# REGULATION OF HEART PUMPING

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# OBJECTIVES

- Describe the autonomic control on contractility, excitability, force of contraction on heart muscle, SA node and AV node.
- Discuss the factors affecting cardiac output (Dec Total peripheral resistance + Venous return)
- Frank starling law and its limitation.
- Alveolar pressure affecting venous return and mean systemic filling pressure.

# Cardiac output:

- **Cardiac output (CO) is the volume of blood pumped by *each ventricle per minute***
- **= 5 liters */min***
- ***Cardiac Output = Stroke Vol x Heart Rate***

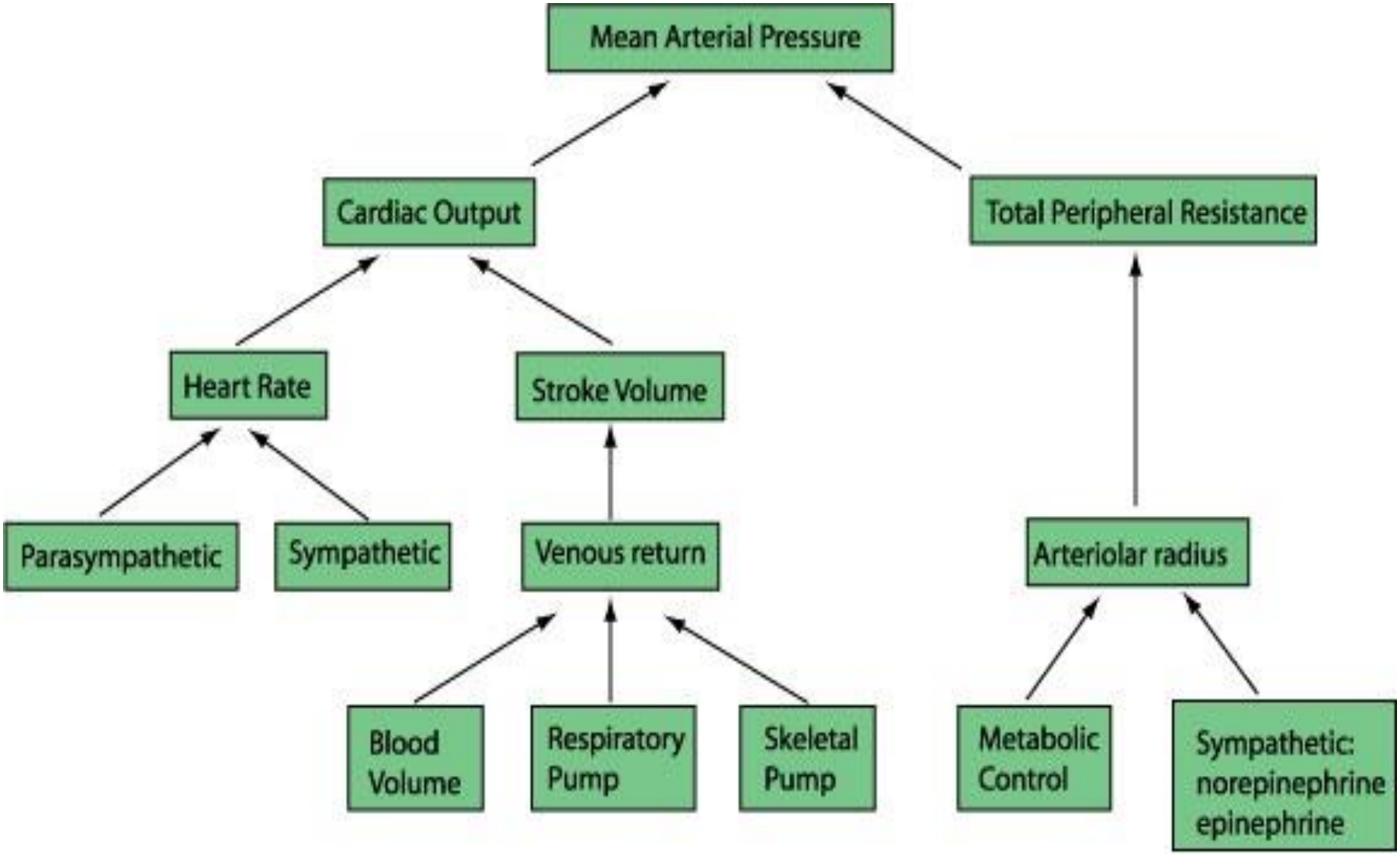
# Cardiac out put is

Heart rate  is 70 beats per minute

- By SA node rhythmicity;
- The stroke volume is 70 ml per beat
- Average cardiac output= 4900 ml/min, or
- 5 liters/min:
- Cardiac output (CO) = Heart rate x stroke volume
- 70 beats/min  70 ml/beat
- 4900 ml/min  5 liters/min

- **EJECTION FRACTION**: The amount of blood which left ventricle pumps out from the end diastolic volume.
- Ejection fraction is the fraction of the end-diastolic volume that is ejected with each beat.
- It is stroke volume (SV)/ divided by end-diastolic volume (EDV):= 58%).

- Each minute the right ventricle pumps 5 liters of blood through the lungs.
- The left ventricle pumps 5 liters through the systemic circulation.


Mean Arterial Pressure
Cardiac Output
Total Peripheral Resistance
Heart Rate
Stroke Volume
Parasympathetic
Sympathetic
Venous return
Arteriolar radius
Blood Volume
Respiratory Pump
Skeletal Pump
Metabolic Control
Sympathetic: norepinephrine epinephrine

# STROKE VOLUME

- It means that Stroke Volume is dependent upon Venous return.
- Venous Return is dependent upon
  - Respiratory Pump
  - Skeletal muscle pump
  - Blood Volume

# HEART RATE

Heart Rate is mainly controlled through autonomic nervous system.

1. Intrinsic control
2. Extrinsic control
   - Sympathetic causing Inc. Heart Rate
   - Parasympathetic causing Dec. Heart Rate

- During exercise, cardiac output can increase to 20 to 25 liters per minute.
- To as high as 40 liters per minute in trained athlete.

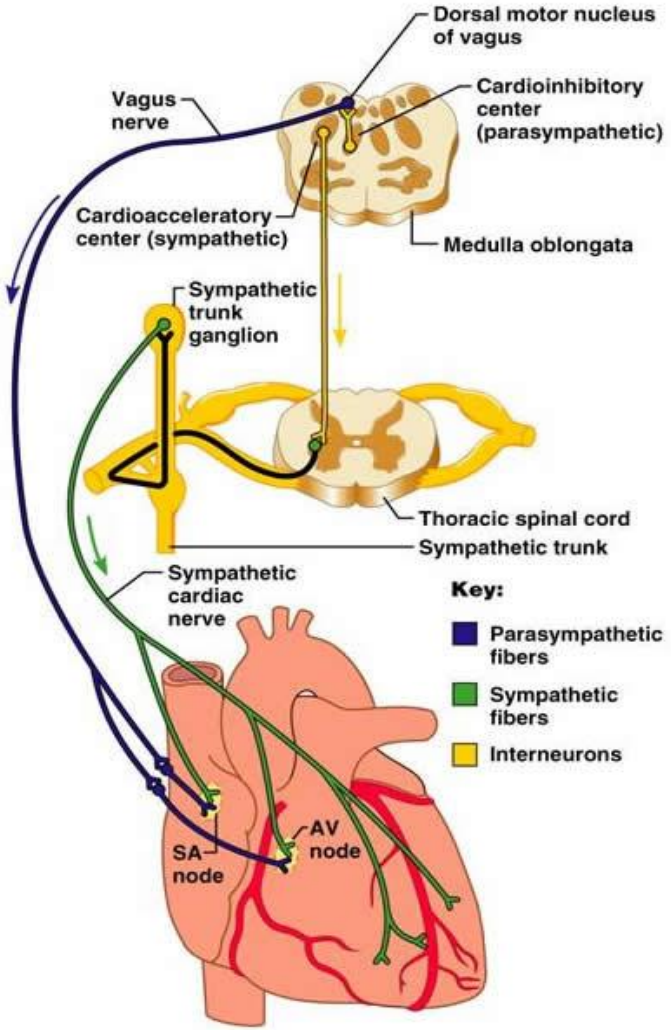
# Cardiac Reserve:

- The difference between the cardiac output at rest and the maximum volume of blood the heart can pump per minute is called the **cardiac reserve.**
- The output per minute per square meter of body surface (the **cardiac index**) averages 3.2 L.

- Both Heart Rate and Stroke Volume are affected by Autonomic nervous system.

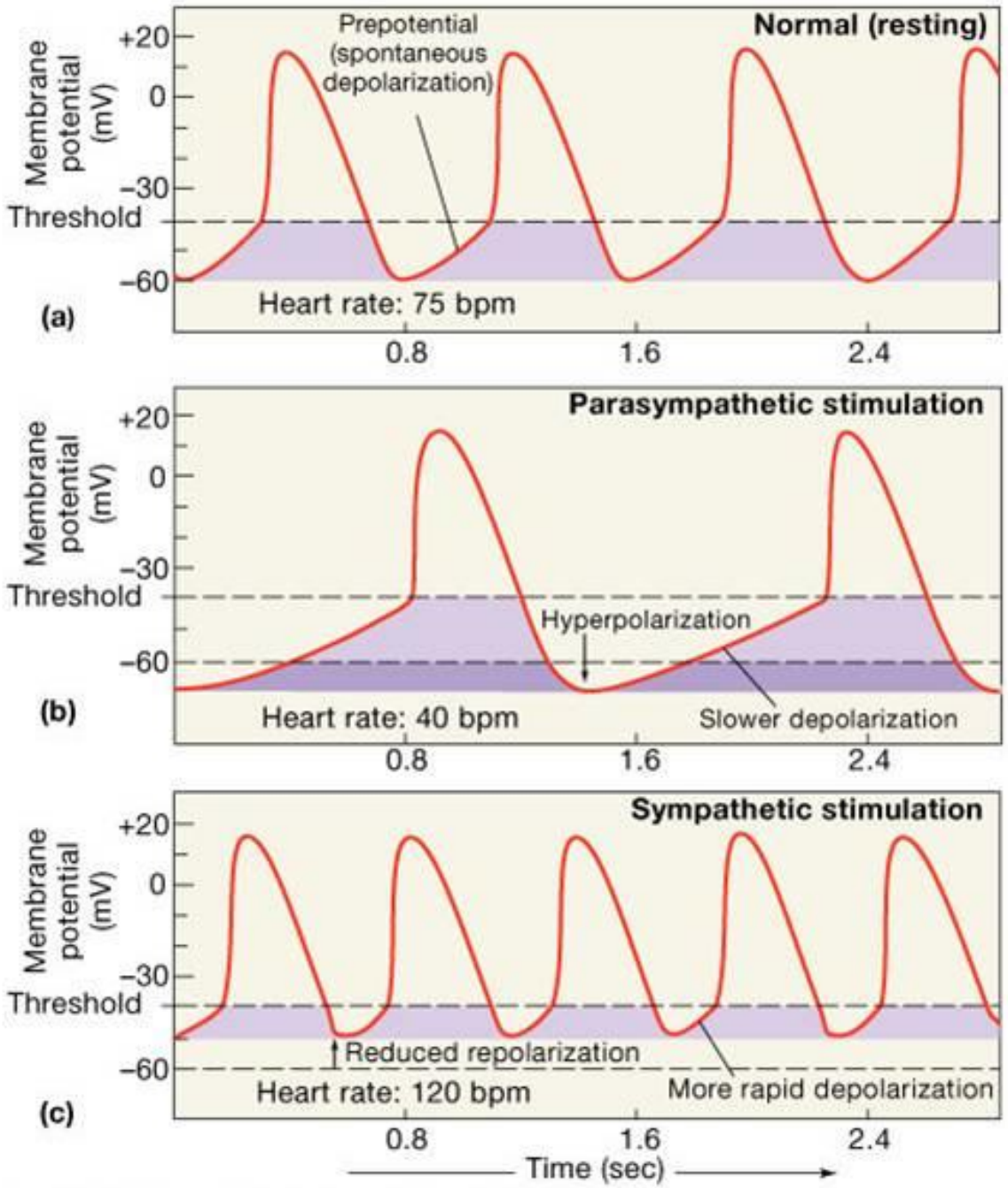
# Effect of Autonomic Nervous System on cardiac out put

Both the parasympathetic and sympathetic nervous system effects the heart by altering the activity of the cyclic AMP, second-messenger system in the innervated cardiac cells.

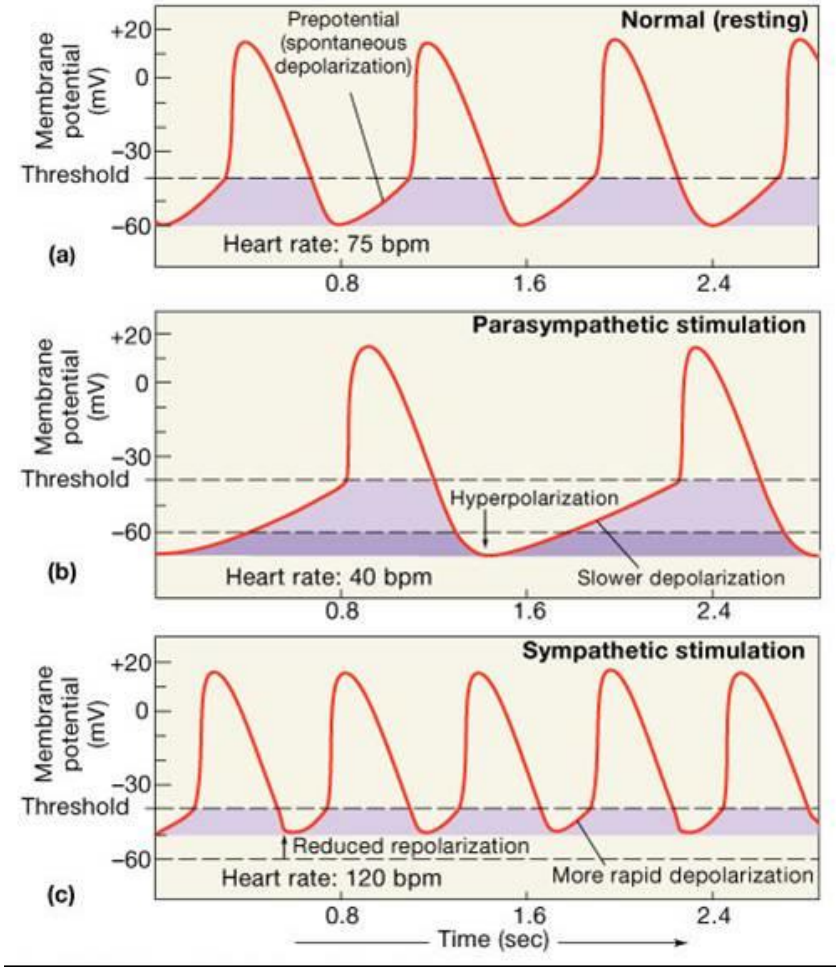


# PARASYMPATHETIC EFFECT

- Acetylcholine released from the vagus nerve binds to a muscarinic receptor
- Inhibitory G protein that reduces activity of the cyclic AMP pathway.
- The parasympathetic nervous system's Influence on the SA node is to decrease the heart rate.

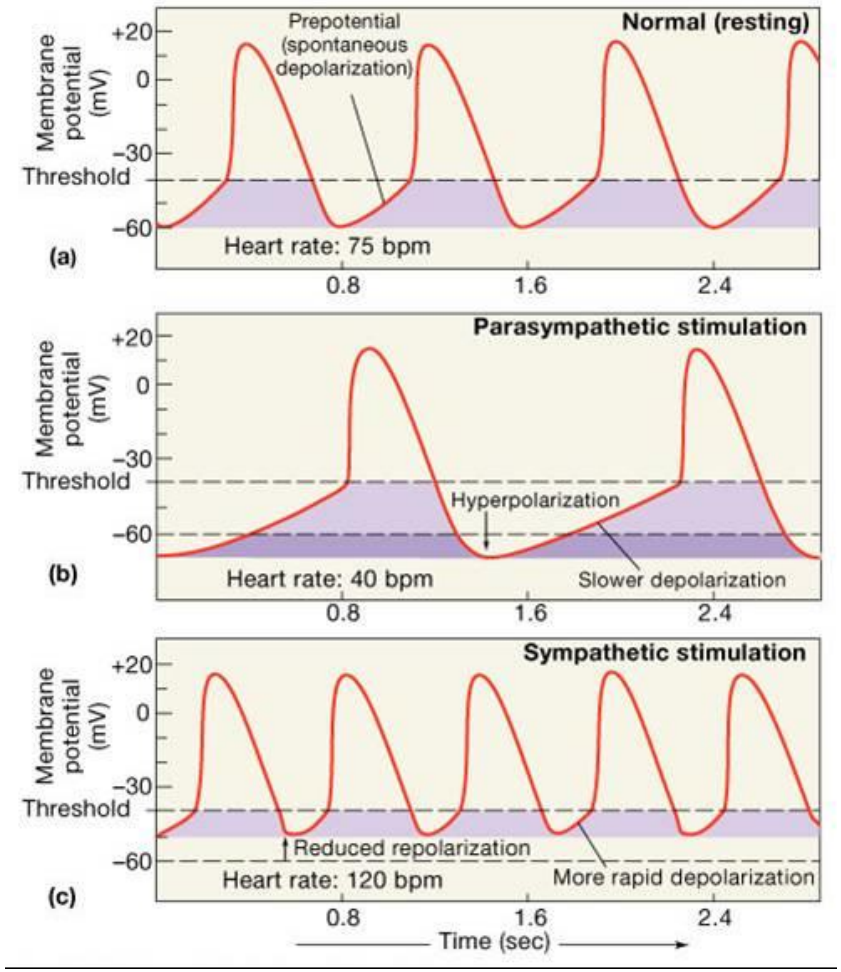

Normal (resting)
Prepotential (spontaneous depolarization)
Membrane potential (mV)
+20
0
−30
−60
Threshold
Heart rate: 75 bpm
(a)
0.8
1.6
2.4
Parasympathetic stimulation
Hyperpolarization
Heart rate: 40 bpm
Slower depolarization
(b)
Sympathetic stimulation
Reduced repolarization
Heart rate: 120 bpm
More rapid depolarization
(c)
Time (sec)

- Ach slows heart rate primarily by increasing K permeability of the pacemaker cells.
- **1. Enhanced K permeability hyperpolarizes the SA node.**
- **2. The increase in K permeability contributes to late development of the pacemaker potential.**



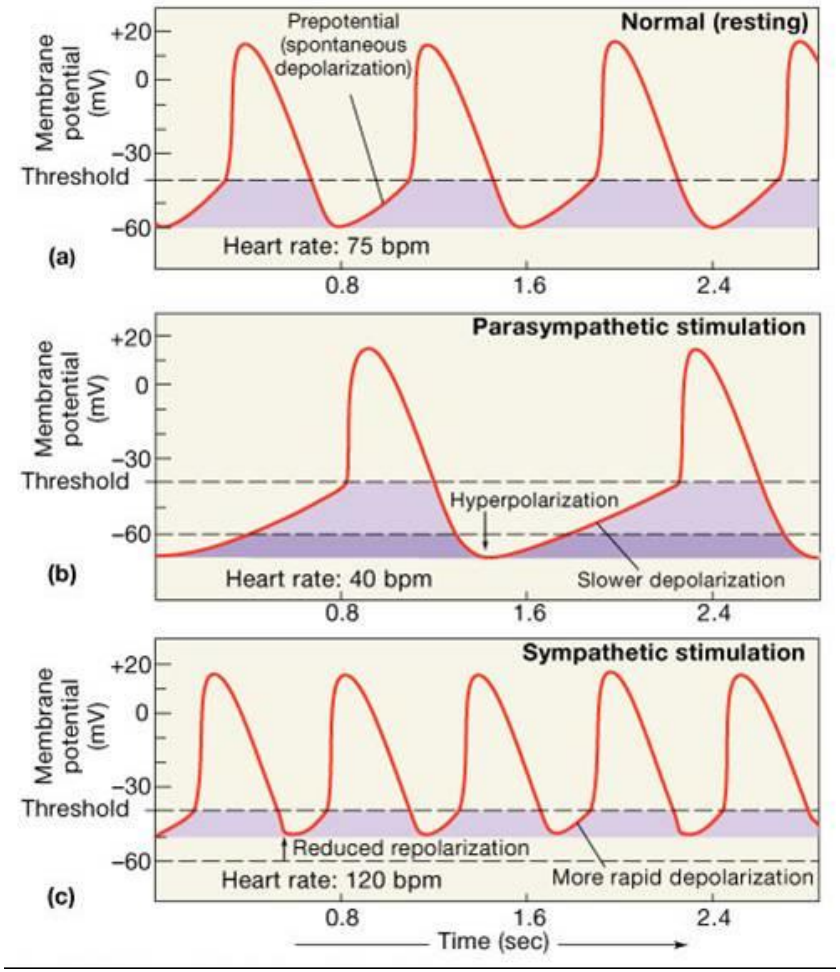
# PARASYMPATHETIC EFFECT ON AV NODE

- Decreases the node's excitability
- Prolonging transmission of impulses to the ventricles , AV nodal delay.
- By increasing K permeability.



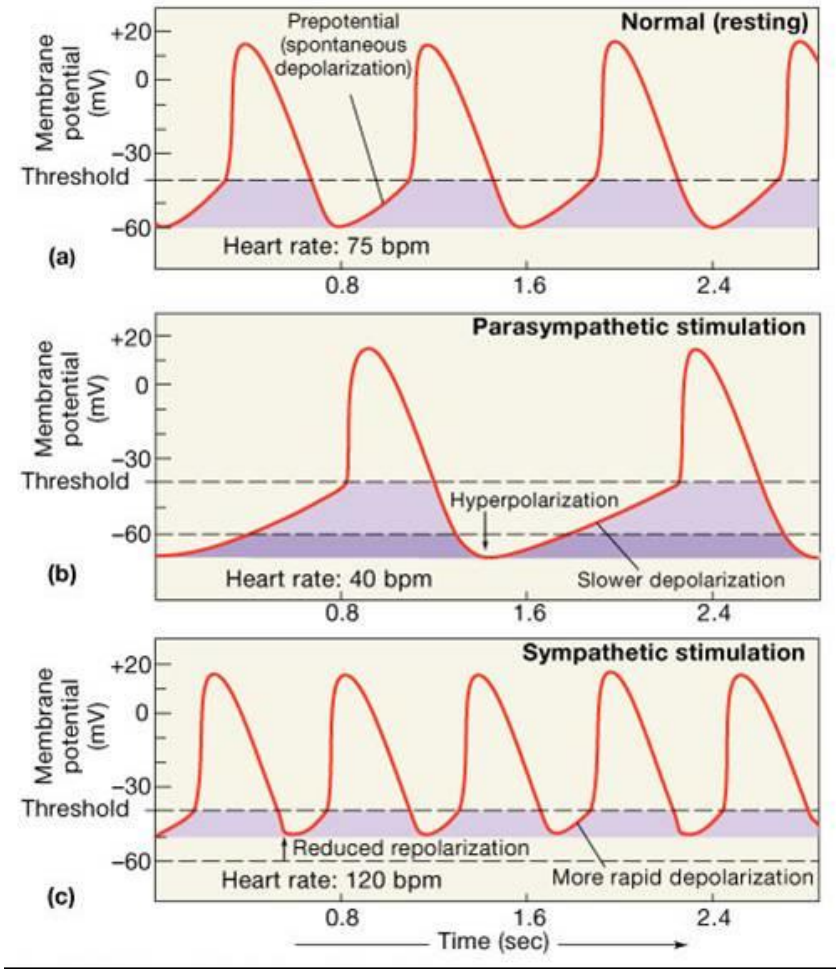
# ATRIAL MUSCLE

- Shortens the action potential
- Reducing the slow  Ca2 channel, the plateau phase is shortened.
- The  atrial contraction is weakened.



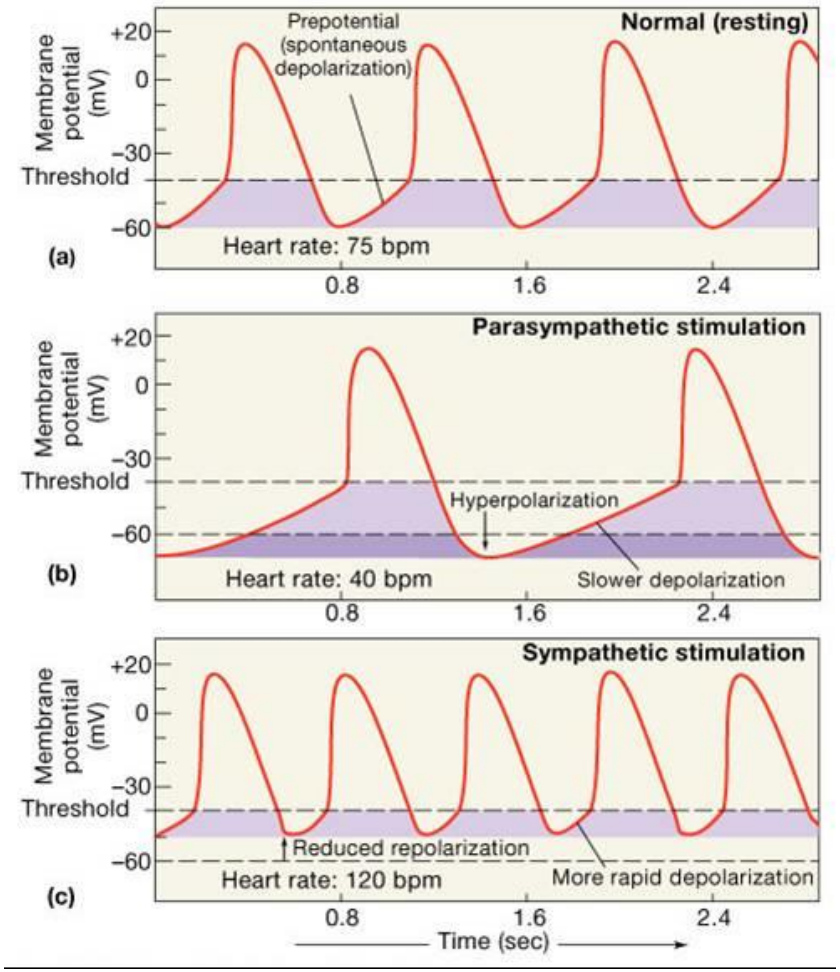
# Sympathetic Effects

- The sympathetic neurotransmitter Norepinephrine binds with
- Alpha 1 adrenergic receptor
- Stimulatory G protein
- Accelerates the cyclic AMP pathway in the target cells.



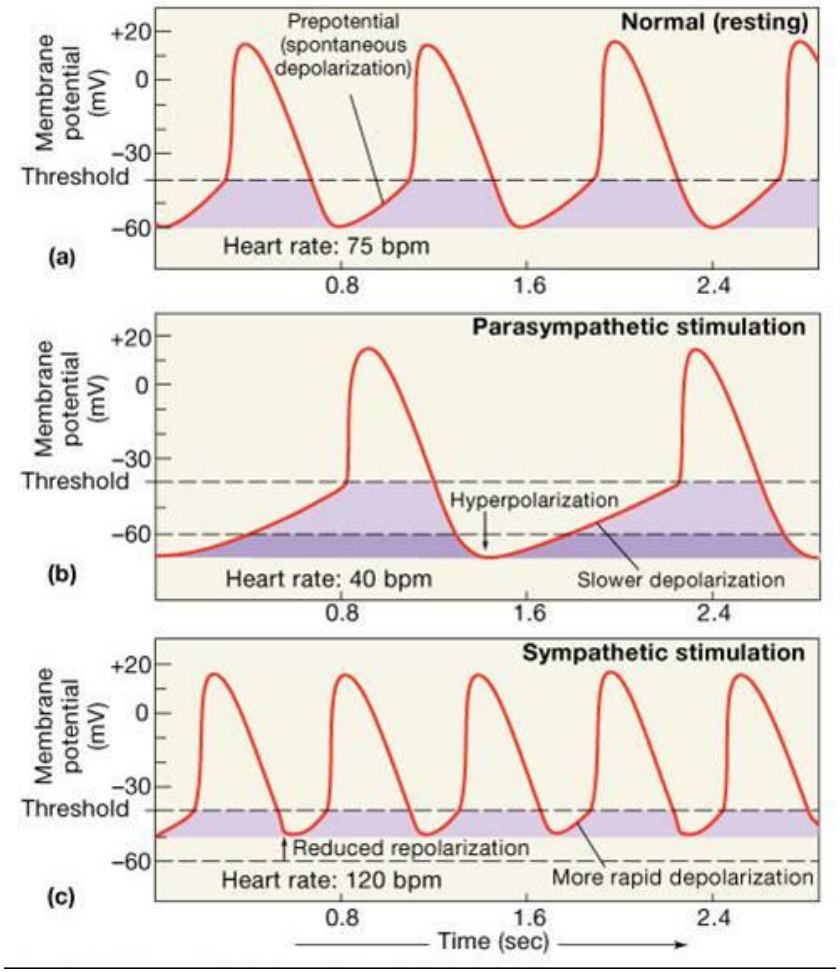
# SA NODE

- Speed up depolarization, the rate of depolarization increases
- Greater inward movement of Na and Ca2 through the augmented If and T-type Ca2 channels.



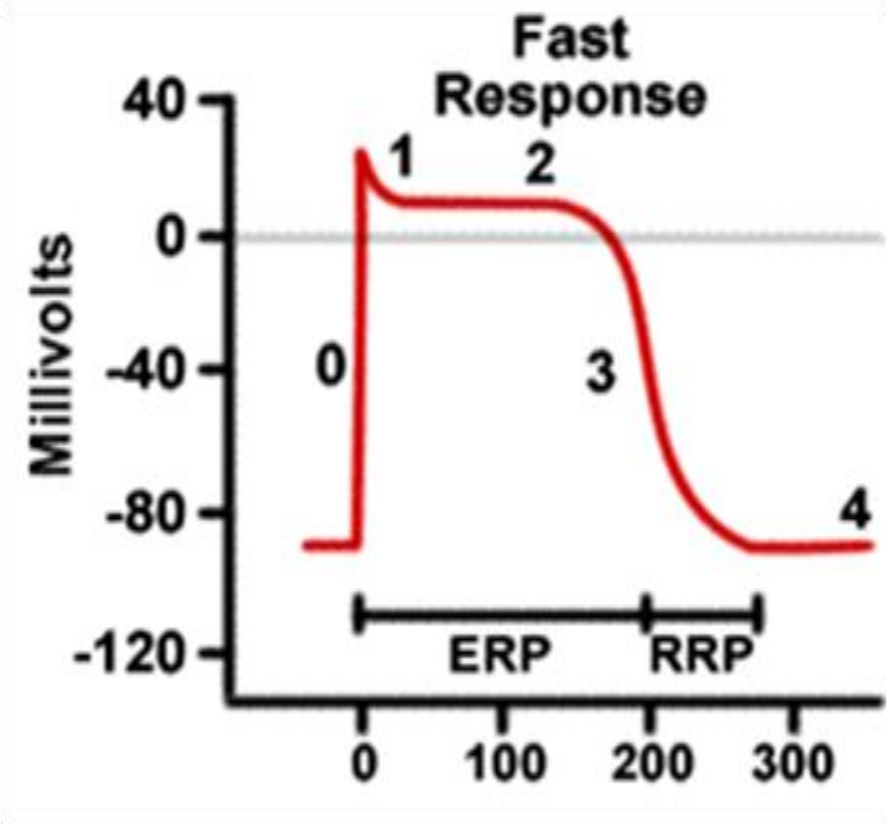
# AV NODE

- Sympathetic stimulation of the AV node reduces the AV nodal delay
- By increasing conduction velocity
- By enhancing the slow, inward Ca2 current.
- Speeds up spread of the action potential throughout the specialized conduction pathway.



# ATRIAL AND VENTRICULAR MUSCLE

- Increases contractile strength In the atrial and ventricular contractile cells.
- By increasing inward Ca2 movement through prolonged opening of L-type Ca2 channels.
- Enhances and Intensifies in Excitation-contraction-coupling.

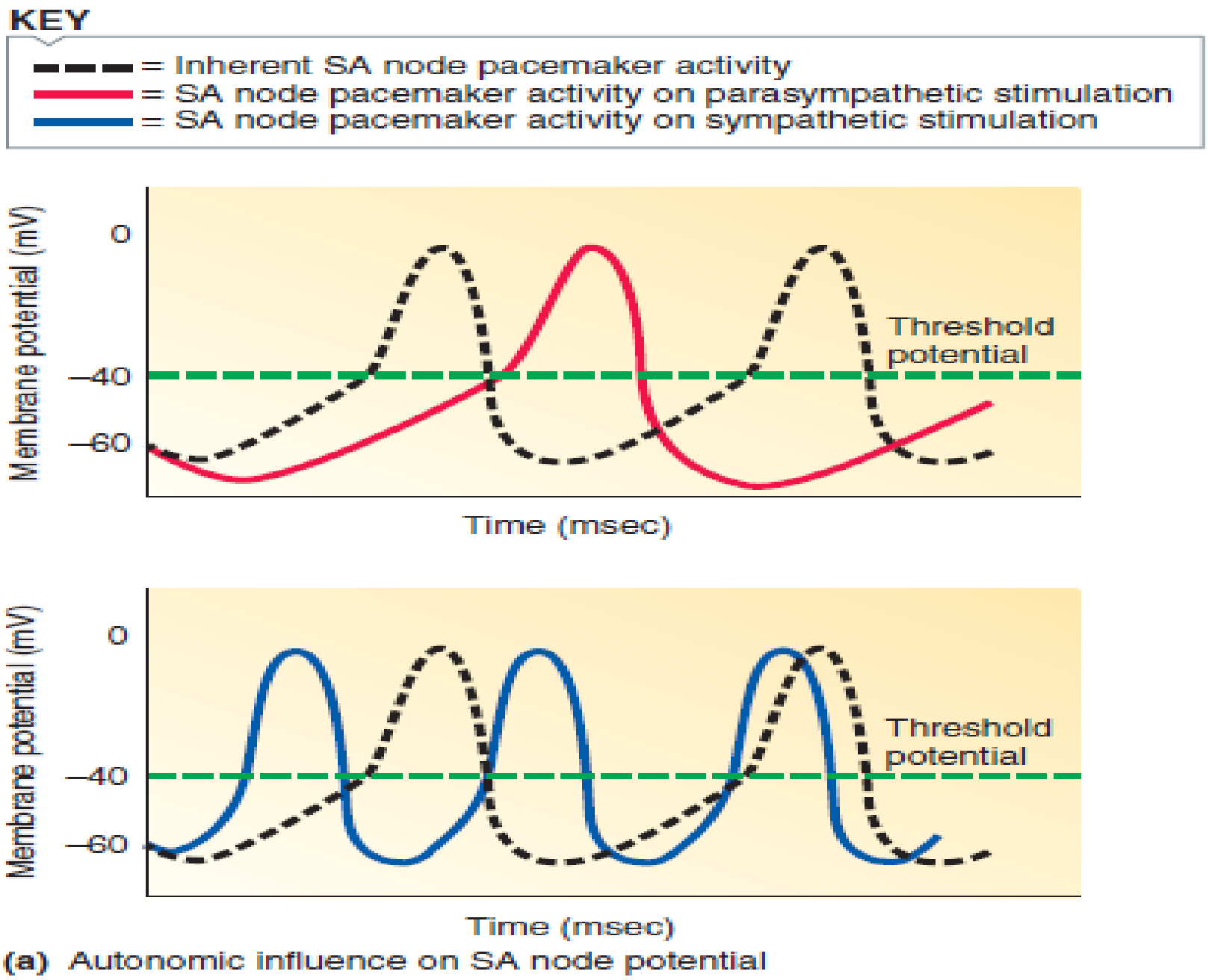


- Sympathetic stimulation also speeds up relaxation by enhancing the active Ca2 pump in the sarcoplasmic reticulum that removes Ca2 from the cytosol.

# SYMPATHETIC EFFECTS

Improve its effectiveness as a pump by

- Increasing heart rate
- Increasing force of contraction
- Decreasing the delay between atrial and ventricular contraction.
- Decreasing conduction Time.




**(a)** Autonomic influence on SA node potential

## TABLE 9-1 Effects of the Autonomic Nervous System on Heart Activity

| Area Affected | Effect of Parasympathetic Stimulation | Effect of Sympathetic Stimulation |
|---|---|---|
| **SA node** | Decreases the rate of depolarization to threshold; decreases the heart rate | Increases the rate of depolarization to threshold; increases the heart rate |
| **AV node** | Decreases excitability; increases the AV nodal delay | Increases excitability; decreases the AV nodal delay |
| **Ventricular conduction pathway** | No effect | Increases excitability; hastens conduction through the bundle of His and Purkinje cells |
| **Atrial muscle** | Decreases contractility; weakens contraction | Increases contractility; strengthens contraction |
| **Ventricular muscle** | No effect | Increases contractility; strengthens contraction |
| **Adrenal medulla (an endocrine gland)** | No effect | Promotes secretion of epinephrine, a hormone that augments sympathetic nervous system actions |
| **Veins** | No effect | Increases venous return, which increases the strength of cardiac contraction via intrinsic control |

# ADRENAL GLAND SECRETION

- The Epinephrine, a hormone secreted from adrenal medulla on sympathetic stimulation.
- Epinephrine acts to increase heart rate.

# FACTORS INCREASING STROKE VOLUME

- (1) *intrinsic control by venous* return
- (2) *extrinsic control by* sympathetic stimulation of the heart.
- Both factors increase stroke volume by increasing the strength of heart contraction.

- Depends on the direct correlation between end-diastolic volume and stroke volume.
- As more blood returns to the heart, the heart pumps out more blood.

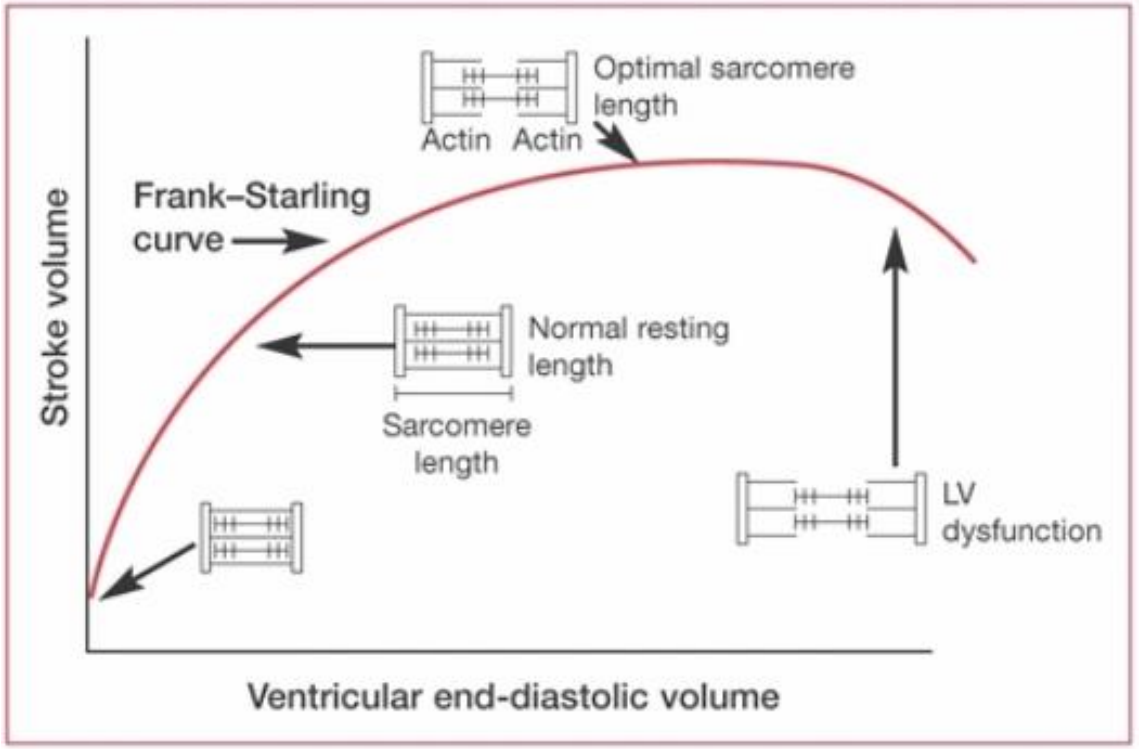
- **EDV** is often referred to as "preload," and it influences stroke volume in the following way
- Two physiologists, Frank and Starling, demonstrated that the strength of ventricular contraction increased with an enlargement of EDV (i.e , stretch of the ventricles)
- This relationship has become known as the Frank Starling law of the heart

# FRANK STARLING LAW

- Starling's Law of Heart This law states that in a healthy heart with normal cardiac output, the amount of blood that is pumped out of the heart (stroke volume) should return in full (end diastolic volume).
- The greater the volume of blood that leaves the heart, the greater the volume that will return and vice versa.

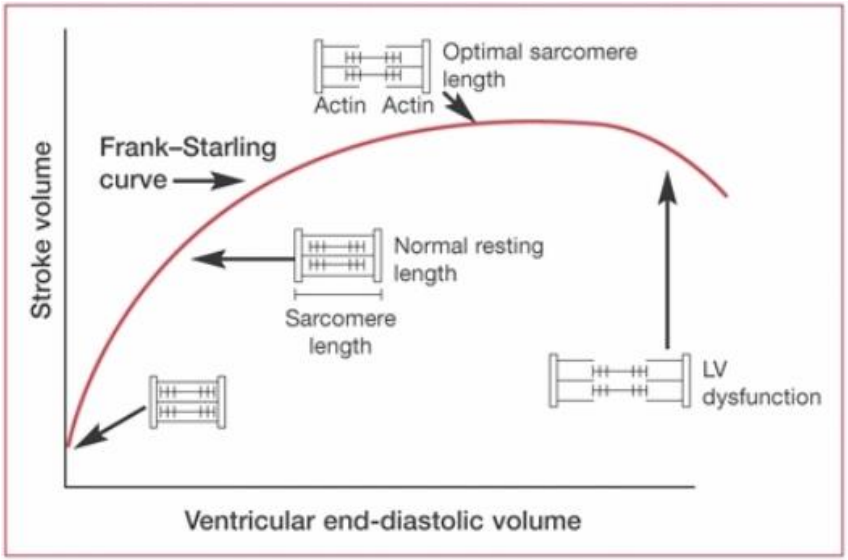
# LENGTH TENSION RELATION

- This intrinsic control depends on the length–tension relationship of cardiac muscle, which is similar to that of skeletal muscle.

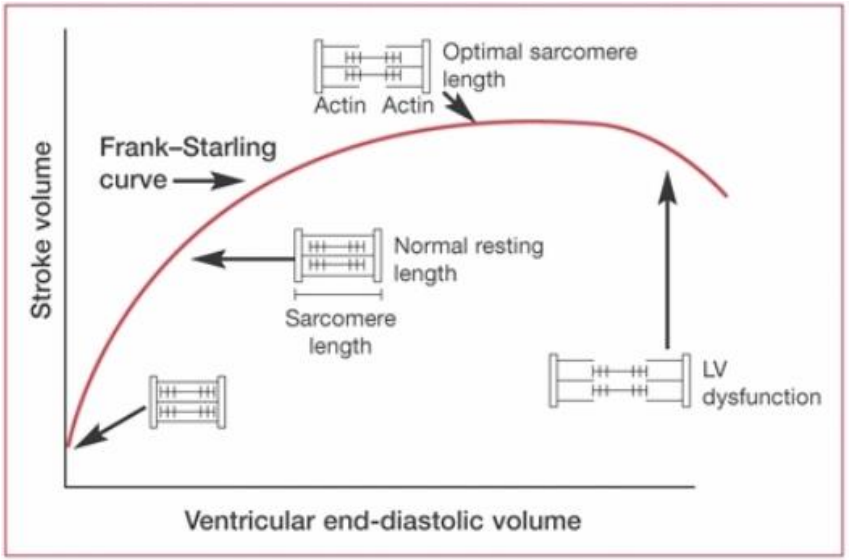


# Relationship with End Diastolic Volume

- The greater the diastolic filling, the larger
- the end-diastolic volume (EDV), and the more the heart is  stretched.
- The more the heart is stretched, the longer the initial cardiac fiber length before contraction.

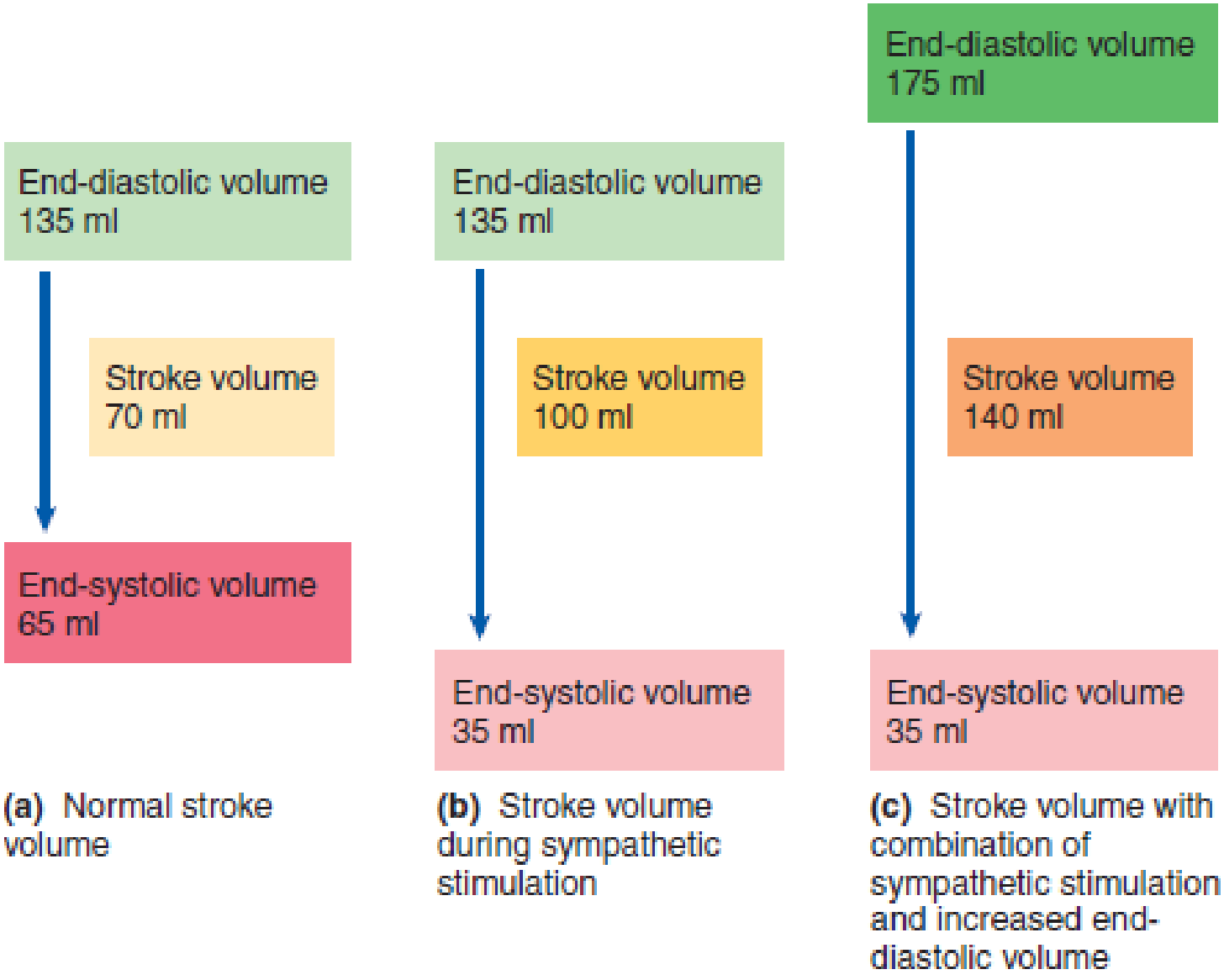


- The increased length results in a greater force on the subsequent cardiac contraction
- and thus in a greater stroke volume.
- This intrinsic relationship between EDV and stroke volume is known as the **Frank–**
- **Starling law of the heart.**



# Relationship with Venous Return

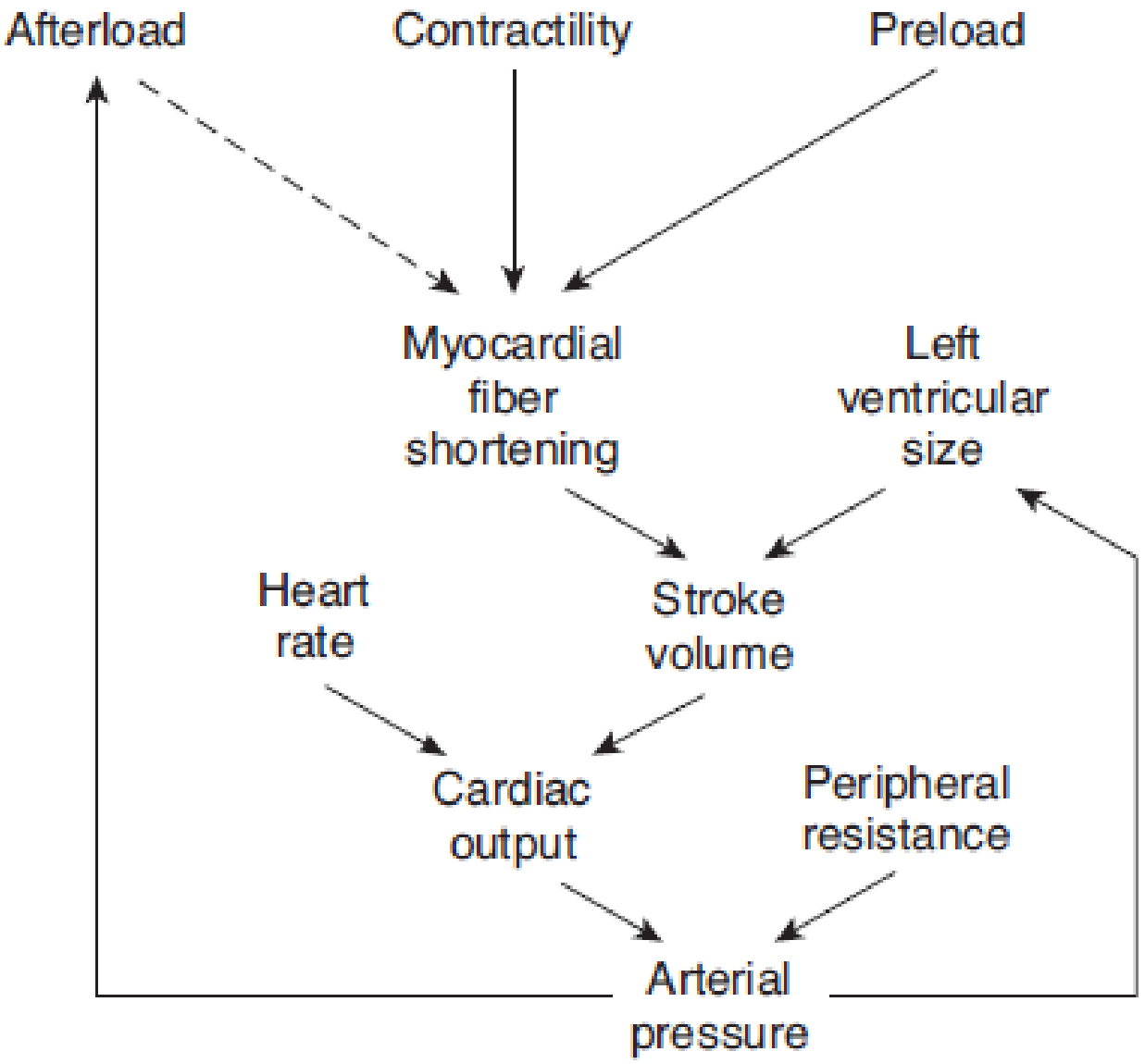
- The right side of the heart ejects a larger stroke volume, more blood enters the pulmonary circulation, so venous return to the left side of the heart increases accordingly.
- The increased EDV of the left side of the heart causes it to contract more forcefully




**(a)** Normal stroke volume

**(b)** Stroke volume during sympathetic stimulation

**(c)** Stroke volume with combination of sympathetic stimulation and increased end-diastolic volume


Afterload
Contractility
Preload
Myocardial fiber shortening
Left ventricular size
Heart rate
Stroke volume
Cardiac output
Peripheral resistance
Arterial pressure

# Autonomic effects on heart rate & conduction velocity

**Dromotropic Effects:**

- Produces changes in conduction velocity primarily of AV node.

- Negative Dromotropic Effect --- dec Conduction Velocity through the AV node slowing the conduction of action potential from atria to the ventricles & vice versa.

# Parasympathetic effects on heart rate & conduction velocity

- SA node, atria & AV node have parasympathetic vagal innervation
- Acetylcholine is the neurotransmitter
- Dec in heart rate
- Dec the rate of phase 4 depolarization
- Dec inward Na current

# Parasympathetic effects on heart rate & conduction velocity

- Dec in conduction velocity via AV node
- Action potentials carry more slowly from the atria to the ventricles
- Dec inward ca+ current & inc outward K+ current

# Sympathetic effects on heart rate & conduction velocity

- Nor epinephrine is the neurotransmitter
- Inc in heart rate
- Inc the rate of phase 4 depolarization
- Inc inward Na current
- More action potentials occur per unit time

# Sympathetic effects on heart rate & conduction velocity

- Inc in conduction velocity via AV node
- Action potentials carry more rapidly from the atria to the ventricles
- Ventricular filling may be compromised
- Inc inward ca+ current

**Ionotropic Effects:**

- Produces changes in the heart's contractility.
- Related to intracellular Ca+ accumulation

- Positive ionotropic agents increases the contractility & vice versa

# Positive Ionotropism

**Factors:**

- Increased heart rate (more action potentials / unit time --- more Ca+ --- more contraction)

- Sympathetic stimulation by (catecholamines) Inc inward Ca+ current

# Negative Ionotropism

**Factors:**

- Parasympathetic stimulation by (Acytylcholine) Dec inward Ca+ current --- Dec force of contraction

# Factors affecting myocardial excitability

**Cardiac Innervation:**

- Sympathetic NS → ↑ excitability.
- Parasympathetic NS (vagus) → ↓ excitability.

**Effect of ions concentration in ECF:**

- ↑ $Ca^{2+}$ → ↑ excitability.
- ↑ $K^{+}$ → ↓ excitability.

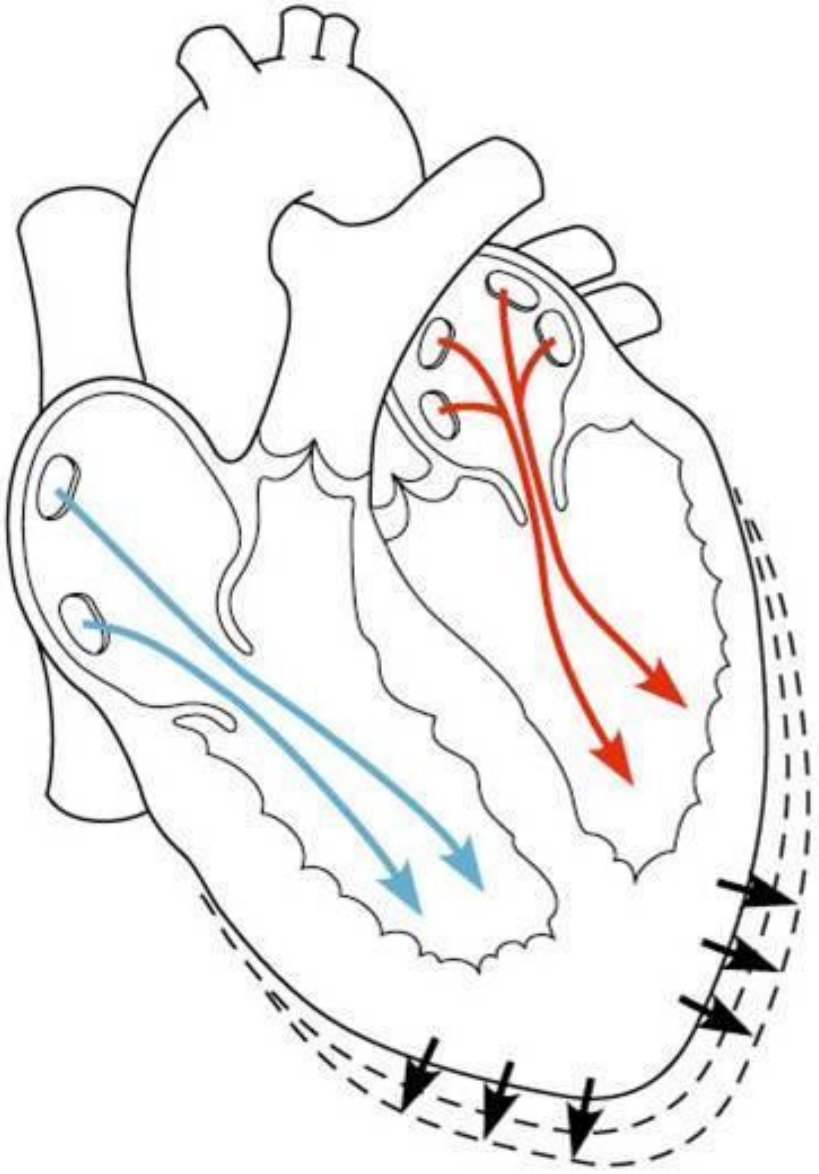
**Physical factors:**

- ↑ temperature → ↑ excitability.
- ↓ temperature → ↓ excitability.

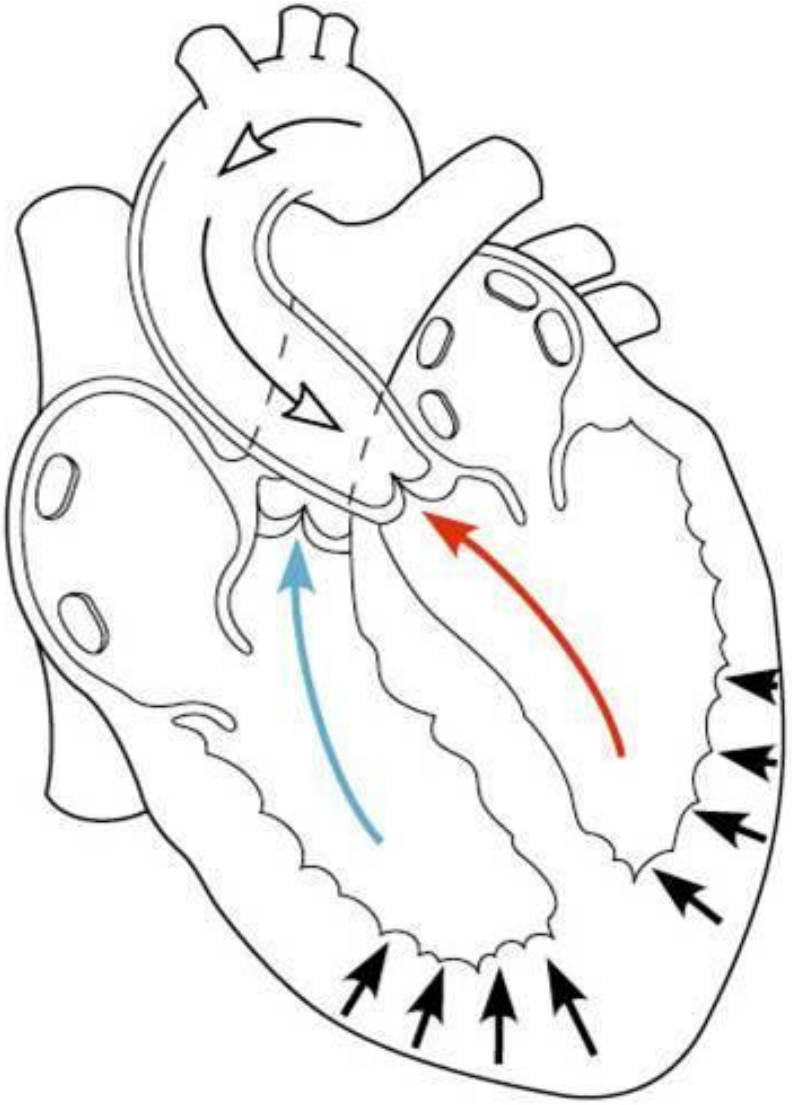
# PRE-LOAD & AFTER LOAD

- Preload is the muscle length prior to contractility, and it is dependent of ventricular filling (or end diastolic volume.)
- The most important determining factor for preload is venous return.

- Afterload is a measure of the pressure that must be generated by the ventricles to force the semilunar valves open.
- The greater the afterload, the smaller the stroke volume.

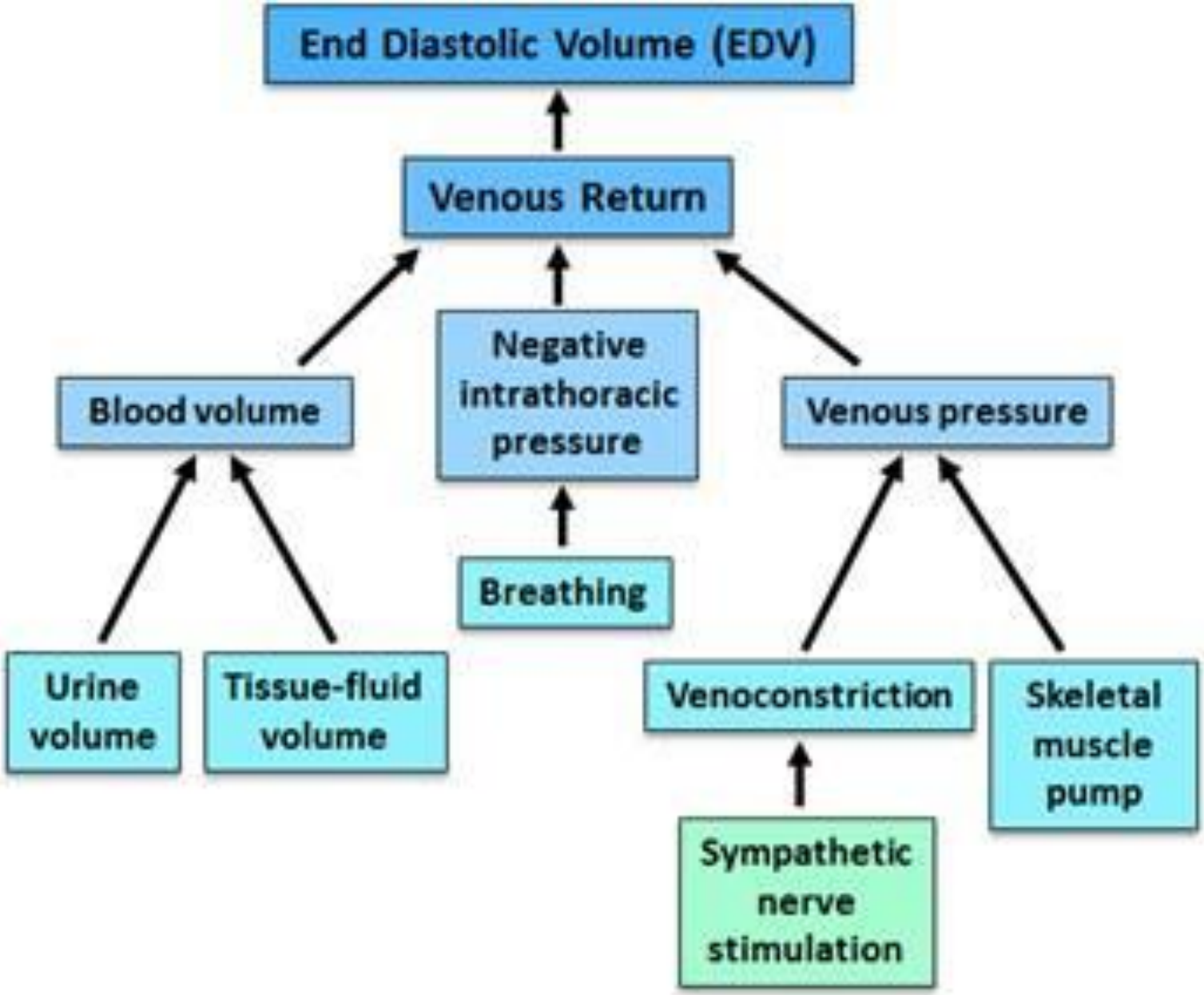


(a) Preload



(b) Afterload

- The Pre-Load is the degree to which the myocardium is stretched before it contracts and
- The
- After-Load is the resistance against which blood is expelled.


End Diastolic Volume (EDV)
Venous Return
Blood volume
Negative intrathoracic pressure
Venous pressure
Urine volume
Tissue-fluid volume
Breathing
Venoconstriction
Skeletal muscle pump
Sympathetic nerve stimulation

# EFFECT OF RESISTANCE

- Under most normal conditions, the long-term cardiac output level varies reciprocally with changes in total peripheral Resistance.
- Then, when the total peripheral resistance
- increases above normal, the cardiac output falls; conversely,
- when the total peripheral resistance decreases, the cardiac output increases.

- Cardiac Output = Arterial Pressure/ Total Peripheral Resistance

- The normal human heart can pump an amount of venous return up to about 2.5 times the normal venous return ,
- before the heart becomes a limiting factor in the control of cardiac output.

- two types of factors usually can make the heart a better pump than normal.
- (1) Nervous Stimulation
- (2) Hypertrophy of the Heart Muscle.

- A long-term increased workload, causes the heart muscle to increase in mass and contractile strength,
- same way that heavy exercise causes skeletal muscles to hypertrophy.

- When there is combination of nervous excitation of the heart and hypertrophy, as occurs in marathon runners,
- The total effect can allow the heart to pump as much 30 to 40 L/min, about 21/2 times normal.

# FACTORS CAUSING HYPOEFFECTIVE HEART

- Coronary artery blockage
- Inhibition of nervous excitation of the heart
- Pathological factors that cause abnormal heart
- rhythm or rate of heartbeat
- Valvular heart disease
- Increased arterial pressure against which the
- heart must pump, such as in hypertension
- Congenital heart disease
- Myocarditis
- Cardiac hypoxia

# INCREASE VENOUS RETURN

- DECREASED IN TOTAL PEIPHERAL RESISTANCE:
- Beri-beri
- Arterio-venous Fistula
- Hyperthyroidism
- Anemia
- Anxiety
- Pulmonary disease

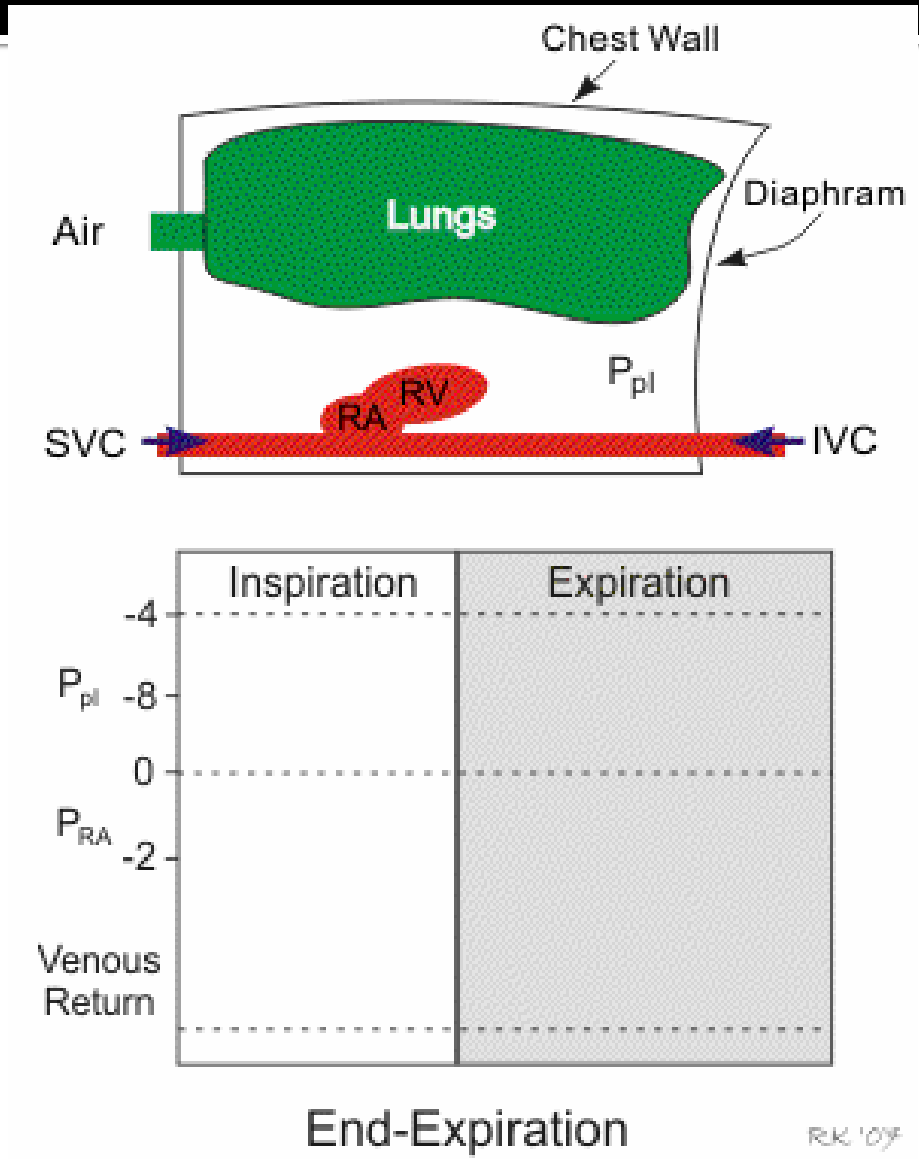
- Conditions that cause abnormally low cardiac output.
- These conditions fall into two categories:
- (1) Abnormalities in pumping effectiveness of the heart
- (2) Decrease in venous return

- **Decreased Cardiac Output Caused by Cardiac Factors.**
- 1) *Severe coronary blood vessel*
- *blockage and consequent Myocardial Infarction,*
- *(2) Severe valvular heart disease,*
- *(3) Myocarditis, (4) Cardiac Tamponade,*
- *and (5) Cardiac Metabolic Derangements.*

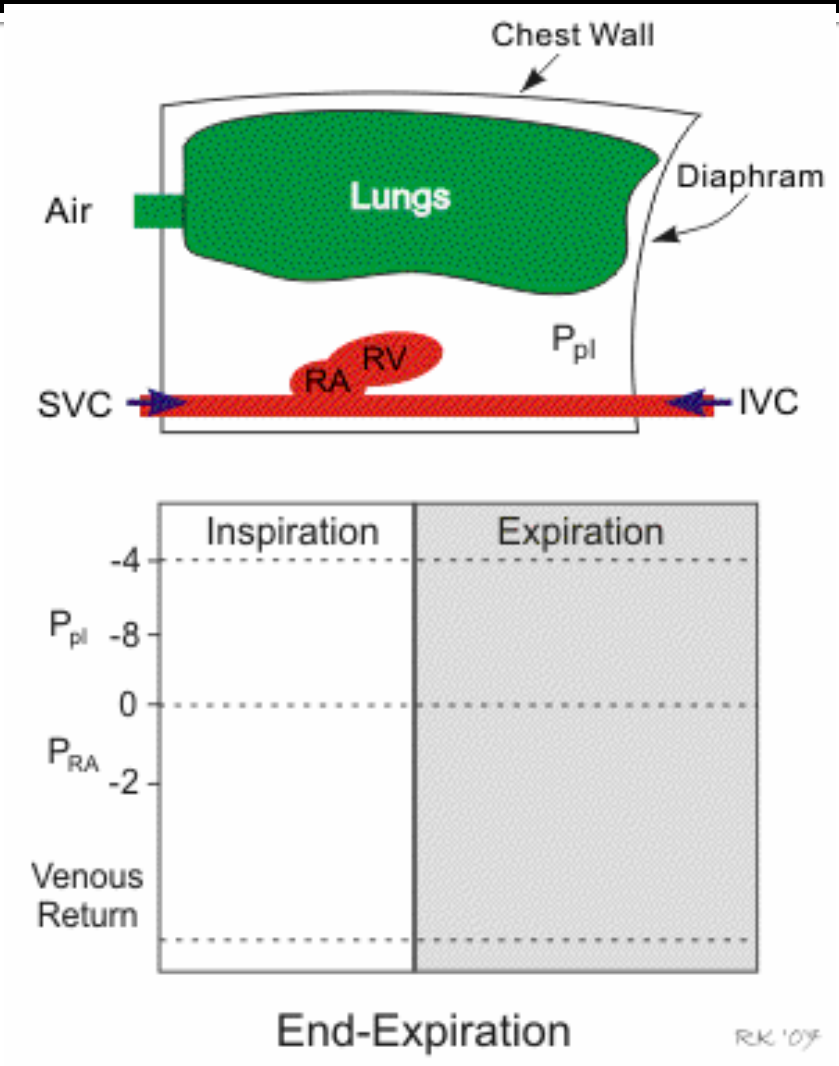
- **Decrease in Cardiac Output Caused by Non-cardiac Peripheral**
- **Factors—Decreased Venous Return.**
- *1.Decreased blood volume*
- *2. Acute venous dilation*
- *3. Obstruction of the large veins.*
- *4. Decreased tissue mass, especially decreased skeletal muscle mass.*

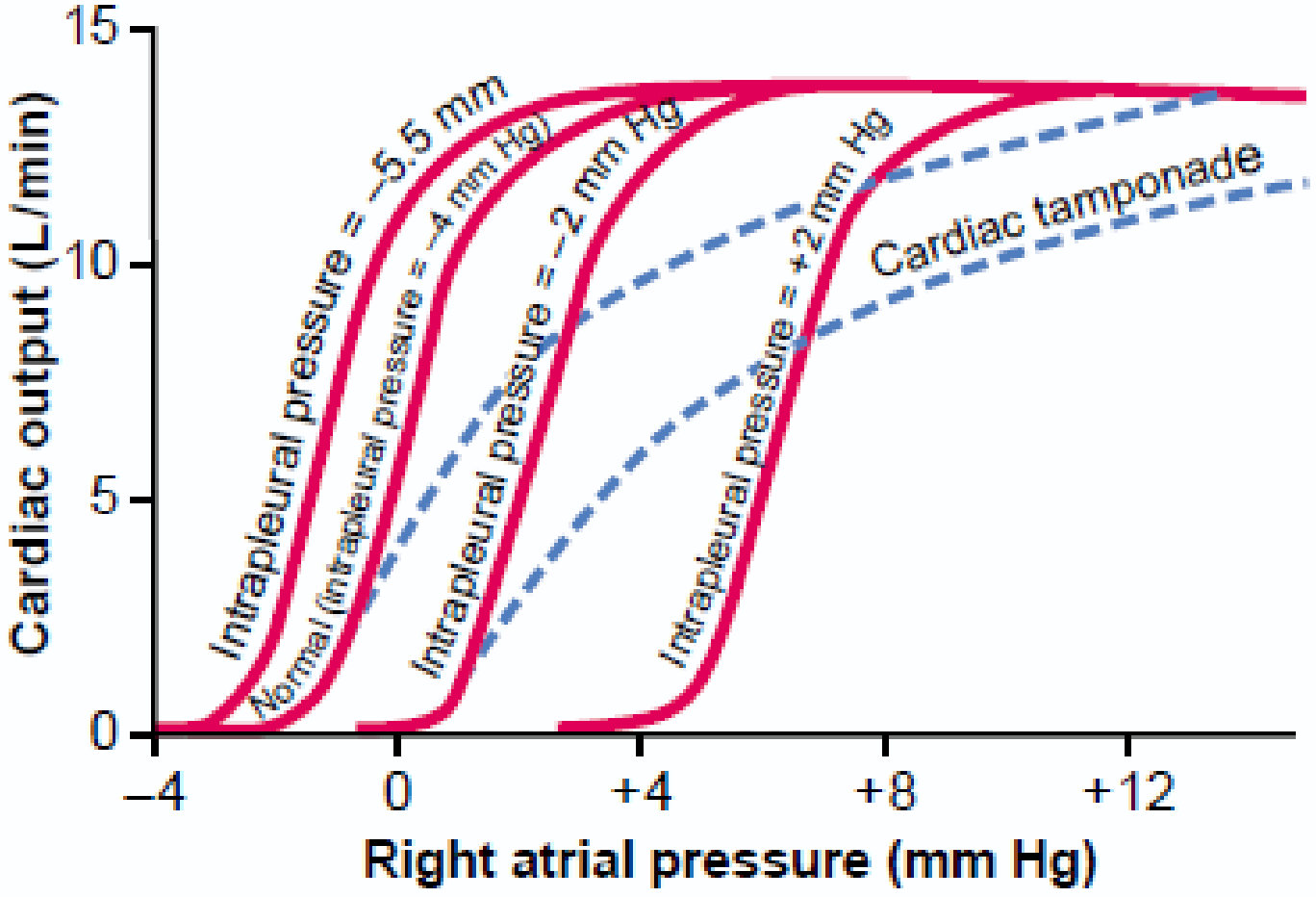
# RESPIRATION & VENOUS RETURN

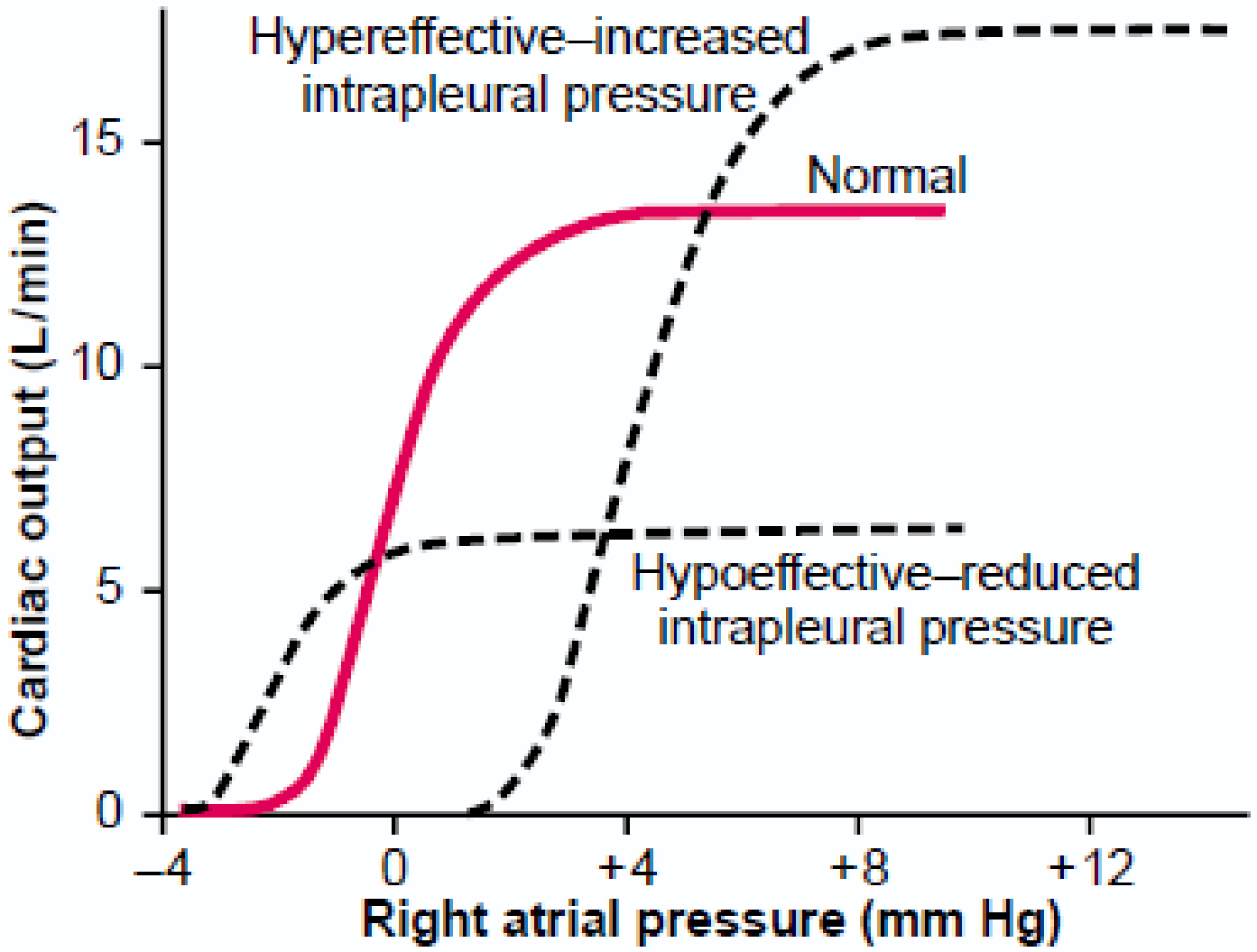
- INTRA-PLEURAL PRESSURE
- *Cyclical changes of intrapleural pressure during*
- *respiration, which are about ±2 mm Hg during*
- normal breathing but can be as much as
- ±50 mm Hg during strenuous breathing.



- *Breathing against a negative pressure, which shifts* the curve to a more negative right atrial pressure (to the left).
- 3. *Positive pressure breathing, which shifts the curve to* the right.



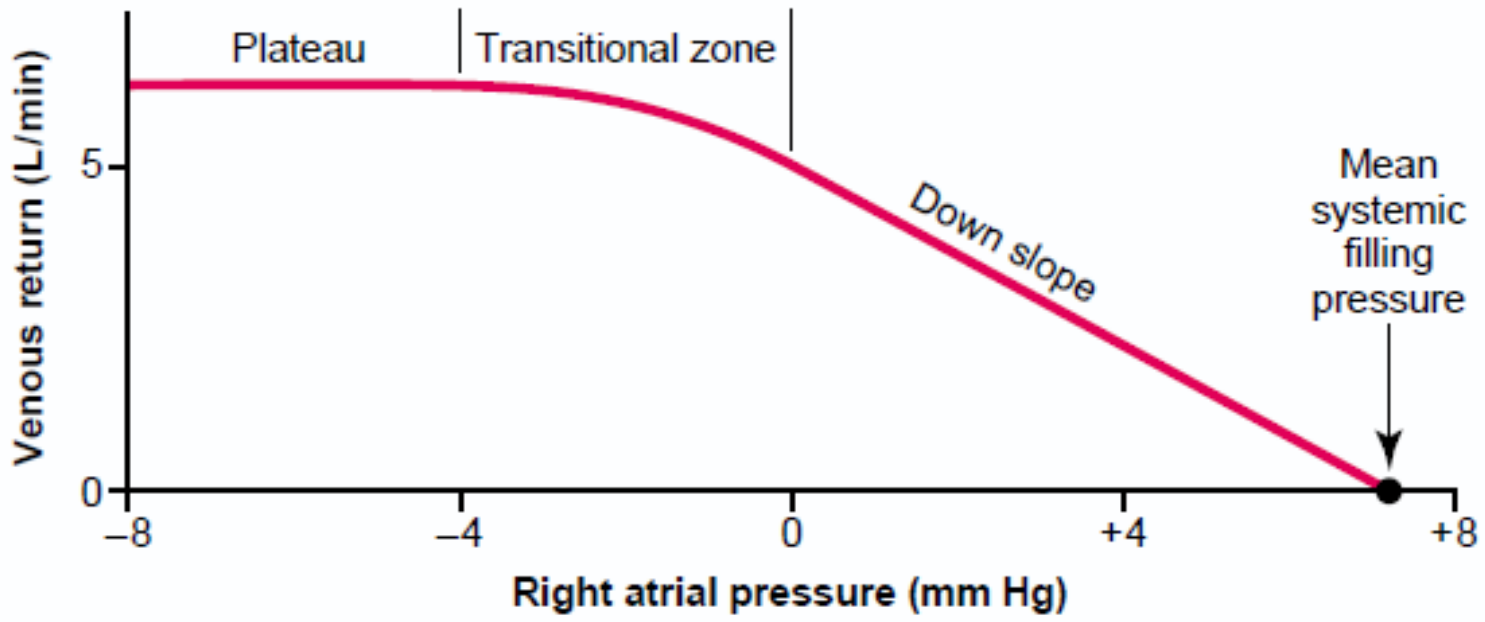

Cardiac output (L/min)
15
10
5
0
–4
0
+4
+8
+12
Right atrial pressure (mm Hg)
Intrapleural pressure = –5.5 mm Hg
Normal (Intrapleural pressure = –4 mm Hg)
Intrapleural pressure = –2 mm Hg
Intrapleural pressure = +2 mm Hg
Cardiac tamponade


Hypereffective–increased intrapleural pressure
Normal
Hypoeffective–reduced intrapleural pressure
Cardiac output (L/min)
15
10
5
0
–4
0
+4
+8
+12
Right atrial pressure (mm Hg)

- Three principal factors that affect venous return to the heart from the systemic circulation.

- They are as follows:
- 1. *Right atrial pressure*
- 2. Degree of filling of the systemic circulation
- (measured by the *mean systemic filling pressure),*
- 3. *Resistance to blood flow between the peripheral*
- vessels and the right atrium.

- Filling Pressure Mean Circulatory:
- The pressure within the circulatory system when all flow is stopped (e.g. by stopping the heart).


Plateau
Transitional zone
Down slope
Mean systemic filling pressure
Venous return (L/min)
5
0
–8
–4
0
+4
+8
Right atrial pressure (mm Hg)

- **Measurement of CO :**
- Measurement of CO
  Electromagnetic/ultrasonic (transit time) flow meter.
- Oxygen Fick method:
- CO = (Rate of O2 absorbed by lungs)
- [O2]la - [O2]rv Indicator dilution method:
  Inject cold saline (or dye) into RA, measure temperature (or concentration) in aorta.