

## **Cardiovascular Physiology**

Cardiovascular system is one of the systems of the human organism , that is responsible for:

1. supplying the tissue and cells of the organism by the needed oxygen and nutrients
2. helping it to get rid of carbon dioxide and waste products of metabolism.
3. participating in protection of the body and wound healing .
4. regulation of body temperature , fluid - electrolytes balance , and acid - base balance.

Cardiovascular system is composed of three major components , that form the circulation :

- 1- The heart : as a pumping organ of the system.
- 2- Blood vessels : as containers, through which the circulation occurs .
- 3- The blood : as transport medium of the circulation.

### **Physiologic anatomy of the heart**

Heart is a hollow muscular organ , that is located in the middle mediastinum between the two bony structures of the sternum and the vertebral column .

It has a shape of clenched fist , which weighs about 300 grams ( with mild variation between male and female ).

Heart has an apex that is anteriorly , inferiorly , and leftward oriented , and a base , that is posteriorly , superiorly and rightward oriented .

In addition to its apex and base the heart has anterior , posterior and left surfaces.

**Chambers of the heart :** Heart has four chambers : two atria and two ventricles . The two right and left atria are separated from the two ventricles by the fibrous skeleton , which involves the right ( tricuspid ) and left ( bicuspid ) valves. Right and left atria are separated from each other by the interatrial septum .

The two ventricles are separated by the interventricular septum. Interventricular septum is muscular in its lower thick part and fibrous in its upper thin part.

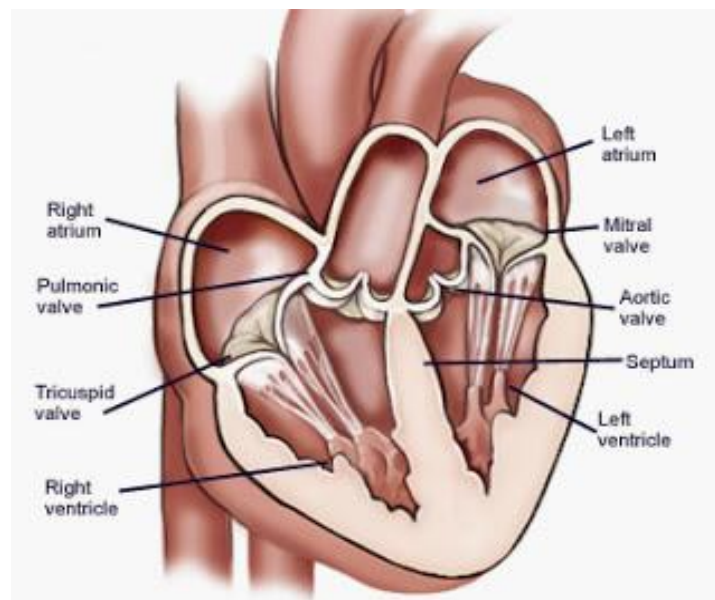
The two atria hold the blood returning from the veins and empty it only in a given right moment into the ventricles. Ventricles pump the blood into the arteries .

### **Heart valves :**

There are four valves in the heart : Two atrioventricular valves and two semi-lunar valves:

1. Atrioventricular ( AV ) valves: These valves are found between the atria and ventricles , depending on the number of the leaflets , the right atrioventricular valve is also called tricuspid valve (has three leaflets ) , while the left one is called bicuspid valve (has two leaflets ) .

The leaflets of the valves are attached to fibrous threads (composed of collagen fibers ) , known as chordae tendineae , which from their side are attached to papillary muscles in the ventricles. These valves prevent backward flow of blood from ventricles during the systole.



2. Semi-lunar valves : These valves are located on the base of the arteries ( aorta and pulmonary artery ) . They prevent the backward flow of blood from the arteries into ventricles.

The structure of the semilunar valves is quite different from that of the

AV valves , as they have crescent-shaped cusps that do not have chorda tendinea , instead these cusps are like pockets which are filled of blood when it returns to the ventricles from the lumen of arteries during the diastole , so they get closed and prevent the backward flow of blood.

### **Properties of cardiac muscle**

Cardiac muscle is a striated muscle like the skeletal muscle , but it is different from the skeletal muscle in being involuntary and syncytial .

Syncytium means that cardiac muscle cells are able to excite and contract together due to the presence of gap junctions between adjacent cardiac cells.

Cardiac muscle has four properties , due to which the heart is able to fulfill its function as a pumping organ. Studying and understanding these properties is essential for students to understand the cardiac physiology as a whole.

1.Rhythmicity ( Chronotropism ) : means the ability of heart to beat regularly ( due to repetitive and stable depolarization and repolarization ) . Rhythmicity of heart is a myogenic in origin , because cardiac muscles are automatically excited muscles and does not depend on the nervous stimulus to initiate excitation and then contraction . The role of nerves is limited to the regulation of the heart rate and not to initiate the beat.

There are many evidences that approve the myogenic and not neurogenic origin of the rhythmicity of cardiac muscle . For example :

- \* transplanted heart continues to beat regularly without any nerve supply.
- \* Embryologically the heart starts to beat before reaching any nerves to them.
- \* Some drugs that paralyze the nerves ( such as cocaine ) do not stop the heart in given doses.

Spontaneous rhythmicity of the cardiac muscle due to the existence of excitatory - conductive system , which is composed of self- exciting non- contractile cardiac muscle cells . The SA node of the mentioned system excites in a rate , that is the most rapid among the other components of the system ( 110 beats /minute ) , which makes it the controller or ( the pacemaker ) of the cardiac rhythm of the entire heart.

Mechanism , responsible for self- excitation in the SA node and the excitatory conductive system is due to the following properties of the cell

membrane of these cells :

- 1- Non-gated sodium channels
- 2- Decreased permeability to potassium
- 3- existence of slow and fast calcium channels.

These properties enable the cations ( sodium through the none-gated sodium voltage channels , calcium through calcium slow channels) to enter the cell and depolarize the cell membrane without need for external stimulus.

The resting membrane potential of non-contractile cardiac cell is -55 - -60 millivolts ( less than that of excitable nerve cells (-70) ) . The threshold is also less negative than that of nerve cells ( -40 millivolts ).

The decreased permeability to potassium from its side decrease the eflux of potassium during the repolarization phase of the pacemaker potential . All of these factors give the pacemaker potential its characteristic shape

Repeating of the pacemaker potential between the action potentials of contractile muscle cells is the cause of spontaneous rhythmicity of cardiac muscle cells.

*Factors , affecting the rhythmicity of the cardiac muscle :*

I.some Factors that increase the rate ( positive chronotropic factors) :

1. sympathetic stimulation : as its neurotransmitter norepinephrine increases the membrane permeability to sodium and calcium.
2. Catecholaminic drugs have positive chronotropic effect.
3. Thyroid hormones : have positive chronotropic effect , due to the fact that these drugs increase the sensitivity of adrenergic receptors to adrenaline and noreadrenaline .

II.some Factors that decrease rhythmicity ( negative chronotropic):

- 1.Vagal stimulation : the basal level of vagal stimulation inhibits the sinus rhythm and decrease it from 110-75 beats/ minute. This effect due to increasing the permeability of the cardiac muscle cell to potassium , which causes rapid potassium eflux , which increases the negativity inside the cardiac cells (hyperpolarization ) .
2. metabolism and stops rhythmicity.
3. Cholenergic drugs ( such as methacholine , pilocarpine..etc) have

negative chronotropic effect.

4. Hypercapnia ( excessive CO<sub>2</sub> production ).

2. Excitability ( Bathmotropism ) : Excitability means the ability of cardiac muscle to respond to signals. Here we are talking about contractile muscle cells that are excited by the excitatory conductive system and generate an action potential.

Cardiac action potential is similar to action potential in nerve and skeletal muscle tissue , with one difference , which is the presence of plateau phase . Plateau phase is unique for cardiac muscle cells .

The resting membrane potential for cardiac muscle is about -80 mV.

When the cardiac muscle is stimulated an action potential is generated .

The action potential in cardiac muscle is composed of four phases , which are :

1. Depolarization phase (Phase 0 ) :

A result of opening of sodium channels , which increase the permeability to sodium , which will lead to a rapid sodium influx into the cardiac muscle cell.

2. Repolarization : Repolarization in cardiac muscle is slow and triphasic :

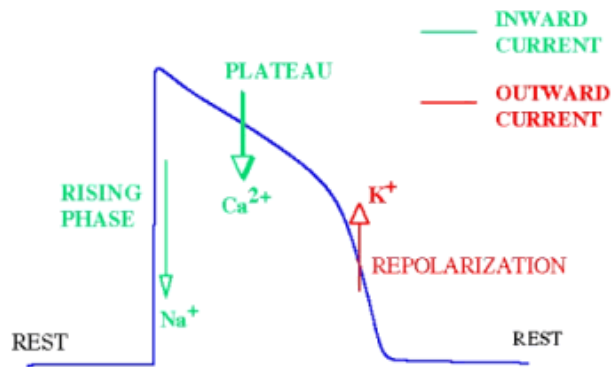
a. Phase 1 (early partial repolarization ) : A small fast repolarization , results from potassium efflux and chloride influx.

b. Phase 2 ( Plateau ) : After the early partial depolarization , the membrane remains depolarized , exhibiting a plateau , which is a unique phase for the cardiac muscle cell. Plateau is due to opening of slow calcium-sodium channels , delay closure of sodium channels , and to decreased potassium efflux.

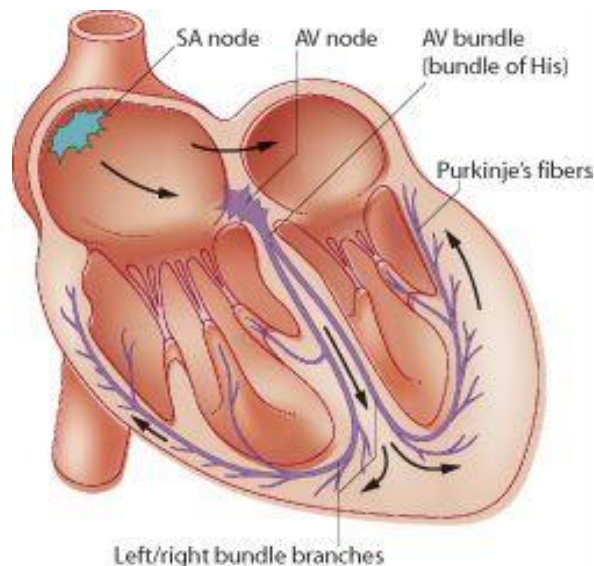
c. Phase 3 ( Rapid repolarization) : opening of potassium channels and rapid efflux of potassium.

d. Phase 4 ( Returning to resting level) in other words : The phase of complete repolarization. This due to the work of sodium-potassium pump.

## CARDIAC ACTION POTENTIAL



3. Conductivity : Means ability of cardiac muscle to propagate electrical impulses through the entire heart ( from one part of the heart to another) by the excitatory -conductive system of the heart. Excitatory conductive system of the heart involves:



1. Sinoatrial node ( SA node) : Here the initial impulses start and then conducted to the atria through the anterior inter-atrial pathway ( to the left atrium) , to the atrial muscle mass through the gap junction, and to the Atrioventricular node ( AV node ) through anterior, middle , and posterior inter-nodal pathways.

The average conductive velocity in the atria is 1m/s.

2- AV node : The electrical impulses can not be conducted directly from the atria to the ventricles , because of the fibrous skeleton , which is an electrical isolator , located between the atria and ventricles. So the only

conductive way is the AV node . But there is a delay in the conduction occurs in the AV node .

This delay is due to:

- \* the smaller size of the nodal fiber.
- \* The less negative resting membrane potential
- \* fewer gap junctions.

There are three sites for delay:

- \* In the transitional fibers , that connect inter-nodal pathways with the AV node ( 0.03 ) .
- \* AV node itself ( 0.09 s ) .
- \* In the penetrating portion of Bundle of Hiss ( 0.04 s ) .

This delay actually allows atria to empty blood in ventricles during the cardiac cycle before the beginning of ventricular contraction , as it prevents the ventricles from the pathological high atrial rhythm.

The average velocity of conduction in the AV node is 0.02-0.05 m/s

3- Bundle of Hiss : A continuous with the AV node that passes to the ventricles through the inter-ventricular septum. It is subdivided into : Right and left bundle. The left bundle is also subdivided into two branches: anterior and posterior branches .

4- Purkinje`s fibers: large fibers with velocity of conduction 1.5-4 m/s. the high velocity of these fibers is due to the abundant gap junctions , and to their nature as very large fibers as well.

The conduction from AV node is a one-way conduction . This prevents the re-entry of cardiac impulses from the ventricles to the atria.

Lastly: The conduction through the ventricular fibers has a velocity of 0.3-0.5 m/s.

4. Contractility : Means ability of cardiac muscle to convert electrical energy of action potential into mechanical energy ( work).

The excitation- contraction coupling of cardiac muscle is similar to that of skeletal muscle , except the lack of motor nerve stimulation. Cardiac muscle is a self-excited muscle , but the principles of contraction are the same . There are many rules that control the contractility of the cardiac muscles, which are:

1. All or none rule: due to the syncytial nature of the cardiac muscle. There are atrial syncytium and ventricular syncytium . This rule makes the heart an efficient pump.

2. Staircase phenomenon : means gradual increase in muscle contraction following rapidly repeated stimulation..

3. Starling`s law of the heart: The greater the initial length of cardiac muscle fiber , the greater the force of contraction. The initial length is determined by the degree of diastolic filling .The pericardium prevents overstretching of heart , and allows optimal increase in diastolic volume. Thankful to this law , the heart is able to pump any amount of blood that it receives. But overstretching of cardiac muscle fibers may cause heart failure.

### **Cardiac cycle**

The mechanical events , occurring in the heart within one beat ( from the beginning of a heart beat the next beat ).

Cardiac cycle involves five stages . The first two of five are responsible for filling the ventricles. During these two stages , the blood moves from the atria to fill the ventricles. The other three stages are responsible for emptying the ventricles and ejecting blood into the arterial system.

To understand the events of the cardiac cycle lets imagine that we are describing events occurring with one half of the heart ( right or left) because the same events occur simultaneously in the other one.

Phases of cardiac cycle :

1. Early diastole ( also called the atrial diastole , or complete heart diastole) : During this phase :

- \* Atria are relaxed
- \* Ventricles are relaxed
- \* Semilunar valves are closed
- \* Atrioventricular valves are open

During this phase the blood moves passively from the venous system into the ventricles ( about 80 % of blood fills the ventricles during this phase.

2. Atrial systole : During this phase :

- \* Atria are contracting
- \* Ventricles are relaxed
- \* AV valves are open
- \* Semilunar valves are closed
- \* Atrial pressure increases.the a wave of atrial pressure appears here.
- \* intraventricular pressure increases due to the rush of blood then decrease due to continuous relaxation of ventricles.



The remaining 20% of blood is moved to fill the ventricles during this phase , due to atrial contraction.

3. *Isovolumetric contraction* : During this phase :

- \* Atria are relaxed
- \* Ventricles are contracting
- \* AV valves are closed
- \* Semilunar valves are closed
- \* First heart sound

The ventricular fibers start to contract during this phase , and the intraventricular pressure increases. This result in closing the AV valves , but the pressure is not yet enough to open the semilunar valves , so the blood volume remain unchanged , and the muscle fibers length also remain unchanged , so we call this phase as isovolumetric contraction ( iso : the same , volu= volume , metric= length).

4. *Ejection phase* : Blood is ejected from the ventricles into the aorta and pulmonary artery

During this phase :

- \* Ventricles are contracting
- \* Atria are relaxed
- \* AV valves are closed
- \* Semilunar valves are open
- \* First heart sound
- \* Intraventricular pressure is increased , due to continuous contraction
- \* increased aortic pressure .

5. *Isovolumetric relaxation*: This phase due to backflow of blood in aorta and pulmonary system after the ventricular contraction is up and the ventricles relax . This backflow closes the semilunar valves .

During this phase :

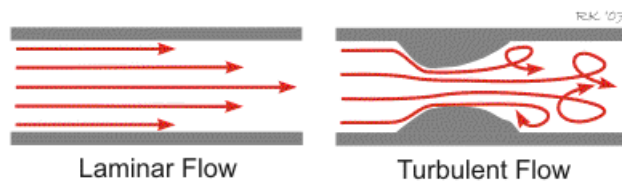
- \* Ventricles are relaxed
- \* Atrial are relaxed
- \* Semilunar valves are closed .
- \* AV valves are closed.
- \* Ventricular pressure falls rapidly
- \* Atrial pressure increases due to continuous venous return. the v wave appears here.
- \* Aortic pressure : initial sharp decrease due to sudden closure of the

semilunar valve , followed by secondary rise in pressure , due to elastic recoil of the aorta .

## Heart sounds

Heart sounds are a result of beating heart and resultant blood flow . that could be detected by a stethoscope during auscultation .

Physiologically , blood flow has a laminar pattern , which means that blood flows in form of layers , where the central layer is the most rapid . Laminar blood flow could be turned into turbulent one .



Turbulent blood flow is a result of stenotic ( narrowed ) valves or blood vessels , insufficient valves , roughened vessels` wall or endocardium , and many diseases . The turbulent blood flow causes noisy murmurs inside or outside the heart.

Heart sounds ( especially first and second sounds ) are mainly a result of closure of the valves of the heart . While the third sound is a result of vibration of ventricular wall and the leaflets of the opened AV valves after rapid inflow of blood from the atria to ventricles . Third heart sound is physiologic in children but pathological in adults.

The fourth heart sound is a result of the atrial systole and vibration of the AV valves , due to blood rush during atrial systole . It is inaudible neither in adults nor in children . It is just detectable by the phonocardiogram .

Characteristic of heart sounds :

1. First heart sound ( S1 , lub ) : a soft and low pitch sound, caused by closure of AV valves.
2. Second heart sound ( S2 , dub ) : sharp and high pitch sound . caused by closure of semilunar valves
3. Third heart sound ( S3 ) : low pitched sound.
4. Fourth heart sound ( S4 ) very low pitched sound.

As we notice : the first three sounds are related to ventricular activity , while the fourth heart sound is related to atrial activity.

Closure of valves is not the direct cause for heart sounds , but sharp

blocking of blood of backward returning of blood by the closing valve is the direct cause.

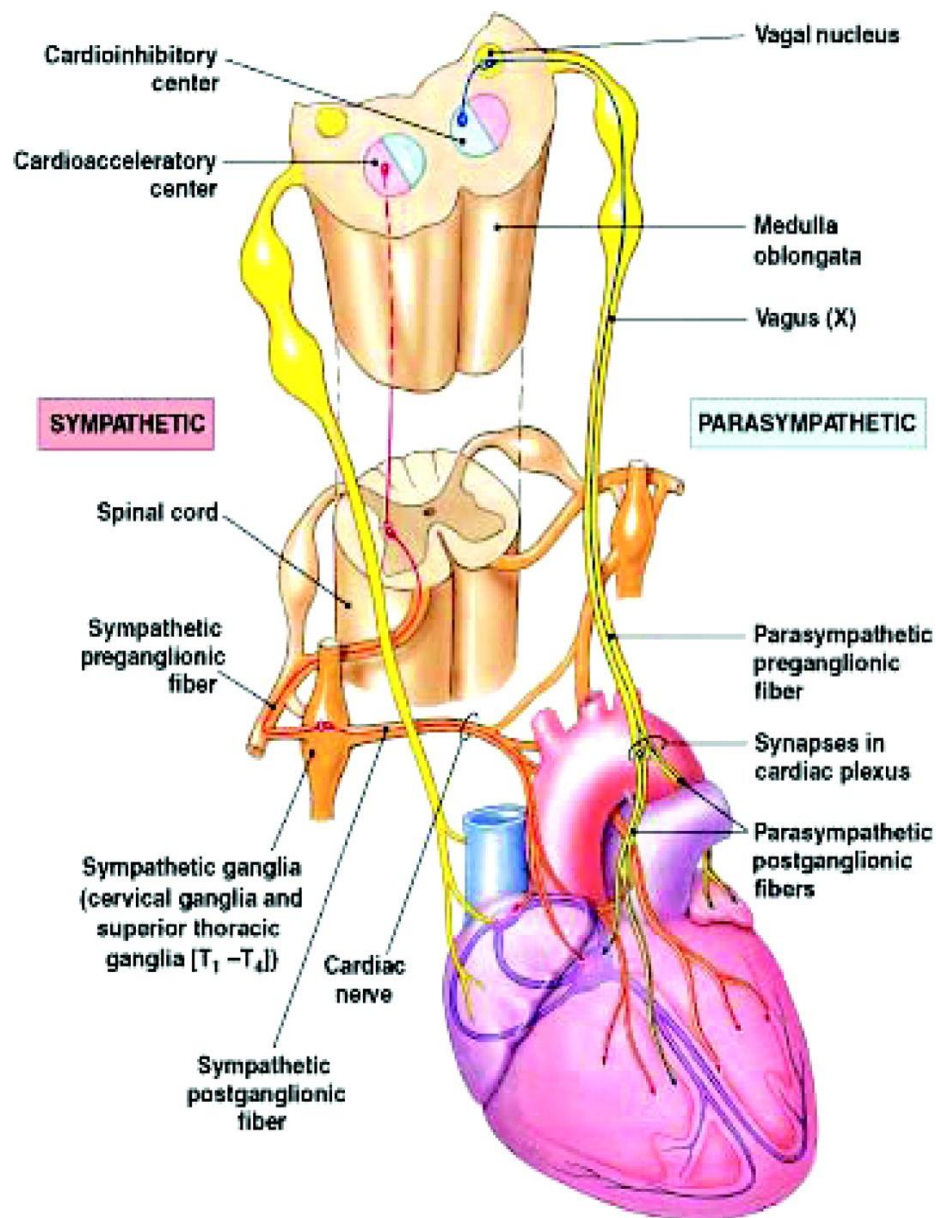
Exam

### **Innervation of the heart**

Heart as a visceral organ receives autonomic nerve fibers from higher centers in the midbrain , as it sends to the brain afferent sensory fibers that transmits sensory information about pain, pressure and O<sub>2</sub> concentration to the brain.

The higher centers , responsible for innervation of the heart are located in the medulla oblongata. They are :

1. Cardioacceleratory Center ( CAC): The nerve fibers descends from this center in the spinal cord.
- 2- Cardioinhibitory Center ( CIC) : Parasympathetic fibers , arising from this center travel via the vagus nerve , and then rely in the terminal ganglia in the atrium .



## Cardiac Output

Cardiac output is the amount of blood , pumped by each ventricle within one minute of time. It is also called minute volume.

Cardiac output has two determinants , which are :

1- Stroke volume : The amount of blood , pumped by the heart within one beat ( one cardiac cycle) . So the stroke volume equals the difference between end diastolic volume and end systolic volume.

2- Heart rate : The frequency of heart beating within one minute of time.

So: Cardiac output ( CO ) = Stroke volume ( SV) X Heart rate ( HR).

We know that the average heart rate in a healthy adult person is about 70

beats per minute , and the stroke volume is about 70 ml , so we can estimate cardiac output by multiplying these two values :

$70 \times 70 = 4900 \text{ ml ( about 5 L) / minute.}$

The venous return ( VR ) , which is the amount of blood returning to the heart by veins . So cardiac output and venous return express the blood flow around the circulation , so they are equal in equilibrium.

Factors affecting cardiac output :

As far as cardiac output is determined by stroke volume and heart rate , so any factor that affect one or both of those determinants would affect the cardiac output as a whole.

Stroke volume is affected by three factors :

- 1- Preload ( venous return)
2. Contractility power of the heart
- c. Afterload ( vascular resistance) .

### **Regulation of cardiac output :**

Regulation of cardiac output is extrinsic and intrinsic:

Extrinsic regulation of cardiac output : Means that cardiac output is regulated by extra-cardiac regulatory factors , which adjust the heart rate and stroke volume . They are:

1. Autonomic nervous system : sympathetic and parasympathetic. The autonomic nervous system regulates the cardiac output by : 1. Changing the heart rate 2. Changing the power of contraction 3. Altering the circulatory pressure:

Increased sympathetic input , due to excitation , exercise , or others affect the cardiac output by increasing both heart rate and stroke volume . We have to notice here that increased heart rate may decrease the filling time of the heart and decreases the end-diastolic volume , but in the same time it will increase the contraction power of the myocardium (increased sympathetic input increases the contraction power about 60-70% above the normal) , which will decrease the end systolic volume (ESV) and so increases the cardiac output.

The forceful contraction from its side also leads to rapid relaxation that acts as suction force which causes more filling even during short diastole. In the same time , the increased sympathetic input causes vasoconstriction and this will increase the mean circulatory pressure and

the venous return.

Increased parasympathetic input in rest will decrease the heart rate, but will not affect the contractility of the heart, and will decrease the cardiac output (to its normal level) as an end result.

2. Humoral factors : such as hormones affecting heart and blood vessels ( Epinephrine , Norepinephrine , Acetylcholine , thyroid hormones , and others)

**Intrinsic regulation of cardiac output :** Intrinsic regulatory factors operate by inherent mechanism of cardiac tissue. They are subdivided into:

a. Heterometric regulation ( mechanisms involve changes in myocardial fiber length - Starling law) : When there is an increase in initial length of the myocardial fiber's length, this will cause more forceful contraction of the fiber. So when there is expansion of the ventricles as a result of increased filling of blood, the ventricles will contract more forcefully. This is called Starling law.

b. Homometric regulation : Mechanisms don't involve changes in myocardial fiber length.

This usually occurs after the heterometric mechanism, as follows:

After the heterometric phenomenon (5 minutes later), a gradual return of end-diastolic volume to its normal level, with rapid decrease of end-systolic volume, but the stroke volume remains increased.

This phenomenon is related to the previous one (heterometric), which caused increased power of contraction, and better metabolic state in the ventricles, and decreased peripheral resistance (due to maximum rate of arterial pressure, which has developed during the previous phenomenon).