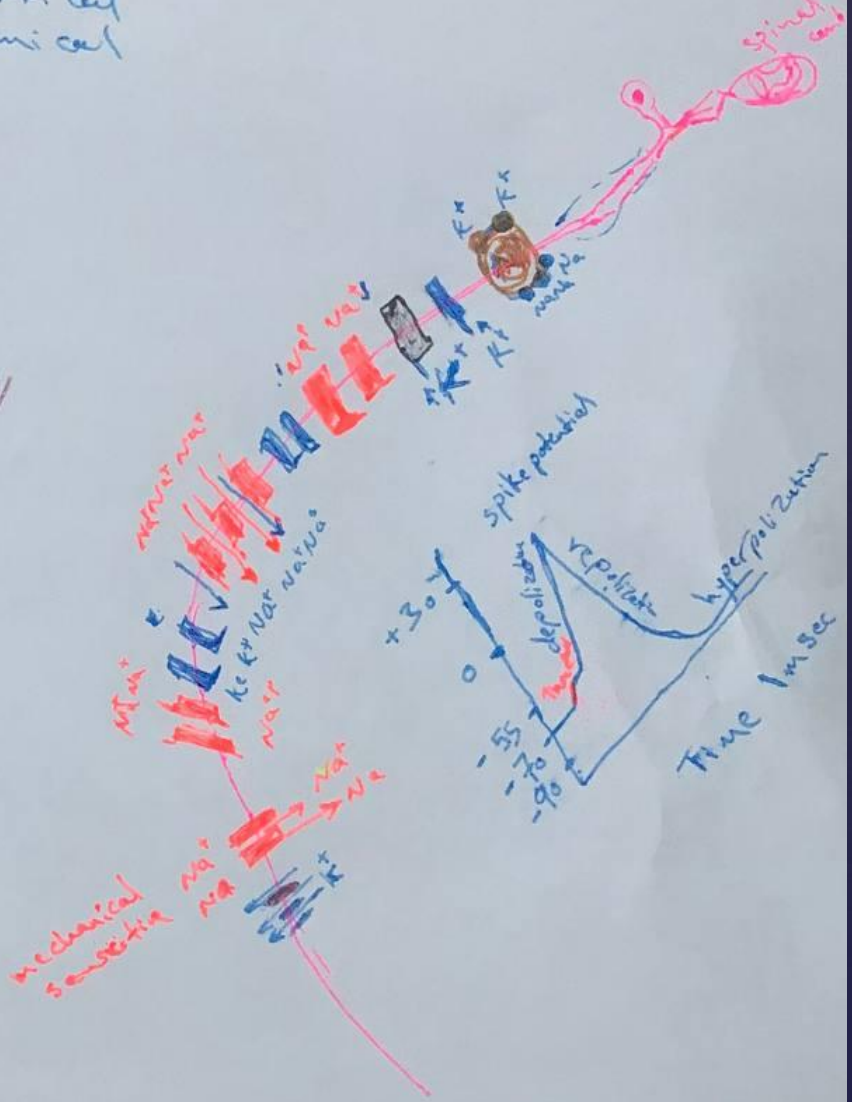
non activated

(-70)-(-90) mv

-55 mv
Threshold

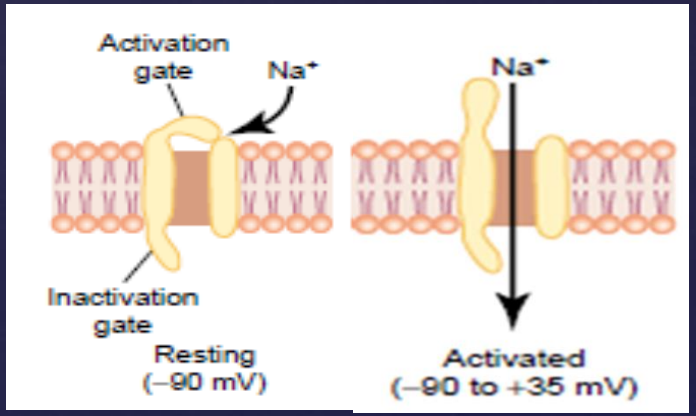
+30mV



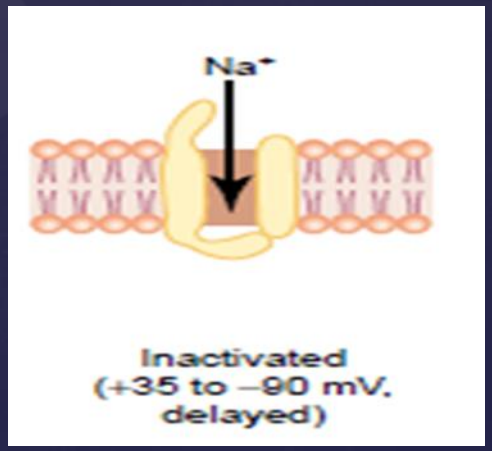


Development of the AP:

- When a cell membrane is stimulated by a physical or a chemical stimulus, **the cell membrane permeability to Na+ is dramatically increased.**
- Sodium channels open and the sodium ions rush through the channels to the inside the cell **causing the inside the membrane to become positive** with respect to the outside.
- This is called ***depolarization***.

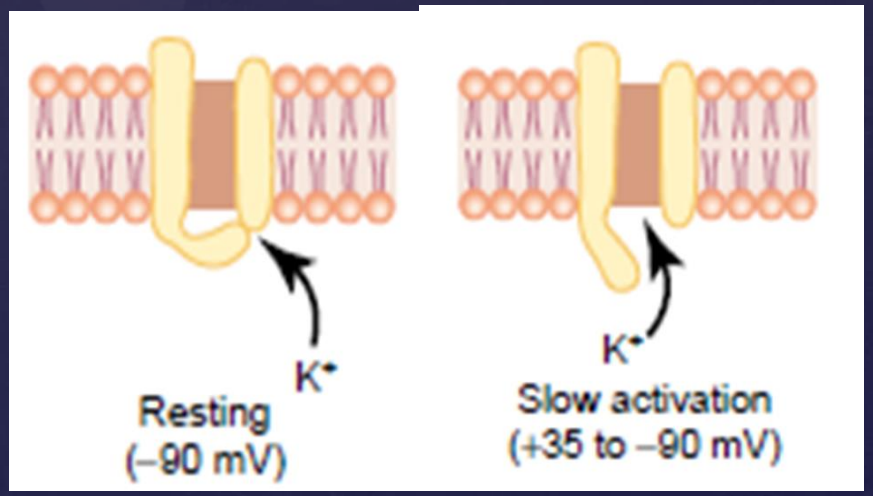


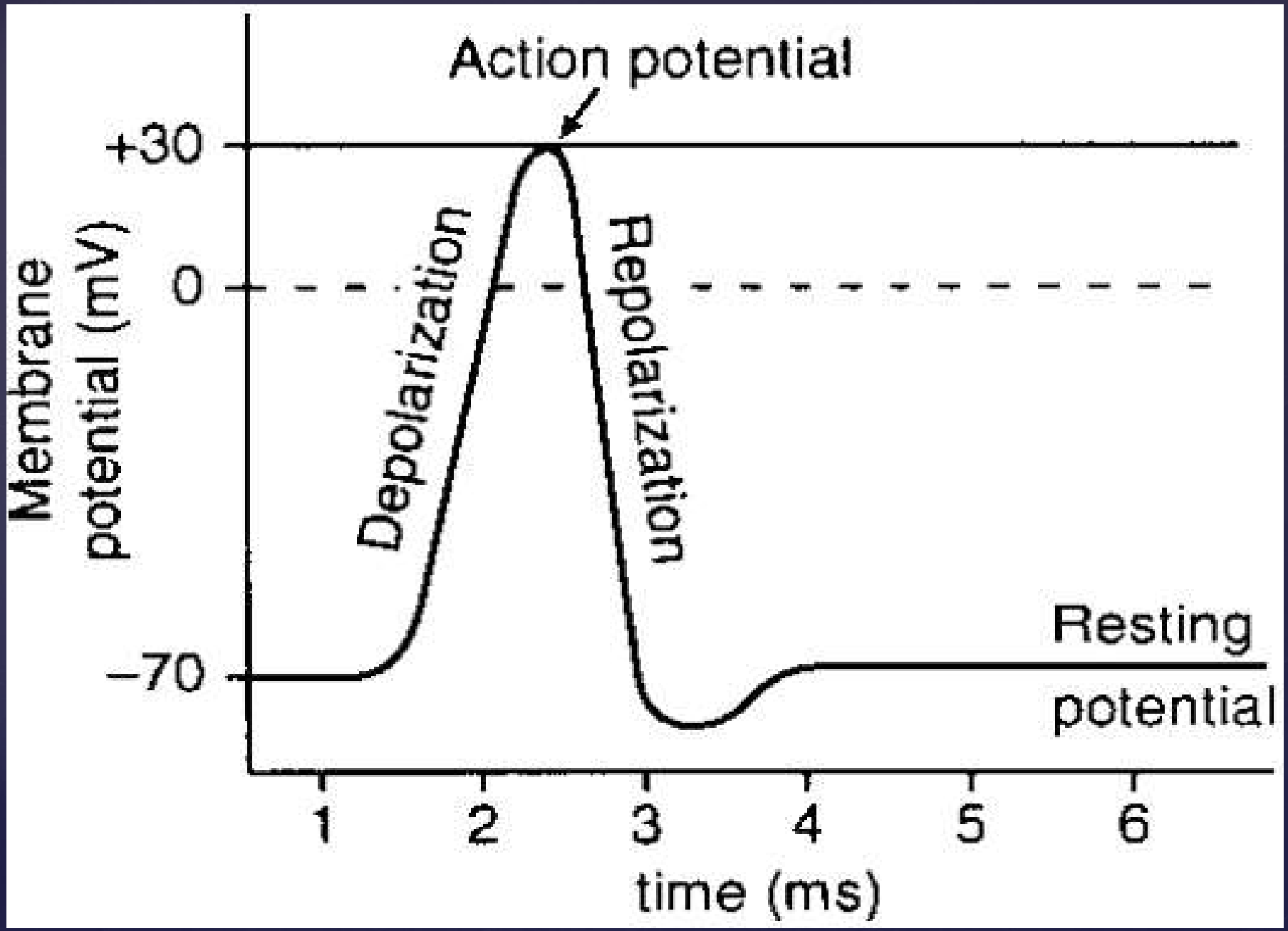
- The membrane potential becomes
- **reversed and reaches +35 mV.**



Towards the end of depolarization, sodium permeability decreases and pottasium permeability increases.

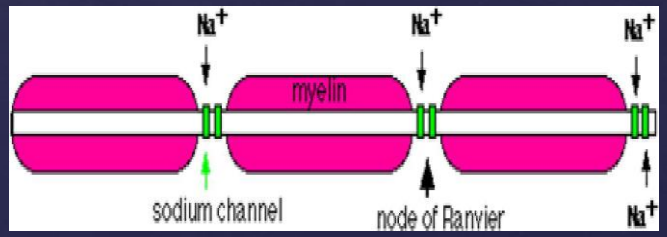
- K+ions leave the cell down their concentration gradient, **causing the inside the membrane to return quickly to its original potential.**
- This is called ***repolarization.***
- **The membrane potential**
- **brought back to -70 mV**




Action potential
+30
0
−70
Membrane potential (mV)
Depolarization
Repolarization
Resting potential
1
2
3
4
5
6
time (ms)

PROPAGATION OF THE ACTION POTENTIAL:

- An action potential elicited at any one point on an excitable membrane usually excites adjacent portions of the membrane, resulting in propagation of the action potential along the membrane.
- This transmission of the depolarization process along a nerve or muscle fiber is called a nerve or muscle impulse



An excitable membrane **has no single direction of propagation,** but the action potential **travels in all directions away from the stimulus**—even along all branches of a nerve fiber—until the entire membrane has become depolarized

Generation of action potential (AP):

The AP can be divided in five phases:

1. **The resting potential.**
2. **Threshold.**
3. **The rising phase.**
4. **The falling phase.**
5. **The recovery phase.**

Resting potential When the neuron is at rest, **only a small of K+ channels are open**, permitting K+ ions to enter and exit the cell based on electrochemical forces.

Threshold

- As a depolarizing stimulus arrives the membrane, a **few Na+ channels open permitting Na+ ions to enter the neuron.**
- **The increase in positive ions inside the cell depolarizes the membrane (making it less negative).**

Rising phase

- If the depolarization reaches the threshold potential, **additional voltage-gated Na+ channels open.**

As positive Na+ ions rush in to the cell the voltage across the membrane rapidly **reverses and reaches its most positive value**

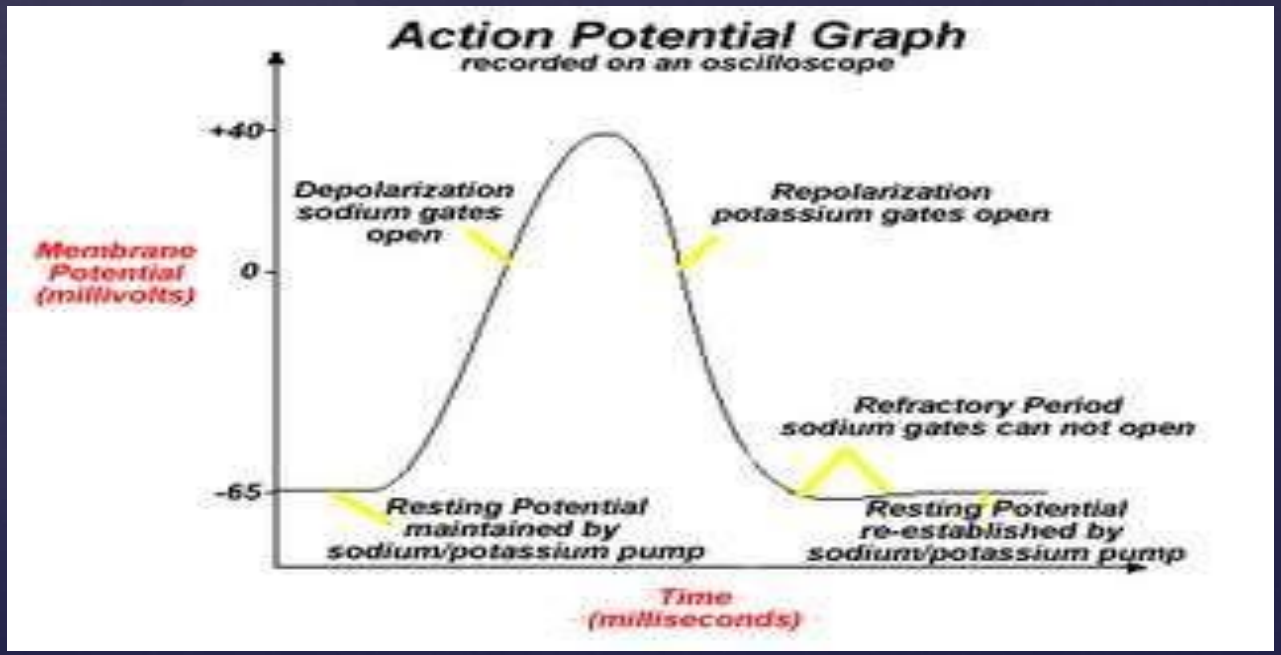
Falling phase :At the peak of AP, two process occur simultaneously;

1. First: **many of the voltage-gated Na+ channels begin to close.**
2. Second: **many more k+ channel open, allowing positive charges to leave the cell**.

- This causes the Membrane Potential to begin to shift back toward the **Resting Membrane Potential.**
- As the Membrane Potential approaches the Resting Potential , **voltage-gated K+ channels are maximally activated and open.**

Recovery phase

- This undershoot occurs because more K+ channels are open.
- The return to steady state continues as the additional K+ channels **that opened during the Action Potential now close.**
- **The AP is now determined by the subset of the K+ channels that are normally open during the membrne's resting state.**



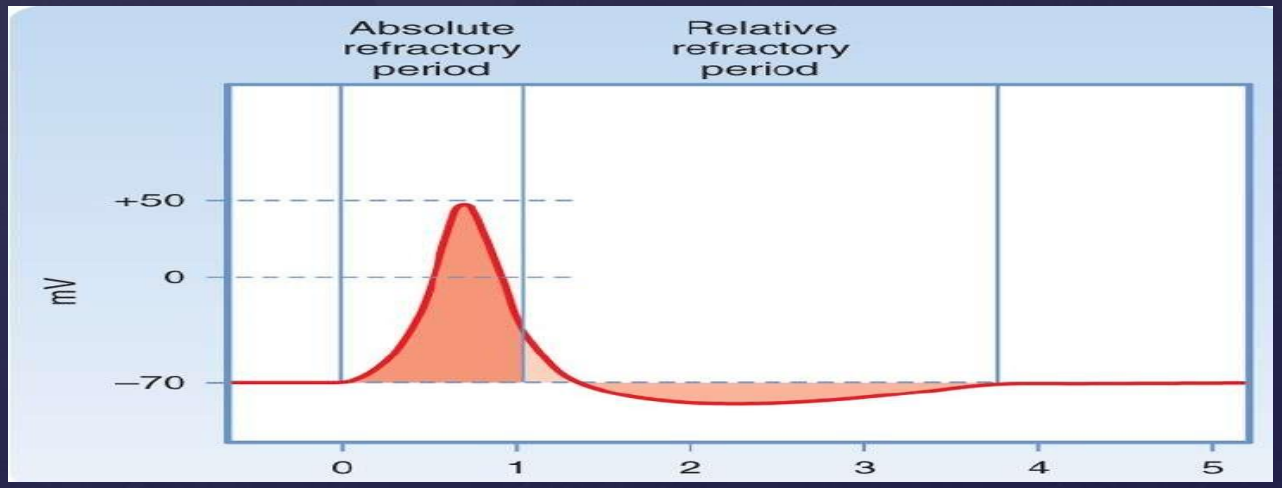
All-or-Nothing Principle

- Also called **All or None Law.**
- Applies to all normal **excitable tissues.**
- The depolarization process travels over the entire membrane if conditions are right, but it does not travel at all if conditions are not right.
- A law stating that certain structures, such as a neuron or a muscle fiber, either **respond completely** (all) or **not at all** (none) to a stimulus.
- **There is no partial nerve impulse in a neuron, or partial contraction of a fiber muscle.**
- If the stimulus is any strength above threshold, the nerve or muscle fiber will either give a complete response or no response.

Refractory period

- It is the period which **an excitable cell cannot generate another AP in response to a *normal* threshold stimulus.**
- **Types of refractory period**:

1. ***Absolute refractory period:*** in which cannot initiate a second AP even a very strong stimulus.
   - This period coincide with the period of voltage-gated Na+ channel activation gates are inactivating and cannot reopen; they first must return to the resting state.
1. ***Relative refractory period:*** during which a second action potential can be evoked, but only if the stimulus strength is increased.
   - It coincides with the period when the voltage-gated K+ channels are still open after inactivated Na+ channels have returned to their resting state.



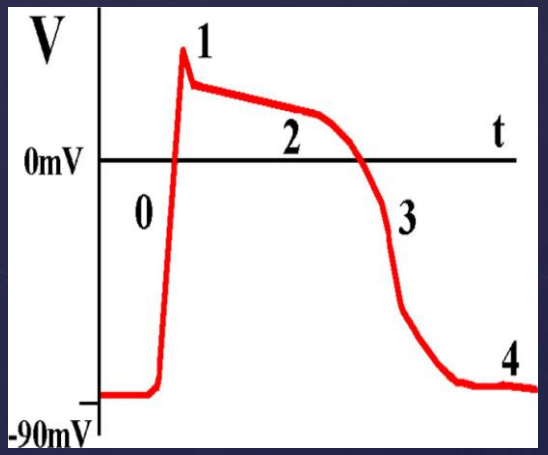
Cardiac muscle action potential:

Phases

- 0: depolarization (Na+ influx through fast Na+ channels)
- 1: short repolarization (K+ efflux through K+ channels, Cl- influx as well)
- 2: plateau phase (Ca++ influx through slow Ca++ channels)
- 3: repolarization (K+ efflux through K+ channels)
- 4: resting

The plateau ends when the **calcium - sodium channels close** and **permeability to potassium ions increases**

Duration is about 250 msec



Smooth muscle resting membrane potential may be about -55mV

- Action potential is similar to nerve AP
- But AP is not necessary for its contraction
- Smooth muscle contraction can occur by hormones