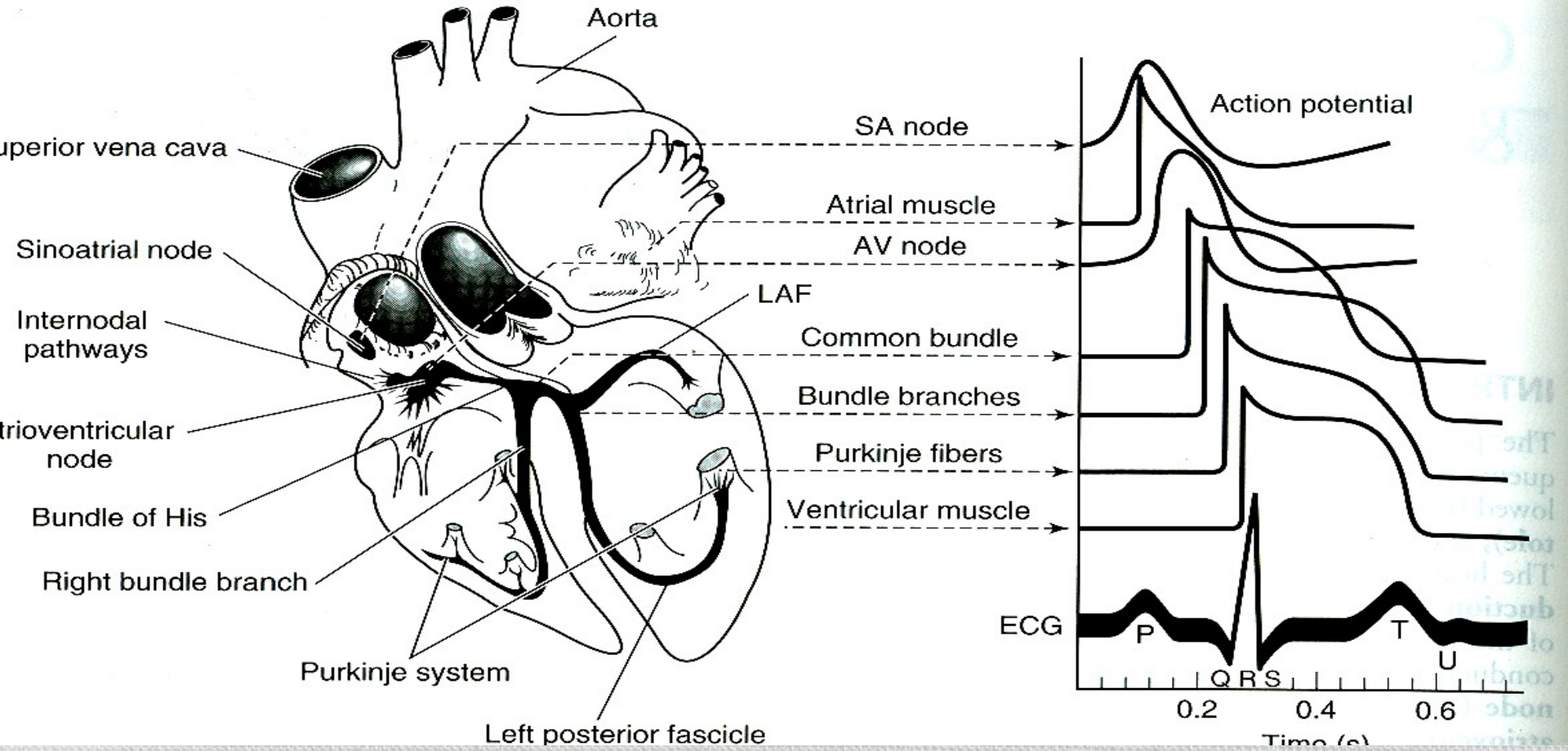
CARDIOVASCULAR PHYSIOLOGY



INTRODUCTION

- The circulatory system – body's transport system.
  - ✓ A vital pipeline for transporting materials.
- Three basic components –
  - ✓ The heart is the pump.
    - o Blood flows down a pressure gradient.
  - ✓ The blood vessels – passageways.
  - ✓ Blood – transport medium.

FUNCTIONAL ANATOMY OF THE HEART

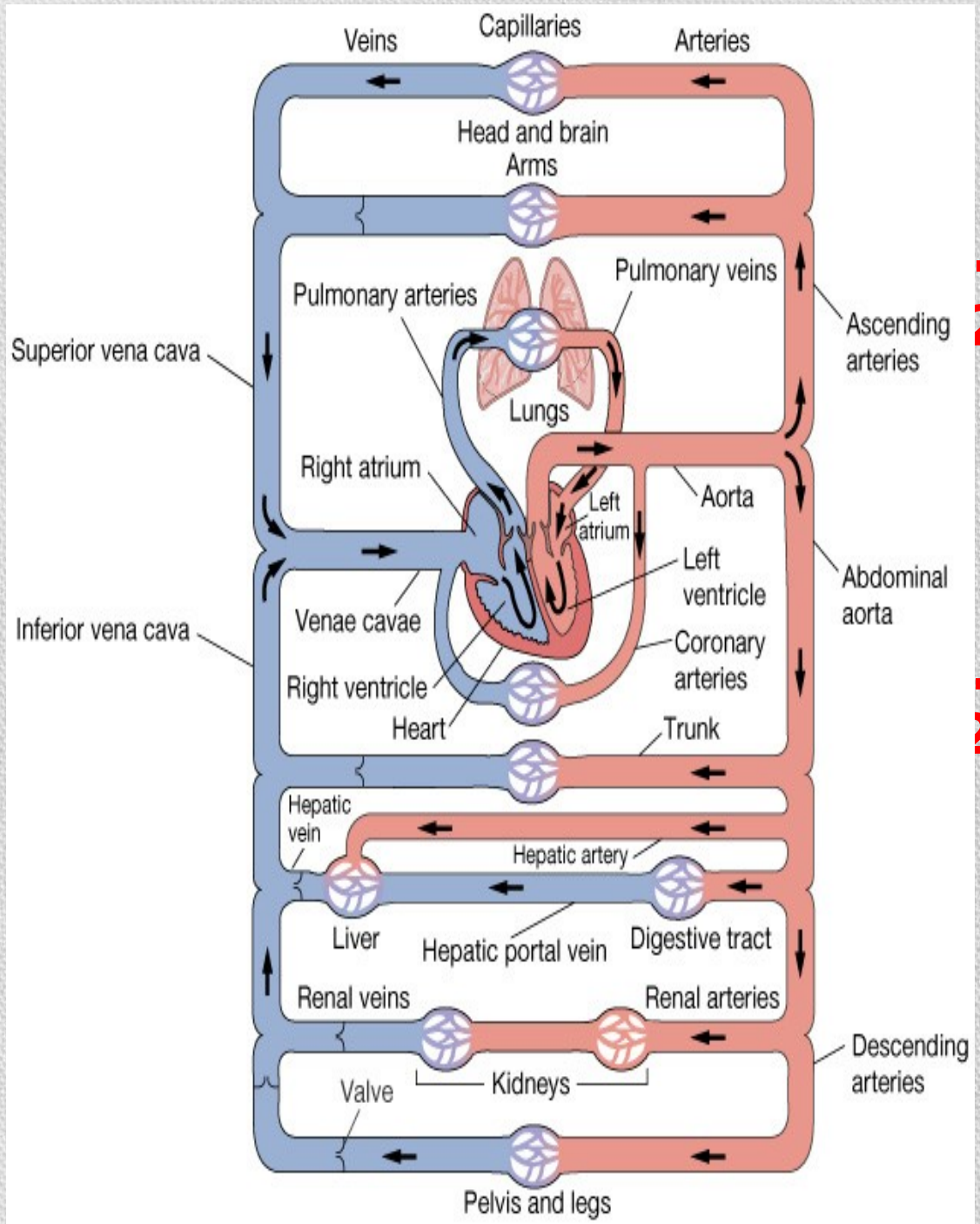
- Within about 3 weeks after conception, the heart of the developing embryo starts to function.
- It is the first organ to become functional.
  - ✓ To pick up and distribute to the developing tissues the supplies so critical for survival and growth.
- It is located in the center of the thoracic cavity.
- The heart is enclosed and anchored in place by the pericardium.
  - ✓ Parietal and visceral membranes of the

CHAMBERS AND CIRCULATION

- Heart consists –
  - ✓ The right and left atria - acts as a receiving chamber;
  - ✓ The right and left ventricles - act as delivery chamber.
- The right pump (right atria and right ventricle) are separated from the left pump (left atria and left ventricle) by septum.
  - ✓ Septum prevents blood mixing from the two pumps.
- Between the atria and ventricles, there is a fibrous

Chambers and circulation cont'd…

- The connective tissue of the fibrous skeleton also forms rings.
  - ✓ Annuli fibrosi – providing a foundation for support of the valve flaps.
- There are two distinct but linked circuits in the human circulation – pulmonary and systemic circuits.
  - ✓ The pulmonary circuit transports blood to and from the lungs.
  - ✓ The systemic circuit transports oxygenated blood to



PULMONARY CIRCULATION

1. LOW RESISTANCE
2. LOW PRESSURE (25/10 mmHg)

SYSTEMIC CIRCULATION

1. HIGH RESISTANCE
2. HIGH PRESSURE (120/80 mmHg)

PARALLEL SUBCIRCUITS

UNIDIRECTIONAL FLOW

Chambers and circulation cont'd…

	Source	Arteries	O_2 Content of Arteries	Veins	O_2 Content of Veins	Termination
Pulmonary Circulation	Right ventricle	Pulmonary arteries	Low	Pulmonary veins	High	Left atrium
Systemic Circulation	Left ventricle	Aorta and its branches	High	Superior and inferior venae cavae and their branches*	Low	Right atrium

HEART VALVES

- Valves – the one-way flow of blood.
  - ✓ Consists of thin flaps of flexible but tough fibrous tissue whose movements are passive.
- Two sets
  1. Atrioventricular (AV) valves – found b/n atria and ventricles.
     - ✓ The right AV valve (tricuspid valve) – three cusps or leaflets.

Heart valve cont'd…

2. The semilunar valves – separate the ventricles from their associated arteries.

   - ✓ The pulmonary valve – between the right ventricle and the pulmonary artery and
   - ✓ The aortic valve – between the left ventricle and the aorta.

- Valves prevent backward flow of blood.
  - ✓ There are no valves between the venae cavae or the pulmonary veins and the atria into which they

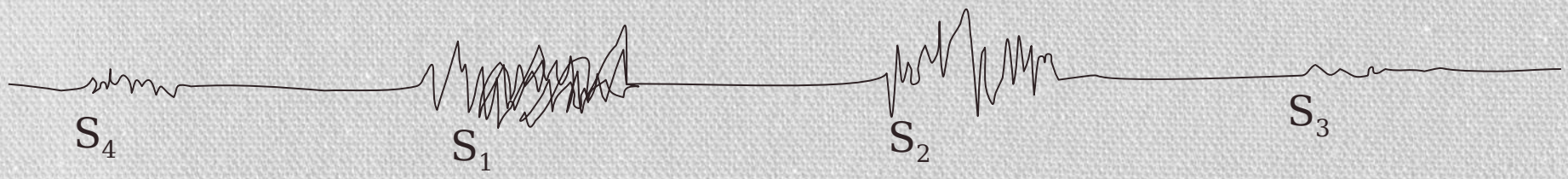
HEART SOUNDS

- Closer of valves produces sounds.
- Means of identification

1. Auscultation –
   - ✓ Direct/immediate auscultation
   - ✓ Stethoscope mediated auscultation
2. Phonocardiographic based recording

Heart sound cont'd…

- 4-separate audible heart sounds (S_1, S_2, S_3 and S_4)



1. S_1: is always audible, has a LUBB-sound
2. S_2: is always audible, has DUBB-sound
3. S_3: is audible in children and in adults during exercise
4. S_4: is audible very rarely

WALL OF THE HEART

- Heart has three layers –
  - ✓ Epicardium – the outermost layer – thin membrane.
  - ✓ Myocardium – the middle thickest layer – muscular layer.
  - ✓ Endocardium – the innermost layer – thin delicate layer.

PROPERTIES OF CARDIAC MUSCLE

- **The basic properties of cardiac muscle include:**
  - ✓ **Automaticity,**
  - ✓ **Rhythmicity (chronotropism),**
  - ✓ **Conductivity (dromotropism),**
  - ✓ **Excitability (bathmotropism) and**
  - ✓ **Contractility (inotropism).**

ELECTRICAL ACTIVITY OF THE HEART

- *Autorhythmicity* is the property of cardiac muscle which enables the heart to initiate its own impulse at constant rhythmical intervals.
  - ✓ This is because of the presence of the specialized *pacemaker tissue* in the heart.
- The pacemaker tissue makes a *conduction system* that normally spreads impulses through the heart.
- The conducting system of the heart consists of specialized fibers of the heart muscle present as:

i. Sinoatrial (SA) node.

- The conduction system of the heart is composed of modified cardiac muscle that has *fewer striations* and *indistinct boundaries.*
- Pacemaker – from which rhythmic impulses for heart beat are produced.
- Sinoatrial (SA) node *acts as a primary pacemaker* because the rate of impulse generation by SA node is the highest.
  - ✓ *SA node* is located in the wall of right atrium, just to the right of the opening of superior vena cava.

Electrical activity cont'd…

- The cells present in the SA node and AV node are called *slow fibers* and the other cells are called *fast fibers.*
  - ✓ Depending on the membrane potential and the shape and conduction velocity of the action potential.
- The slow fibers of the pacemaker tissue have a unique feature, i.e. leakage of resting membrane for Na^+
  - ✓ While the resting membrane of fast fibers is relatively impermeable to Na^+.

Electrical activity cont'd…

- ✓ *This slow entry of Na^+ in the cells slowly raises the potential to -55 mV* (i.e. causes slow depolarization) due to the presence of non selective channels.

- ✓ In pacemaker (SA node) fibers, have no RMP but have pacemaker potential (–55 mV to –60 mV).

- Nodal tissues (SA node) possess certain funny (f) channels

- ✓ Because of their unusual activation following hyperpolarization, associated with increased permeability to both sodium and potassium but dominant effect is that of sodium conductance

Electrical activity cont'd…

- Because of their activation during hyperpolarization of the membrane (-40 to -60 mV).

- This slow entry of Na^+ in the cells through funny (f) channels causes slow depolarization that forms the initial part of pacemaker potential.

- Then the 'T' (transient) calcium channels open up and there is slow influx of Ca^{2+} causing further depolarization in the same at slower rate till a threshold level of -40 mV is reached.

  ✓ Thus calcium current (I_{ca}) due to the opening of 'T calcium channels' forms the later part of pacemaker

Electrical activity cont'd…

- ✓ Thus, it is important to note that the depolarization in SA node is mainly due to influx of Ca^{2+} rather than Na^{+}.
- ✓ Consequently, the depolarization is not as sharp as in the other myocardial fibers.

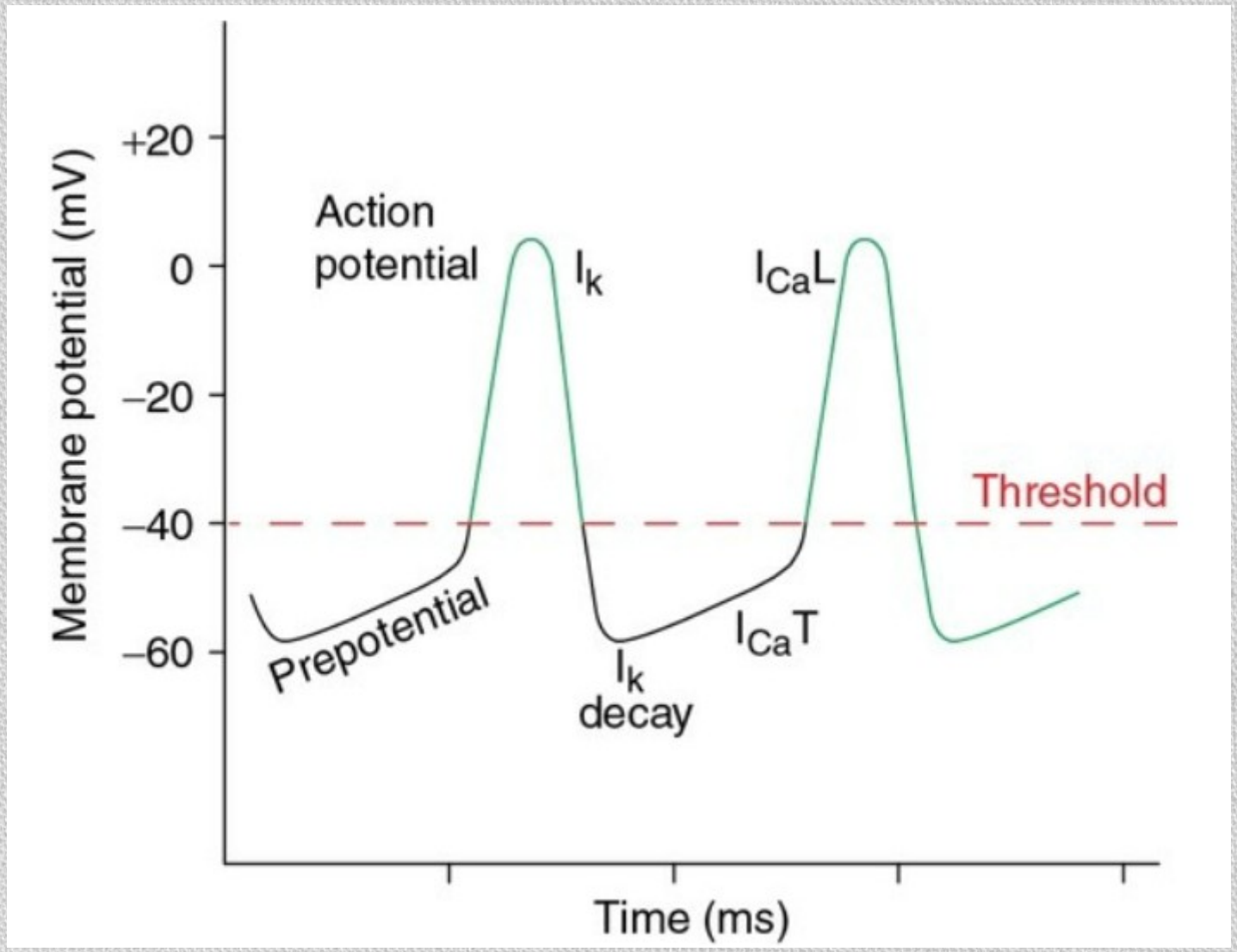
- At the end of depolarization, potassium channels open up and calcium channels close.
  - ✓ This causes K^{+} to diffuse out of the fibers resulting in rapid repolarization to -55 to -60 mV.
- Again, due to the unique feature of slow fibers of the

Electrical activity cont'd…

- ✓ The resting potential does not become stable but slow depolarization starts due to slow influx of Na^+ making initial part of prepotential.
  - o In this way, impulses are generated at regular intervals of time (autorhythmicity).

- Spontaneous rhythmical electrical impulses arise from the SA node and spread in all directions to
  - ✓ Cardiac muscles of atria,
  - ✓ Interatrial tract to left atrium and
  - ✓ Internodal tracts to AV node

Electrical activity cont'd…



Electrical activity cont'd…

- SA node is richly innervated by parasympathetic fibers from the right vagus.
- Normal activity of vagus liberates acetylcholine from its nerve endings which increases the permeability of SA nodal fibers for potassium producing hyperpolarization (due to rapid efflux of K^+).
  - ✓ This hyperpolarization slows the firing rate of SA node from its automatic rate of 90–120 impulses/min to the actual heart rate of about 72 beats/min.

Electrical activity cont'd…

- *Mechanism of action:*

  - ✓ This action of Ach is mediated by M2 receptors via βγ subunit of G protein, which opens the special set of K^+ channels and slows the depolarizing effect of Na^+ channels (I_h).

  - ✓ Activation of M2 receptors also decreases cyclic adenosine 3'5' monophosphate in the pacemaker cells and slows the Ca^{2+} channels opening, thus decreasing the firing rate.

    - o Decrease in the rate of transmission of impulses

Electrical activity cont'd…

- Strong parasympathetic stimulation may even completely block the transmission and ventricles may stop beating for 4–10 s.

- If it happens, Purkinje system initiates the rhythm causing ventricular contraction at a rate of 15–40/min.

  ✓ This phenomenon is called *vagal escape.*

- Stimulation of sympathetic nerves causes release of norepinephrine at the nerve endings.

  ✓ Probably this increases permeability of cardiac muscle fibers to calcium by opening up 'L calcium

Electrical activity cont'd…

- ✓ This increases the rate of sinus rhythm, and rate of conduction of impulse as well as excitability in all the portions of the heart.
- ✓ Force of contraction of atria and ventricles also increases greatly.

- *Mechanism of action:*

- ✓ Norepinephrine released acts by binding to β_1 receptors on the nodal tissue and increases intracellular cAMP, which facilitates the opening of long-lasting Ca^{2+} channels.

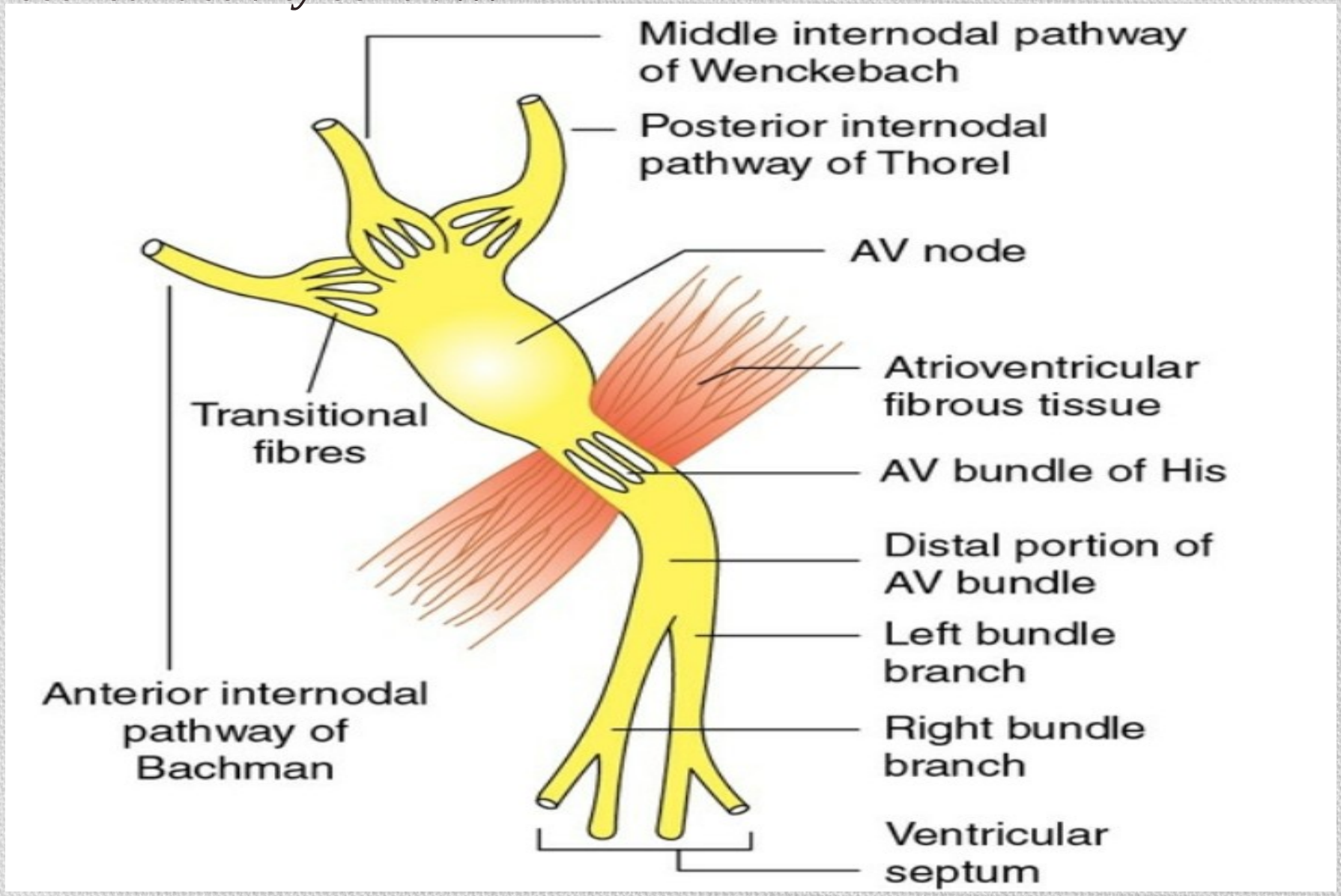
ii. Internodal conduction pathway.

- It transmit pacemaker potential generate from SA node to next structure.
- It has to types:
  - ✓ *Interatrial tract (Bachman's bundle)* is a band of specialized muscle fibers that run from SA node to left atrium.
    - o It causes simultaneous depolarization of the atria, since the velocity of conduction of impulse in this tract is faster than the rest of the atrial muscles.

Electrical activity cont'd…

- *Anterior internodal pathway of Bachman* leaves the anterior end of SA node and passes anterior to the superior vena cava opening.
  - It then descends on the atrial septum and ends in the AV node.
- *Middle internodal pathway of Wenckebach* leaves the posterior end of SA node and passes posterior to superior vena cava opening.
  - It then descends on the atrial septum to end in the AV node.

Electrical activity cont'd…



iii. Atrioventricular (AV) node.

- The AV node is strategically located just beneath the endocardium on the right side of lower part of atrial septum, near the tricuspid valve.

  ✓ It is located at the base of right atrium.

- It is stimulated by the excitation wave that travels through internodal tracts and atrial myocardium.

- From it, the cardiac impulse is conducted to ventricles by the AV bundle.

  - *The AV node* serves as the only pathway through

Electrical activity cont'd…

- If there is destruction of the AV node, then atria and ventricles beat independent of one another, i.e. atria at the rate of 72 beats/min and ventricles at a slower rate (30–40 beats/min).
  - ✓ There is a complete dissociation of atrial and ventricular beating and is called idioventricular rhythm.
  - The physiological advantage of the AV nodal delay – allows full ventricular filling.
- Both SA node and AV node are richly supplied by the sympathetic as well as parasympathetic nerves.

iv. AV bundle or the bundle of His .

- The AV bundle arises from the AV node, descends through the fibrous skeleton of the heart separating the atria from the ventricles and enters the interventricular septum.
  - ✓ It divides into right bundle branch (RBB) for right ventricle and left bundle branch (LBB) for the left ventricle.

v. The bundle branches

- The AV bundle is the only connecting tissue between atria and ventricles.
- The branches break up and become continuous with the plexus of Purkinje fibres.
- It travel down the septum toward the apex.

Electrical activity cont'd…

- ✓ And then reverse direction, traveling back toward the atria along the outer ventricle walls.

- This route of conduction of the impulse facilitates ejection of blood from the ventricles.

vi. Purkinje fibers

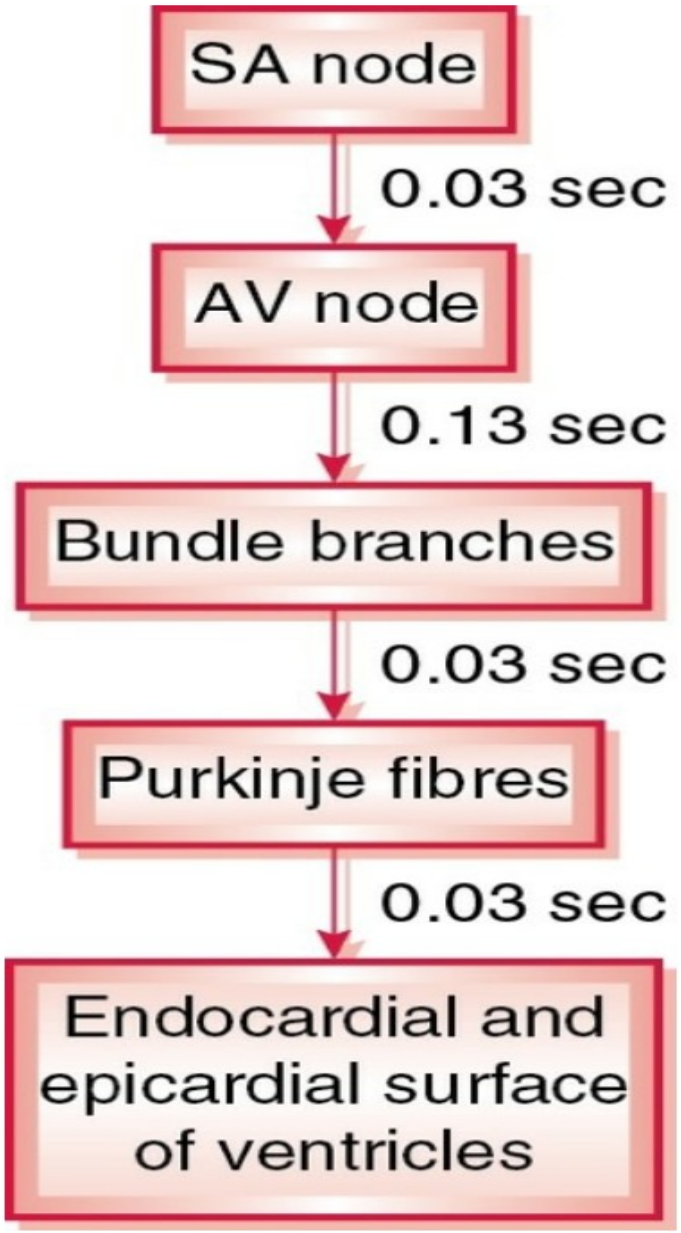
- It extend from the bundle branches.

- ✓ Terminate on the true cardiac muscle cells of the ventricles.

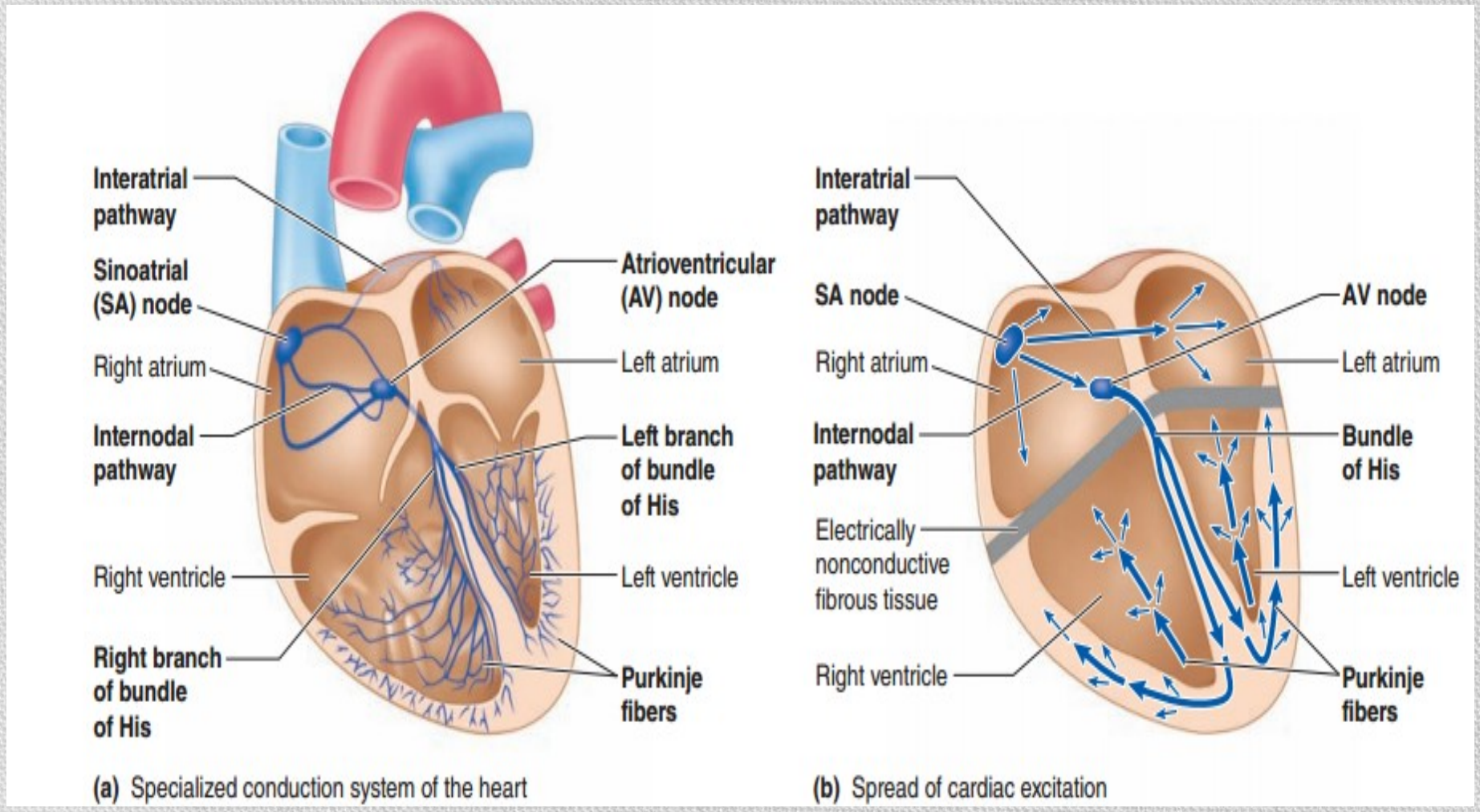
- ✓ It is very rapid and results in the functional

Electrical activity cont'd…

- These are spread out deep to the endocardium and reach all parts of the ventricles, including the bases of papillary muscles.
- Thus, total time required for conduction from SA node to endocardial surface is 0.22 s.



Electrical activity cont'd…



ELECTROPHYSIOLOGY OF THE HEART

- The action potential generated in the ventricular muscle –
  - ✓ The resting membrane potential is stable.
  - ✓ The slope of the depolarization phase is much steeper.
  - ✓ There is a lengthy plateau phase – approximately 300 msec.

Electrophysiology cont'd…

Electrical potentials in cardiac muscle

- The resting membrane potential (RMP) of a normal cardiac muscle fiber is -85 to -95 mV.

- The cardiac muscle being an excitable tissue produces an action potential *(electrical phenomenon)* when stimulated and responds by contracting *(mechanical phenomenon).*

  - ✓ When stimulated, each cardiac muscle fiber shows an electrical activity known as propagated action potential.

- The action potential recorded from a single cardiac

Electrophysiology cont'd…

i. Phase 0: Rapid depolarization.

- The phase 0 (upstroke) is characterized by the depolarization which proceeds rapidly, an overshoot is present, as in skeletal muscle and nerve.
- In mammalian heart, depolarization lasts about 2 ms.
- In this phase, amplitude of potential reaches up to +20 to +30 mV.
- *Ionic basis.*
  - ✓ It is due to the rapid opening of voltage-gated Na^+

Electrophysiology cont'd…

Phase 1: Initial rapid repolarization.

- Rapid depolarization is followed by a very short-lived slight rapid repolarization.
- The membrane potential reaches from +30 mV to -10 mV during this phase.
- *Ionic basis.*
  - ✓ It is due to closure of Na^+ channels and opening of fast K^+ channels resulting in transient outward

Electrophysiology cont'd…

Phase 2: Plateau.

- During plateau phase, the cardiac muscle fiber remains in the depolarized state.
- The plateau lasts for about 100–200 ms.
- This plateau in action potential explains the 5–15 times longer contraction time of the cardiac muscle as compared to the skeletal muscle.
- *Ionic basis*.
  - ✓ Very slow repolarization during the plateau phase is due to:

Electrophysiology cont'd…

- Closure of a distinct set of K+ channels called the inward-rectifying K^+ channels.

Phase 3: Repolarization.

- During this phase, complete repolarization occurs and the membrane potential falls to the approximate resting value of -80 mV.
  - ✓ This phase lasts for about 50 ms.
- *Ionic basis.*
  - ✓ The slow repolarization results from closing of Ca^{2+}

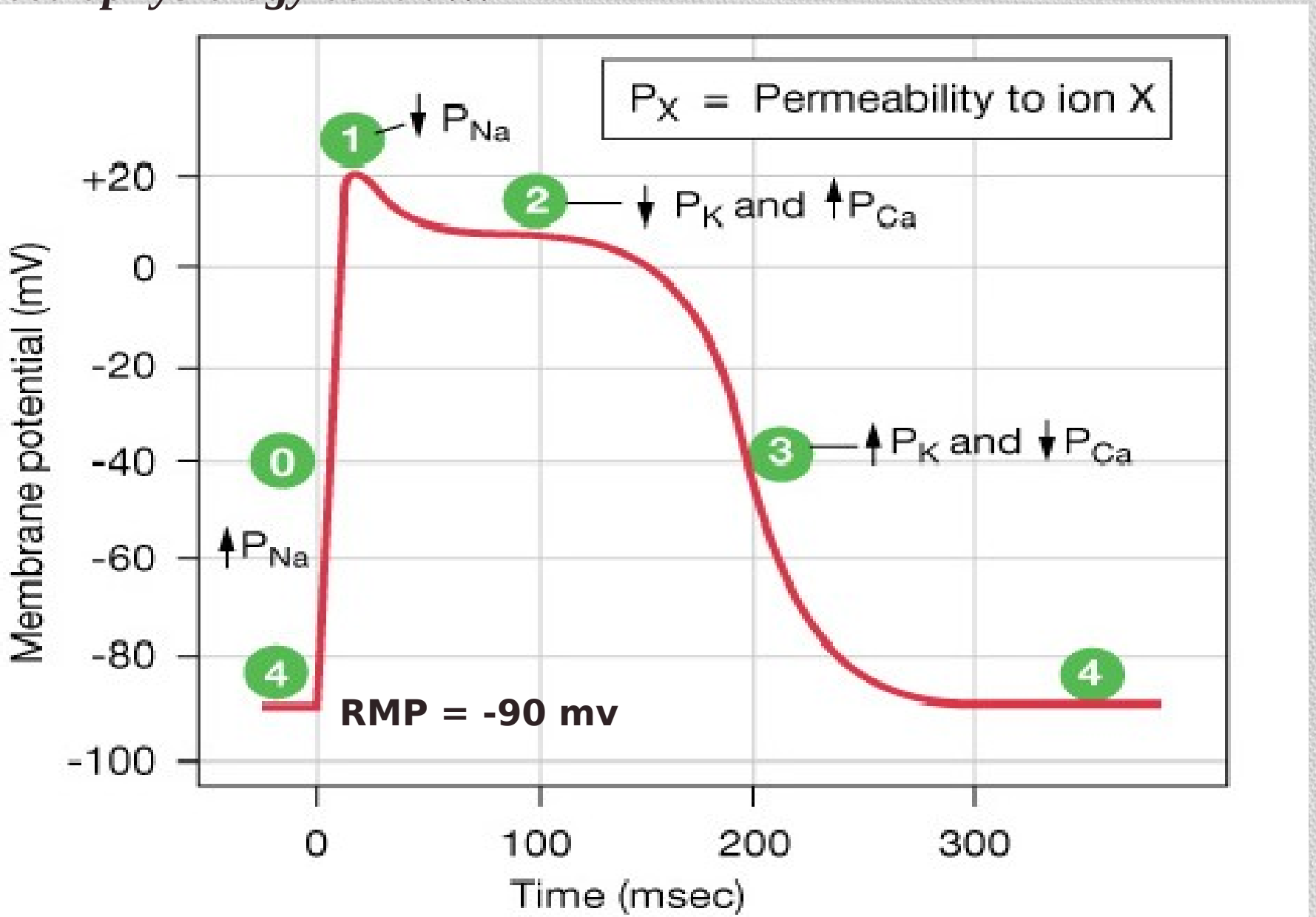
Electrophysiology cont'd…

- *Delayed outward rectifying K^+ channels,* which are voltage-gated and are activated slowly and
- *Ca^{2+}*-activated channels which are activated by the elevated sarcoplasmic Ca^{2+} levels.

Phase 4: Resting potential.

- In this phase of RMP (also called as polarized state), the potential is maintained at -90 mV.
- *Ionic basis.*
  - ✓ The RMP is maintained by a resting K^+ current, the largest contributor to which is the inward rectifying

Electrophysiology cont'd…



Refractory period

- Refractory period refers to the period following action potential during which the cardiac muscle does not respond to a stimulus.
- Cardiac muscle has a long refractory period (250–300 ms in ventricles and about 150 ms in atria).
- It is of two types as follows.

1. Absolute refractory period (ARP).

   ✓ During this period the cardiac muscle does not show any response at all.

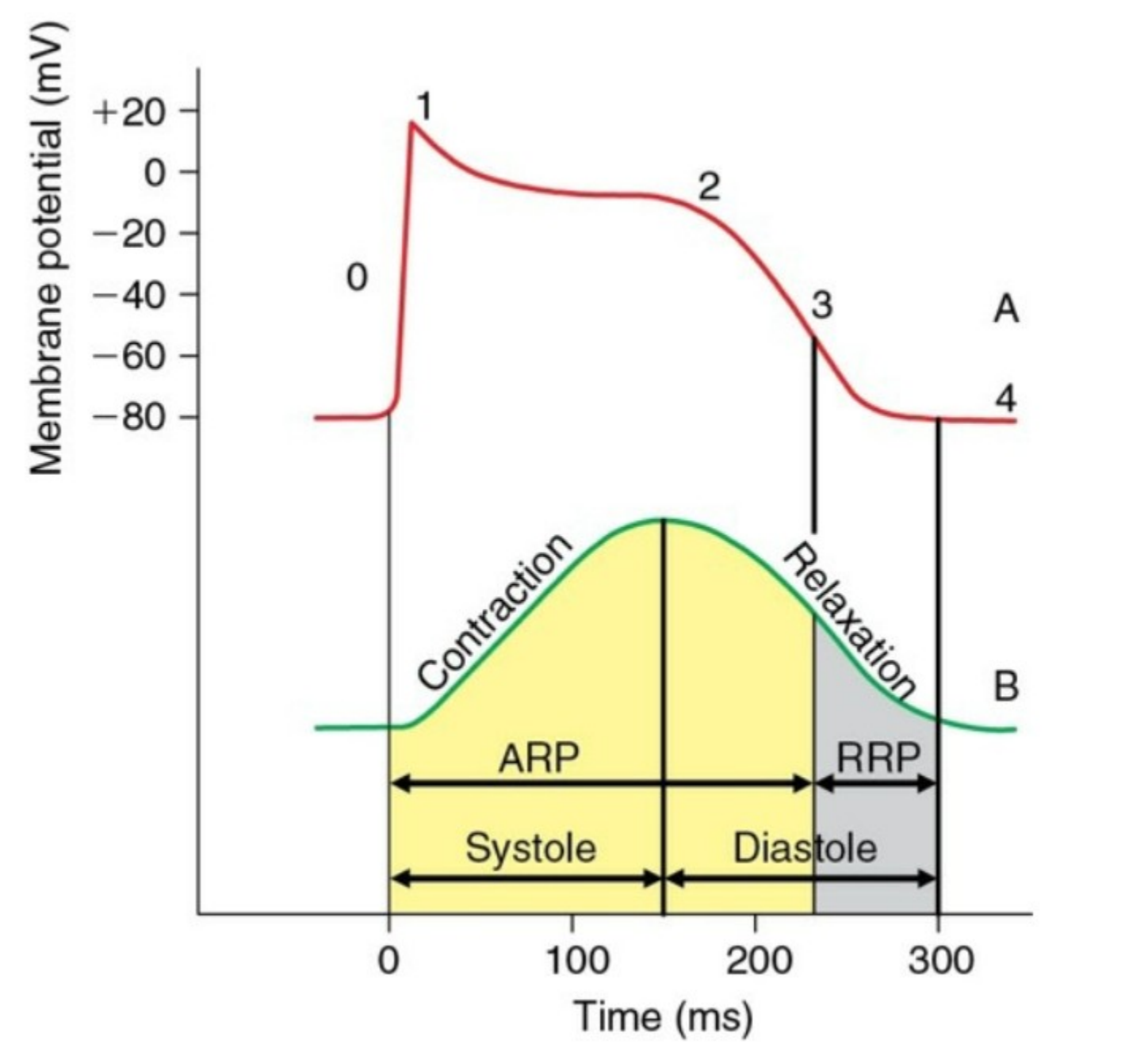
Electrophysiology cont'd…

- ✓ It extends from phase 0 to half of phase 3 of action potential, i.e. until the membrane potential reaches approximately 50 mV during repolarization.
- ✓ Normal duration of ARP in ventricles is about 180–200 ms.

2. Relative refractory period (RRP).

- ✓ During this period the muscle shows response if the strength of stimulus is increased to maximum.
- ✓ It extends from second half of the phase 3 to phase 4 of the action potential. Normal duration of RRP in

Electrophysiology cont'd…



Significance of long refractory period in cardiac muscle.

- The cardiac muscle is refractory to any stimulus during the contraction phase (systole), therefore, the complete summation of contractions and thus tetanus cannot be produced in the cardiac muscle.
- This property is very useful.
- Since the heart has to function as a pump, it must relax, get filled up with blood and then contract to pump out the blood.
- A tetanized heart would be useless as a pump.

Excitation–contraction coupling phenomenon in cardiac muscles

- The events which link the electrical phenomenon with mechanical phenomenon constitute the *excitation–contraction coupling phenomenon.*

- Excitation–contraction coupling refers to the sequence of events by which an excited plasma membrane of a muscle fiber leads to cross-bridge activity by increasing sarcoplasmic calcium concentration.

- The sequence of events during excitation–contraction coupling in the cardiac muscles is similar to those observed in a skeletal muscle.

ECC cont'd…

- With the following exception:

  - ✓ In cardiac muscle, the AP originates spontaneously in the heart's pacemaker cells and spreads into the contractile cells through gap junctions.

  - ✓ In cardiac contractile cells, the slow Ca^{2+} channels lie primarily in the transverse (T) tubules.

    - These voltage-gated channels open during an AP.

  - ✓ In cardiac muscles (as against that in skeletal muscles), extra Ca^{2+} ions diffuse into the sarcoplasm from T-tubules without which the

ECC cont'd…

- ✓ This entering Ca^{2+} triggers the opening of nearby Ca^{2+}-release channels in the adjacent lateral sacs of the SR.
  - o Termed Ca^{2+}-induced Ca^{2+} release.
- ✓ Because of this, strength of cardiac muscle contraction depends to a great extent on Ca^{2+} concentration in ECF.
  - o Whereas, skeletal muscle contraction is hardly affected by the calcium concentration in ECF.
- ✓ 90% of the Ca^{2+} needed for muscle contraction

ECC cont'd…

- ✓ Cardiac contraction lasts about three times longer than the contraction of a single skeletal muscle fiber.
  - o 300 msec compared to 100 msec.
- ✓ Removal of Ca^{2+} from the cytosol by energy-dependent mechanisms in both the plasma membrane and the SR restores the blocking action of troponin and tropomyosin.
  - o So contraction ceases and the heart muscle relaxes.

Relaxation of cardiac muscle

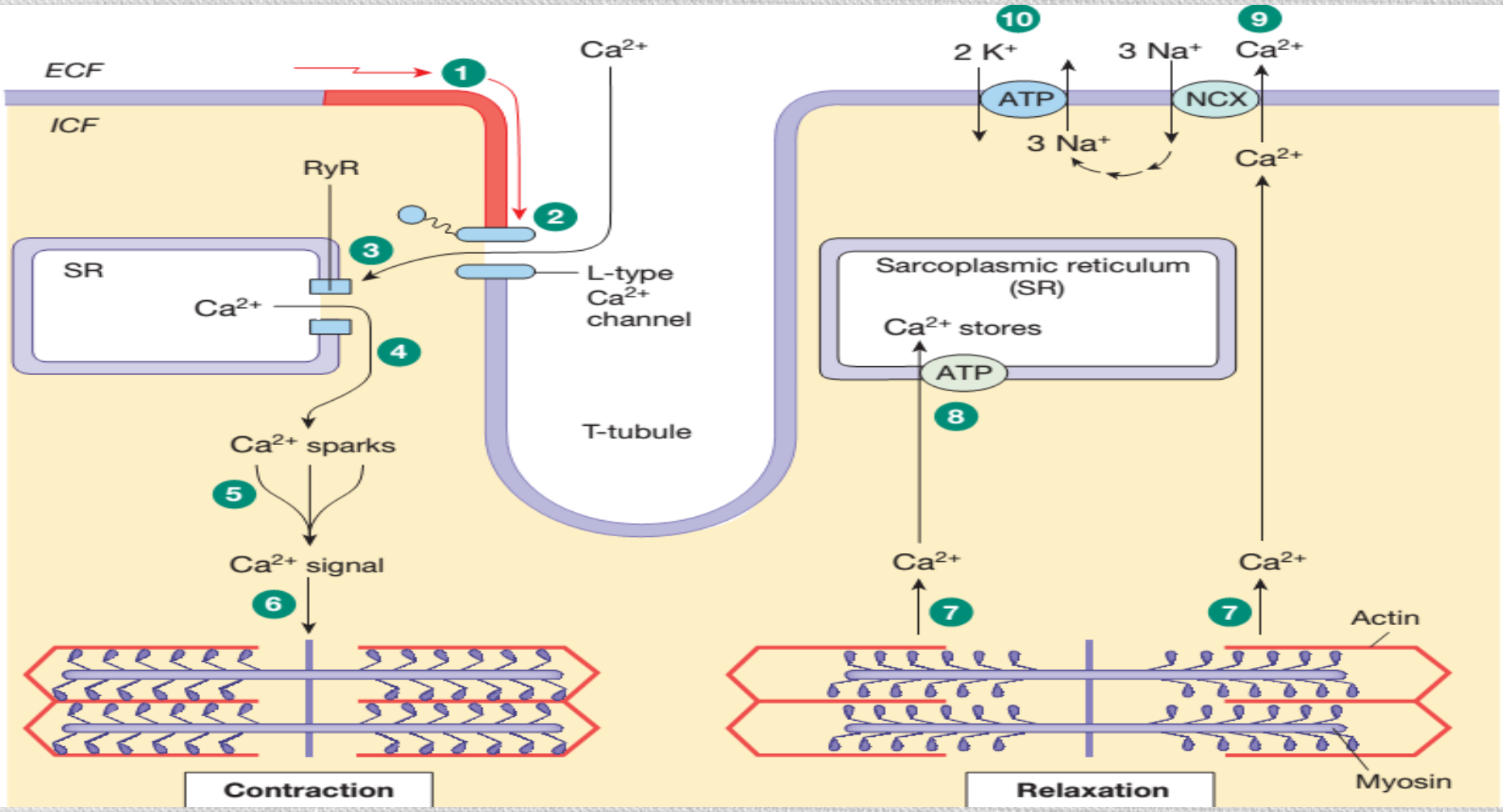
- Relaxation of cardiac muscle occurs when levels of Ca^{2+} ions fall in the cardiac muscle fibers.

- During diastole, the Ca^{2+} ions are extruded out of the cardiac muscle fiber by a carrier system operating at the sarcolemma in which two Na^{+} ions are exchanged for each Ca^{2+} ion extruded.

  - ✓ Thus, the rate of Ca^{2+} ion extrusion depends on the gradient of Na^{+} created by Na^{+}-K^{+} ATPase.

- Inhibition of this secondary active transport of Ca^{2+} ions, e.g. by digitalis or other cardiac glycosides raises the intracellular Ca^{2+} concentration and thereby

ECC cont'd…


ECF
ICF
RyR
SR
Ca^{2+}
Ca^{2+}
L-type Ca^{2+} channel
T-tubule
Ca^{2+} sparks
Ca^{2+} signal
1
2
3
4
5
6
Contraction
10
2 K^+
3 Na^+
ATP
NCX
3 Na^+
9
Ca^{2+}
Ca^{2+}
Sarcoplasmic reticulum (SR)
Ca^{2+} stores
ATP
8
Ca^{2+}
Ca^{2+}
7
7
Actin
Myosin
Relaxation

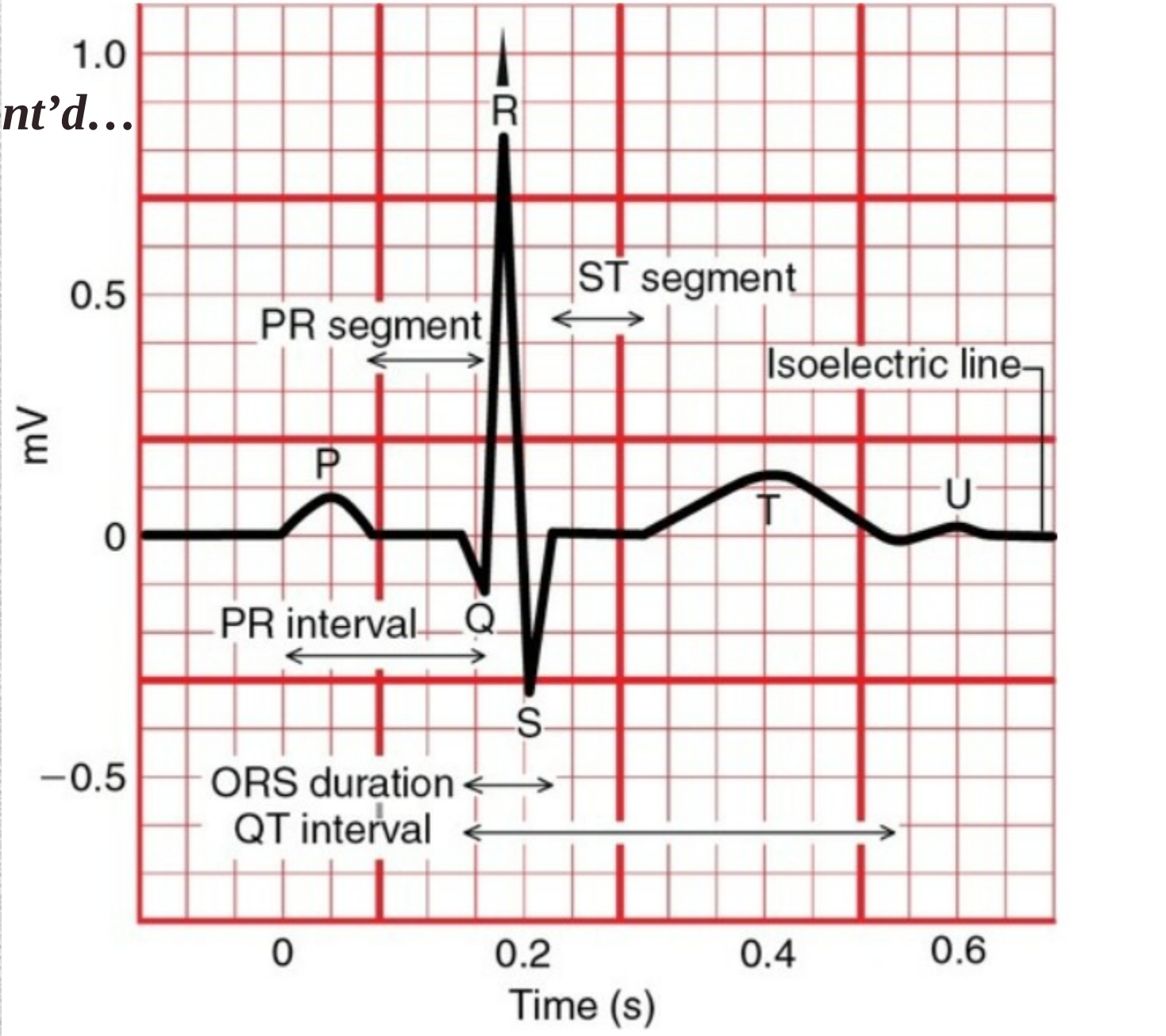
ELECTROCARDIOGRAPHY

- William Einthoven, a Dutch physiologist, originally developed the technique of electrocardiography.
  - ✓ He was awarded the Nobel prize in 1924 for his contribution and is called the father of modern electrocardiography.
- *Electrocardiography (ECG)* refers to extracellular recording of the summed-up electrical events of all the cardiac muscle fibers generated with each heart beat.
- Electrically, heart behaves as a *dipole,* i.e. a two-terminal battery in which the excited part (depolarized

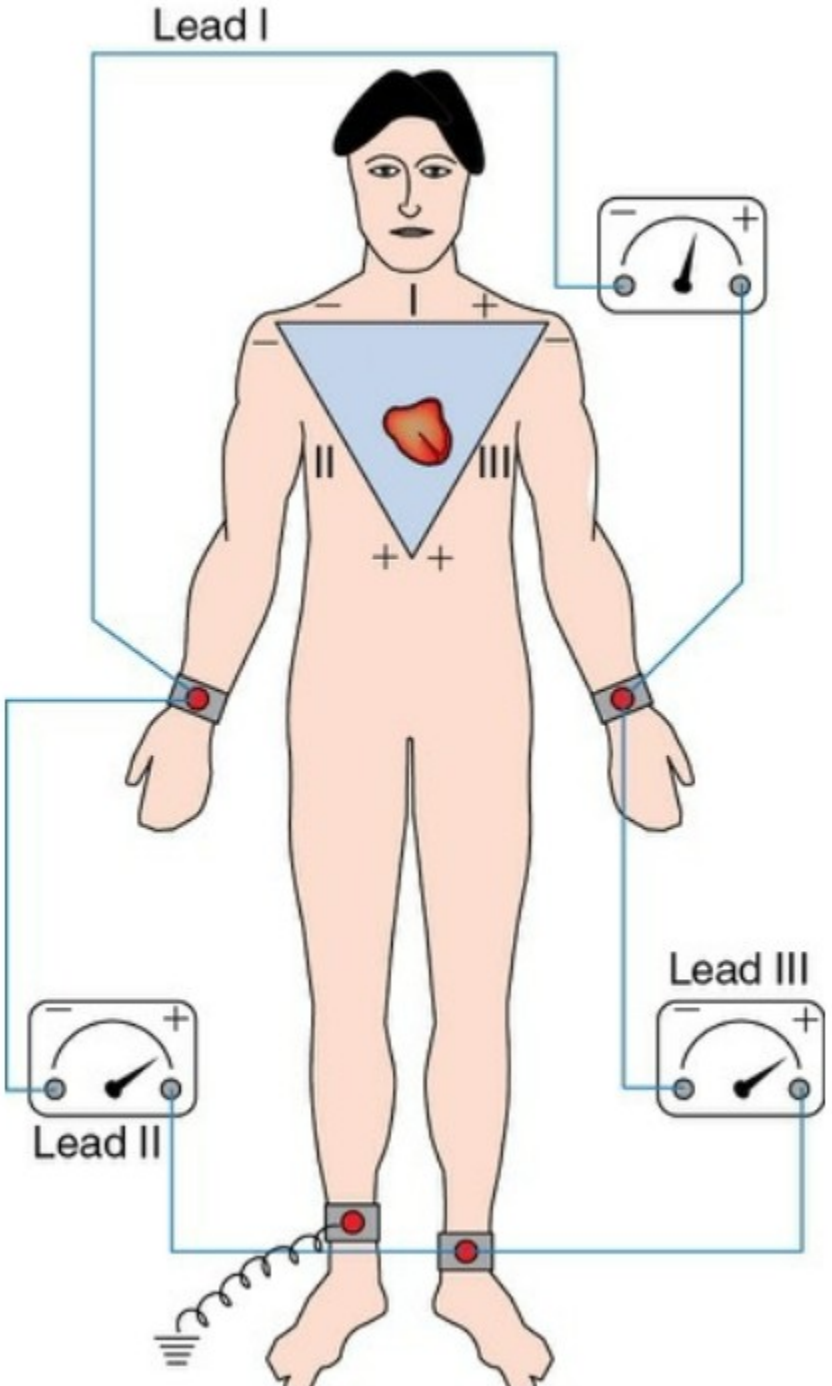
ECG cont'd…

- Thus, ECG is nothing but the surface recording of the potential difference between the two poles of the heart dipole at a given time.
- The record of the potential fluctuations during the cardiac cycle is called the *electrocardiography*.
- The machine used to record these potential fluctuations is called *electrocardiograph,* which is essentially a sensitive galvanometer.

ECG cont'd…


1.0
0.5
0
−0.5
mV
R
ST segment
PR segment
Isoelectric line
P
T
U
PR interval
Q
S
QRS duration
QT interval
0
0.2
0.4
0.6
Time (s)

ECG cont'd…



ECG cont'd…

- The ECG provides information concerning:-
  - ✓ Relative size of heart chambers
  - ✓ Various disturbances of rhythm and electrical conduction
  - ✓ Extent and location of ischemic damage to the myocardium
  - ✓ Effects of altered electrolyte concentrations
  - ✓ Influence of certain drugs.

CARDIAC CYCLE

- The period of time from beginning of one heartbeat to beginning of the next.
- It consists of two phases –
  - ✓ Systole – chambers contract and eject the blood.
  - ✓ Diastole – chambers relax allowing blood to fill them.
- Atria and ventricles undergo phases of systole and diastole.

Cardiac cycle cont'd…

1. *Ventricular filling.*

   - ✓ When the ventricle has completely relaxed and pressure in the ventricle is lower than pressure in the atrium,
     - o The AV valve opens.
   - ✓ During the entire diastolic filling period, the semilunar valve is closed.
   - ✓ Occurs during ventricular diastole.
   - ✓ Three phases –

Cardiac cycle cont'd…

a. *The initial phase of filling* – rapid – occurred passively.

b. *The second phase of filling (diastasis)* – slower and occurred passively.

c. *The third phase of ventricular filling* results from atrial contraction – active process – 25% of the blood.

- The volume of blood in the ventricles at the end of the filling period – end-diastolic volume (EDV).

Cardiac cycle cont'd…

2. *Isovolumetric contraction.*

- ✓ Occurs during ventricular systole.
- ✓ When the ventricular myocardium begins to contract.
  - o Ventricular pressure is almost instantly greater than atrial pressure.
- ✓ The AV valve closes – results in the first heart sound ("lub").
- ✓ Neither filling of the ventricle nor ejection of blood

Cardiac cycle cont'd…

c. Ejection phase

- ✓ Eventually, the build-up of ventricular pressure overtakes the aortic pressure and the aortic valve is pushed open.
  - o At this point, ejection, or ventricular emptying, takes place.
- ✓ The chamber does not eject all of the blood within it.
- ✓ Some blood remains in the ventricle following

Cardiac cycle cont'd…

- ✓ The volume of blood pumped out of each ventricle per beat – the stroke volume (SV).
  - o About 70 ml in a healthy adult heart at rest.

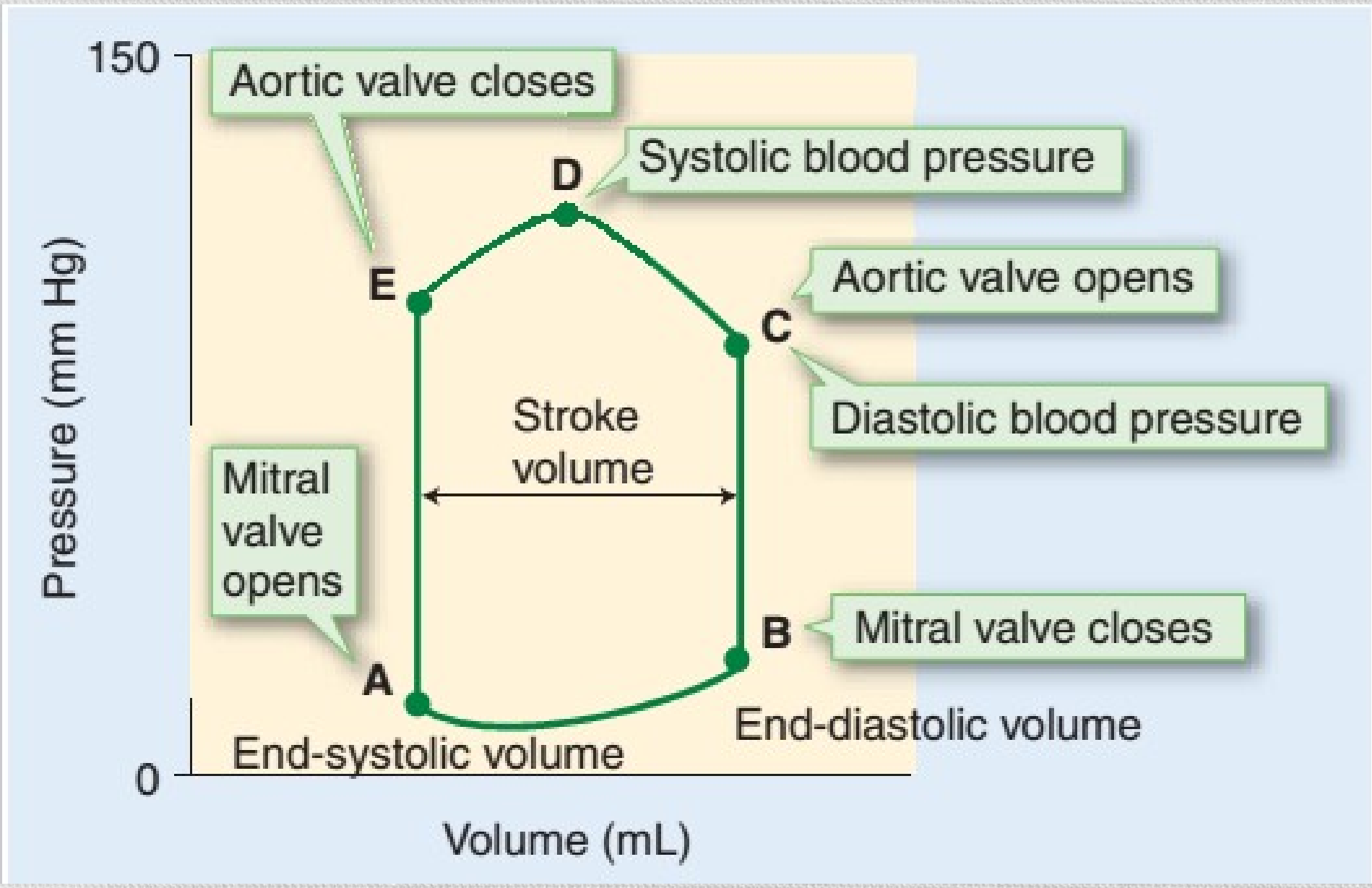
d. Isovolumetric relaxation

- ✓ After systole, the ventricles abruptly relax.
- ✓ The blood in the distended artery is immediately pushed back toward the ventricle down the pressure gradient.
- ✓ The backward movement of blood snaps the aortic

Cardiac cycle cont'd…

- ✓ Atrial pressure is close to zero, the AV valve remains closed.
- ✓ During this phase of isovolumetric relaxation, both valves leading into and out of the chamber are closed.
- ✓ As with isovolumetric contraction, no change takes place in the blood volume of the ventricle during this phase of isovolumetric relaxation.

Cont'd…


150
Aortic valve closes
D
Systolic blood pressure
E
Aortic valve opens
C
Diastolic blood pressure
Stroke volume
Mitral valve opens
B
Mitral valve closes
A
End-diastolic volume
End-systolic volume
0
Pressure (mm Hg)
Volume (mL)

END-DIASTOLIC VOLUME, END-SYSTOLIC VOLUME, AND STROKE VOLUME OUTPUT.

- **EDV:** the volume of blood in the ventricle at the end of ventricular diastole.
  - ✓ During diastole, normal filling of the ventricles increases the volume of each ventricle to about 120 to 130 milliliters.
  - ✓ When the heart contracts strongly, the EDV can be decreased to as little as 10 to 20 milliliters.
  - ✓ When large amounts of blood flow into the

EDV, ESV and SV cont'd…

- ✓ Then, as the ventricles empty during systole, the volume decreases about 70 milliliters, which is called the stroke volume output.

- **SV:** the volume of blood ejected from the ventricle during ventricular systole.

- ✓ By both increasing the end-diastolic volume and decreasing the end-systolic volume, the stroke volume output can be increased to more than double normal.

  - SV = VEDV – VESV = 70 – 80 ml

EDV, ESV and SV cont'd…

- **ESV:** the volume of blood that remains in the ventricle at the end of ventricular systole.
- **Ejection fraction:** the blood proportion that enters the ventricles during diastole to the amount ejected.
  - ✓ Is the fraction of the EDV that is ejected, usually equal to about 60%.
  - ✓ $EF = {}^{SV}/_{EDV}\ ^{x100} = 60\% - 70\%$.
- **Cardiac output:** the volume of blood ejected from the heart per minute.

EDV, ESV and SV cont'd…

- **The Cardiac index:** is an assessment of the cardiac output value based on the patient's size.

  - ✓ To find the cardiac index, divide the cardiac output by the person's body surface area (BSA).

  - ✓ The normal range for CI is 2.5 to 4 L/min/m^2.

CARDIAC OUTPUT

- The volume of blood ejected from the heart per minute.
- It is the amount of blood pumped by each ventricle in one minute.
- Is the product of heart rate (HR) and stroke volume (SV)
  - ✓ CO = SV x HR = 5 - 6 L/min.
- HR – number of heart beats per minute.

CO cont'd…

Factors Affecting Stroke Volume

- *Preload* – degree of ventricular stretch by the amount of blood enter the ventricle during relaxation (EDV).
- *Contractility* – contractile force of cardiac cell due to factors other than EDV.
- *Afterload* – pressure exerted by blood in the large arteries leaving the heart (MAP).

VARIATIONS IN CARDIAC OUTPUT

Physiological causes of variations in cardiac output

- ***Age.***
  - ✓ Because of less body surface area, children have more cardiac index than adults.
- ***Sex.***
  - ✓ Since the body surface area is less in females, they have more cardiac index than the males.
- ***Diurnal variation.***

CO cont'd…

- ✓ In the early morning, cardiac output is low which increases in the day time depending upon the basal condition of the individual.

- ***Environmental temperature.***

  - ✓ Moderate change in environmental temperature does not cause any change in cardiac output.

  - ✓ A high environmental temperature is associated with an increase in the cardiac output.

- ***Anxiety and excitement***

  - ✓ They are reported to increase the cardiac output by

CO cont'd…

- ***Eating***
  - ✓ It is associated with an increase in cardiac output approximately by 30%.
- ***Exercise***
  - ✓ It may increase the cardiac output up to 700% depending upon the vigorousness of exercise.
- ***Pregnancy.***
  - ✓ An increase in cardiac output to the tune of 45–60% is reported during the later months of the

CO cont'd…

- ***High altitude.***
  - ✓ The cardiac output is increased at high altitude due to release of adrenaline as a consequence to hypoxia.
- ***Posture change.***
  - ✓ Sitting or standing from lying down position may decrease the cardiac output by 20–30% because of pooling of blood in lower limbs.

CARDIAC OUTPUT CONTROL MECHANISMS

- The cardiac output is regulated by two mechanisms:
  - ✓ Intrinsic and
  - ✓ Extrinsic.

Intrinsic autoregulation (Frank–Starling mechanism)

- The force of contraction of cardiac muscle fibers like that of skeletal muscle fibers depends upon its preload.
- The preload determines the initial length (resting length) of the muscle fibers

CO cont'd…

- According to *Frank–Starling law* of heart, 'within physiological limits' the force of contraction of *cardiac muscle* is proportionate to the initial length of muscle fibers.
- In the heart, end-diastolic volume forms the preload.
- Thus, the stretching of the cardiac muscle fibers to increase their initial length depends upon the end-diastolic volume.
- Therefore, precisely, the Frank–Starling law of heart can be stated as, within physiological limits the force

CO cont'd…

- Since, in this intrinsic regulation mechanism, cardiac muscle fibers are stretched to increase their initial length, it is also termed as *heterometric mechanism.*

- The relationship between ventricular stroke volume and end-diastolic volume is called the *Frank–Starling curve.*

Factors affecting end-diastolic volume

- The end-diastolic volume refers to the *venous return* to the heart during diastole.
  - ✓ Therefore, the factors that normally operate to regulate end-diastolic volume, i.e. the degree to which cardiac muscle is stretched are the same which affect the venous return.
- Up to physiological limits the cardiac output is directly proportional to the venous return.
  - ✓ Thus, over any significant period of time, venous return must equal cardiac output

CO cont'd…

- For individual at rest, the cardiac output and venous return are approximately 5 L/min.

- A complicated interaction of neural, humoural and physical factors determine the flow rate.

- Factors affecting venous return are:

1. Respiratory pump.

- Normally the intrapleural (intrathoracic) pressure at the end of expiration is

  ✓ about -3 mmHg

CO cont'd…

- During inspiration, the intrathoracic pressure becomes more negative (about -5 mmHg):
  - ✓ *Due to which the diameter of inferior vena cava is increased and pressure inside it is reduced; and there occurs descent of diaphragm which increases the intra-abdominal pressure.*
    - o The decreased pressure inside the inferior vena cava coupled with increased intraabdominal pressure during inspiration results in increased flow of blood into the right atrium.
    - o This mechanism of increased blood flow during

CO cont'd…

- This respiratory pump operates strongly in forced respiration and in severe muscular exercise increasing the venous return.

2. Cardiac pump.

- The cardiac pump influences the venous return by two kinds of forces: 'vis-a-tergo' and 'vis-a-fronte'.

- ***Vis-a-tergo*** refers to the forward push from behind, i.e. the propelling force which pushes the blood from veins into the right atrium.

  ✓ Vis-a-tergo results from the myocardial contraction

CO cont'd…

- ***Vis-a-fronte*** refers to the suction force acting from the front which basically pulls the blood from the great veins into the right atrium.

- This suction force is created by ventricular contraction and has following two components:

  ✓ *Ventricular systolic suction* results from pulling down of the fibrous AV ring causing enlargement of atrial lumen and thus decreasing the intra-atrial pressure which sucks blood from the inferior vena cava and superior vena cava.

CO cont'd…

- ✓ *Ventricular diastolic suction* results from the opening of AV valves allowing rapid flow of blood from atria to ventricles.
  - o The sudden decrease in atrial pressure in turn sucks blood from the great veins.
  - o So, a decrease in ventricular compliance, i.e. an increase in the ventricular stiffness produced by myocardial infarction, infiltrative diseases and other abnormalities will decrease the venous return.

CO cont'd…

3. Muscle pump.

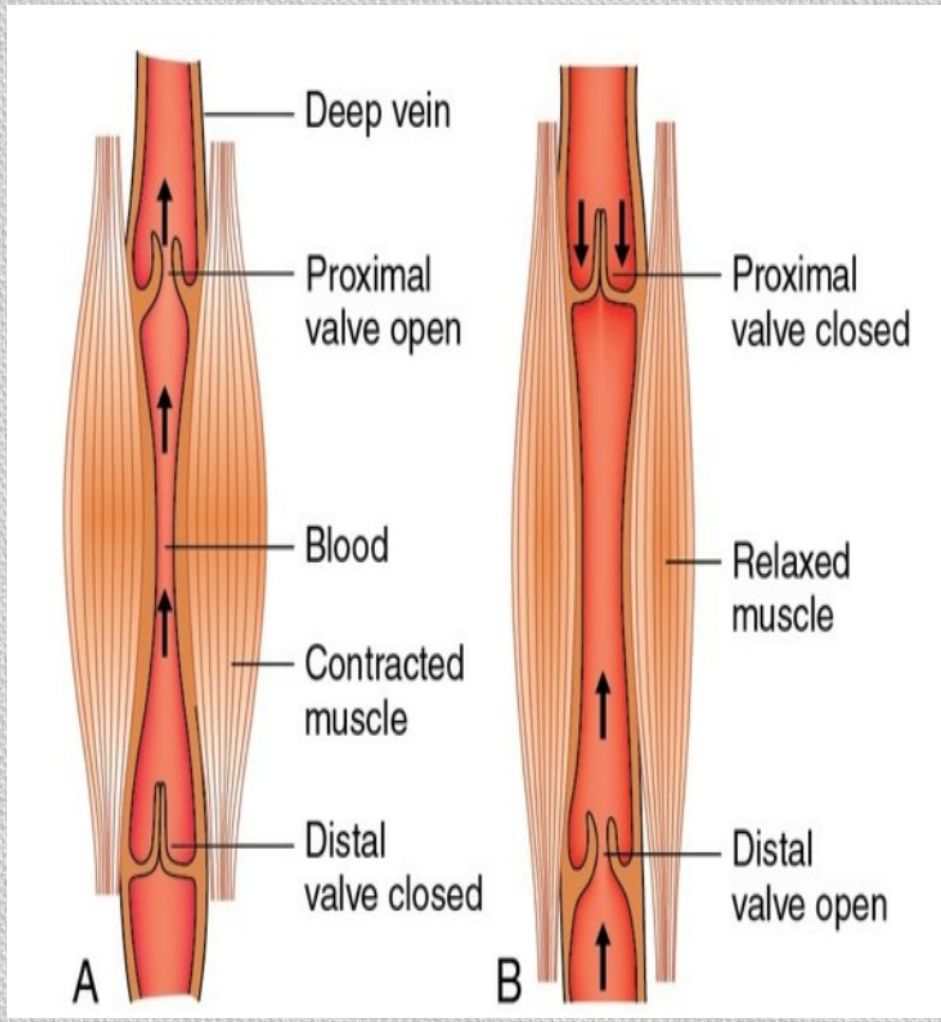
- The muscle pump mechanism is responsible for flow of blood from the veins of the limbs to the heart.
  - ✓ Therefore, increased pumping action of skeletal muscles will increase the venous return and decreased pumping of skeletal muscles will decrease the venous return.
- Two types of veins are present in the limbs:
  - ✓ Superficial and deep veins.

CO cont'd…

- Blood flows from the superficial veins into deep veins through communicating veins.
- Due to the presence of valves in the limb veins the blood flows in one direction, i.e. from periphery towards heart and not in reverse direction.
- *When the skeletal muscles contract*, the deep veins present in between the muscles are compressed and due to increased pressure the valve present proximal to the contracting muscle is opened up while the valve present on distal end is tightly closed and in this way the blood is propelled up towards the heart.

CO cont'd…

- So, due to back flow the proximal valve is closed and the distal valve is opened and blood is sucked up.
- *With rhythmic contractions of skeletal muscles* in this way, the blood is squeezed out of the limbs towards the heart.



CO cont'd…

4. Blood volume.

- The mean circulating filling pressure (MCFP) which is equivalent to mean systemic filling pressure (MSFP) refers to the equilibrated pressure measured everywhere as a result of stoppage of blood flow in systemic circulation when heart stops pumping.

- The level of MSFP influences the venous return.

  ✓ Greater the MSFP more the venous return and lower the MSFP lesser the venous return.

CO cont'd…

- The MCFP in turn depends upon the level of blood volume.
  - ✓ Thus, the increased blood volume increases the venous return and a decreased blood volume decreases the venous return.

5. Sympathetic discharge.

- On sympathetic stimulation, there occurs increase in the venous tone which decreases the capacity of the venous system (veins are capacitance vessels).

CO cont'd…

- At normal blood volume, a strong sympathetic stimulation raises the MCFP from 7 to 17 mmHg.
  - ✓ And inhibition of sympathetics decreases the MCFP from 7 to 4 mmHg (due to venous dilatation) and thus decreases the venous return.

6. Standing body position

- It is associated with a decreased venous return due to peripheral pooling of the blood.

7. Resistance to venous return.

CO cont'd…

- Normally, 2/3rd resistance to venous flow is offered by veins and 1/3rd by the arteries.
- Resistance decreases the venous return.
- The venous resistance is considered to be more important regarding venous return, as the veins being capacitance vessels, rise in the venous pressure is less effective to push the blood towards the heart.
- On the other hand, as with increased resistance in arterioles or small arteries, with little accumulation of blood in the arteries there is great increase in the pressure (30 times as compared to veins) which

CO cont'd…

Extrinsic regulation (autonomic neural mechanism)

- In this mechanism, stroke volume increases due to *increased myocardial contractility* without any increase in the initial muscle length.
  - ✓ Therefore, it is also called *homometric mechanism.*
- The homometric regulation is governed by autonomic neural mechanism as:

i. Sympathetic activity

- ✓ *Stimulation of the sympathetic nerves* to the heart

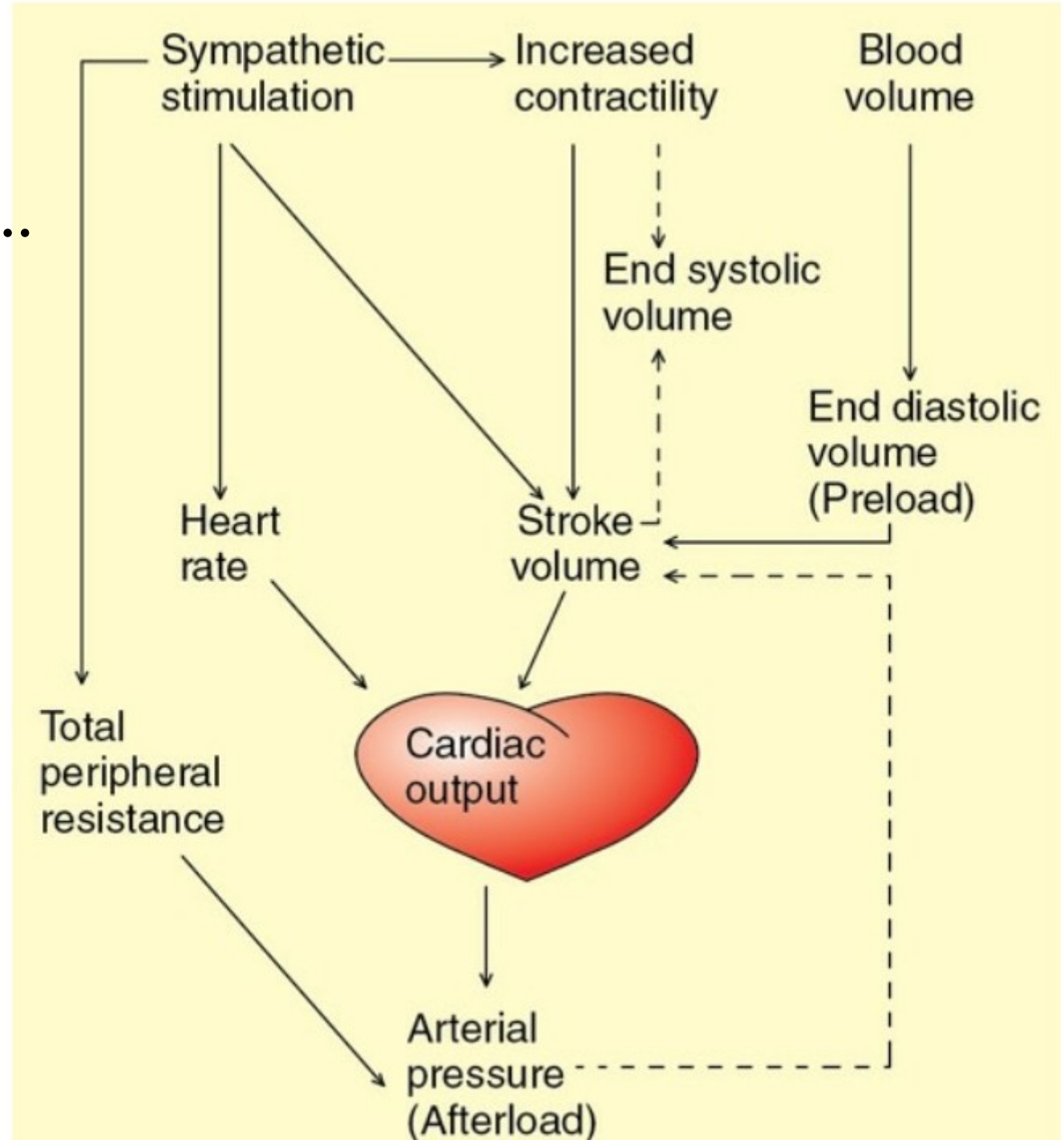
CO cont'd…

- ✓ The positive inotropic effect of the norepinephrine liberated at the sympathetic nerve endings is augmented by circulating norepinephrine.

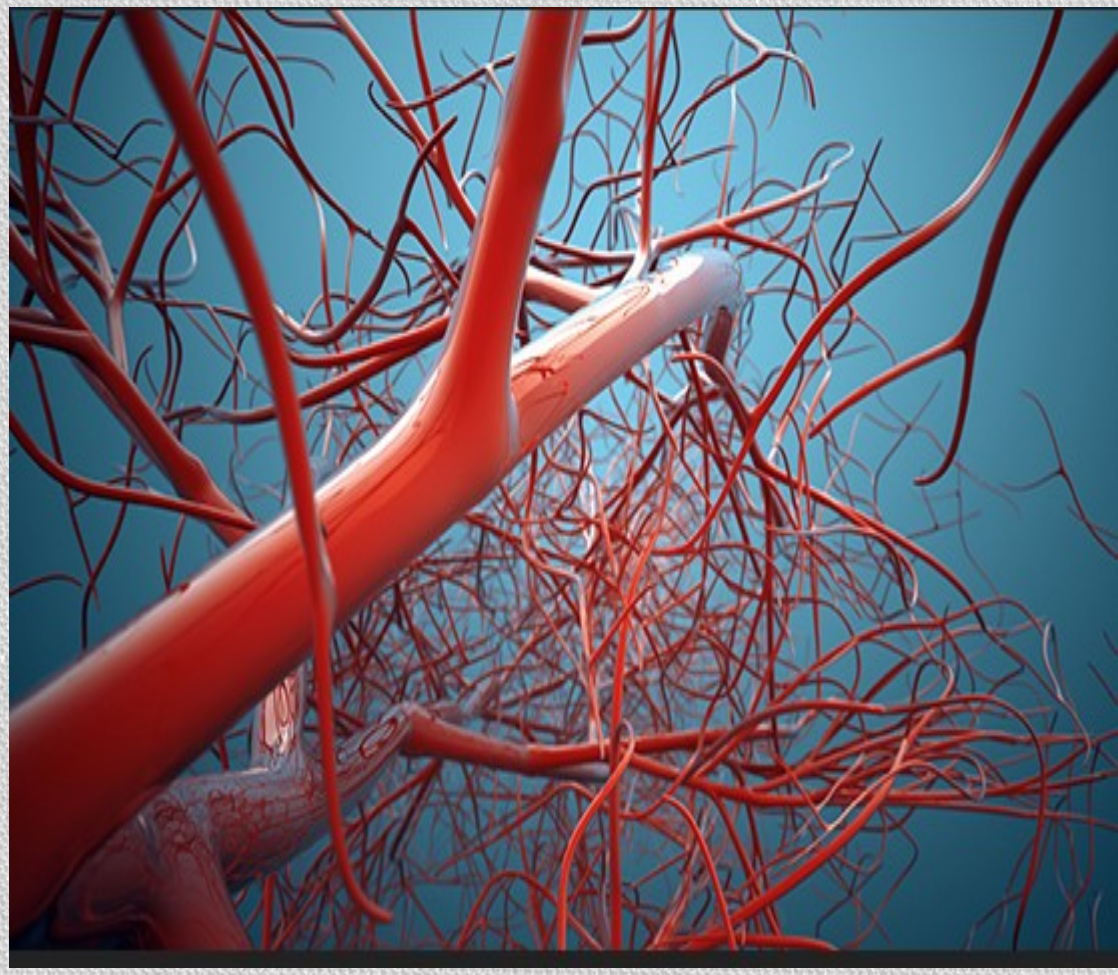
ii. Parasympathetic activity.

- ✓ There is a negative inotropic effect of parasympathetic (vagal) stimulation.
- ✓ This effect, however, is not much because vagal fibers are mainly distributed to the atria and not much to the ventricles.

CO cont'd…


Sympathetic stimulation
Increased contractility
Blood volume
End systolic volume
End diastolic volume (Preload)
Heart rate
Stroke volume
Total peripheral resistance
Cardiac output
Arterial pressure (Afterload)

PHYSIOLOGY OF VASCULAR SYSTEM



STRUCTURE OF BLOOD VESSELS

- Histologically, walls of most of the blood vessels except the capillaries consist of three coats.

- General structural characteristics of a large artery are:

1. Tunica intima.

- It is the innermost coat of the vessel wall.

- In large arteries, from inside-out, it consists of:

  - ✓ *Endothelial lining,* which is very smooth and silky, and consists of single layer of cells.

Blood vessels cont'd…

- It lies in contact with blood.

✓ *Basal lamina* is a thin layer of glycoprotein which lines the external aspect of the endothelium.

✓ *Subendothelial connective tissue* is a delicate layer of connective tissue which lies outside the basal lamina.

✓ *Internal elastic lamina* is a thin membrane formed by elastic fibres.

2. Tunica media.

Blood vessels cont'd…

- It consists of smooth muscles and elastic tissue.
- The ratio of these two tissues varies from vessel to vessel.
- On the outside, tunica media is limited by a membrane formed by elastic fibres called the *external elastic lamina.*

3. Tunica adventitia.

- It is the outermost coat of the vessel wall.
- It is made of connective tissue in which collagen fibres

Blood vessels cont'd…

- *Important points* to be noted are:
  - ✓ Fibrous elements in the intima and adventitia (mainly collagen) run longitudinally (i.e. along the length of the vessel).
  - ✓ Elastic tissue and smooth muscles forming tunica media run circularly.
  - ✓ Elastic fibres forming internal and external elastic laminae are often in the form of fenestrated sheets.

CLASSIFICATION OF BLOOD VESSELS

- The blood vessels in the adult human stretch for about 100,000 km through the internal body landscape!
- The vessel types vary in length, diameter, wall thickness, and tissue makeup.
  - ✓ The five main types of blood vessels are arteries, arterioles, capillaries, venules, and veins.

ARTERIAL SYSTEM

- They are vessels that are adapted for carrying blood away from the heart under relatively high pressure to other organs.
- They serve as rapid-transit passageways to the organs and as a pressure reservoir.
- In terms of relative size and function, arteries can be divided into :-

  i. Elastic arteries,

  ii. Muscular arteries, and

ELASTIC ARTERIES

- Elastic arteries are the largest arteries in the body.
  - ✓ They have the largest diameter among arteries (2.5 cm to 1 cm) .
  - ✓ But their vessel walls are relatively thin.
  - ✓ Because their large lumens make them low-resistance pathways.
- They have well-defined internal and external elastic laminae.
- Elastic arteries are pressure reservoirs.

Arteries cont'd …

- Although elastic arteries also contain substantial amounts of smooth muscle.
  - ✓ They are relatively inactive in vasoconstriction.
- Thus, in terms of function, they can be visualized as simple elastic tubes.
- It include aorta, pulmonary trunk, brachiocephalic, subclavian, common carotid, and common iliac arteries.

MUSCULAR ARTERIES

- Muscular arteries account for most of the named arteries.
- They contains more smooth muscle and fewer elastic fibers in tunica media than elastic arteries.
  - ✓ Thus, muscular arteries are capable of greater vasoconstriction and vasodilation to adjust the rate of blood flow.
- Because the muscular arteries continue to branch and ultimately distribute blood to each of the various organs.

ARTERIOLES

- They are microscopic vessels that regulate the flow of blood into the capillary networks of the body’s tissues.

  ✓ ~ 400 million.

- They have a lumen diameter ranging from 300 µm down to 15 µm.

- The wall thickness of arterioles is one-half of the total vessel diameter.

- They have fenestrated internal elastic lamina that disappears at the terminal end.

Arteries cont'd …

- Arterioles are the main resistance vessels in the vascular tree.
  - ✓ Because their radius is small enough to offer considerable resistance to flow.
    - o Because of this they are known as resistance vessels.
- The high degree of arteriolar resistance causes: -
  - ✓ A marked drop in mean pressure as blood flows through these small vessels.
    - o On average, the pressure falls from 93 mm Hg to 37

CAPILLARIES

- They are the smallest of blood vessels and form the U-turns that connect the arterial outflow to the venous return.
  - ✓ They have diameters of 5 – 10µm.
  - ✓ Approximately 20 billion in number.
- Capillaries do not function independently.
  - ✓ Instead they form interweaving an extensive network called **capillary beds**.

Capillaries cont'd …

- The flow of blood from an arteriole to a venule through a capillary bed is called the **microcirculation**.
- In most body regions, a capillary bed consists of two types of vessels: -

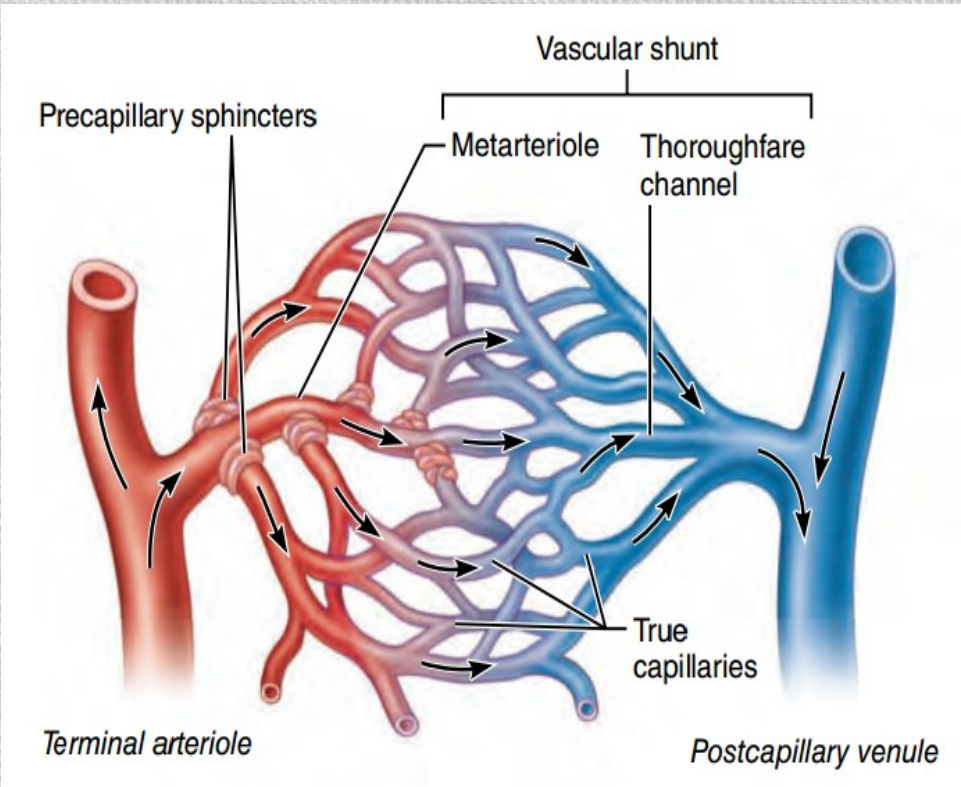
i. A vascular shunt (metarteriole–thoroughfare channel)

- ✓ A short vessel that directly connects the arteriole and venule at opposite ends of the bed.

ii. True capillaries, the actual exchange vessels.

Capillaries cont'd …

- Structurally, there are three types of capillaries :-
  - ✓ Continuous capillaries,
  - ✓ Fenestrated capillaries, and
  - ✓ Sinusoids.



THE CAPILLARY MICROCIRCULATION

- It is the movement of substances between blood and interstitial fluid.
- It is the mission of the entire cardiovascular system.
- Capillaries have the largest collective surface area for the exchange of nutrients and wastes.
- There are no carrier-mediated transport systems across capillaries.
  - ✓ Except those in the brain that play a role in the blood–brain barrier.

Capillaries cont'd …

- **Diffusion** is the most important mechanism for exchange across capillary walls.

- The time available for diffusion as blood flows through the microcirculation is maximized by slow velocity of blood flow.

  - ✓ The velocity of flow is least in the capillaries because blood flow is shared among many parallel vessels, with a large collective cross-sectional area.

- Bulk fluid flow also occurs between plasma and interstitium.

Capillaries cont'd …

$$J_v = K_f\,[(P_c - P_i) - \sigma\,(\pi_c - \pi_i)]$$

- The net driving force for filtration consists of a gradient of hydrostatic pressure that pushes fluid out of plasma and is opposed by a gradient of oncotic pressure.

  - ✓ The individual components of the net driving pressure are referred to as **Starling's forces:**

- **Capillary hydrostatic pressure (*Pc*)** is a force pushing fluid out of the capillaries. Hydrostatic pressure is usually about 35 mm Hg at the arteriolar end of a capillary, decreasing to about 15 mm Hg at the venous end of a capillary.

Capillaries cont'd …

- **Capillary oncotic pressure (πc)** is an osmotic force exerted by plasma proteins, and pulls fluid into the plasma from the interstitium and is approximately 25 mm Hg.

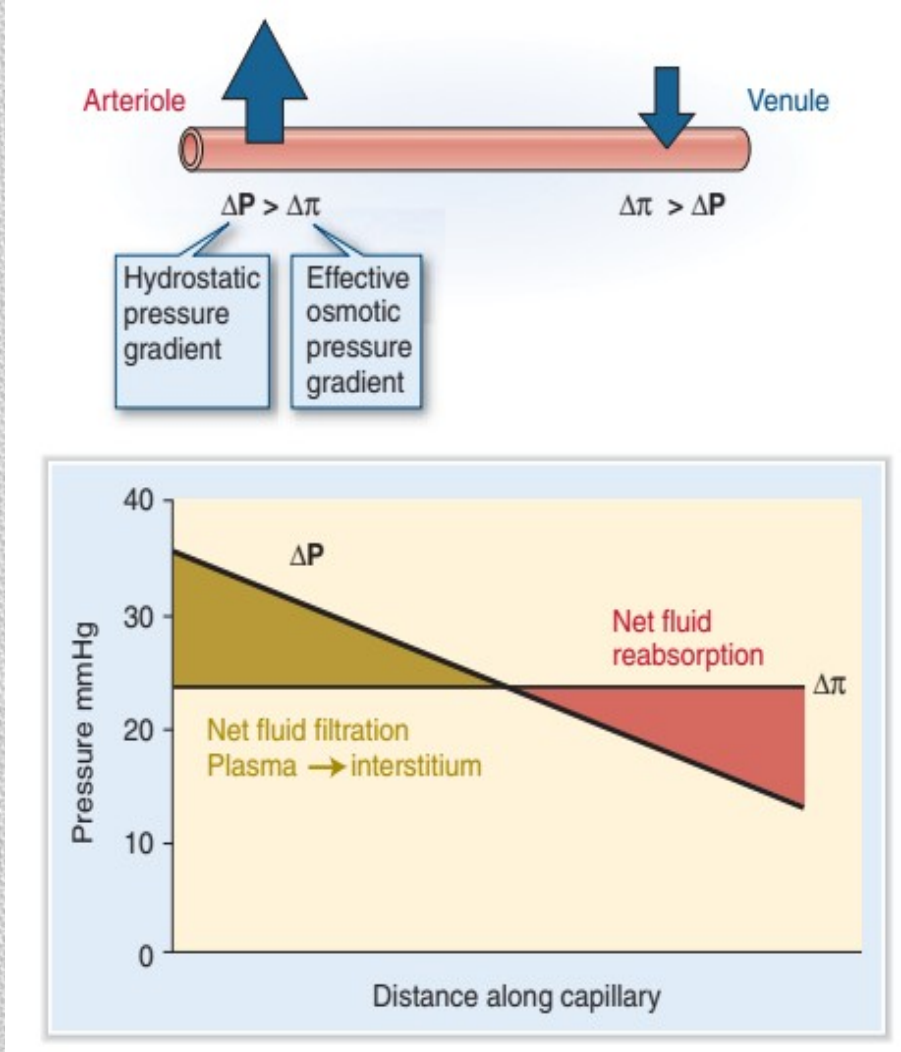
- **Interstitial fluid oncotic pressure (πi)** is normally low because proteins have reflection coefficients of 0.8–1.0 and interstitial protein concentration is low.

- ***Example :*** the following Starling forces were measured in a systemic capillary:

  ✓ Capillary hydrostatic pressure = 30 mm Hg

Capillaries cont'd …

- ✓ Capillary oncotic pressure = 25 mm Hg
- ✓ Interstitial oncotic pressure = 2 mm Hg
- ✓ Net pressure = (*Pc* - *Pi*) - (*πc* - *πi*) mm Hg
- ✓ = (30 - 1) - (25 - 2) mm Hg
- ✓ = +2 mm Hg (favors net filtration)



VEINS

- Blood flows from the capillaries into the venules.
  - ✓ Small vessels consisting mainly of a layer of endothelium and fibrous connective tissue.
- From the venules, the blood flows into veins that become larger as they travel toward the heart.
- The walls of larger veins consist of all layers.
- Anatomical characteristics of veins – have much thinner walls and wider diameters than the arteries they accompany.

Blood vessels cont'd…

- ✓ They are very distensible and are capable of holding large volumes of blood at a very low pressure.
  - o For this reason, the veins are the major compliance vessels.
  - o Approximately 64% of the blood volume is contained within the veins under resting conditions.

- Veins play an important role in regulation of venous return and, consequently, cardiac output.

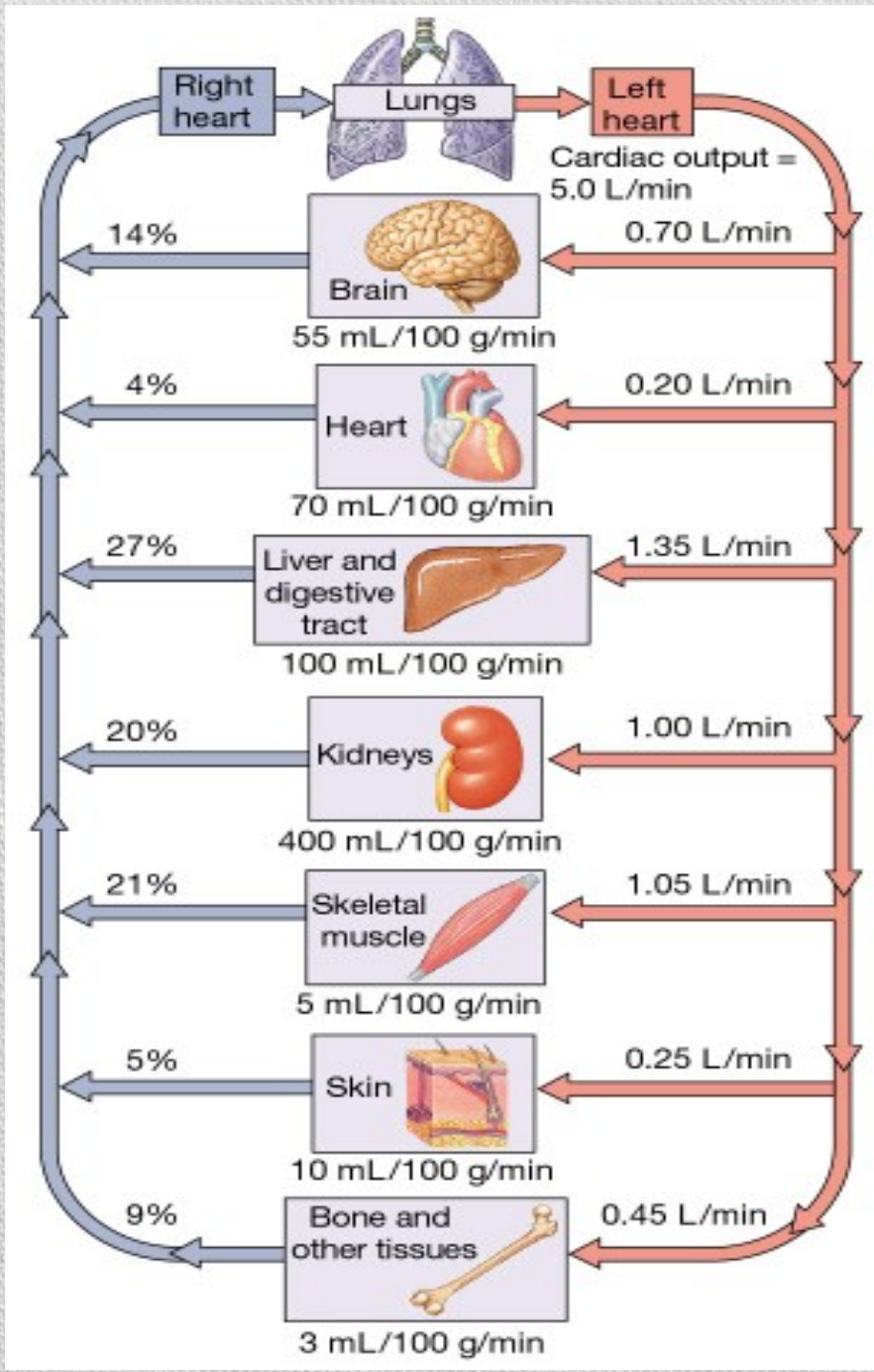
Blood vessels cont'd…

- Another important characteristic is the presence of valves.
  - ✓ Ensure the one-way flow of blood back toward the heart.
  - ✓ They are most abundant in the lower limbs.
- Finally, the venae cavae return blood to the right atrium.
  - ✓ These vessels function primarily as conduits.

Blood vessels cont'd…

Distribution of blood to the body organs

- 65% in veins
- 25% in the arteries
- 5% in capillaries
- 5% in the heart



ARTERIAL BLOOD PRESSUE

- Arterial blood pressure is defined as the lateral pressure exerted by the column of blood on wall of arteries.
- Arterial blood pressure is expressed in four different terms:
  - ✓ Systolic blood pressure
  - ✓ Diastolic blood pressure
  - ✓ Pulse pressure
  - ✓ Mean arterial blood pressure

ABP cont'd …

- **Systolic Blood Pressure (SBP)**
  - ✓ Systolic blood pressure (systolic pressure) is defined as the **maximum pressure** exerted in the arteries **during systole** of heart.
  - ✓ *Normal systolic pressure:* 120 mm Hg (90 mm Hg to 140 mm Hg).
- **Diastolic Blood Pressure (DBP)**
  - ✓ Diastolic blood pressure (diastolic pressure) is defined as the **minimum pressure** exerted in the arteries **during diastole** of heart.

ABP cont'd …

- **Pulse Pressure (PP)**
  - ✓ Pulse pressure is the difference between the SBP and DBP.
  - ✓ *Normal pulse pressure:* 40 mm Hg (30 – 50).
- **Mean Arterial Blood Pressure (MAP)**
- Mean arterial blood pressure is the average pressure existing in the arteries.
  - ✓ It is not the arithmetic mean of systolic and diastolic pressures.

ABP cont'd …

- To determine the mean pressure, diastolic pressure is considered than the systolic pressure.

- It is because, the diastolic period of cardiac cycle is longer (0.53 second) than the systolic period (0.27 second).

✓ *Normal mean arterial pressure:* 93 mm Hg (80 + 13 = 93).

- Mean arterial blood pressure = Diastolic pressure + 1/3 of pulse pressure

Causes of Variations In ABP

- Age – ABP rises as age increases
- Sex – After the age of 50, F > M by 5 mm Hg.
- Time of the day (Diurnal Variation) – in early morning it is slightly low, but reaches maximum at noon.
- Body wt (Body Built) – ABP higher by 10-15 mm Hg in obese.
- After Meals – ABP is increased for few hours after meals due to increase in cardiac output.
- During Sleep – Usually, the pressure is reduced up to 15 to 20 mm Hg during deep sleep.

ABP cont'd …

- However, it increases slightly during sleep associated with dreams

- Gravity – every 1 cm distance below the level of the heart increases pressure by 0.77 mm Hg

- Emotional Conditions – increases ABP due to release of adrenaline.

- After Exercise – After moderate exercise, SBP increases by 20 to 30 mm Hg above the basal level due to increase in rate and force of contraction and stroke volume.

ABP cont'd …

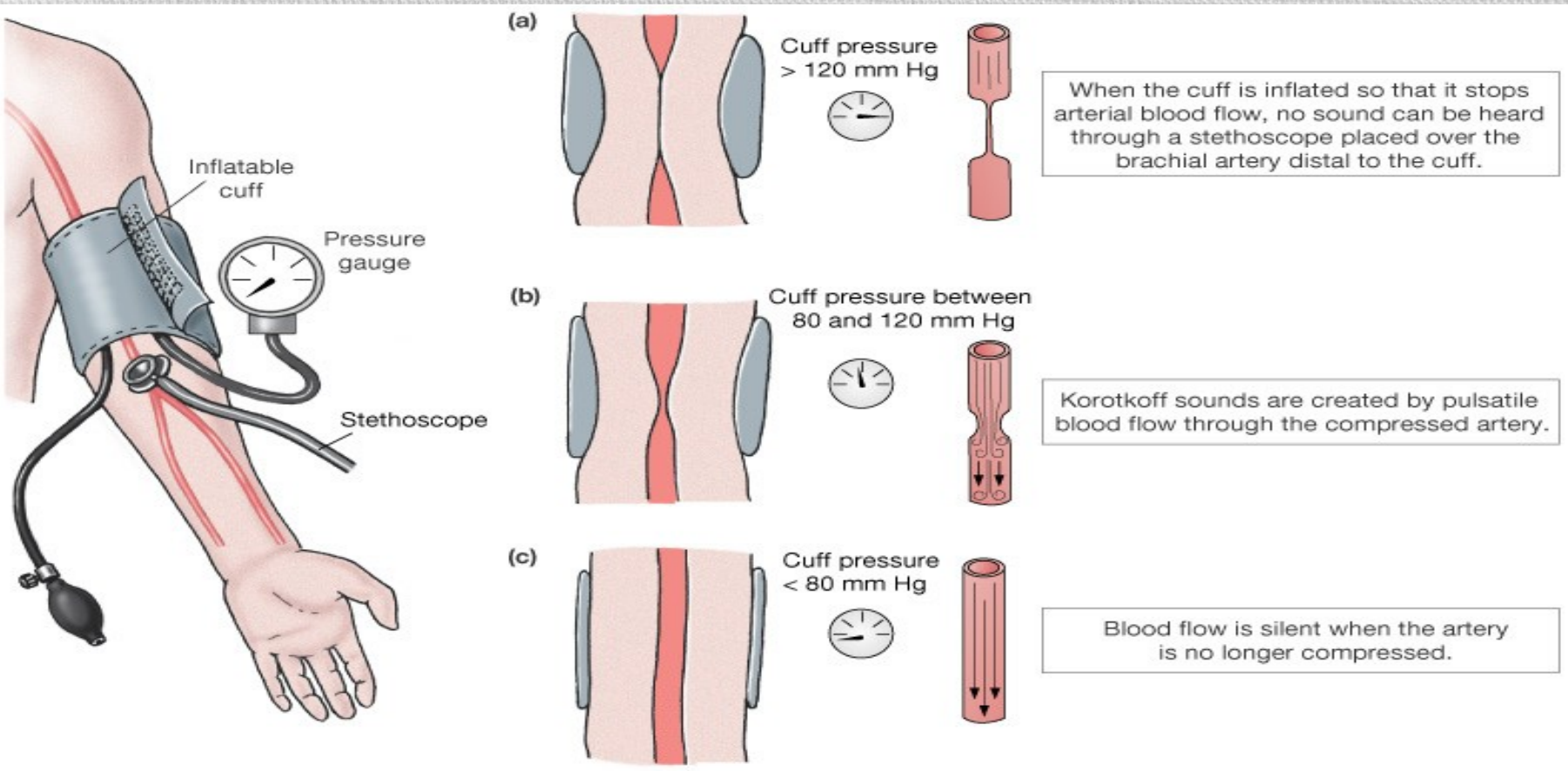
- It is because, the diastolic pressure depends upon peripheral resistance, which is not altered by moderate exercise.

✓ After severe muscular exercise, systolic pressure rises by 40 to 50 mm Hg above the basal level.

- But, the diastolic pressure reduces because the peripheral resistance decreases in severe muscular exercise.

METHOD OF MEASUREMENT OF ABP

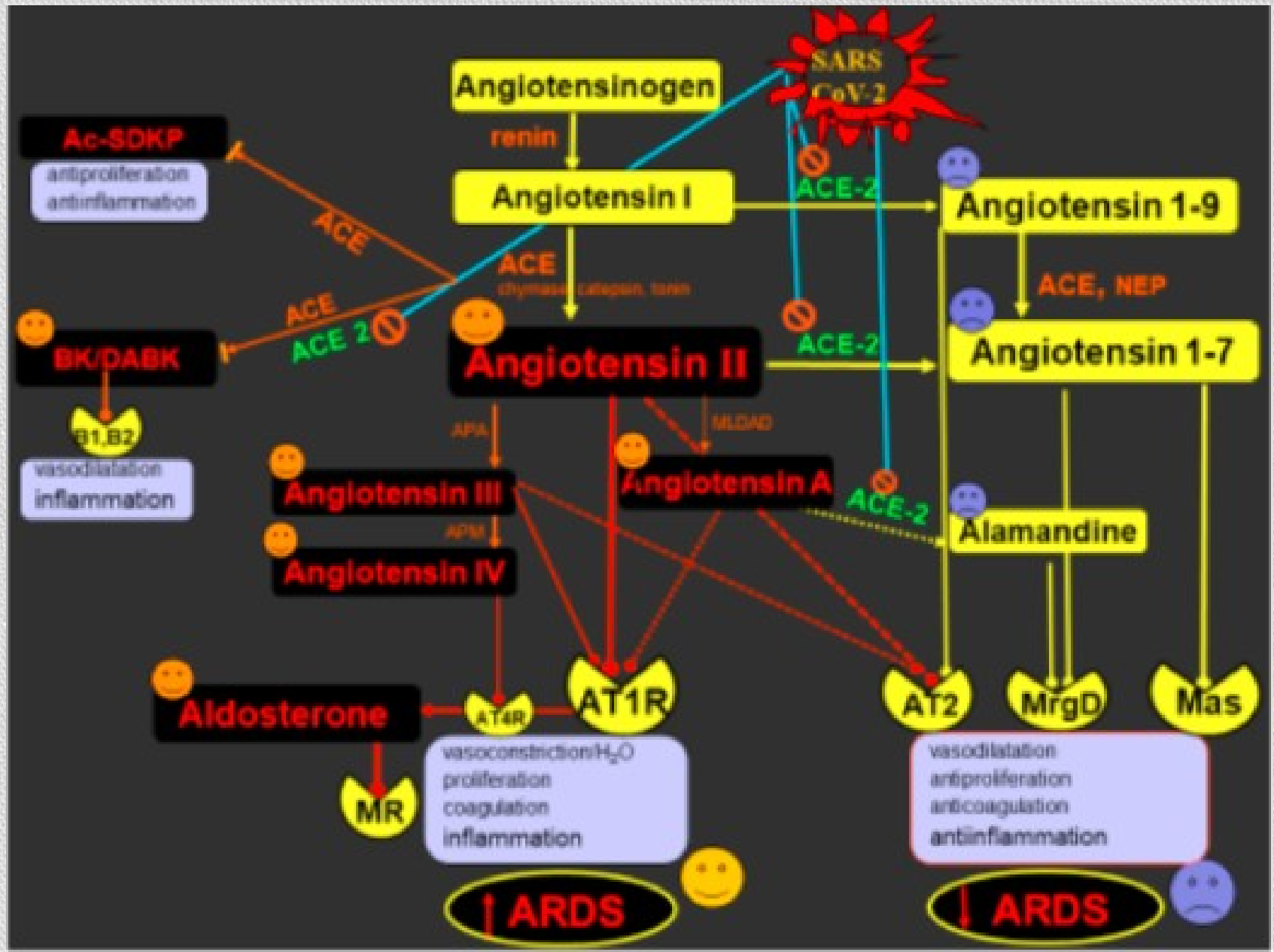
- Direct method/invasive
- Indirect method/non-invasive/auscultatory method



REGULATION OF ABP

1. Short-term controlling mechanisms
   - ✓ CNS ischemic response
   - ✓ Baroreceptor reflex
   - ✓ Chemoreceptor reflex
   - ✓ Atrial stretch reflex
   - ✓ Stress relaxation and reverse stress relaxation
   - ✓ Capillary fluid shift
   - ✓ Hormonal mechanisms: AD, ND, VP
2. Long-term controlling mechanisms
   - ✓ The RAAS

ABP cont'd …


SARS CoV-2
Angiotensinogen
renin
Angiotensin I
ACE
ACE-2
Angiotensin 1-9
ACE, NEP
Angiotensin 1-7
Ac-SDKP
antiproliferation
antiinflammation
ACE
ACE 2
BK/DABK
B1,B2
vasodilatation
inflammation
Angiotensin II
APA
NLGAD
Angiotensin III
Angiotensin A
APM
Angiotensin IV
Alamandine
Aldosterone
MR
AT4R
AT1R
vasoconstriction/H2O
proliferation
coagulation
inflammation
AT2
MrgD
Mas
vasodilatation
antiproliferation
anticoagulation
antiinflammation
ARDS
ARDS