Cardiovascular System

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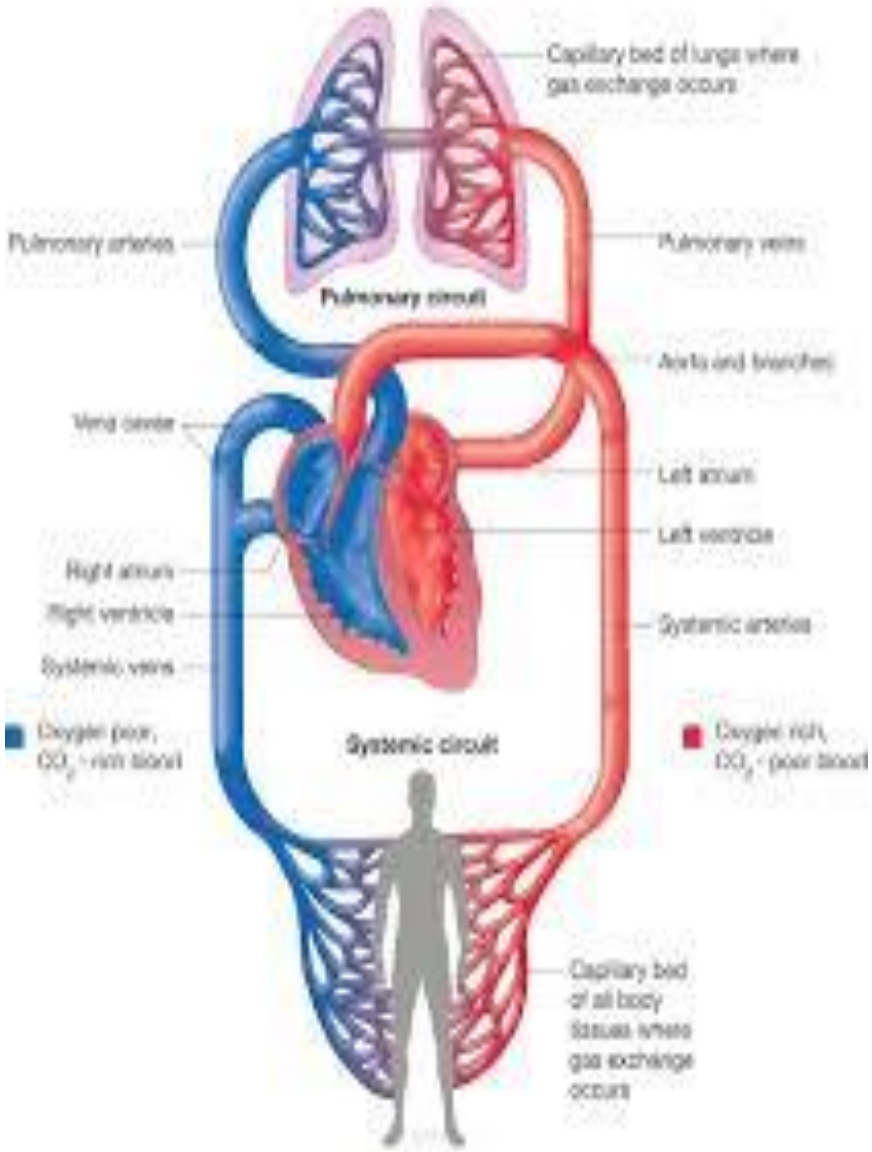
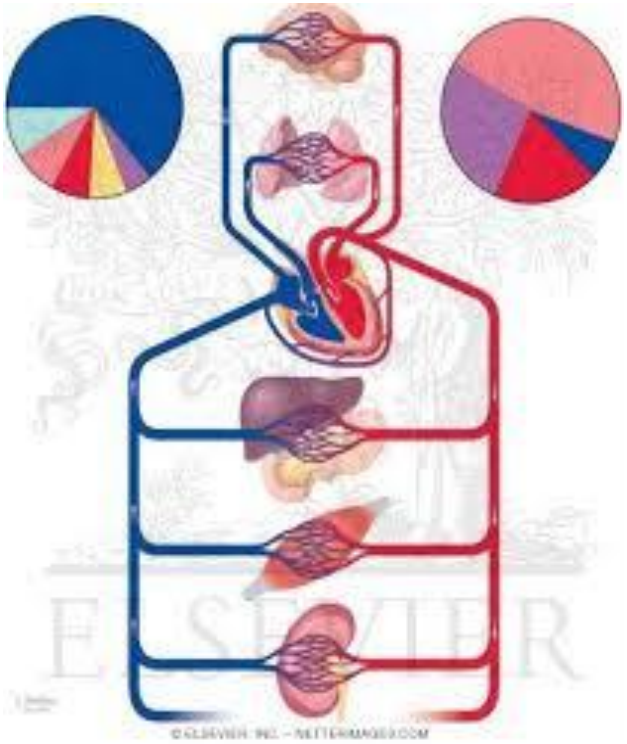
Functions of the Cardiovascular System

- Transport of O2 from the lungs to the tissues.
- Transport of CO2 from the tissues to the lungs.
- Transport of nutrients from the intestine to the tissues.
- Transport of metabolic products from the tissues to the organs of their excretion.
- Transport of hormones from the endocrine glands to their target cells.
- Participation to the regulation of the temperature.


Capillary bed of lungs where gas exchange occurs
Pulmonary arteries
Pulmonary veins
Pulmonary circuit
Aorta and branches
Vena cavae
Left atrium
Left ventricle
Right atrium
Right ventricle
Systemic arteries
Systemic veins
Oxygen poor, CO_2 - rich blood
Systemic circuit
Oxygen rich, CO_2 - poor blood
Capillary bed of all body tissues where gas exchange occurs

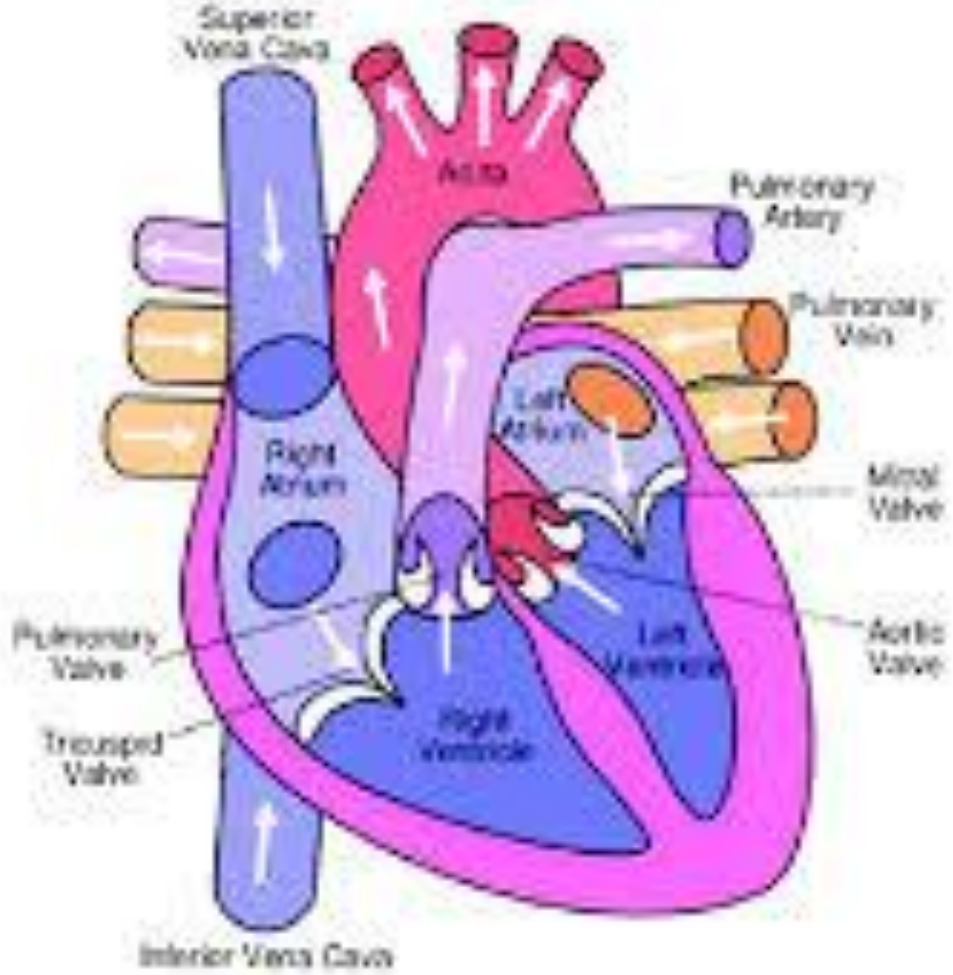
Cardiovascular System

- **The cardiovascular system contains a central part (the heart) and a peripheral part (the blood vessels). The heart is devided in four cavities: left and right atrium, left and right ventricle. The left ventricle pumps blood through the arterial blood vessels of the systemic circulation to the peripheral capillaries. The blood is returned to the right atrium via the systemic veins and is pumped by the right ventricle through the pulmonary artery to the lung capillaries and is returned to the left atrium via the pulmonary veins (pulmonary circulation)**



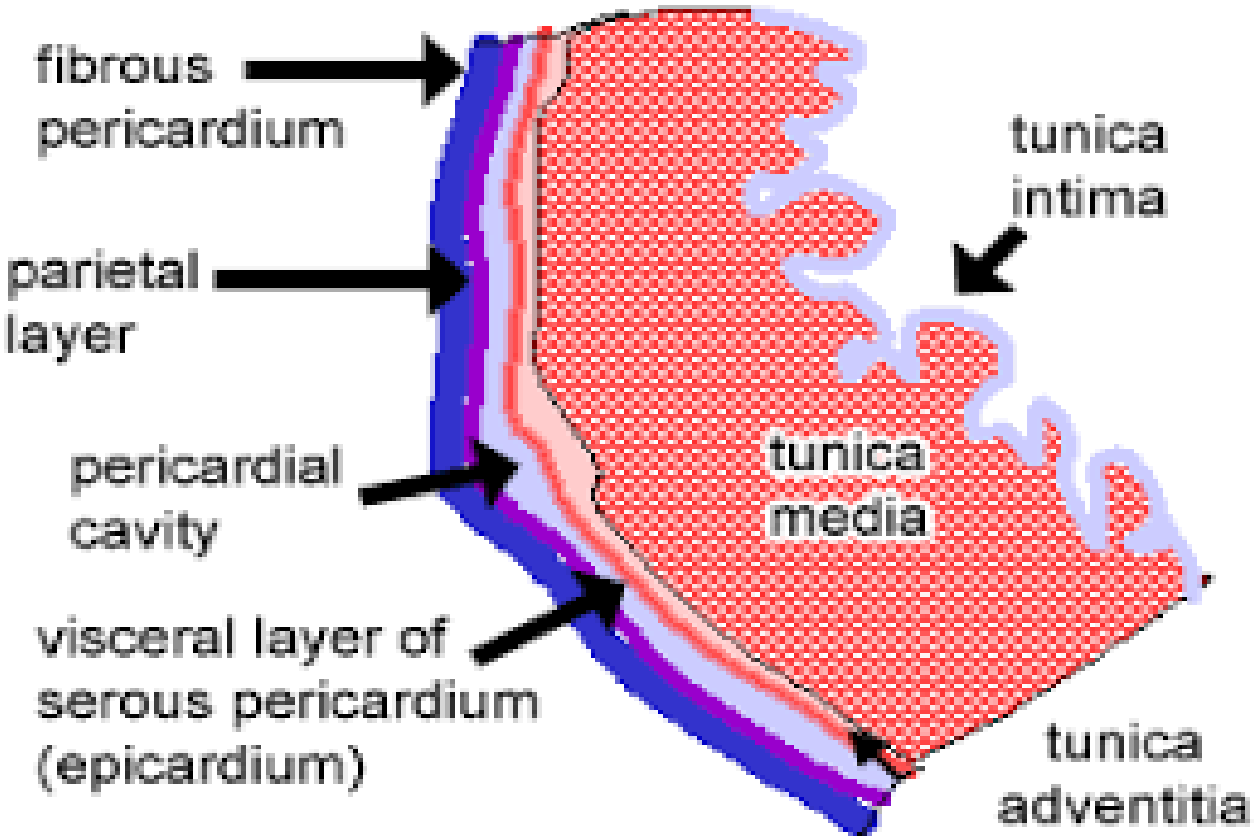
Blood Vessels and Blood Flow

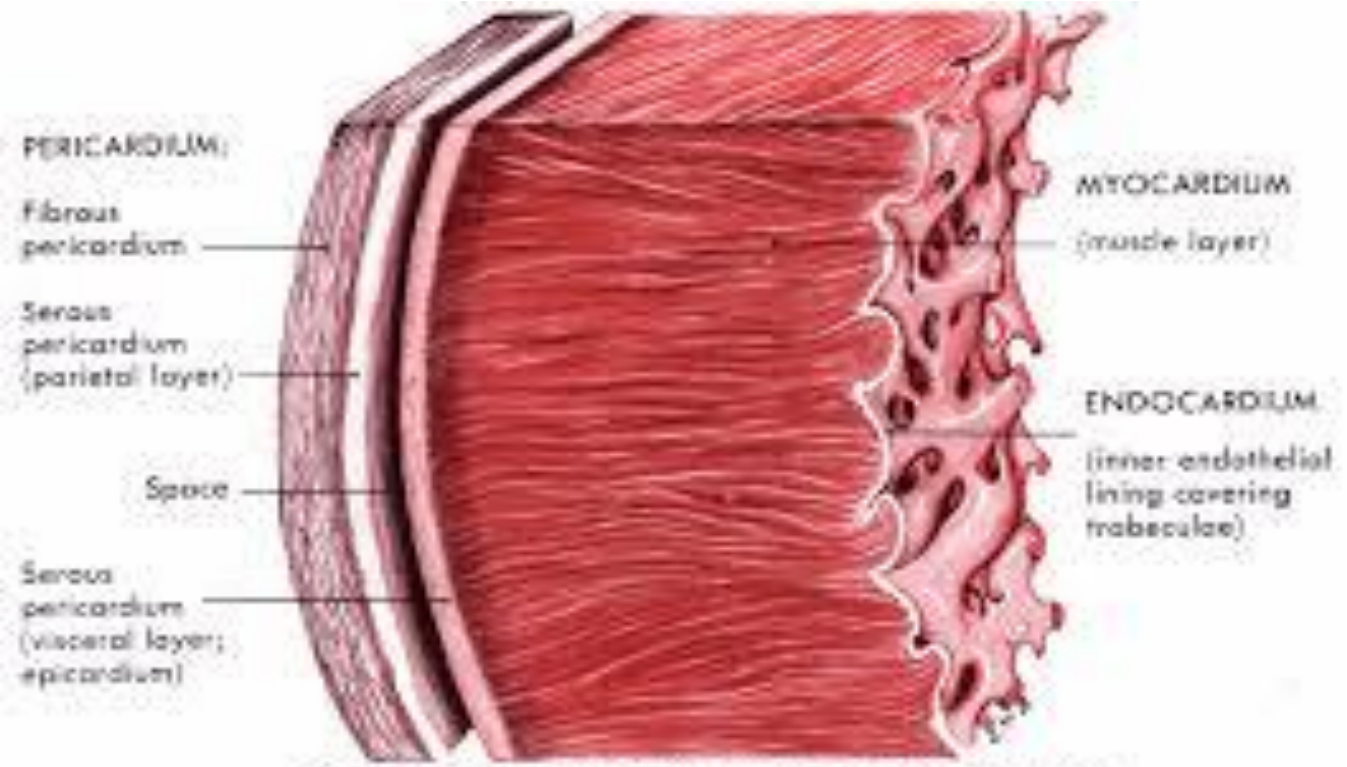
- **In the systemic circulation the blood leaves the left ventricle in the aorta and flows into the arteries which devide and subdivide to form the arterioles via which the blood reaches the network of the capillaries of the different tissues. The capillaries reunite to form the venules from which the blood is passed on to the veins and reenters the right atrium of the heart via the superior and inferior venae caveae.**
- **The arterioles and small arteries together account for about 50% of the total resistence (right side diagram) whereas the veins at rest account for the 65% of the blood volume (left side diagram)**


Superior Vena Cava
Aorta
Pulmonary Artery
Pulmonary Vein
Left Atrium
Right Atrium
Mitral Valve
Pulmonary Valve
Aortic Valve
Tricuspid Valve
Left Ventricle
Right Ventricle
Inferior Vena Cava

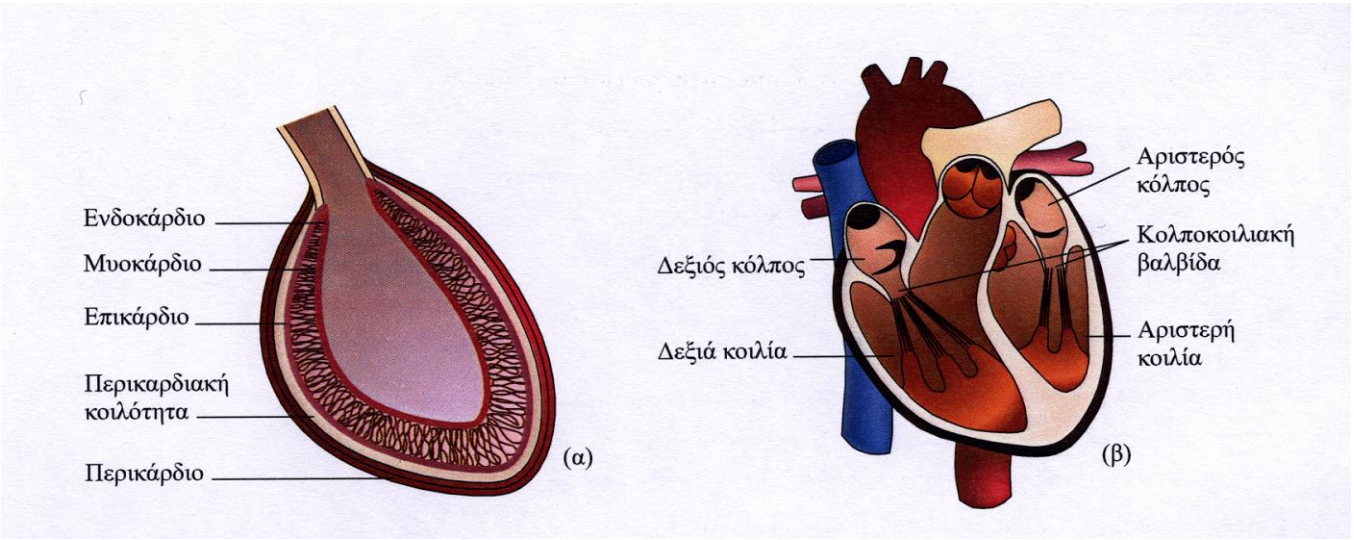
The layers of the walls of the heart

- **The heart has three histological layers .**
- **The luminar surface is known as endocardium and similarly with the tunica intima of the blood vessels is composed of thin epithelial cells (endothelial cells)**
- **The myocrdium, like the tunica media of the blood vessels, is the middle layer of the heart and contains a large quantity of muscle cells .**
- **The pericardium is a fibrous double layered connective sheath that encases the heart. The visceral portion that is in contact with the heart is called epicardium. Between the two layers of the pericardium is located is a very thin cavity filled with liquid, the pericardial cavity.**


fibrous pericardium
parietal layer
pericardial cavity
visceral layer of serous pericardium (epicardium)
tunica intima
tunica media
tunica adventitia

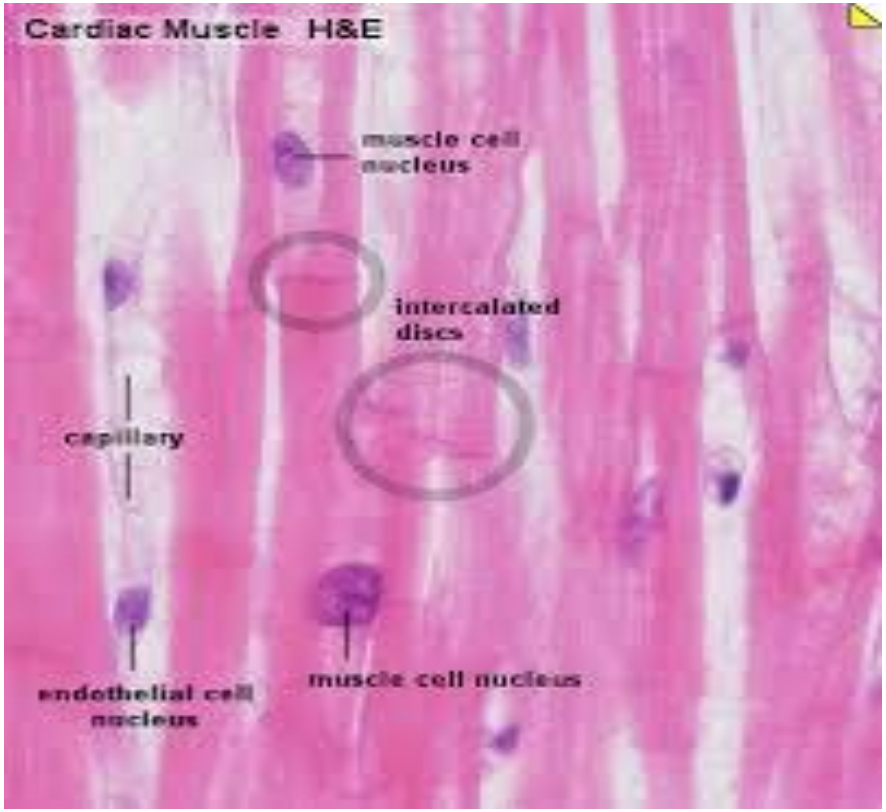


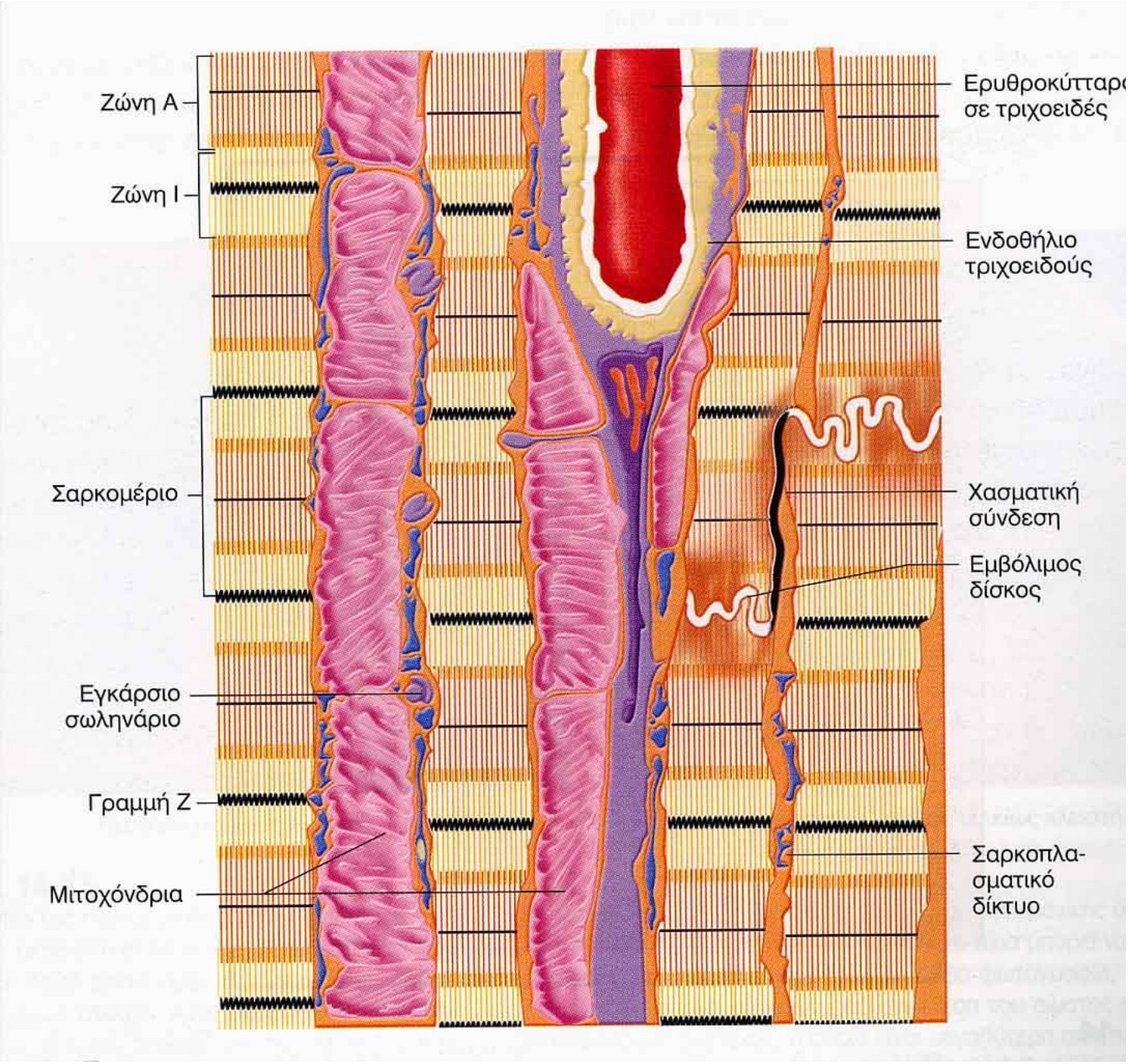
Section of the heart wall showing the components of the outer pericardium (heart sac), muscle layer (myocardium), and inner lining (endocardium).


Ενδοκάρδιο
Μυοκάρδιο
Επικάρδιο
Περικαρδιακή κοιλότητα
Περικάρδιο
(α)
Αριστερός κόλπος
Κολποκοιλιακή βαλβίδα
Δεξιός κόλπος
Αριστερή κοιλία
Δεξιά κοιλία
(β)

The Myocardium

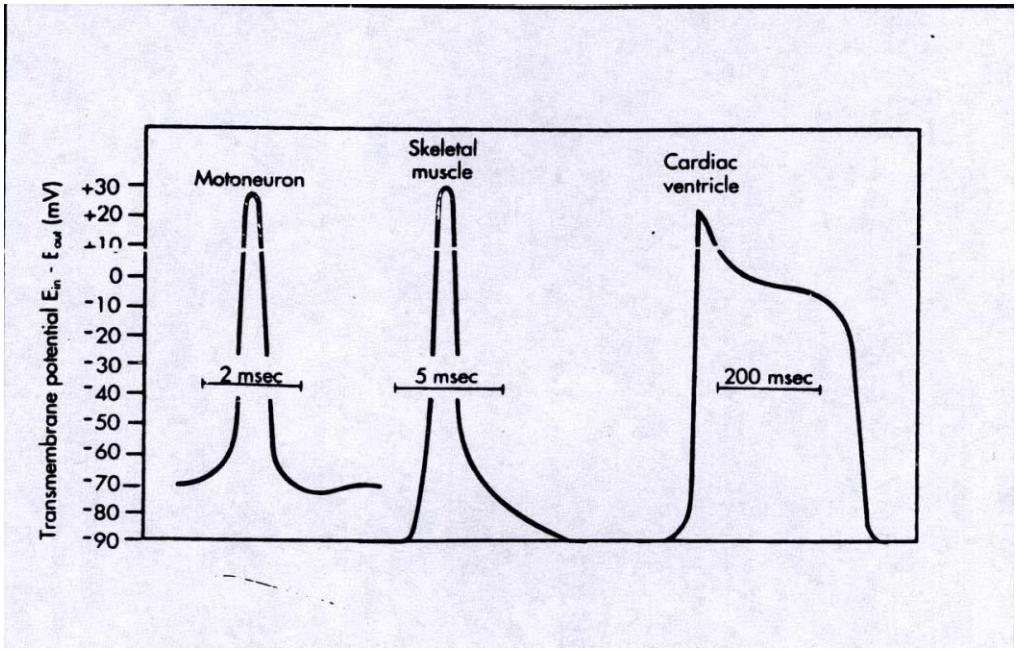
- **The myocardium is the functional layer of the heart and it is composed of individual heart muscle cells (myocardial fibers, very similar to the muscle fibers of the striated muscle), joined together by intercalated discs (εμβόλιμοι δισκοι).**
- **All cardiac muscle cells are electrically linked to one another by structures known as gap junctions (χασματικές συνδέσεις) which allow the action potential to pass from one cell to the next. This means that all atrial cells contract together and then all ventricular cells (law all or none)**

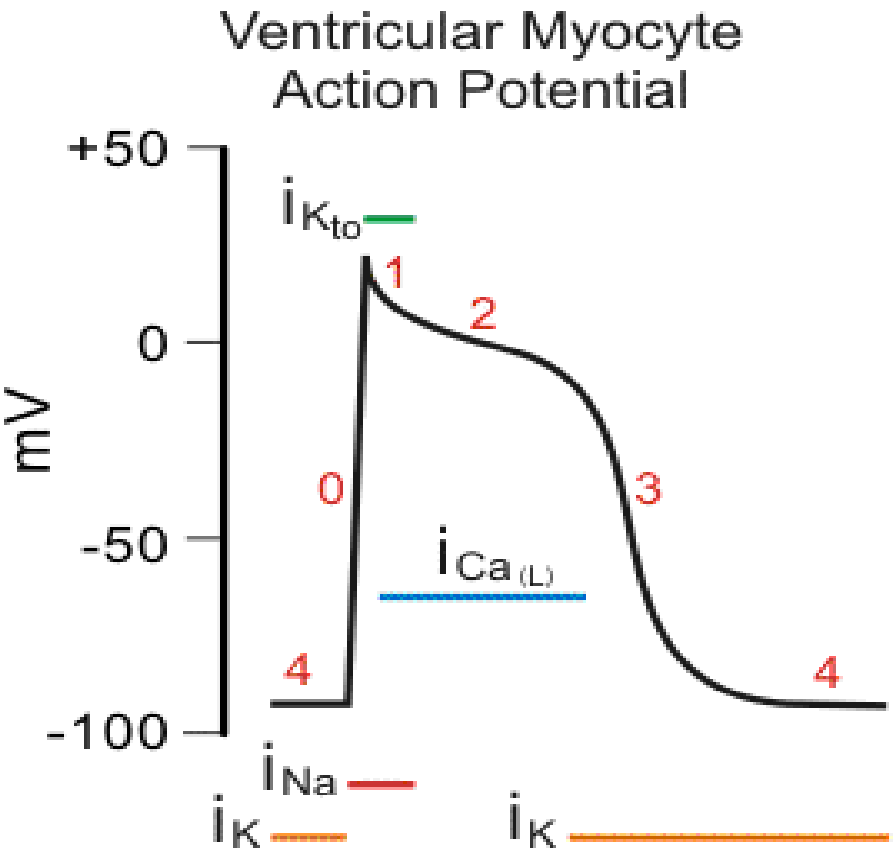

Cardiac Muscle H&E
muscle cell nucleus
intercalated discs
capillary
endothelial cell nucleus
muscle cell nucleus

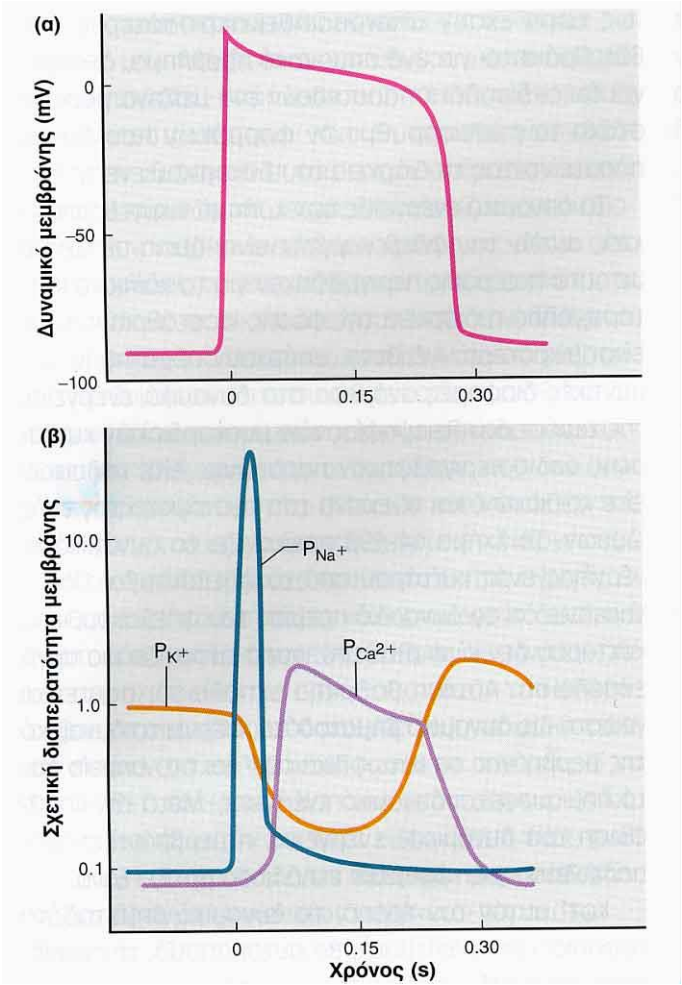

Ζώνη Α
Ζώνη Ι
Σαρκομέριο
Εγκάρσιο σωληνάριο
Γραμμή Z
Μιτοχόνδρια
Ερυθροκύτταρο σε τριχοειδές
Ενδοθήλιο τριχοειδούς
Χασματική σύνδεση
Εμβόλιμος δίσκος
Σαρκοπλασματικό δίκτυο

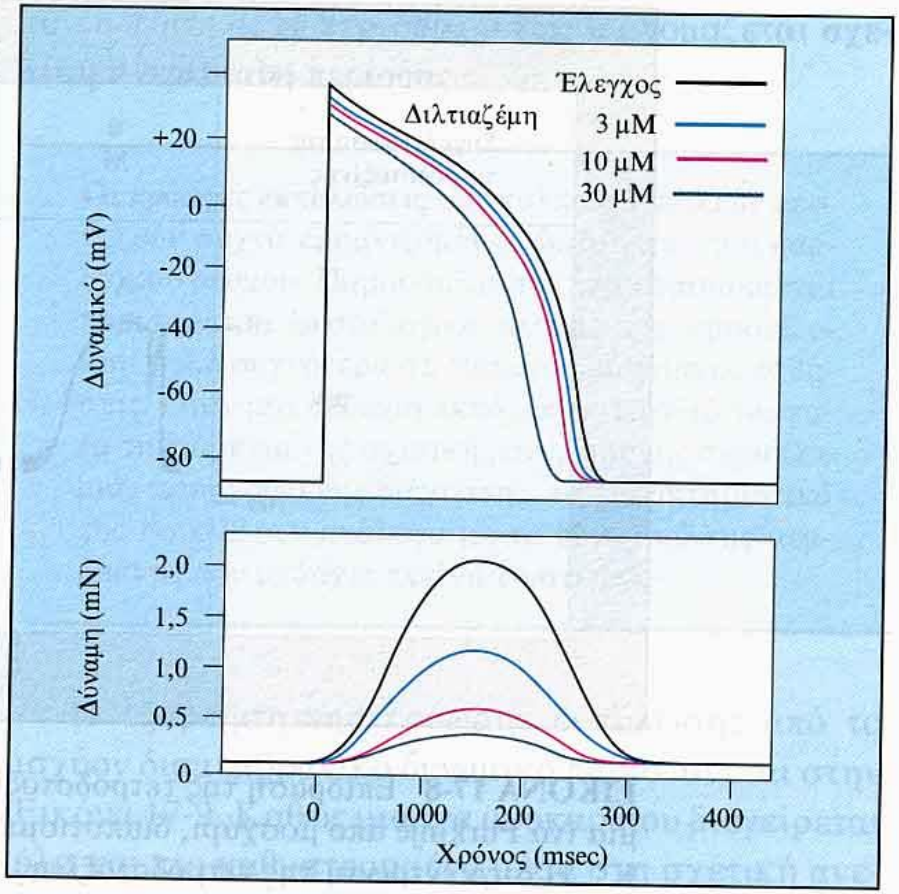
Action Potential

- **The duration of the action potentials of ventricular and atrial myocytes (fast action potentials) is much higher (100-300ms) than the duration of action potentials of the neuronal cells and the cells of the striated muscles.**
- **The resting membrane potential (phase 4) of ventricular myocytes is in the order of -90 mV. The depolarization (phase 0) is produced by the activation of Na channels which increases the membrane conductance (flow) of Na and a rapid influx of sodium into the cell resulting an icrease of voltage up to about +50mV. During the plateau phase (phase 2) , potassium channel permeability is minimized ad this protects the cell from an excessive loss of K. The efflux of K is balanced by the influx of Ca which enters the cell through specific Ca channels (L channels). Finally, repolarization (phase 3) is achieved by a n icrease of the permeability of the membrane to K and a much greater efflux of K The in vitro administration of Diltiazem (Διλτιαζέμη) provokes a dose dependent reduction of the plateau and of isometric contraction of the heart papillary muscle.**


Transmembrane potential $E_{in} - E_{out}$ (mV)
+30
+20
+10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
Motoneuron
2 msec
Skeletal muscle
5 msec
Cardiac ventricle
200 msec

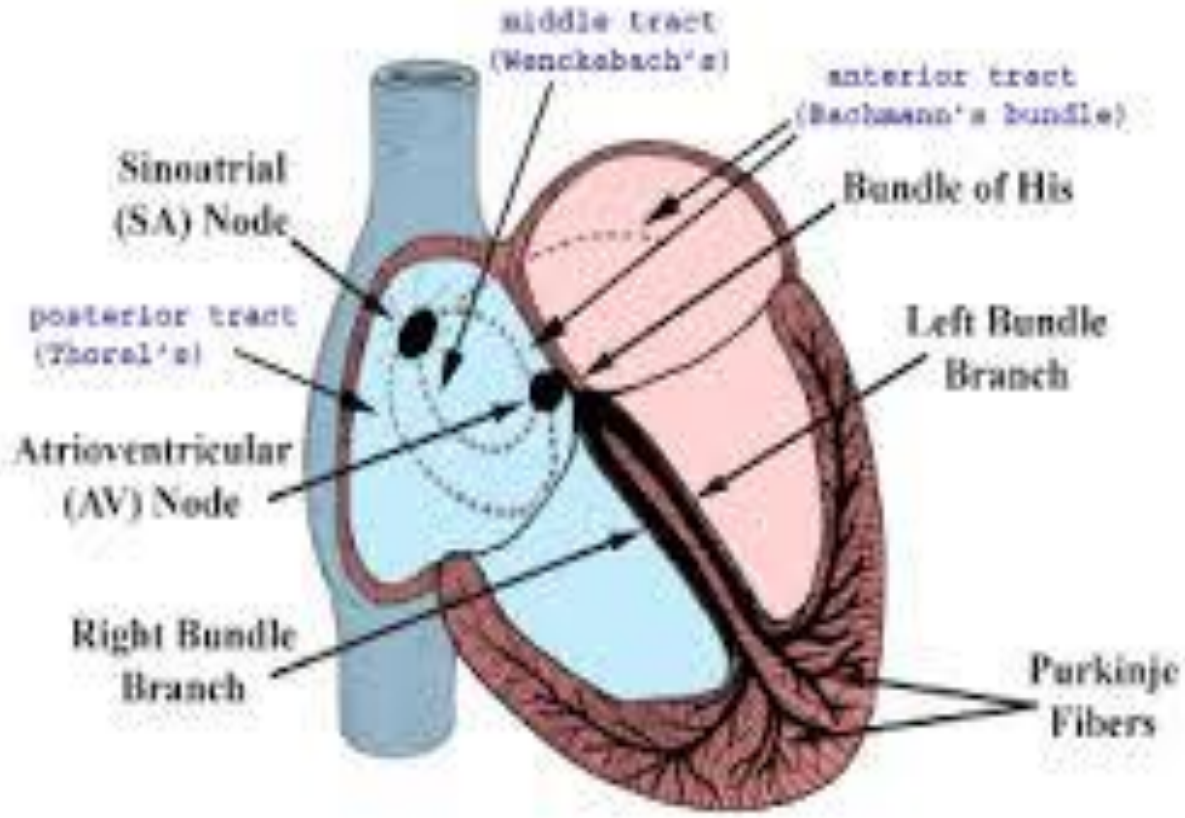

Ventricular Myocyte
Action Potential
+50
0
-50
-100
mV
$i_{K_{to}}$
1
2
0
3
$i_{Ca\,(L)}$
4
4
i_{Na}
i_K
i_K

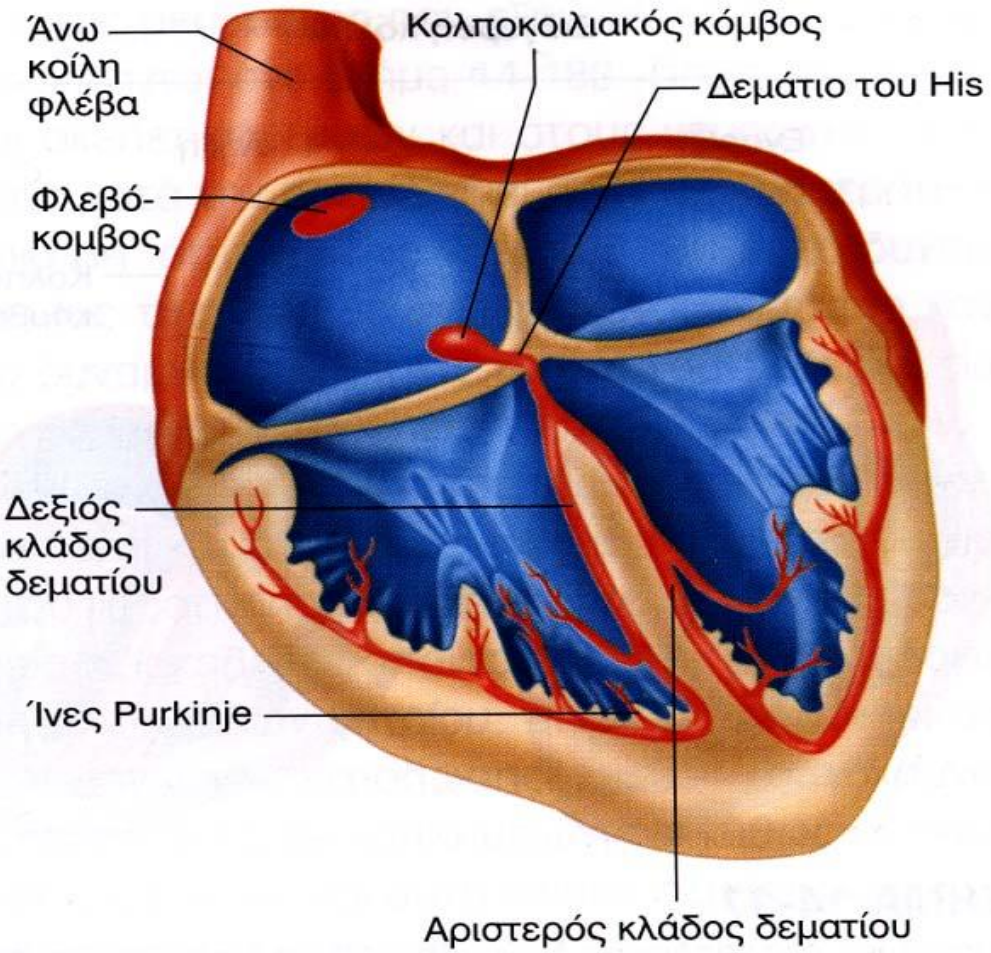

(α)
Δυναμικό μεμβράνης (mV)
0
−50
−100
0
0.15
0.30
(β)
Σχετική διαπερατότητα μεμβράνης
10.0
1.0
0.1
P_{Na^+}
P_{K^+}
$P_{Ca^{2+}}$
0
0.15
0.30
Χρόνος (s)

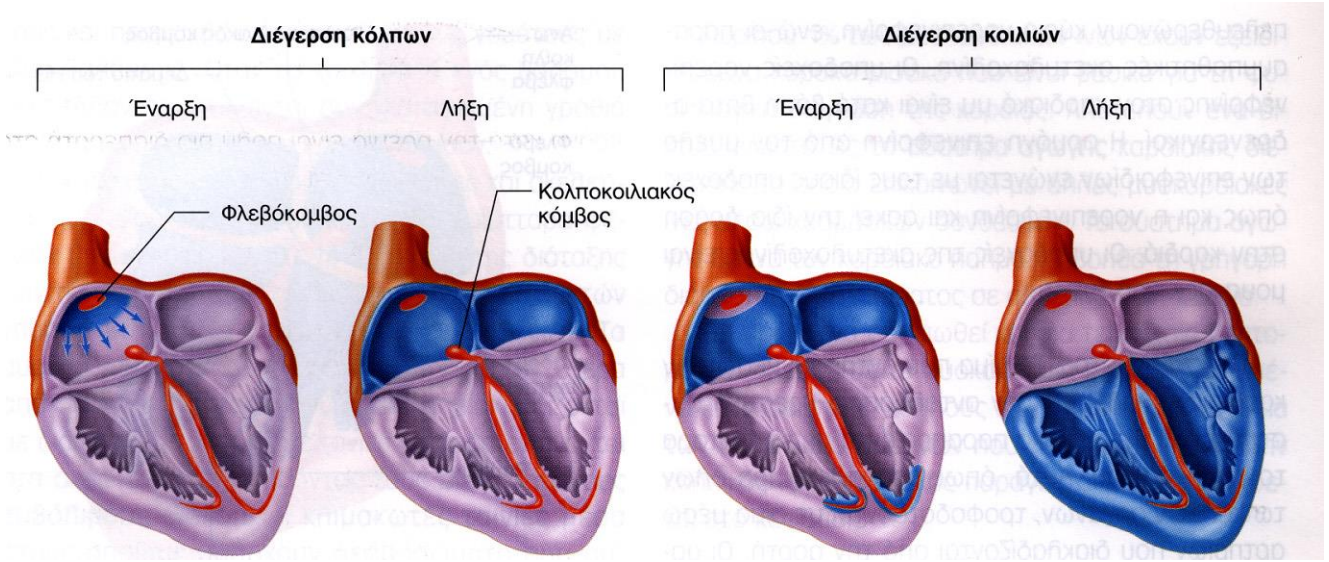

Έλεγχος
Διλτιαζέμη
3 μM
10 μM
30 μM
+20
0
-20
-40
-60
-80
Δυναμικό (mV)
2,0
1,5
1,0
0,5
0
Δύναμη (mN)
0
1000
200
300
400
Χρόνος (msec)

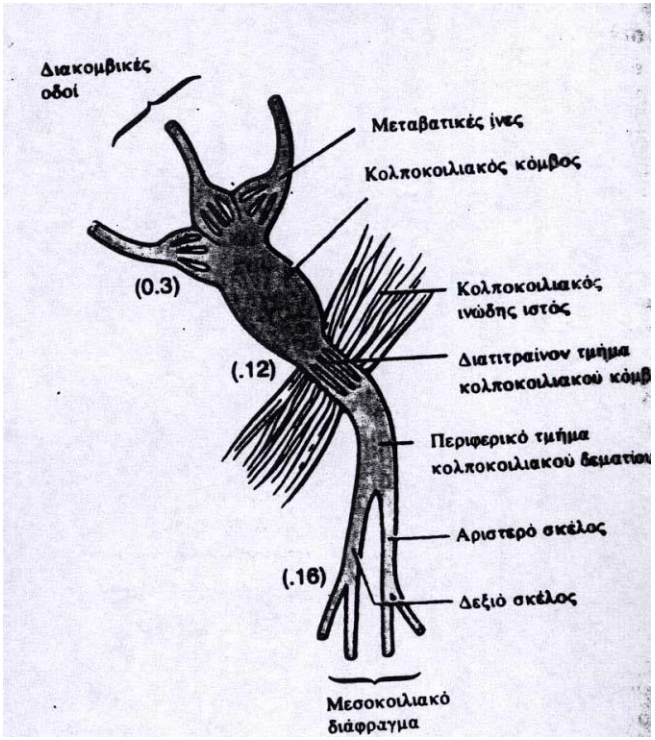
Excitation and Conduction in the Heart

- **Excitation of the heart normally proceeds from the sinooatrial node (SA) which is the physiological pacemaker of the heart. From the SA node excitation spreads through both atria to the atrioventricular node (AV) whence via the Bundle of Hiss and its two branches (left and right) it reaches the Purkinje fibers which carries the impulse to the ventricular muscle.**
- **In AV node the conduction is slowed so that atrial contraction can occur and the ventricles can adequately filled.**
- **When the SA node is destroyed pacemaker cells of AV node generally take over the pacemaker function for the entire heart. Purkinje cells in the ventricles also display automaticity.**


middle tract
(Wenckebach's)
anterior tract
(Bachmann's bundle)
Sinoatrial
(SA) Node
Bundle of His
posterior tract
(Thorel's)
Left Bundle
Branch
Atrioventricular
(AV) Node
Right Bundle
Branch
Purkinje
Fibers

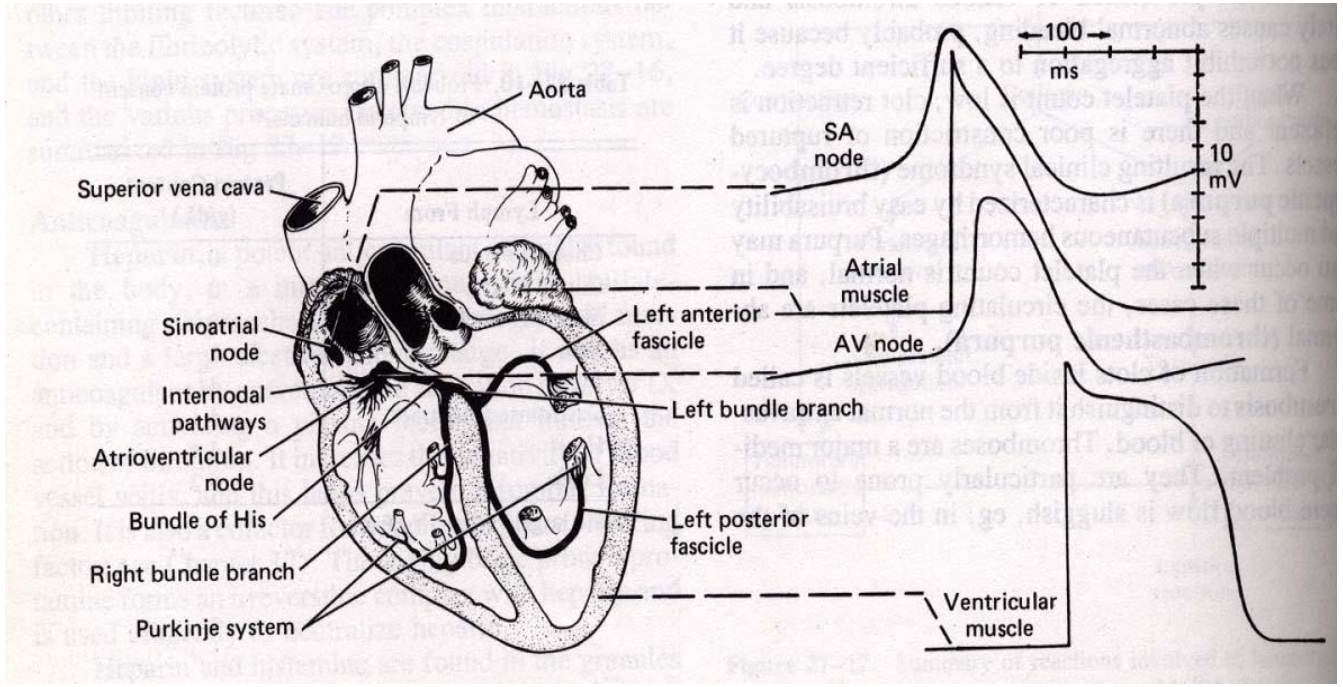

Άνω κοίλη φλέβα
Κολποκοιλιακός κόμβος
Δεμάτιο του His
Φλεβό-κομβος
Δεξιός κλάδος δεματίου
Ίνες Purkinje
Αριστερός κλάδος δεματίου

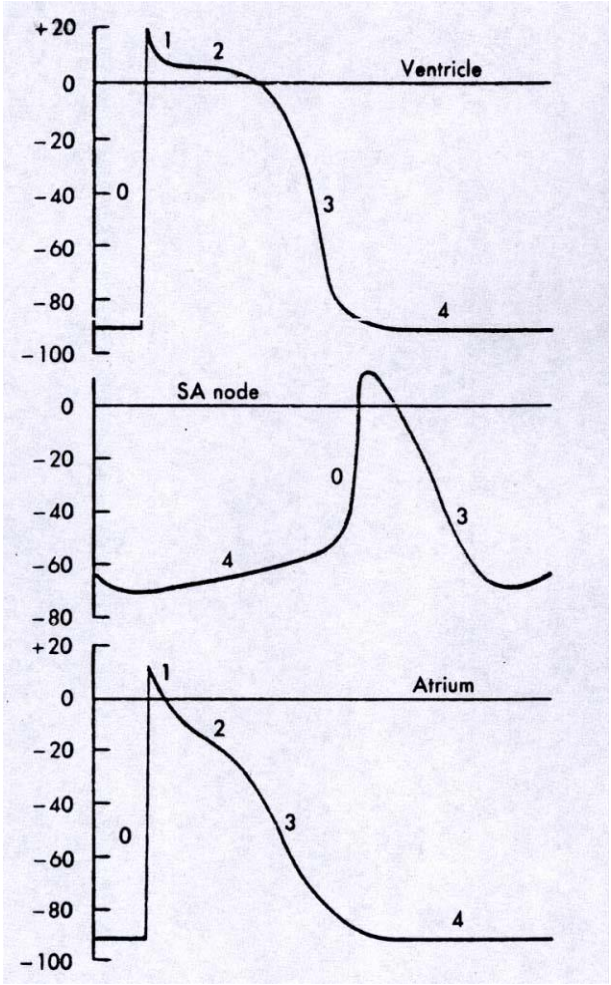

Διέγερση κόλπων
Έναρξη
Λήξη
Διέγερση κοιλιών
Έναρξη
Λήξη
Φλεβόκομβος
Κολποκοιλιακός κόμβος

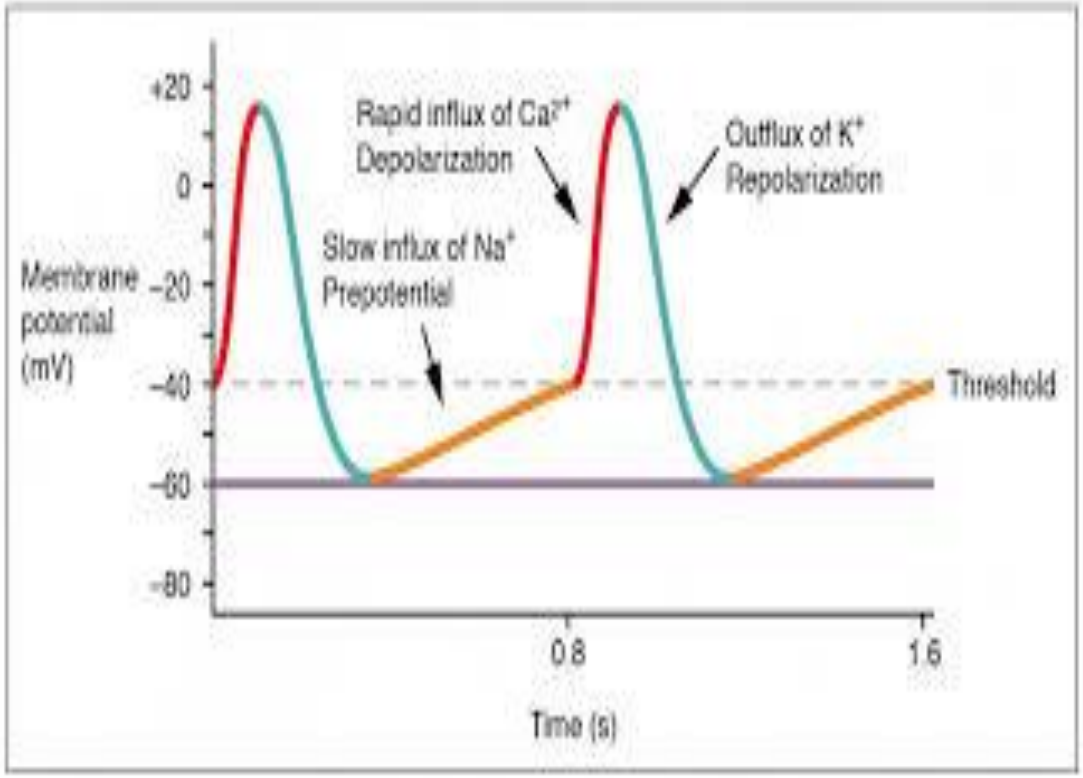

Διακομβικές
οδοί
Μεταβατικές ίνες
Κολποκοιλιακός κόμβος
(0.3)
Κολποκοιλιακός
ινώδης ιστός
(.12)
Διατιτραίνον τμήμα
κολποκοιλιακού κόμβ
Περιφερικό τμήμα
κολποκοιλιακού δεματίου
Αριστερό σκέλος
(.16)
Δεξιό σκέλος
Μεσοκοιλιακό
διάφραγμα

Ionic basis of Automaticity (slow response action potentials)

- **The pacemaker fiber is characterized by a slow diastolic depolarization through the phase 4 (resting membrane potential) until a threshold is attained (around -50mV) and the action potential is then triggered. When the rate of diastolic depolarization is increased (increase of the slope) the threshold is attained earlier and the heart rate increases.**
- **Near the end of the repolarization an inward slow current (if) is activated . This current is carried mainly by Na through specific channels that differ from the fast sodium channels. This current it was dubbed "funny" because its discoverers had not expected to detect such a sodium channel in the pacemaker cells. A second current responsible for the diastolic depolarization is the inward rectifying Ca channel . This current is activated toward the end of the phase 4. Once this channel is activated influx of Ca inside the cell is increased. This influx accelerates the rate of diastolic depolarization which then leads to the action potential upstroke.**

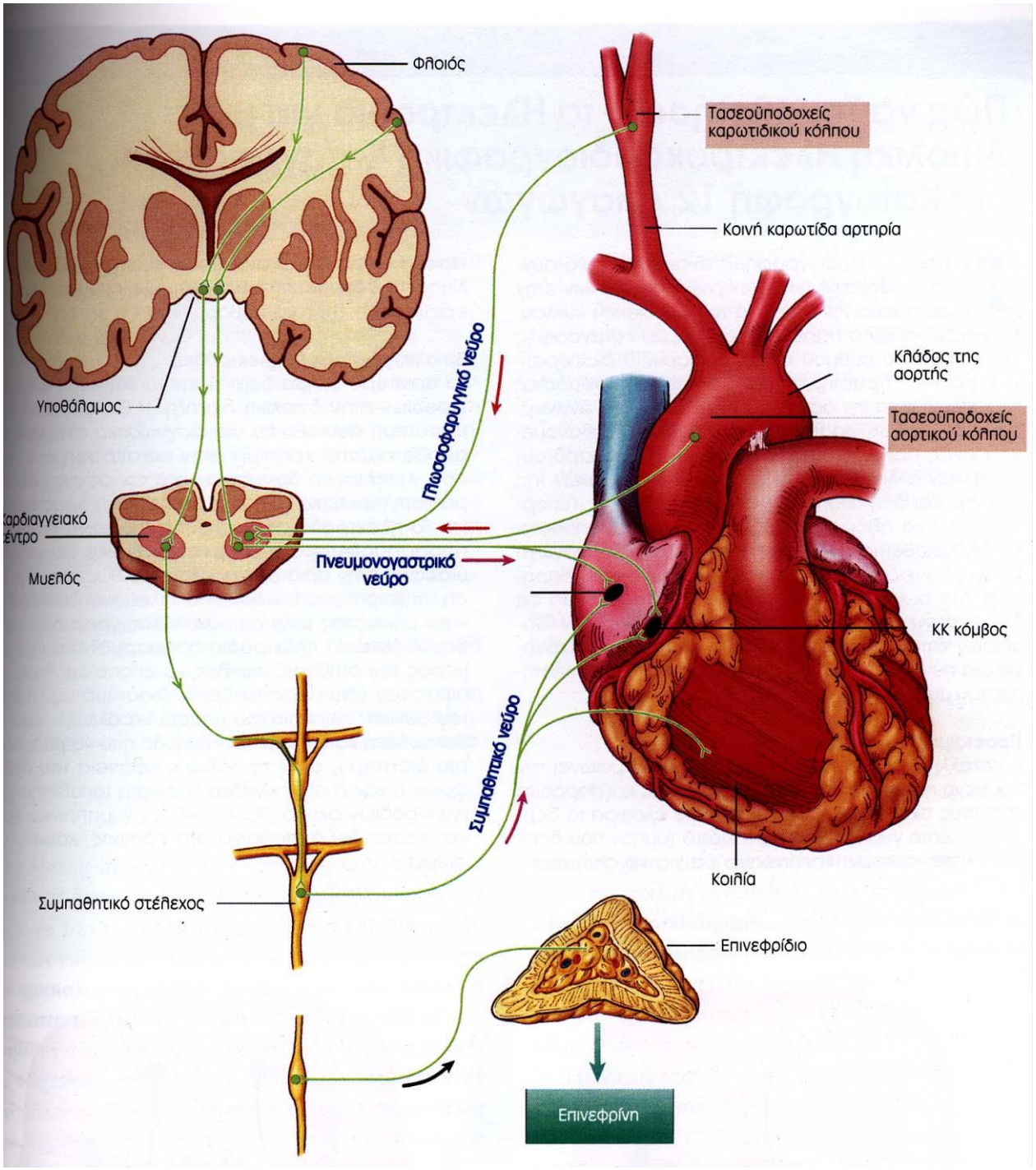

Aorta
Superior vena cava
Sinoatrial node
Internodal pathways
Atrioventricular node
Bundle of His
Right bundle branch
Purkinje system
Left anterior fascicle
Left bundle branch
Left posterior fascicle
100
ms
10
mV
SA node
Atrial muscle
AV node
Ventricular muscle

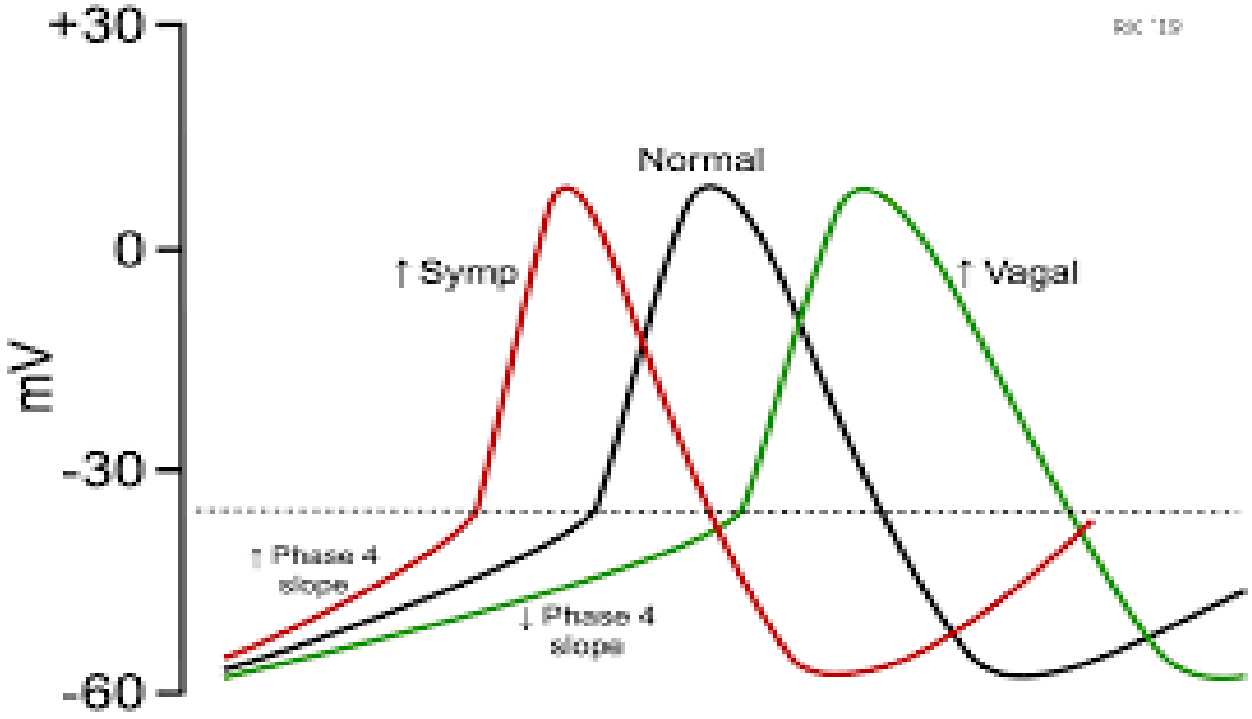

+20
0
-20
-40
-60
-80
-100
Ventricle
0
1
2
3
4
SA node
0
-20
-40
-60
-80
0
3
4
+20
0
-20
-40
-60
-80
-100
Atrium
1
2
3
0
4


+20
0
−20
−40
−60
−80
Membrane potential (mV)
Rapid influx of Ca2+
Depolarization
Outflux of K+
Repolarization
Slow influx of Na+
Prepotential
Threshold
0.8
1.6
Time (s)

Effects of Autonomic Nervous System

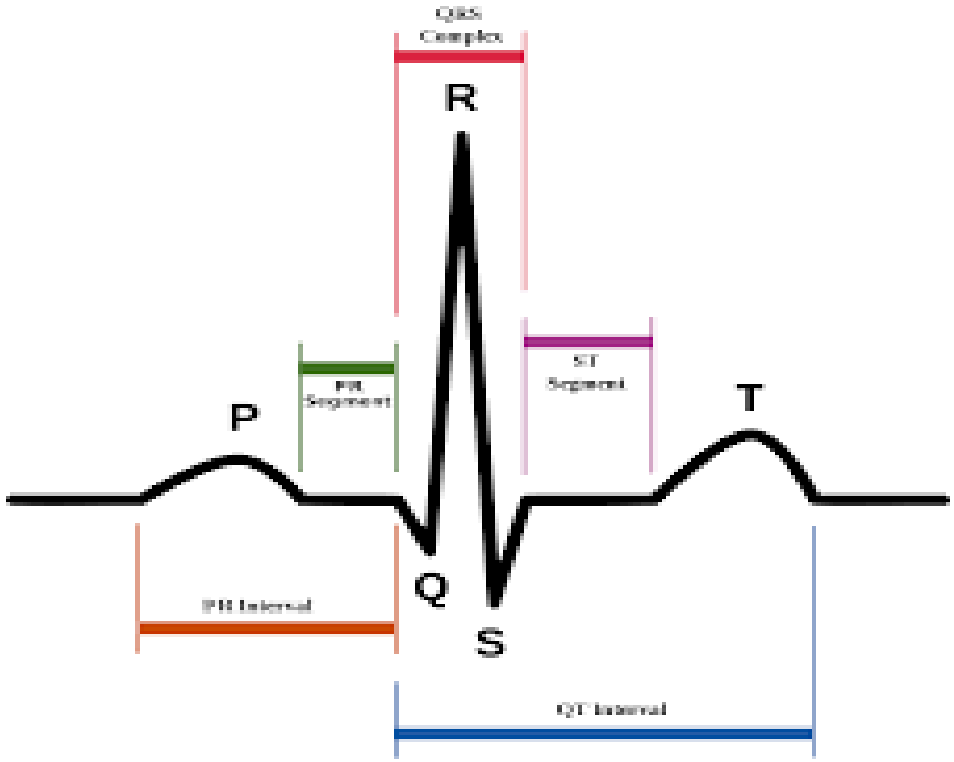
- **The heart is innervated by both sympathetic and parasympathetic nervous system.**
- **When sympathetic nervous system is activated the endocrine gland adrenal medulla is also activated. The neurotransmitter of the sympathetic nervous system is norepinephrine whereas the hormone of the adrenal medulla is epineprine. Both of them exhibit their effects by activating β adrenergic receptors. The adrenergic system increases heart rate (tachycardia) by increasing the slope of diastolic depolarization caused by the augmentation of if and iCa.**
- **The fibers of the parasympathetic nervous system reach the heart through the vagus nerve. The neurotransmitter of the fibers of the parasympatetic nervous system is acetylcholine and exhibits its effects by activating muscarinic muscarinic acetylcholine receptors. Acetylcholine decreases the heart rate (bradycardia)by decreasing the slope of diastolic depolarization caused by the depression of both if and iCa currents and by the induction of hyperpolarization caused by the activation of specific potassium channels.**


Φλοιός
Υποθάλαμος
Καρδιαγγειακό κέντρο
Μυελός
Πλαισοφαρυγγικό νεύρο
Πνευμονογαστρικό νεύρο
Συμπαθητικό νεύρο
Συμπαθητικό στέλεχος
Ταξεοϋποδοχείς καρωτιδικού κόλπου
Κοινή καρωτίδα αρτηρία
Κλάδος της αορτής
Ταξεοϋποδοχείς αορτικού κόλπου
ΚΚ κόμβος
Κοιλία
Επινεφρίδιο
Επινεφρίνη


+30
0
-30
-60
mV
RK '19
Normal
↑ Symp
↑ Vagal
↑ Phase 4 slope
↓ Phase 4 slope

Electrocardiogram (ECG)

- **The ECG is a graphic recording of the changes occurring in the electrical potentials (in mV) between different sites on the skin (*leads)* as a result of cardiac activity. The ECG thus reflects the electrical events connected with cardiac excitation.**
- **An ECG curve is characterized by a series of deflections or waves , the convention being that a positive potential produces an upward deflection, a negative potential a downward deflection. The P wave represents the *atrial depolarization*. The wave for atrial repolarization is not visible on the ECG because it is masked by the succeeding waves . The Q, R and S waves together constitute the QRS complex represent *ventricular depolarization.* Next come the T wave which represents *repolarization of the ventricles.***
- **The PQ segment and the ST segment lie on near 0 mV line. Fully stimulated atria (PQ segment) and ventricles (ST segment) produce no detectable potential. In the PQ interval is included the delay of the propagation of the impulse in AV node.**

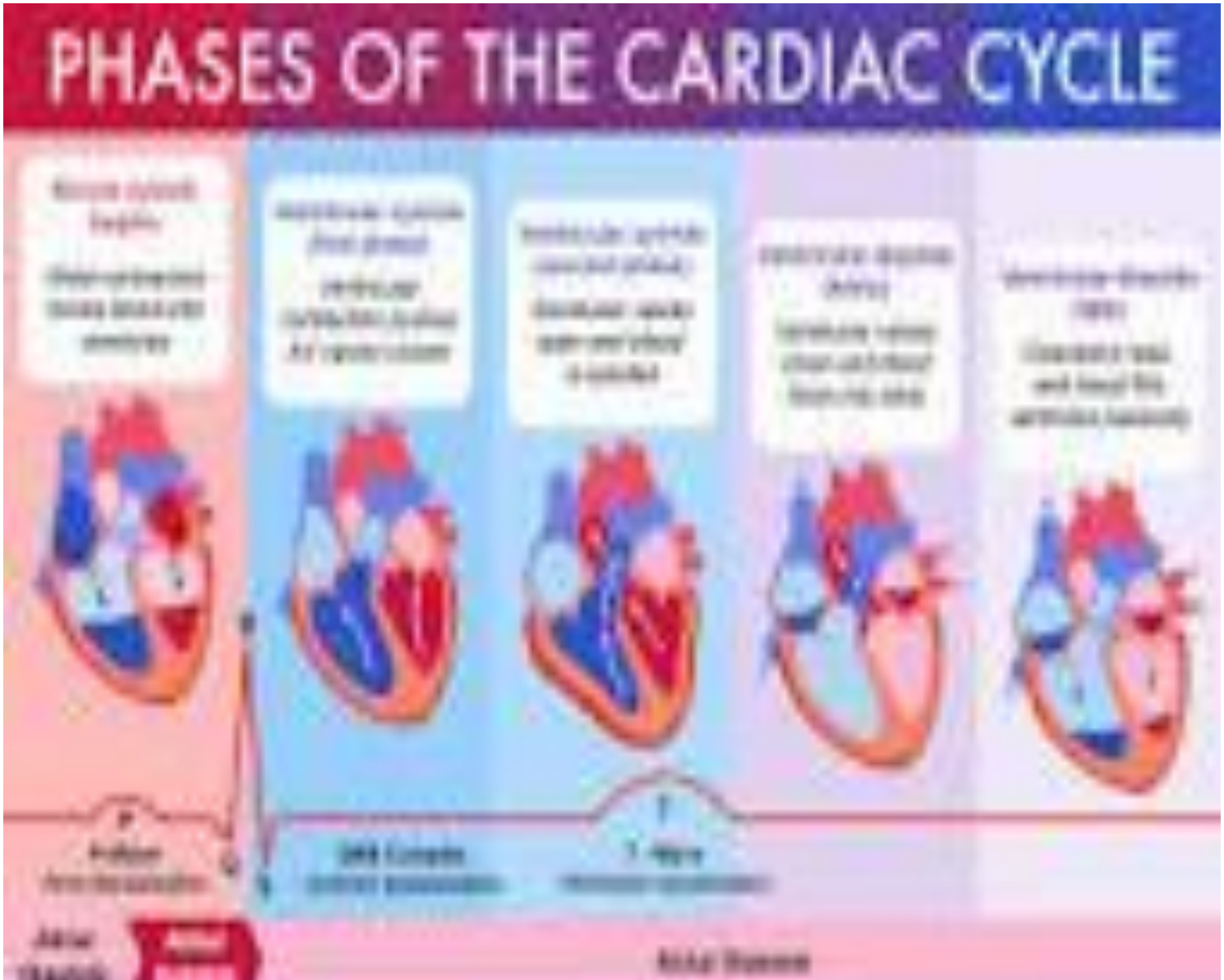

QRS
Complex
R
PR
Segment
ST
Segment
P
T
Q
S
PR Interval
QT Interval

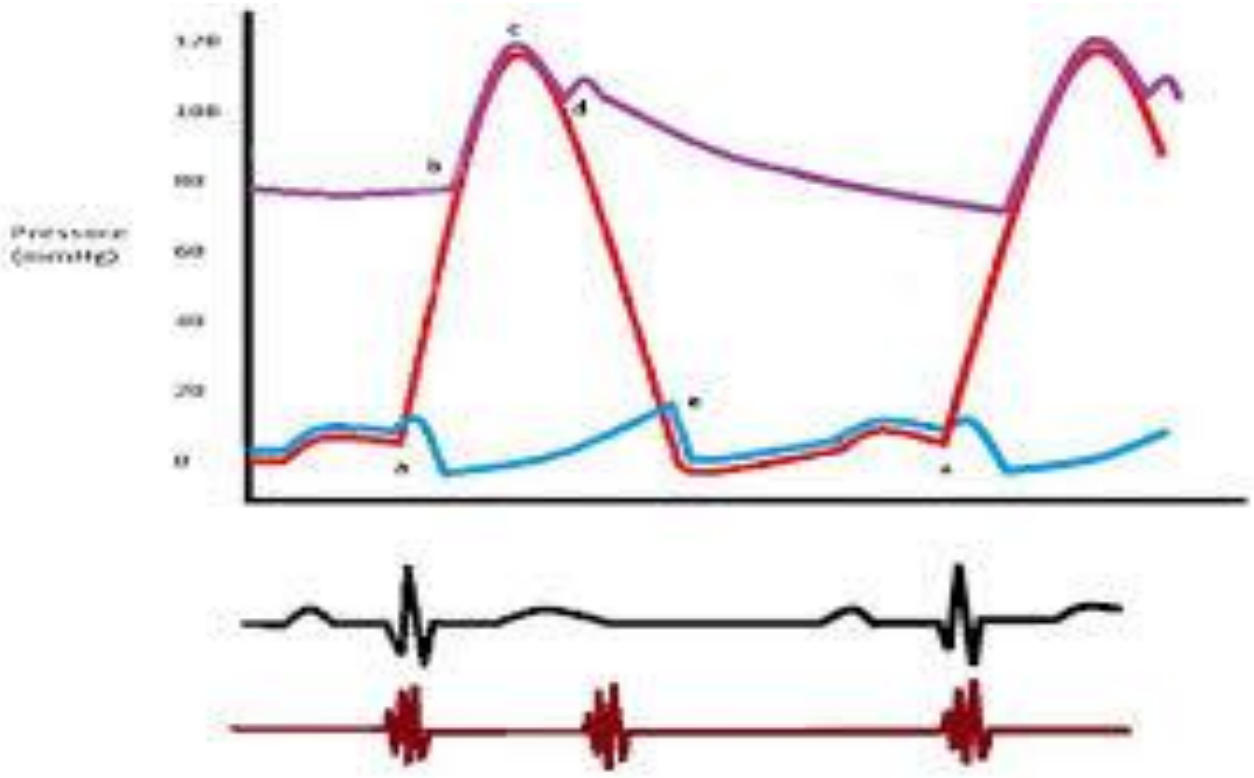
Contraction of the Heart-Cardiac Cycle

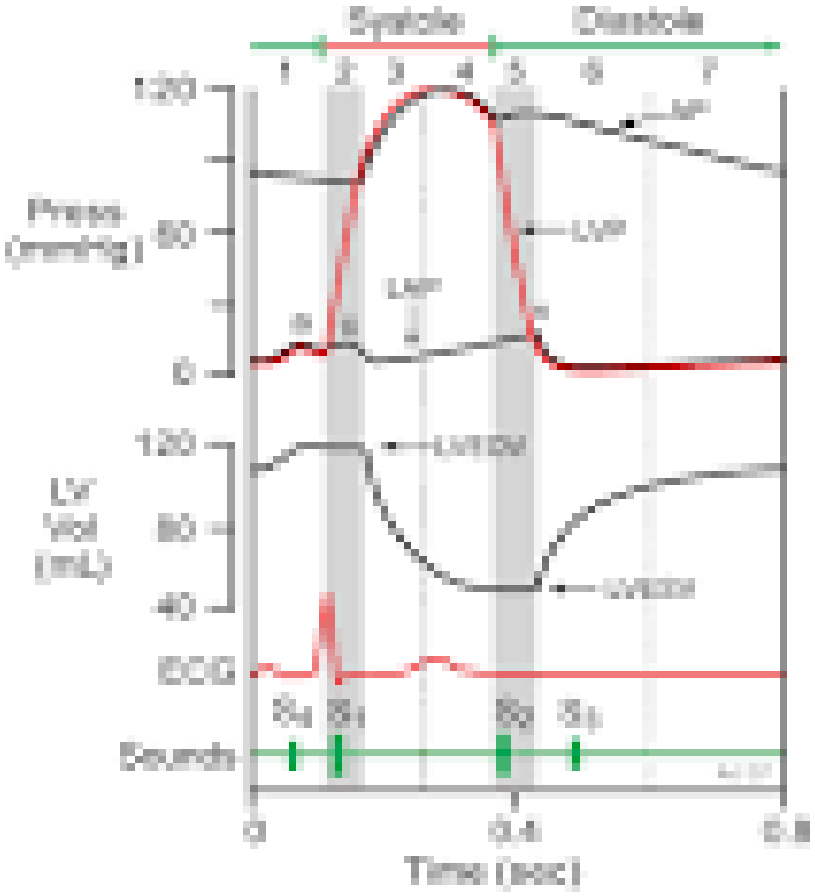
- **The contraction of the myocardial fibers is initiated by the Ca that enters in the cells during the plateau phase of the action potential.**
- **The cardiac cycle is the performance of the heart from the beginning of one heart beat to the beginning of the next. The five phases of the cardiac cycle are accomplished in less than a second and are the following: atrial contraction, isovolumetric contraction of the ventricles, ejection period, isovolumetric relaxation, filling phase of diastole. In diastole both atria and ventricles are relaxed , mitral and tricuspid valve are open whereas aortic and pulmonary valves are closed. Blood flows fro pulmonary veins and vena cava through the atria into the left and right ventricles respectively. The ventricles fill with blood. At the end of the diastole the atria contract squirting a small amount of blood into the ventricles. . The isovolumetric contraction of the ventricles follows. In this phase all four valves are closed . The volume of the blood in the ventricles remains constant but the pressure rise rapidly. . When the pressure in the left ventricle exceeds that in the aorta (diastolic pressure) the aortic valve opens and this marks the beginning of the ejection period during which the pressure in the left ventricle and in the aorta briefly rises (rapid ejection period) to maximum of 120mmHg (systolic pressure) . Systolic and diastolic pressures in the pulmonary artery are 25/8mm Hg. Following the ejection period the ventricles relax (isovolumetric relaxation) and their pressures fall below that of the aorta and pulmonary artery. The mitral and the tricuspid valve open and the valves in the aorta and the pulmonary artery close.**

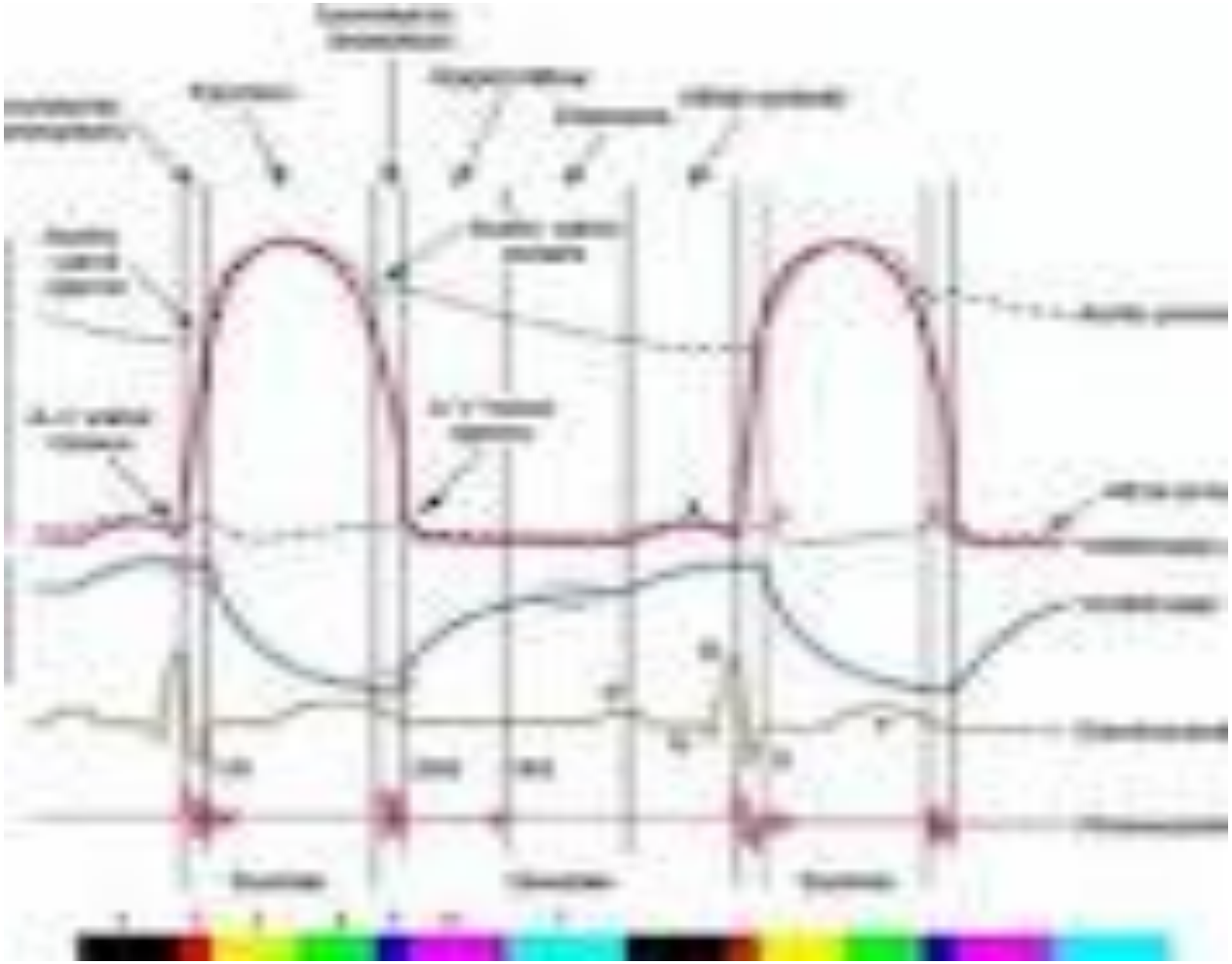
Blood Volumes

- **Normally at the end of the diastole the volume of the blood in each ventricle (end diastolic volume) is about 125 ml but it can rise to as much as 250 ml.**
- **The volume of the blood that remains in each ventricle at the end of the ejection period (end systolic volume) is about 65 ml.**
- **The volume of the blood that is pumped from each ventricle during one beat (stroke volume) is about 70ml.**


PHASES OF THE CARDIAC CYCLE


Pressure (mmHg)
a
b
c
d
e


Systole
Diastole
1
2
3
4
5
6
7
120
80
0
Press
(mmHg)
LVP
LAP
LVP
LAP
120
80
40
LV
Vol
(mL)
LVESV
LVEDV
ECG
S4
S1
S2
S3
Sounds
0
0.4
0.8
Time (sec)

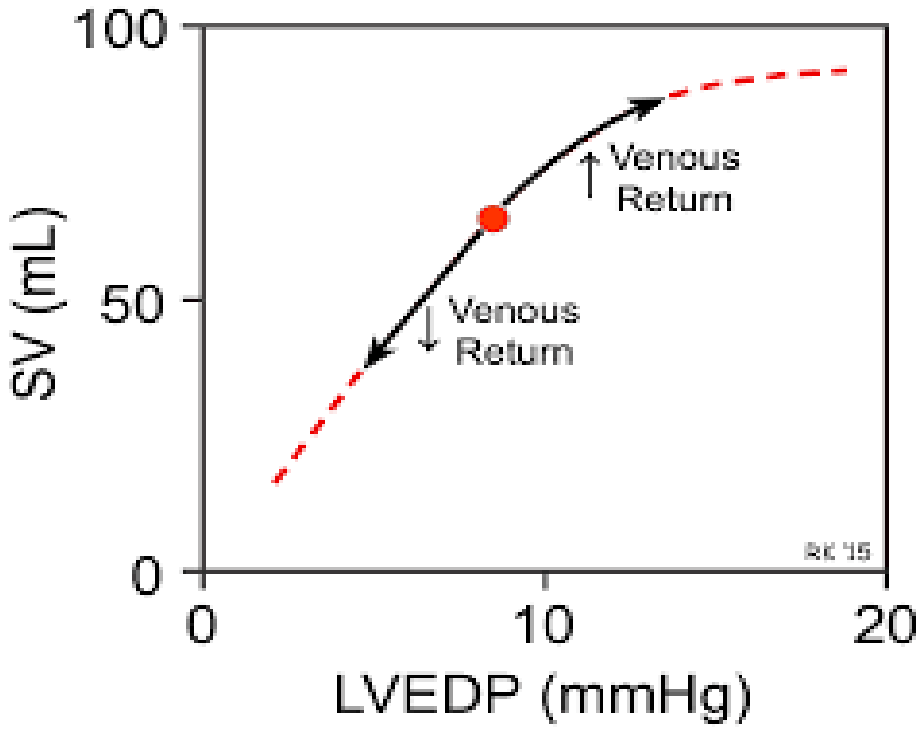


Regulation of heart's contractility –intrinsic factors

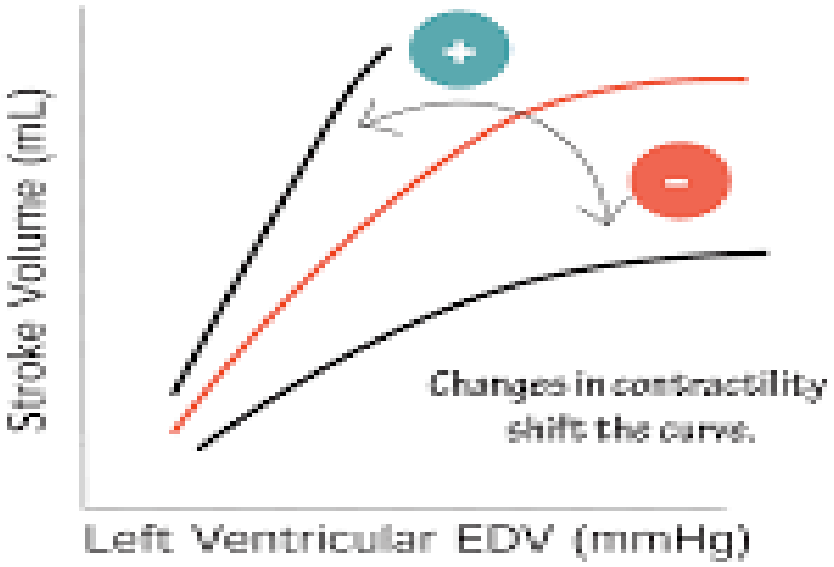
- **In the late 19th century Frank found, using isolated frog hearts, that the strength of ventricular contraction was increased when the ventricle was stretched prior to contraction. In the early 20th Starling and colleagues found that increasing venous return (preload) to the heart which increased end diastolic volume and diastolic pressure of the ventricle led to increased contractility of the ventricle and increased stroke volume. Conversely, decreasing venous return results decreased stroke volume. The ability of the heart to change its force of contraction in response to changes of venous return and therefore of the end diastolic volume is called the Frank=Starling mechanism or law.**
- **This is a very important intrinsic mechanism of regulation heart's contractility and stroke volume.**

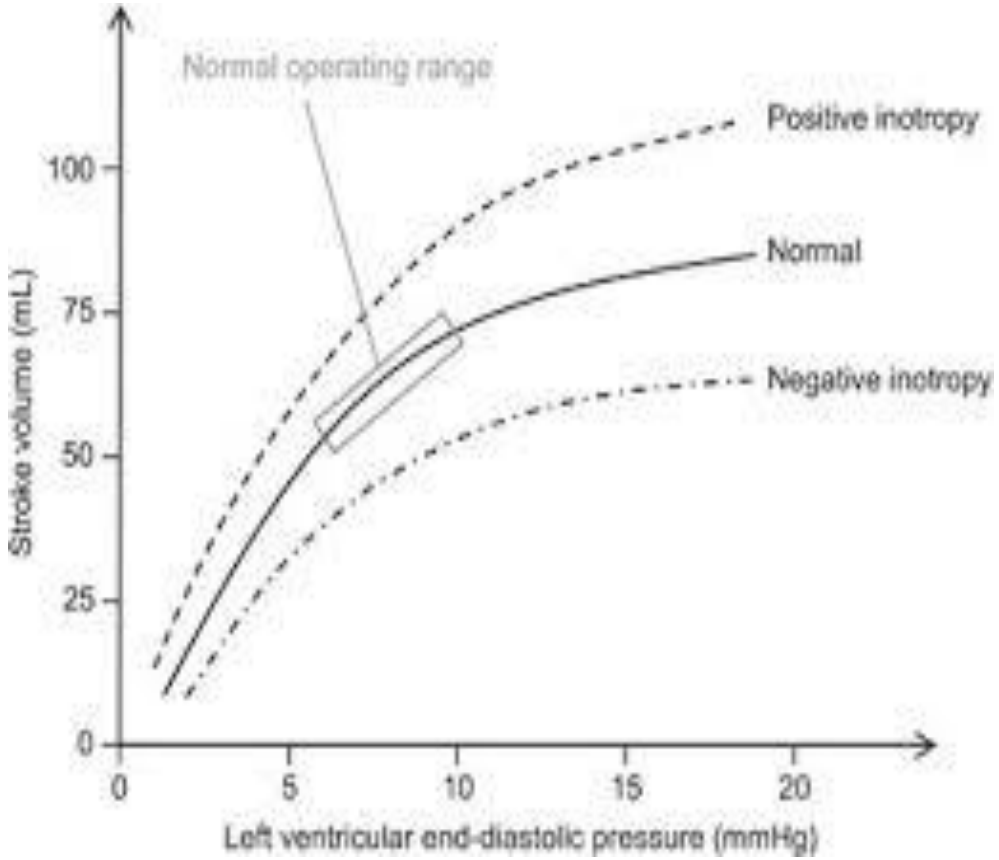
Regulation of Heart's contractility-extrinsic factors

- **Heart's contractility is also affected by several extrinsic factors that increase or decrease heart's contractility and stroke volume. Factors that increase contractility turn Frank – Starling curve to left and up whereas factors that decrease contractility turn the Frank-Starling curve to right and down. Calcium ions is a major factor that increases heart's contractility. Sympathetic nervous system and cardiotonic glycosides (digitalis) increase also myocardial contractility by increasing intracellular concentration of Ca.**
- **Potassium ions, myocardial infarction, barbiturates, β-blockers, Ca-channels antagonists decrease heart's contractility.**


100
50
0
SV (mL)
0
10
20
LVEDP (mmHg)
Venous
Return
Venous
Return

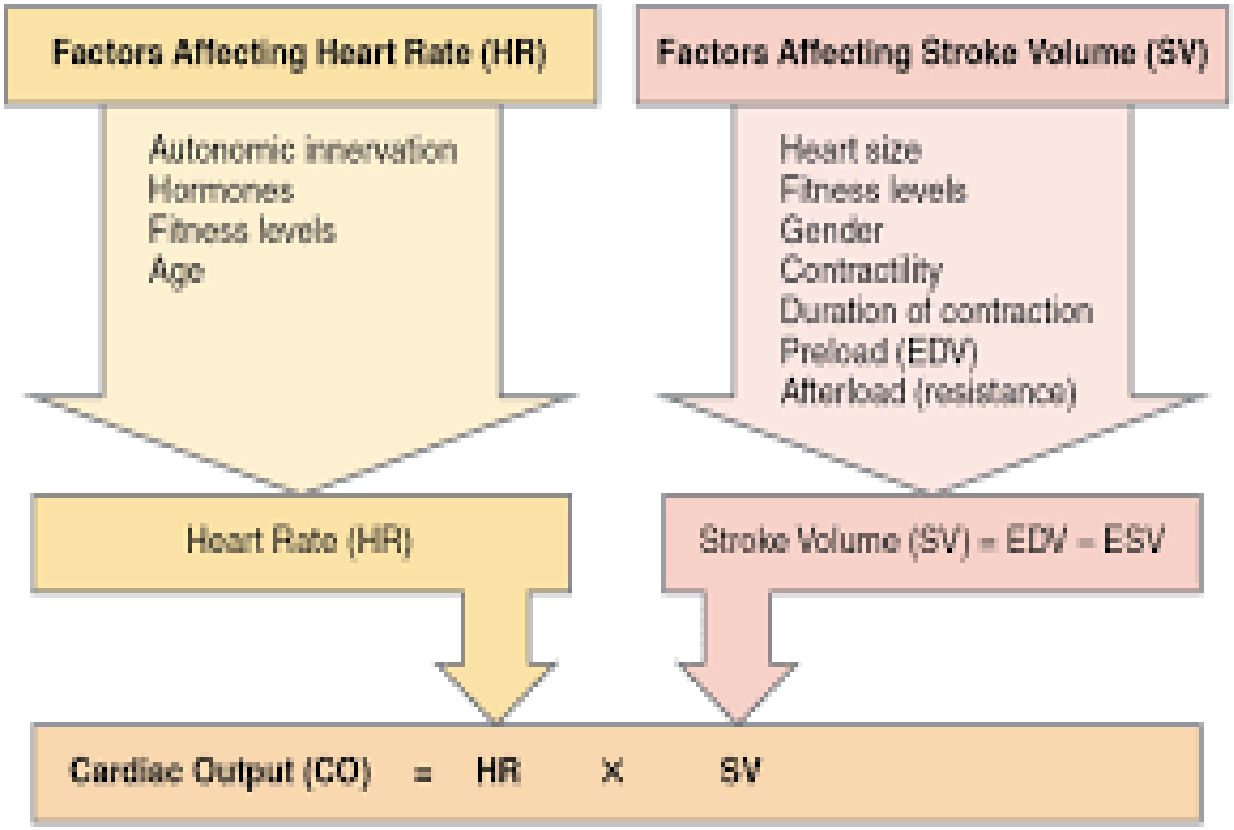
Frank-Starling Law




Normal operating range
Positive inotropy
Normal
Negative inotropy
Stroke volume (mL)
100
75
50
25
0
0
5
10
15
20
Left ventricular end-diastolic pressure (mmHg)

Cardiac Output (CO)

- **Cardiac Output is a term that describes the volume of blood being pumped by each ventricle per minute. Cardiac output is the product of Heart Rate (HR) and the Stroke Volume (SV). For a healthy person weighing 70Kg the CO at rest averages about 5L/min. , assuming a HR of 70beats /min and a SV of approximately 70ml. Probably factors influencing HR and SV influence CO. The major factors that affect HR are Autonomic nervous system and hormones. Sympathetic nervous sytem (norepinephrine) and the hormones of Adrenal Medulla (epinephrine) and Thyroid Gland (T3, T4) increase HR resulting increase of CO. The major factor that affects SV is heart's contractility which, as it is discussed previously , is regulated by the preload and end diastolic volume. Ca, epinephrine and norepinephrine increase heart's contractility resulting increase of CO. In exercise CO can increase up to 25L because of the activation of the Sympathetic system and Adrenal Medulla.**

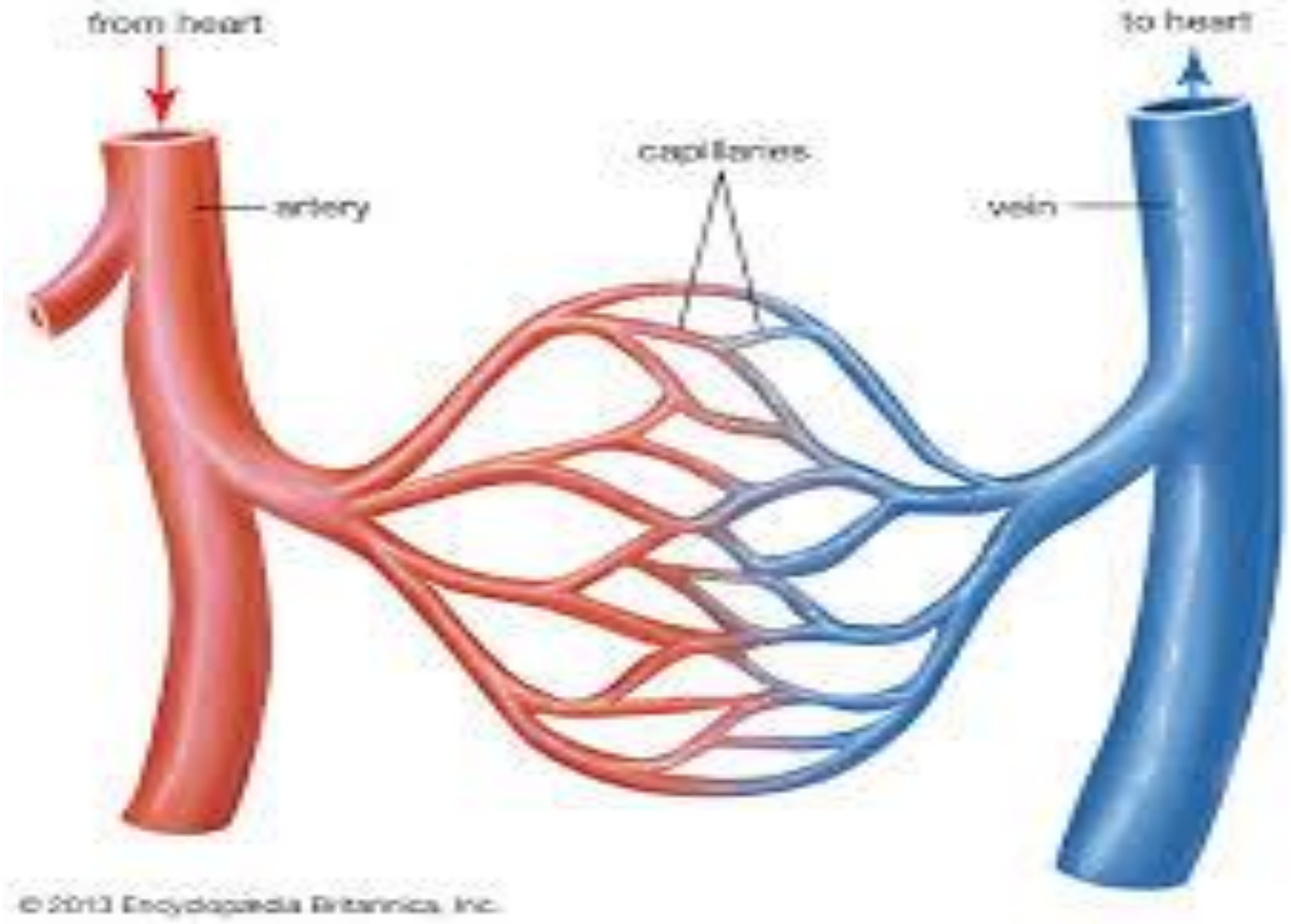

Factors Affecting Heart Rate (HR)
Autonomic innervation
Hormones
Fitness levels
Age
Factors Affecting Stroke Volume (SV)
Heart size
Fitness levels
Gender
Contractility
Duration of contraction
Preload (EDV)
Afterload (resistance)
Heart Rate (HR)
Stroke Volume (SV) = EDV – ESV
Cardiac Output (CO) = HR X SV

PROPERTIES OF THE VASCULATURE

- **Vasculature can be devided in the arterial system, the venous system and the microcirculation which separates the arterial and the venous system.**

Types of blood vessels

- **There are five types of blood vessels, the arteries which carry the blood away from the heart , the arterioles, the capillaries, where the exchange of water and chemicals between the blood and the tissues occurs, the venules and the veins, which carry blood from the capillaries back towards the heart.**


from heart
to heart
capillaries
artery
vein
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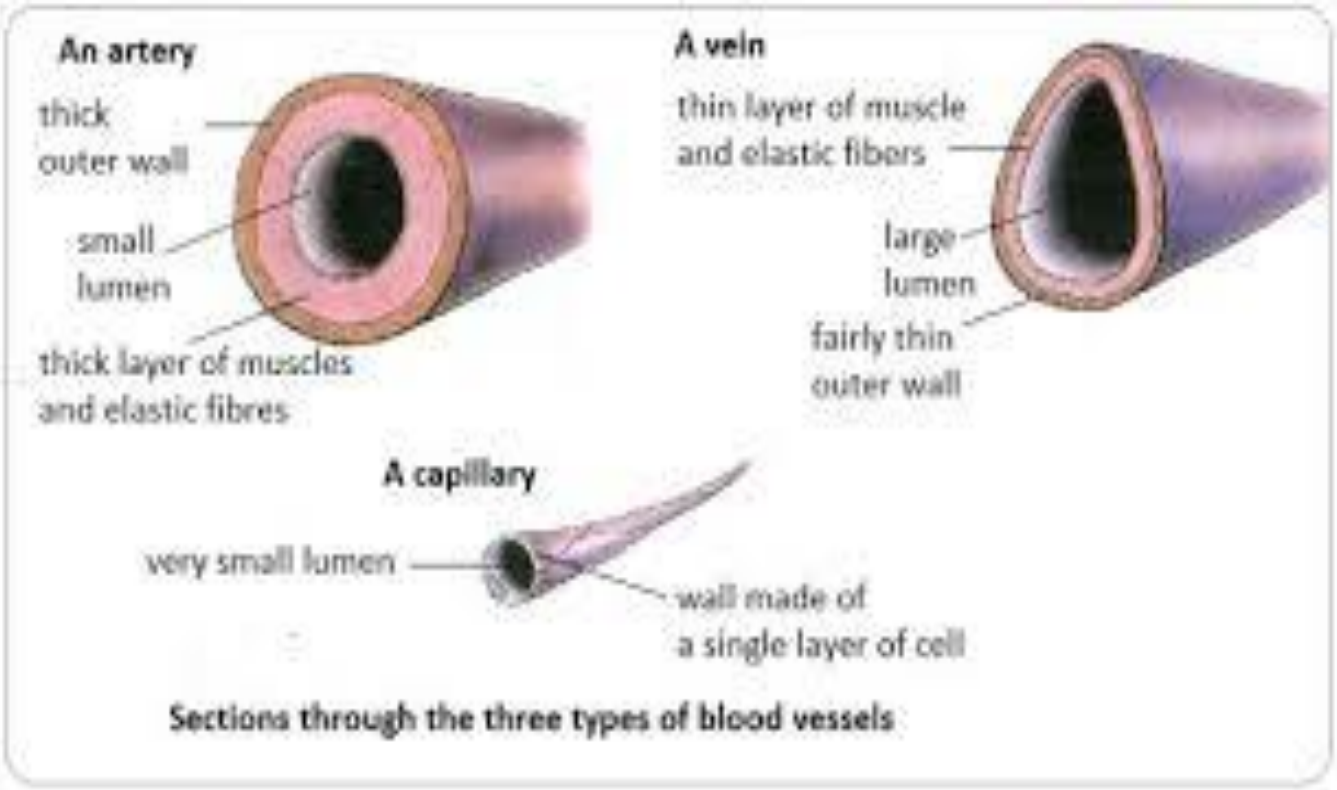
Structure of blood vessels

- **The arteries arterioles and veins have three layers. The inner layer is a single layer of flat epithelial cells (endothelial cells) The middle layer is the thickest layer and consists of vascular smooth muscle which controls the calliber of the vessels. In the elastic arteries (aorta, large arteries) the middle layer contains circularly arranged elastic fibers. The outer layer is entirely made by connective tissue.**
- **Capillaries consist of a single layer of endothelial cells with a supportive basement membrane of connective tissue.**



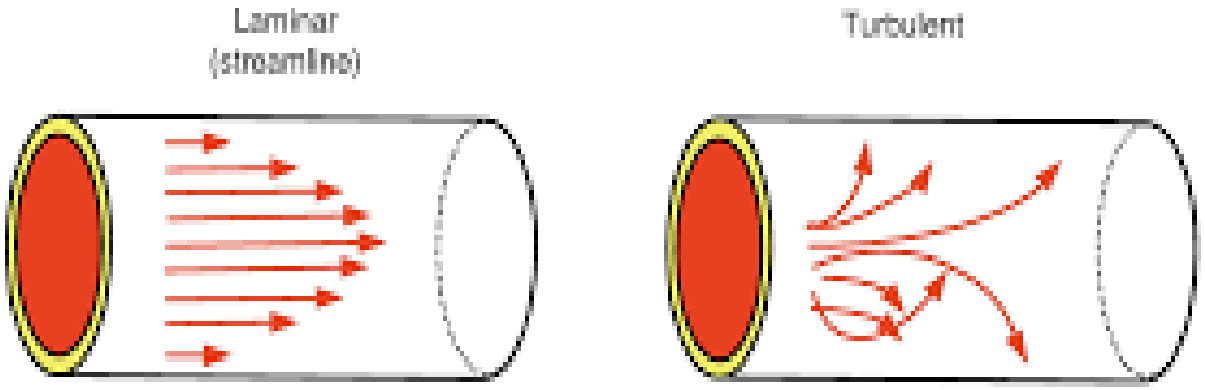
Sections through the three types of blood vessels

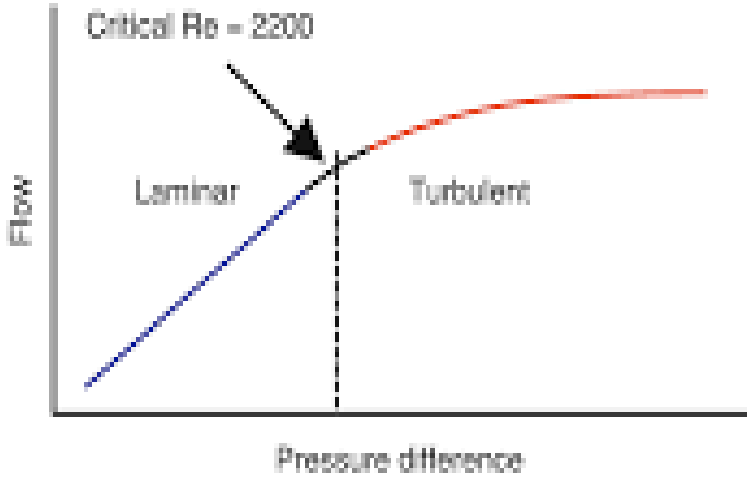
Hemodynamics

- **The physics of fluid flow through rigid tubes provides a basis of understanding the flow of blood through blood vessels even though the blood vessels are not rigid tubes.**
- **Velocity (V) is the distance that a particle of blood travels with regard of time and it is expressed in units of distance per unit time.**
- **Flow (Q) is the volume of blood that passes the cross-sectional area of a blood vessel per unit time.**
- **Velocity (V) and flow (Q) are related to one another by the cross-sectional area (A) of the tube.**
- **$V=Q/A$**

Types of blood flow

- **Blood flow can be laminar or turbulent.**
- **Laminar flow refers to stream line (parallel layers) movement of blood. Blood flow is zero in a very thin layer in contact with the vessel wall and highest at the center of the vessel lumen.**
- **Blood flow in most vessels of the body is laminar. However under certain conditions laminar flow can become turbulent. When this occurs blood does not flow linearly but instead can be described as being chaotic. Turbulence occurs when a critical Reynolds number (Re) is exceeded.**
- $$Re = V.D.p/\eta$$
- **Where V=mean velocity, D=vessel diameter , p=blood density, η=blood viscosity. As can be seen Re increases as velocity increases and viscosity decreases. Therefore, high velocities and low blood viscosity (as occurs with anemia due to reduced hematocrit) are more likely to produce turbulence.**





$Re = \rho v D/\eta$
with

ρ = blood density
v = blood velocity
D = diameter
η = blood viscosity

Relationship between Pressure and Flow

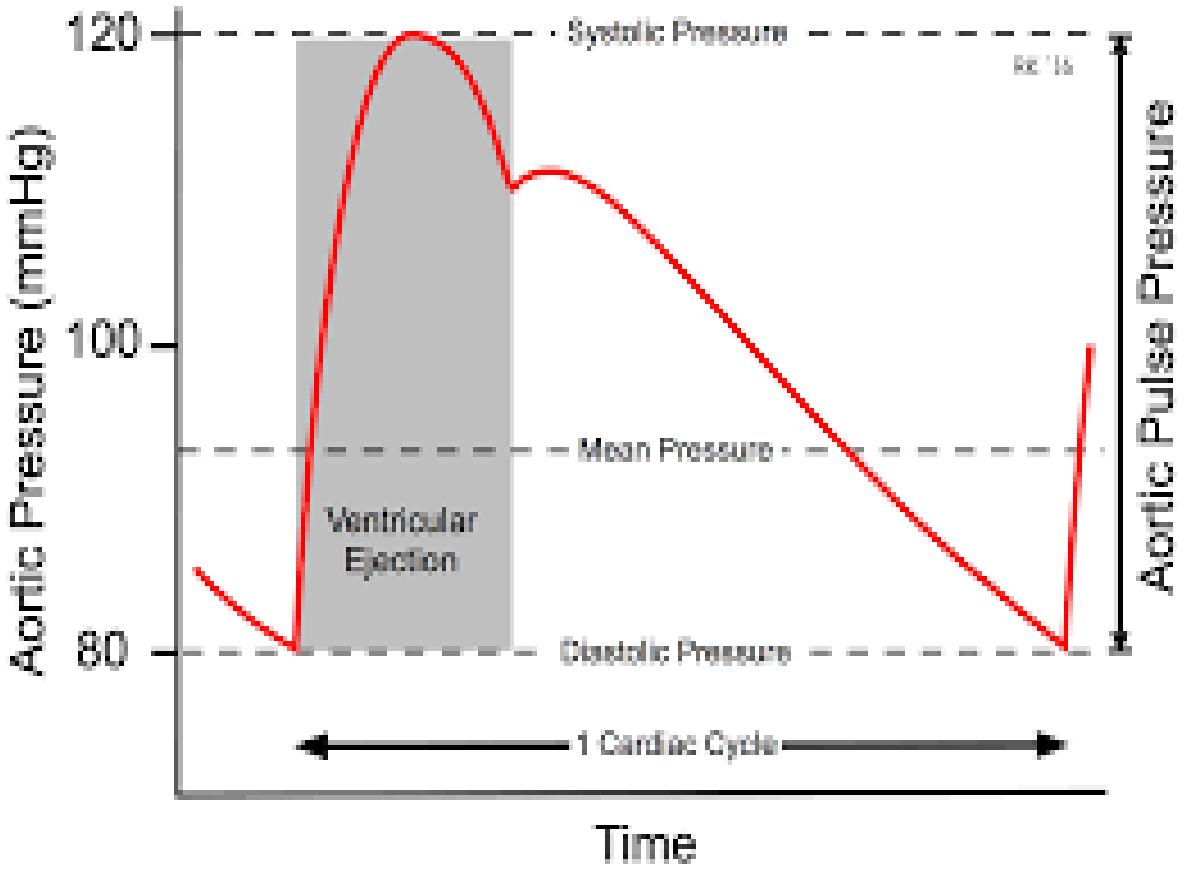
- **The relationship between pressure and flow in a tube is described by the law of Ohm as follows:**
- $$p1-p2=Q.R \quad (1)$$
- **Where p1-p2= the pressure difference between the beginning and the end of the tube, Q=Flow and R=Resistance.**
- **According to the law of Poiseuille:**
- $$R=8\eta l/\pi r4 \quad (2)$$
- **Where η=viscosity of the fluid , l=length of the tube, r=radius.**
- **Therefore**
- $$p1-p2= Q \,.\, 8\eta l/\pi r4 \quad (3)$$

Systemic Circulation

- **If we apply equation 3 in the systemic circulation then:**
- **P1=Arterial pressure (AP) p2=0 because at the end of the systemic circulation p=0, Q= Cardiac output (CO). r=radius. η=viscosity of the blood, l=length of the systemic circulation, r=radius of the resistance vessels (arterioles). Therefore equation 3 can be transformed as follows:**
- $$AP=CO.\ 8\eta l/\pi r4$$
- **Extremely important factor is r because it enters in the equation with the fourth power and can be changed very easily under the effect of neuronal and chemical factors.**
- **l increases and therefore AP with the increase of body weight.**
- **η does not change significantly within a big range of the haematocrit.**

Blood Pressure

- **The general term blood pressure applies to the arterial blood pressure in the systemic circulation. It fluctuates with each heart beat between a maximum value (systolic blood pressure) at the end of the rapid ejection period and a minimum value during cardiac diastole at the end of cardiac cycle. Their geometric mean is the mean pressure and their difference is known as pulse pressure.**

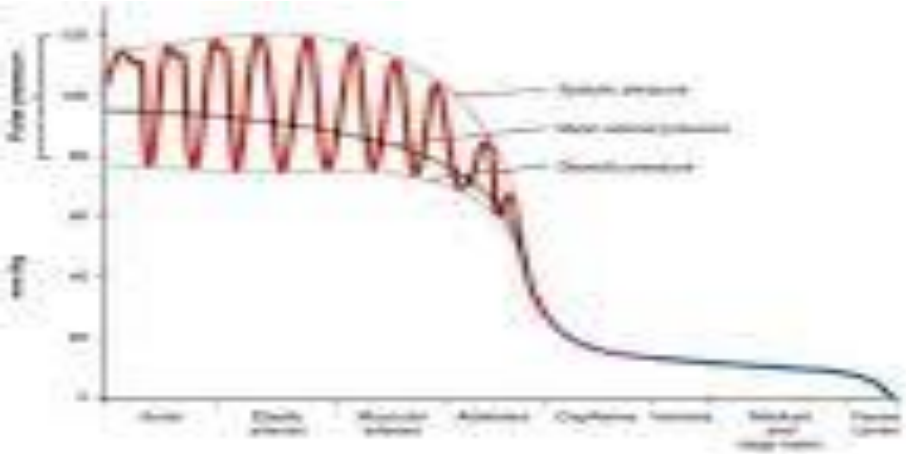

120
100
80
Systolic Pressure
Mean Pressure
Diastolic Pressure
Ventricular Ejection
1 Cardiac Cycle
Aortic Pressure (mmHg)
Aortic Pulse Pressure
Time

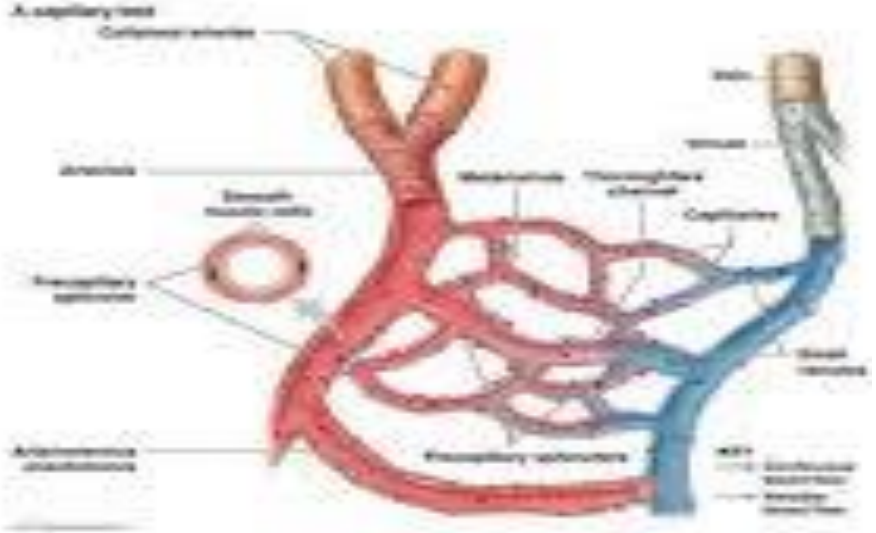
Determinants of Arterial Blood Pressure

- **The determinants of arterial blood pressure are arbitarily devided into "physiological" and "physical" factors.**
- **The two physiological factors are, as it is already mentioned, cardiac output and peripheral resistance. Changes in the size of radius of high resistance vessels play a crucial role in the regulation of peripheral resistance and of blood pressure therefore.**
- **The two physical factors are arterial blood volume and arterial compliance. An increase of arterial blood volume results an increase of arterial blood pressure whereas a decrease arterial blood volume (hemorrhage) has an opposite effect. Arterial compliance is the ability of the aorta and the large arteries to distend and increase volume with increasing pressure. Compliance is calculated using the equation C=dV/dP,dV is the change in volume and dP the change in pressure. Decrease of arterial compliance results increase of pulse pressure.**

Arterioles

- **Arterioles are small diameter blood vessels in the microcirculation that extend and branch from the arteries and lead to the capillaries. They have a thick smooth muscle layer innervated by vasoconstrictive nerve fibers and are the primary site of vascular resistance. Therefore due to the law p1-p2=QR the pressure difference between the beginning and the end of the arterioles is the highest observed in the cardiovascular system. This as will be discussed later, is very important for the function of the capillaries.**



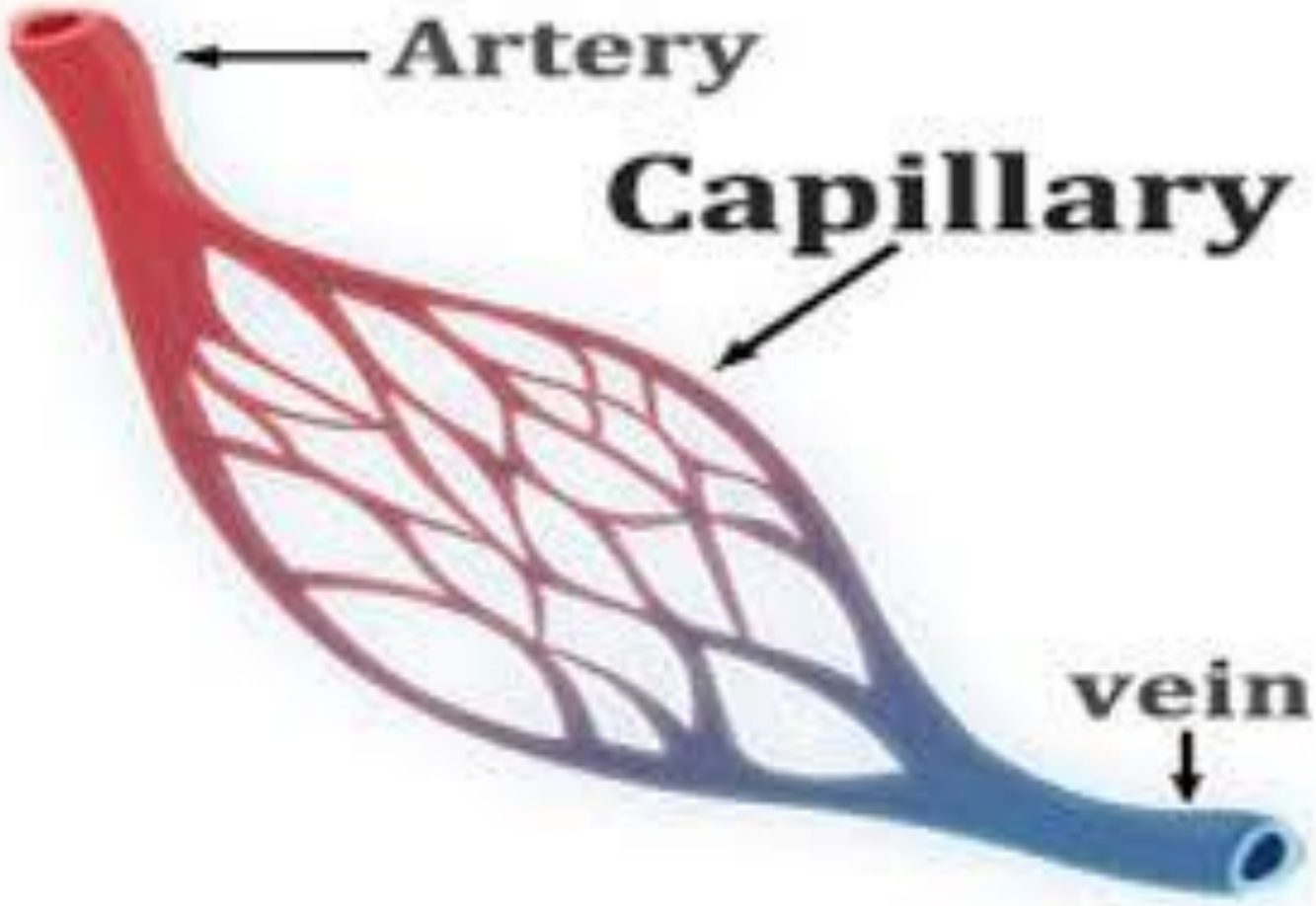


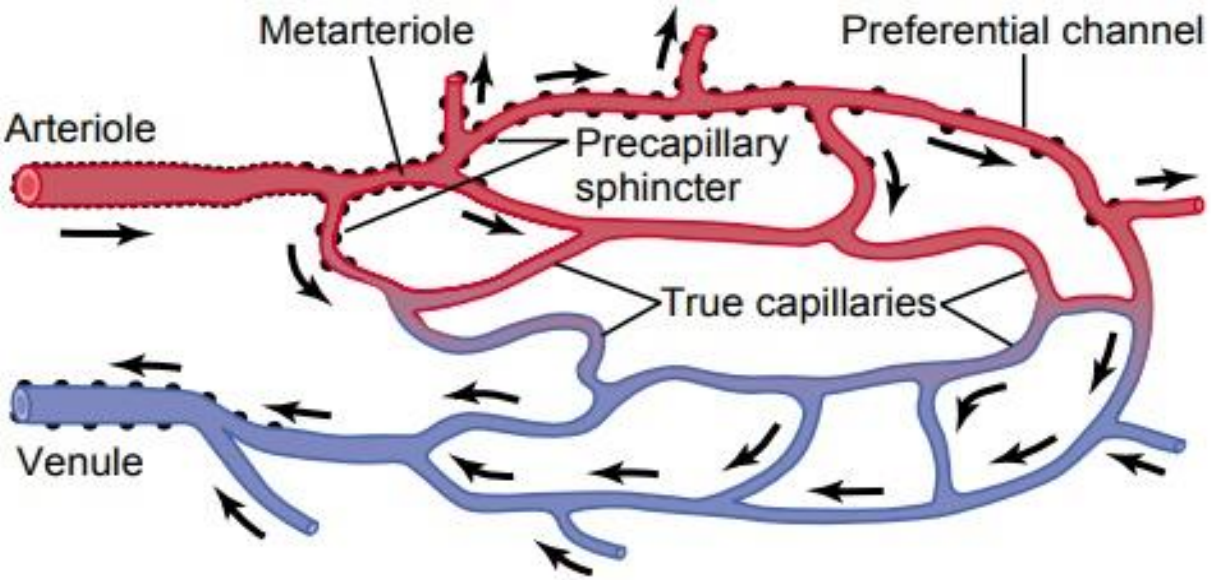
Capillaries

- **Capillaries are small blood vessels from 5 to 10µm in diameter and having a wall of one endothelial cell. These microvessels are the site of exchange of oxygen, CO_2, nutrients and waste between blood and the interstitial fluid of the tissues surrounding the capillaries. Water and substances dissolved in it (except blood cells and proteins) can cross the thin capillary walls through pores of 8nm in diameter through the processes of passive diffusion and filtration. Passive diffusion is the movement of substances from areas of high concentration to areas of low concentration. The rate of passive diffusion is 5000 times higher than the rate of filtration.**

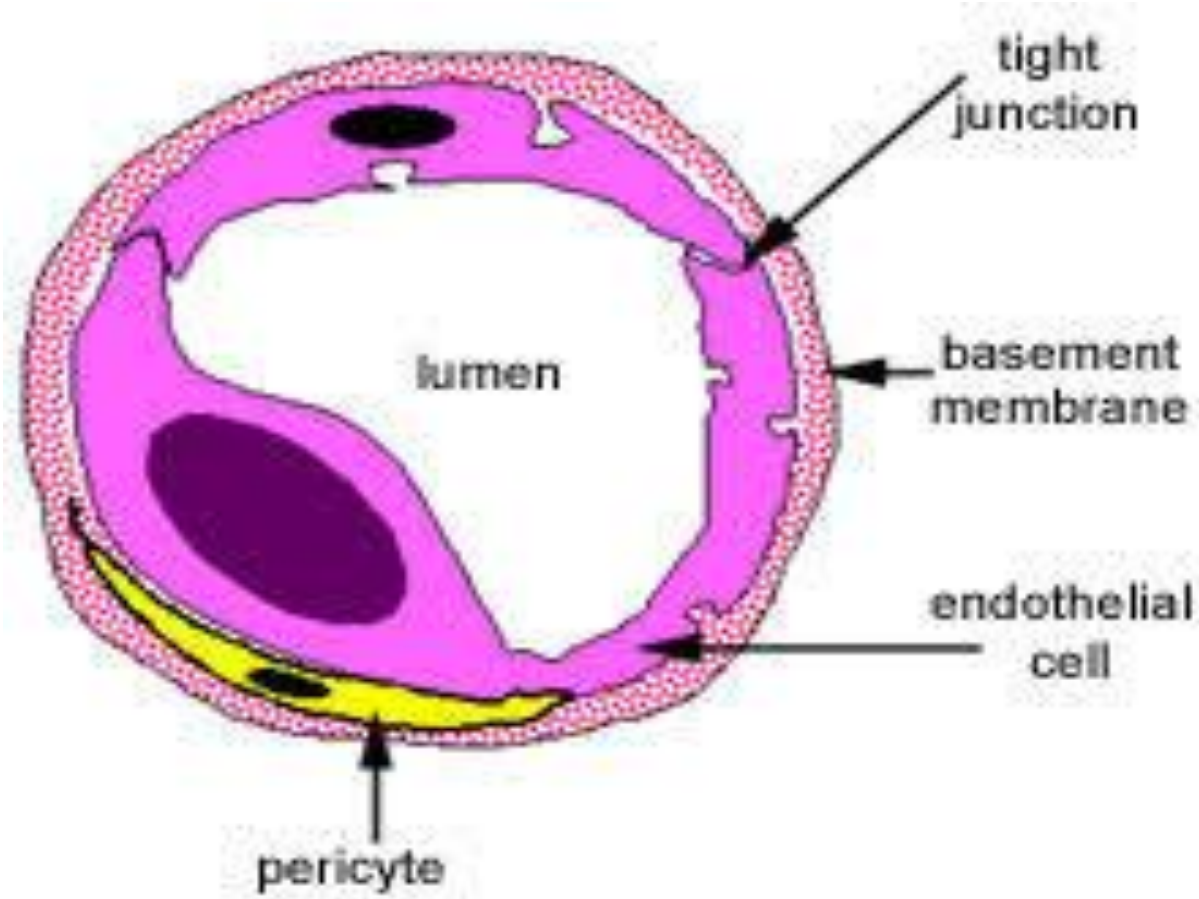
Filtration

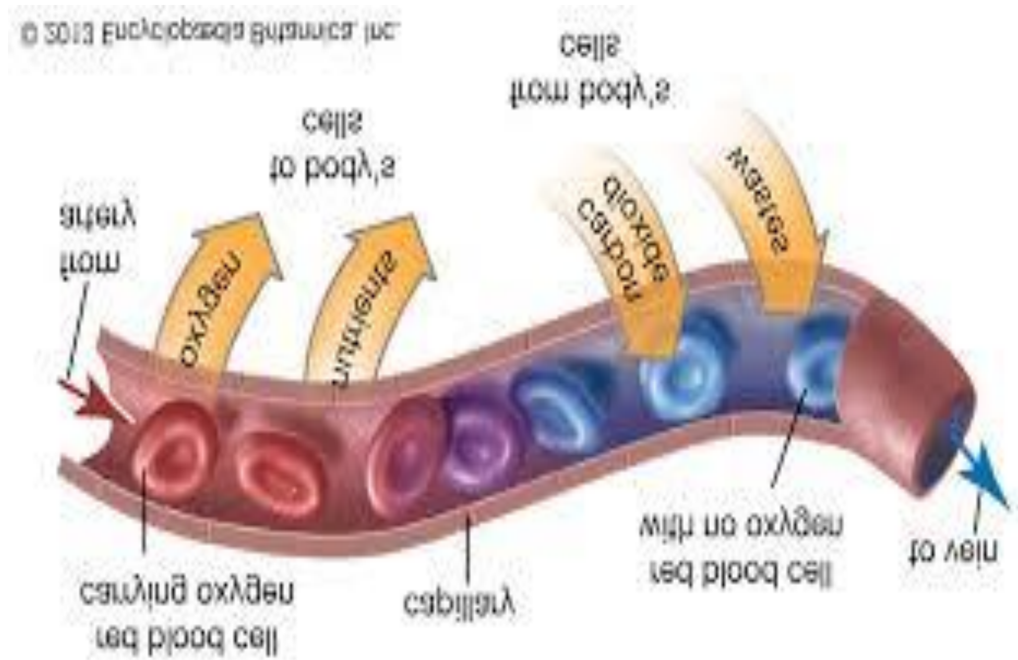
- **The driving pressure for filtration is defined by Starling's equation:**
- **DP=Kf((Pc-Pi)-(πc-πι)**
- **Where: DP=driving pressure, Kf=filtration coefficient, Pc=Capillary hydrostatic pressure, Pi=Interstitial hydrostatic pressure, πc=Capillary oncotic pressure (osmotic pressure of plasma proteins), πi=Interstitial oncotic pressure.**
- **Since Kf is constant and Pi and πi are very low the equation can be transformed as follows: DP= Pc-πc. When DP is positive, fluid will tend to leave the capillary (filtration), when it is negative will tend to enter in the capillary (reabsorption). In the first part of the capillary (arterial) fluid exits the capillary because Pc (35mmHg) is higher than the πc (25mmHg). In mid net filtration is 0 because Pc equals πc(25mmHg). In the second part (venous) fluid reenters in the capillary (reabsorption) since hydrostatic pressure (18mmHg) is less than the πc (25mmHg) . Normally for 100 volumes filtered 90 volumes are reabsorbed and 10 volumes are taken away from the interstitially fluid through the lymphatic capillaries and therefore the volume of the interstitial fluid remains constant. Several pathological conditions increase Pc or decrease πc and may lead to edema (increase of the volume of the interstitial fluid)**
-


Artery
Capillary
vein



Structure of the mesenteric capillary bed. (Redrawn from Zweifach BW: Factors Regulating Blood Pressure. New York: Josiah Macy, Jr., Foundation, 1950.)


tight
junction
lumen
basement
membrane
endothelial
cell
pericyte



from artery
oxygen
nutrients
to body's cells
carbon dioxide
wastes
from body's cells
red blood cell carrying oxygen
capillary
red blood cell with no oxygen
to vein
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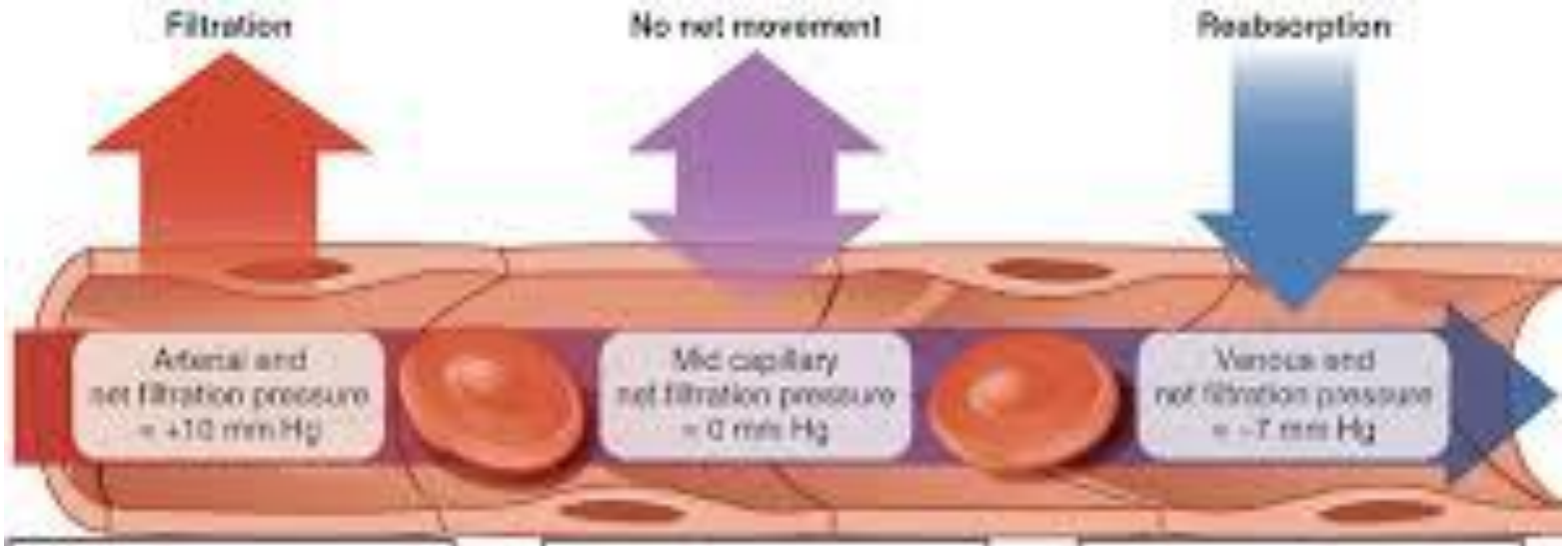


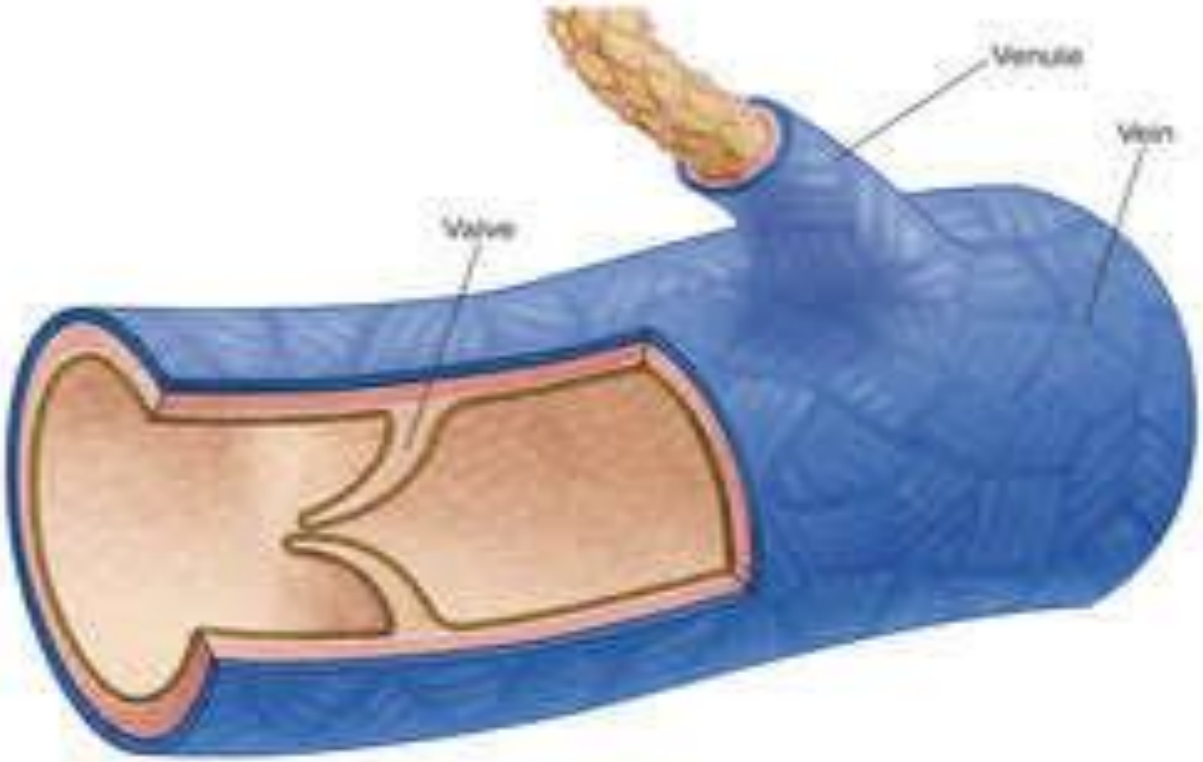
Fluid exits capillary since capillary pressure (35mm Hg) > that blood osmotic pressure (25 mm Hg)

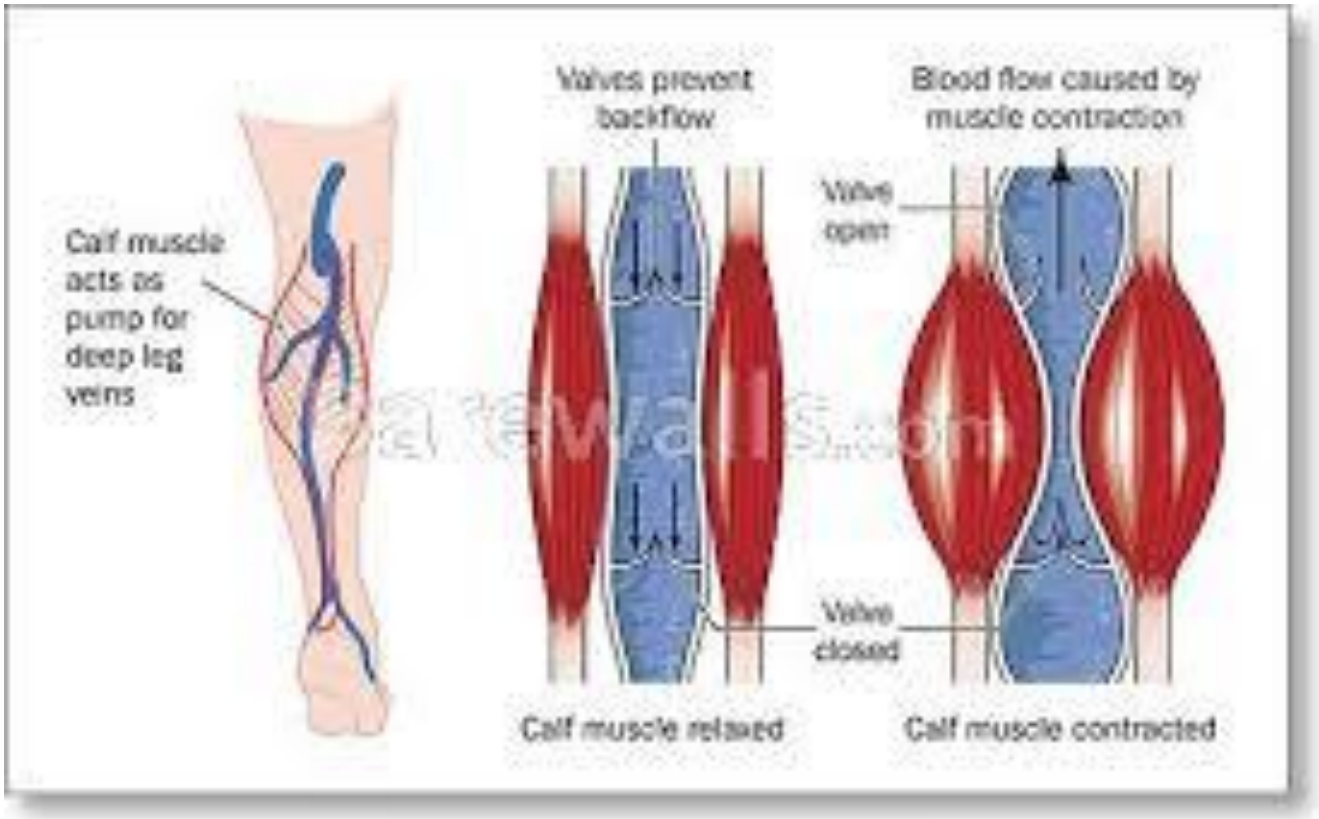
No net movement of fluid since capillary pressure (25 mm Hg) = blood osmotic pressure (25 mmHg)

Fluid re-enters capillary since capillary pressure (18 mm Hg) is less than blood osmotic pressure (25 mm Hg)

Veins

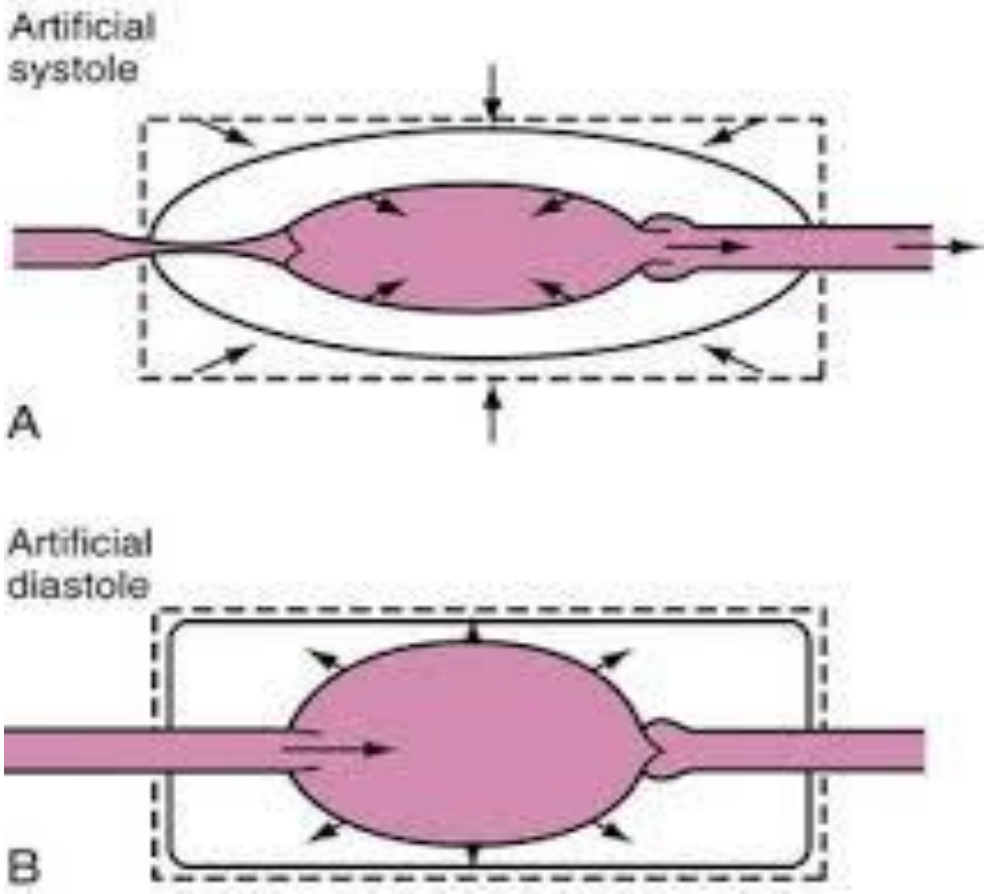
- **Veins serve to return blood from organs to the heart. Veins are also called “capacitance vessels” because most of the blood volume (60%) is contained within veins. Changes of the venous blood volume leads to changes of the blood volume that returns to the heart (preload).**
- **Staying for prolonged period in standing position can cause low venous return to the heart and fainting can occur. To combat this blood return is assisted by the muscle pump and thoracic pump. Muscles involving in the movement of legs contract and help to bring venous blood flow to the heart. Thoracic pump is also assisting to the return of venous blood to the heart. During inspiration the negative pressures in the chest pulls venous blood into the thoracic part of vena cava. During expiration the positive pressure of the chest push out this blood to the heart.**


Venule
Vein
Valve



bwc14738338 Barewalls

Thoracic Pump



Local blood flow regulation

- **Local blood flow regulation refers to intrinsic regulation or control of vascular tone at a local level. meaning within a certain tissue or organ.**
- **The metabolic activity of a tissue governs blood flow in the tissue. Any intervention , for example increase of muscle activity , that results in inadequate oxygen supply prompts the formation and release of vasodilator substances. These substances act locally to dilate the arterioles and precapillary sphincters to increase blood flow and oxygen supply to the tissue. Potassium ions, inorganic phosphate ions, CO_2 , lactate , induce vasodilatation. Adenosine, produced by the brake down of ATP is a major vasodilating metabolite which contributes to the regulation of coronary blood flow . Furthermore, nitric oxide released from the endothelial cells that line the blood vessels, causes vasodilation.**

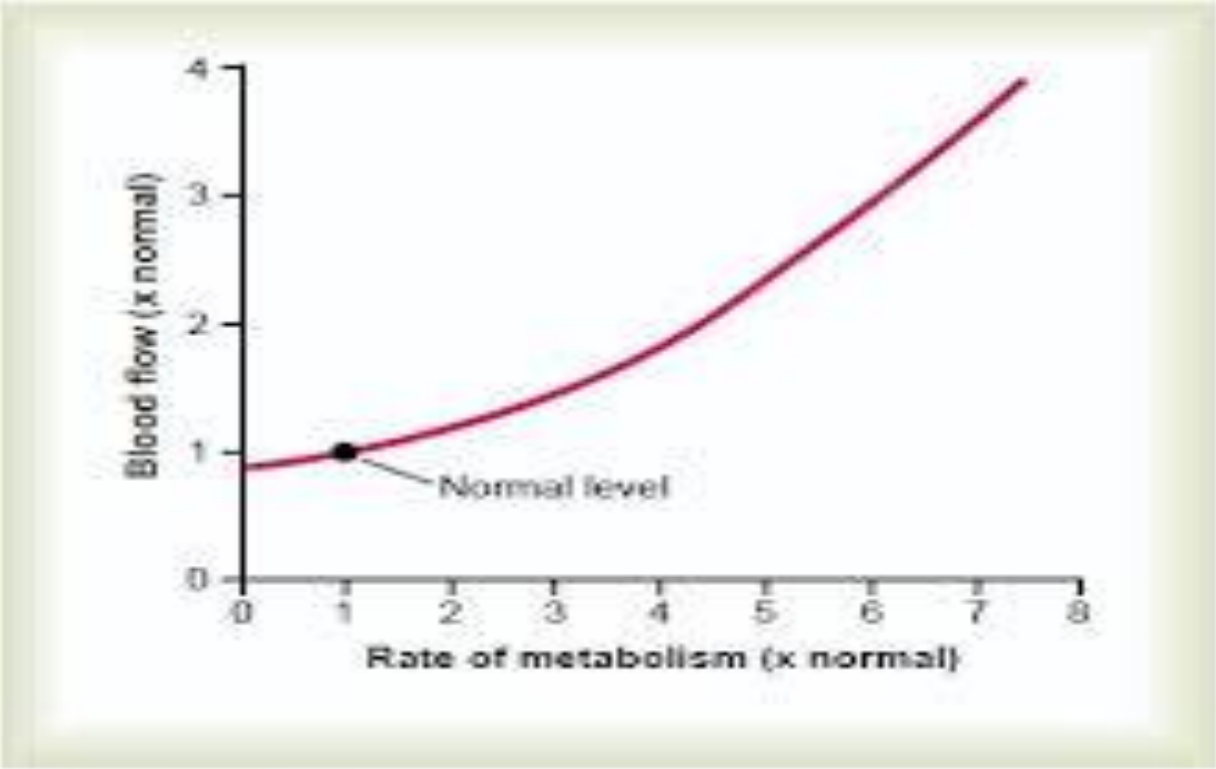


Figure 17–1

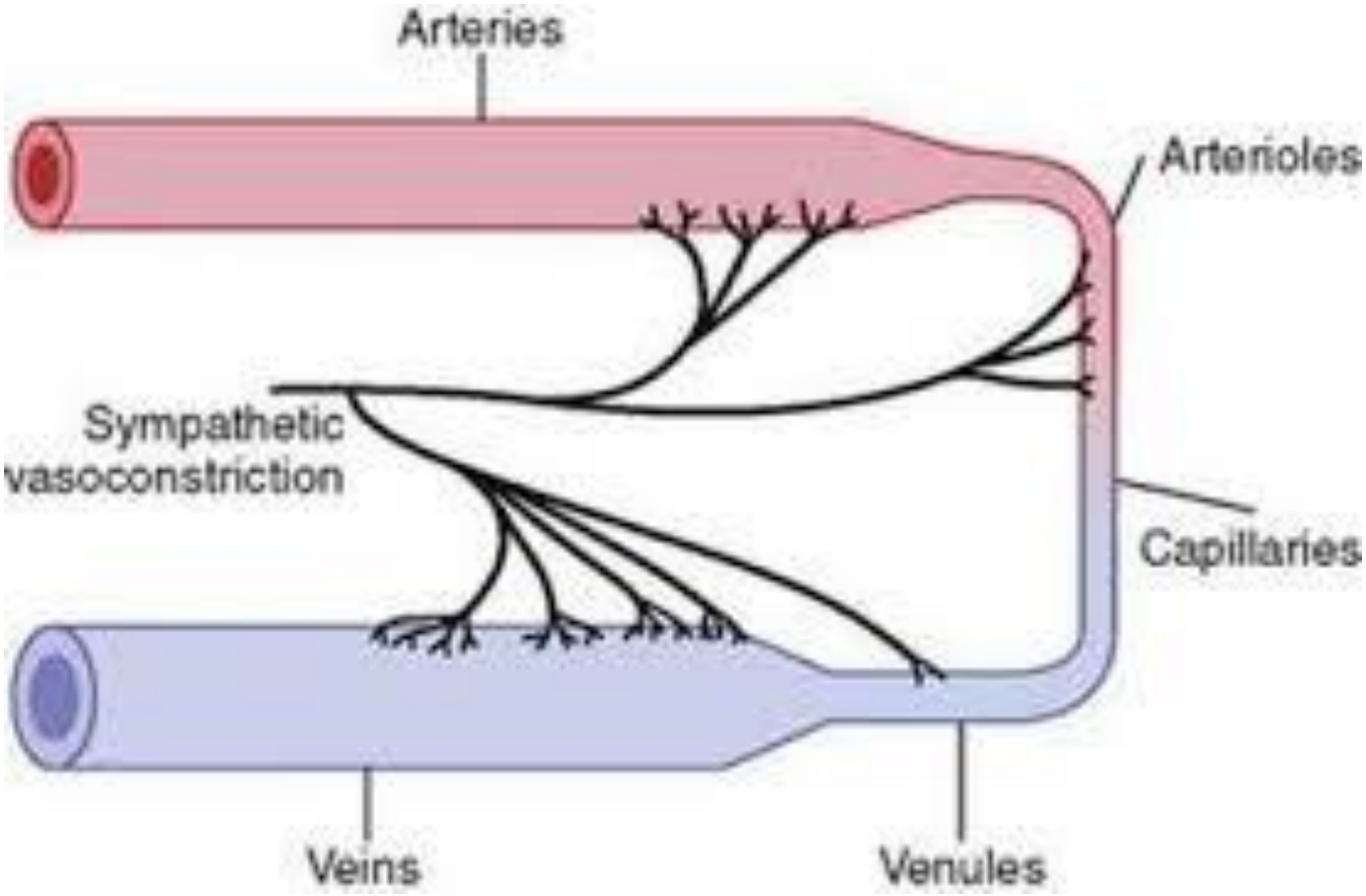
Effect of increasing rate of metabolism on tissue blood flow.

Humoral Control of the diameter of the blood vessels

- **The diameter of the blood vessels is regulated by vasoactive substances of the blood.**
- **A. Vasoconsoconstrictive substances. (increase blood pressure)**
- **-Epinephrine and Norepinephrine released from the adrenal medulla . They exert their vasoconstriction through α1 adrenergic receptors.**
- **Angiotensin II is a peptide that causes vasoconstriction. It is part of the renin-angiotensin system. Angiotensin receptor blockers are used for the treatment of hypertasis.**
- **Vasopressin also called antidiuretic hormmone (ADH) is a peptide synthesized in neurons of the hypothalamus it then travels in the axons of these cells down to the posterior pituitary from where is released into the circulation.**
- **B. Vasodilating substances.**
- **Acetylcholine. Its levels in the blood are very low and therefore its effect is not important**
- **Histamine. In cases of anaphylaxis the high levels of histamine released from must cells and leucocytes cause generalized vasodilatation and fall of blood pressure (allergic shock).**
- **Kinins. They have local effects.**

Neural Contrlol of the diameter of blood vessels

- **The sympathetic nervous system plays a key role in the regulation of the diameter of the blood vessels**
- **Sympathetic vasoconstrictive nerve fibers innervate the smooth muscle layer of the walls of arteries, arterioles (resistance vessels) and veins (capacitance vessels).**
- **The neurotransmitter norepinephrine is released from the terminals to elicit, through the activation of α-adrenergic receptors, constriction of the resistance and capacitance vessels.**
- **Vasoconstriction is very strong in the blood vessels of the skin and does not apply for the blood vessels of brain and heart.**


Arteries
Arterioles
Sympathetic
vasoconstriction
Capillaries
Veins
Venules

Short - term regulation of arterial blood pressure

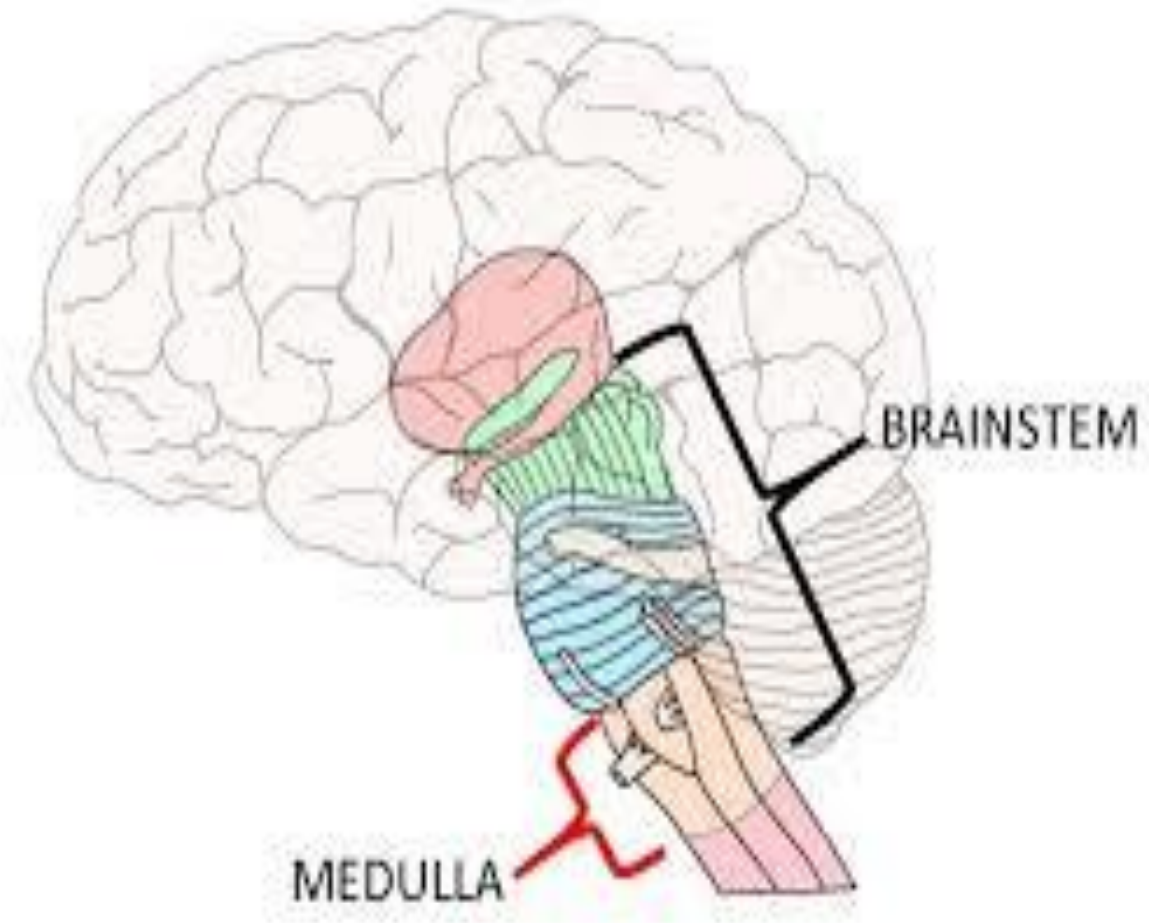
- **Short term regulation of blood pressure is controlled by the autonomic nervous system especially the sympathetic nervous system, through the regulation of the cardiac output and the peripheral resistance .**
- **In the heart activation of the sympathetic system increases heart rate and stroke volume resulting an increase of cardiac output and therefore of the arterial pressure. Deactivation of the of the sympathetic system has the opposite results.**
- **In the vasculature activation of the sympathetic system results constriction of arterioles and of the veins. The constriction of arterioles results an increase of the total resistance and of the blood pressure. The constriction of the veins reduces their capacity resulting increase of the preload which in turn leads to increase of end-diastolic volume , increase of the contractility of the ventricles (Frank- Starling law) increase of stroke volume and cardiac output and finally of arterial blood pressure. Deactivation of the sympathetic system has the opposite results.**

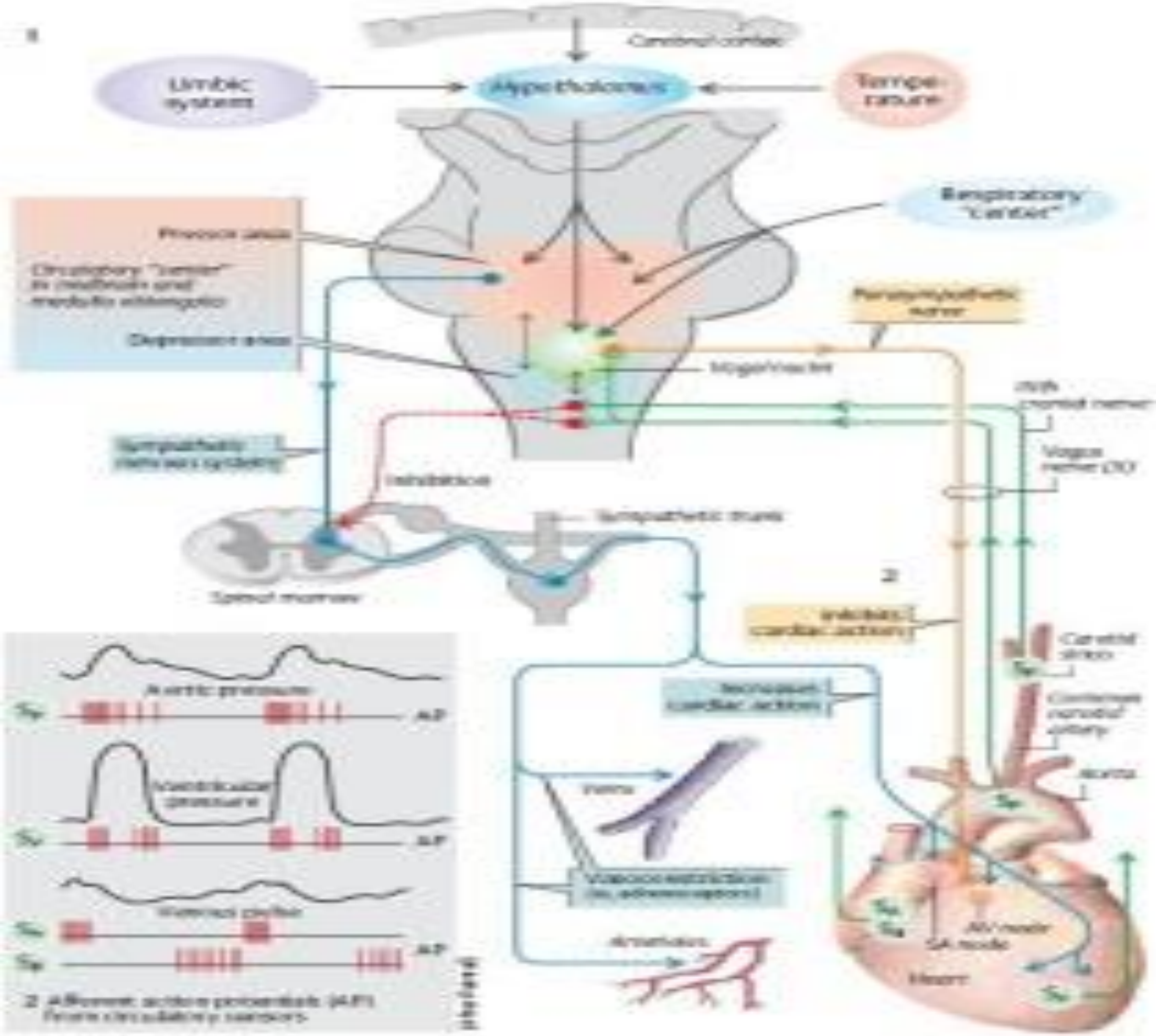
Central regulation of the blood pressure

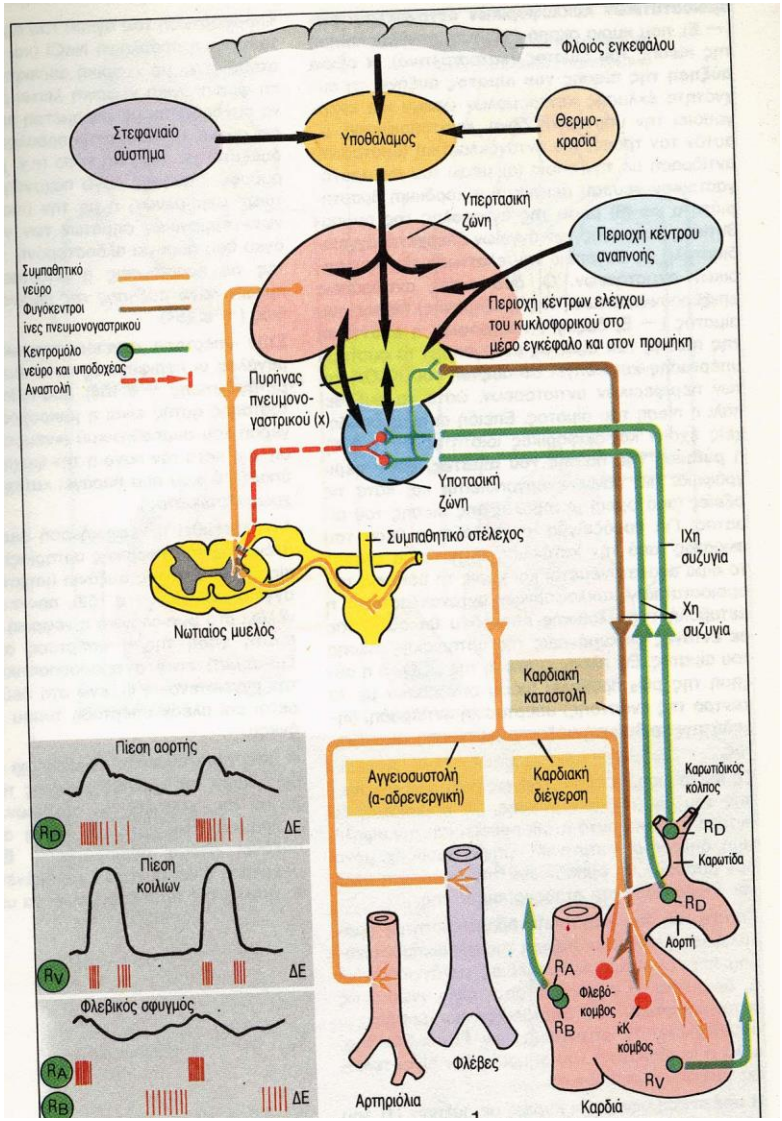
- **Several regions of the medullopontine brain regions influence influence cardiovascular activity through the control of the activity of the sympathetic system. Stimulation of the dorsal lateral medulla (pressor region) evokes , through the activation of the sympathetic system, vasoconstriction, cardiac acceleration and enhanced myocardial activity resulting increase of the arterial blood pressure. Stimulation caudal and ventromedial to the pressure center decreases blood pressure (depressor region). This depressor area exerts its effect by direct inhibition of the cells of the sympathetic regions of the spinal corrd.**
- **The function of these brain regions is regulated by local stimuli (CO_2 stimulates the pressor region), from other brain regions (motor cortex lymbic system, hypothalamus) and from several reflexes. The function of the reflex of baroreceptors of carotid sinus and aorta is extremely important for the short –term regulation of blood pressure.**

The baroreceptor reflex of carotid sinus and aortic arc

- **The baroreceptor reflex is one of the body's homeostatic mechanisms that helps to maintain blood pressure to nearly constant levels. The baroreflex can begin to act in less than the duration of a cardiac cycle (fractions of a second). The system relies on specialized neurons, known as baroreceptors, localized chiefly in the wall of the aortic arch and the carotid sinuses in the beginning of the internal carotid artery. Neuronal fibers connect t activate hem with the depressor center of the medulla. Baroreceptors are stretch receptors and respond to the pressure induced stretching of the wall of blood vessels. An acute increase of blood pressure activates the baroreceptors which , in turn, send neuronal signals that activate the depressor region. The activated depressor region inhibits the pressor regions and the sympathetic neurons of the spinal cord resulting a decrease of blood pressure. A decrease of blood pressure deactivates the baroreceptors resulting a deactivation of the depressor region and in turn activation of the pressor region and of the sympathetic neurons of the spinal cord and therefore an increase of the blood pressure. Thus the baroreceptor reflex is a buffer system that does not permit either an increase or a decrease of blood pressure.**


BRAINSTEM
MEDULLA


Limbic system
Hypothalamus
Tempe-rature
Respiratory "center"
Aortic pressure
Ventricular pressure
AP
Heart


Φλοιός εγκεφάλου
Στεφανιαίο σύστημα
Υποθάλαμος
Θερμο-κρασία
Υπερτασική ζώνη
Περιοχή κέντρου αναπνοής
Περιοχή κέντρων ελέγχου του κυκλοφορικού στο μέσο εγκέφαλο και στον προμήκη
Συμπαθητικό νεύρο
Φυγόκεντροι ίνες πνευμονογαστρικού
Κεντρομόλο νεύρο και υποδοχέας
Αναστολή
Πυρήνας πνευμονο-γαστρικού (x)
Υποτασική ζώνη
Συμπαθητικό στέλεχος
IXη συζυγία
Χη συζυγία
Νωτιαίος μυελός
Καρδιακή καταστολή
Αγγειοσυστολή (α-αδρενεργική)
Καρδιακή διέγερση
Καρωτιδικός κόλπος
Καρωτίδα
Αορτή
Φλεβό-κομβος
κΚ κόμβος
Φλέβες
Αρτηριόλια
Καρδιά
Πίεση αορτής
Πίεση κοιλιών
Φλεβικός σφυγμός
ΔΕ

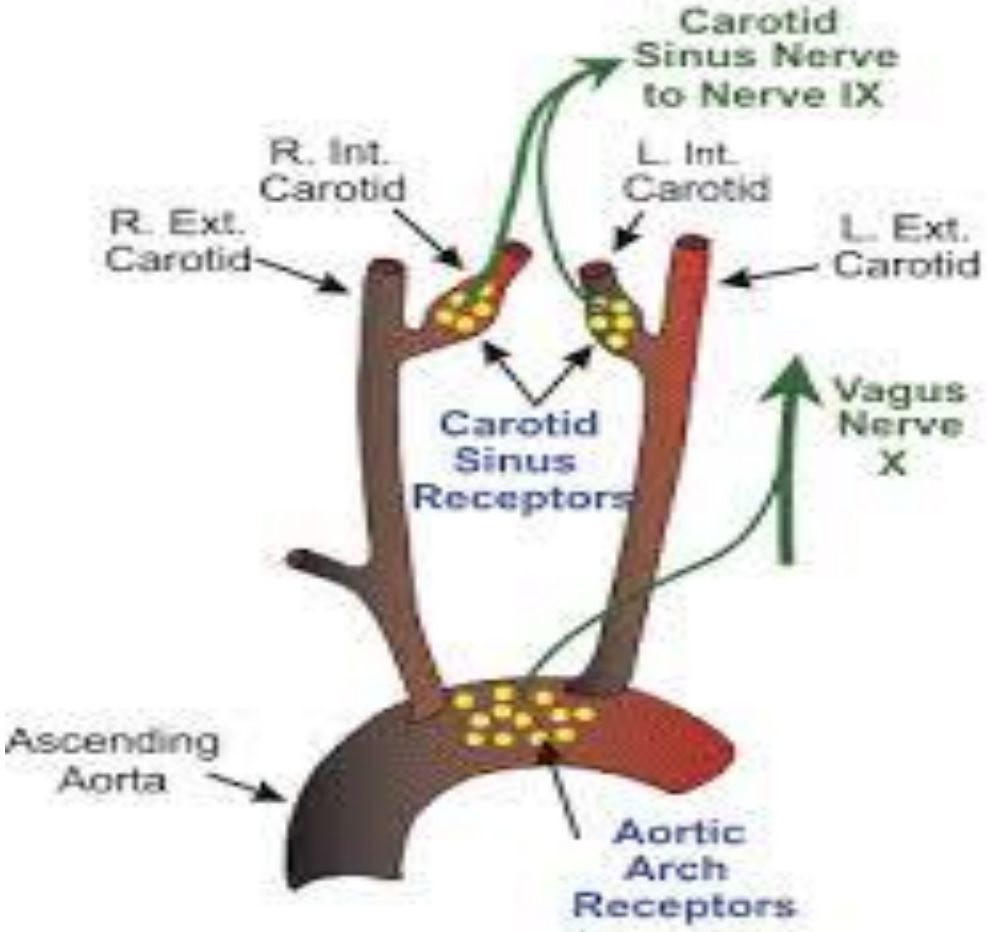
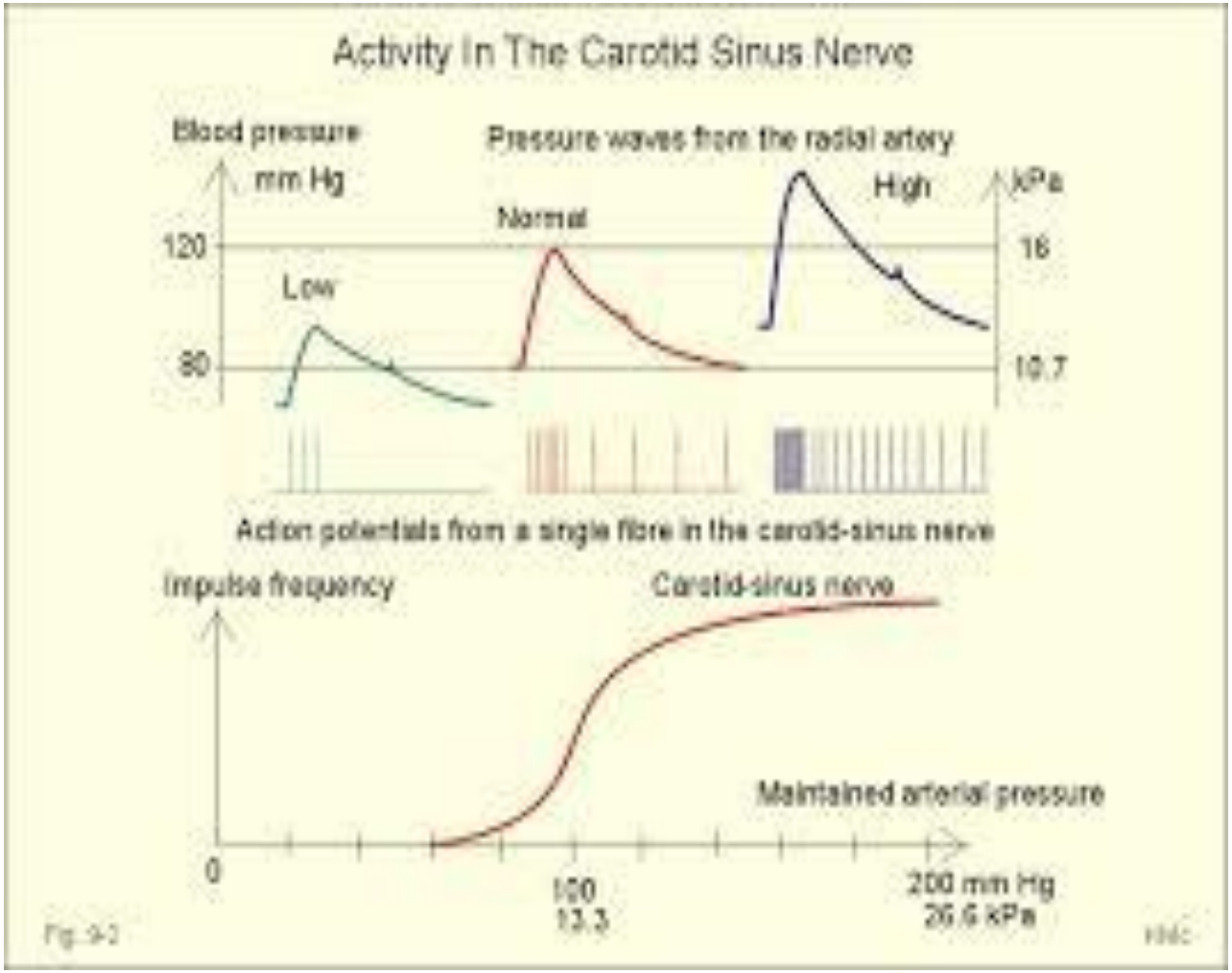


Figure 1. Location and innervation of arterial baroreceptors.


Activity In The Carotid Sinus Nerve
Blood pressure
mm Hg
Pressure waves from the radial artery
kPa
High
Normal
Low
120
80
16
10.7
Action potentials from a single fibre in the carotid-sinus nerve
Impulse frequency
Carotid-sinus nerve
Maintained arterial pressure
0
100
13.3
200 mm Hg
26.6 kPa

Long- term regulation of blood pressure

- **The baroreceptors provide a negative feedback mechanism , veanism ry efficient for short-term regulation of blood pressure.**
- **However in long lasting changes of blood pressure long-term compensatory mechanisms are neded.**
- **There are several physiological mechanisms for long –term regulation of blood pressure the first of which is the renin-angiotensin- aldosterone system. Renin is a peptide hormone released by the juxtaglomerular apparatus of the kidney. Renin is released in response to decreased blood flow to the kidney due to decrease of blood volume and pressure. Renin facilitates the conversion of the blood angiotensinogen to angiotensin II. Angiotensin II is a potent vasoconstrictor and it promotes release of aldosterone. Aldosterone promotes salt retention acting to the distal convoluted tubule of the Kidney. The retention of sodium increases the osmotic pressure of the extracellular fluid. Increased osmotic pressure is a strong stimulus for the release of the Anti-diuretic hormone (ADH). ADH promotes water retention by the kidneys , resulting compensatory increase of blood volume and pressure.**