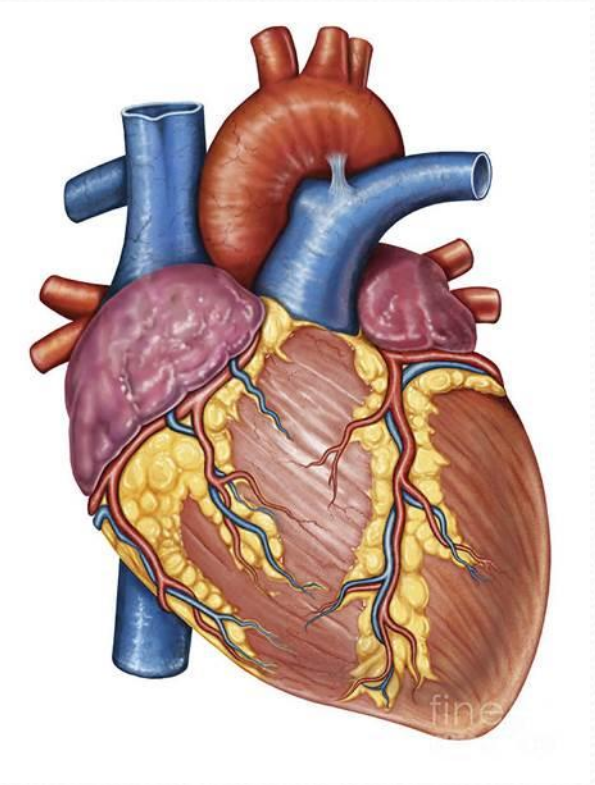
Cardiovascular System Block
Cardiac Output
Regulation of Stroke Volume
(Preload, Contractility & Afterload)



Dr. Hayam Gad

MBBS, MSc, PhD

Associate Professor Of Physiology

College of Medicine, KSU

Learning Objectives

- Define stroke volume, end-systolic volume, and end-diastolic volume
- Define cardiac output, venous return, cardiac index & cardiac reserve
- Understand the concept of preload and afterload
- Understand the determinants of CO and how CO is regulated
- Understand the factors affecting the EDV (the venous return)
- Understand the factors affecting the ESV
- Know how cardiac contractility & heart rate changes affect CO
- Identify the factors that affect heart rate
- Know the method for measurement of CO (The direct Fick's method)
- Describe the factors affecting the SV & CO

Remember What Are ?

- **End-diastolic volume (EDV):**

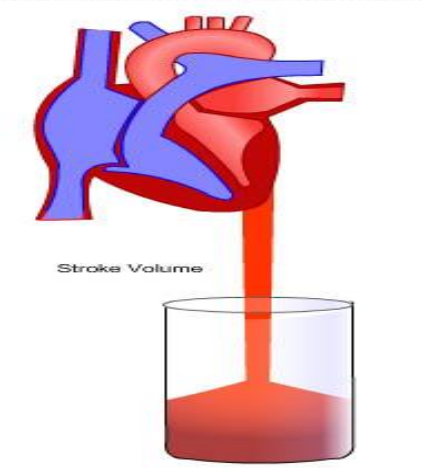
  Volume of blood in ventricles at the end of diastole = **110-130 mL.**

- **End-systolic volume (ESV):**

  Amount of blood left in ventricles at the end of systole = **40-60 mL.**

- **Stroke volume (SV):**

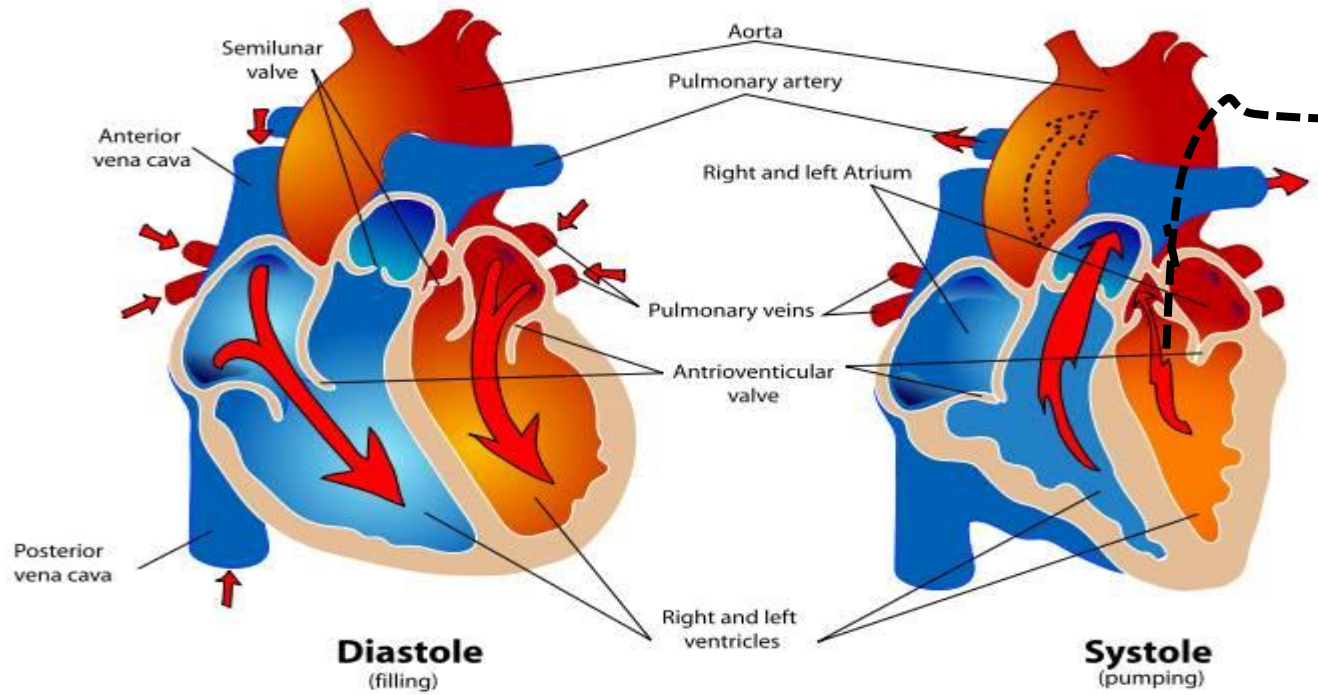
  Amount of blood ejected from ventricles during systole = **70-80 mL/beat.**



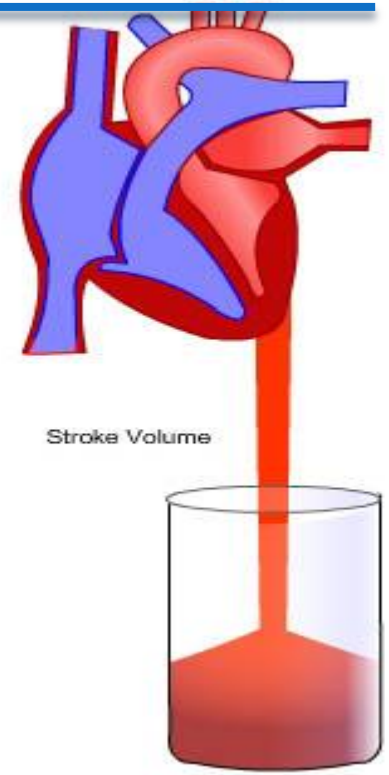
- **Ejection fraction (EF):**

  Fraction of EDV ejected during a heart beat =SV/EDV = **60-65 %.**

The Stroke Volume



Amount of blood ejected from ventricles during systole (per beat) = ***The stroke volume***



Volume of blood in ventricles at the end of diastole (***End-diastolic volume***) ≈110-130 ml

−

Amount of blood left in ventricles at the end of systole (***End-systolic volume***) ≈40-60 ml

=

The stroke volume (70-80 ml)

What determines the stroke volume?

The Cardiac Output

- If the amount of blood pumped by the left ventricle ***per beat*** = ***stroke volume (≈70ml in adult at rest).***

- **What is the amount of blood pumped by the left ventricle *per minute (The Cardiac Output)*?**

  = Stroke volume (SV) X heart rate (HR)

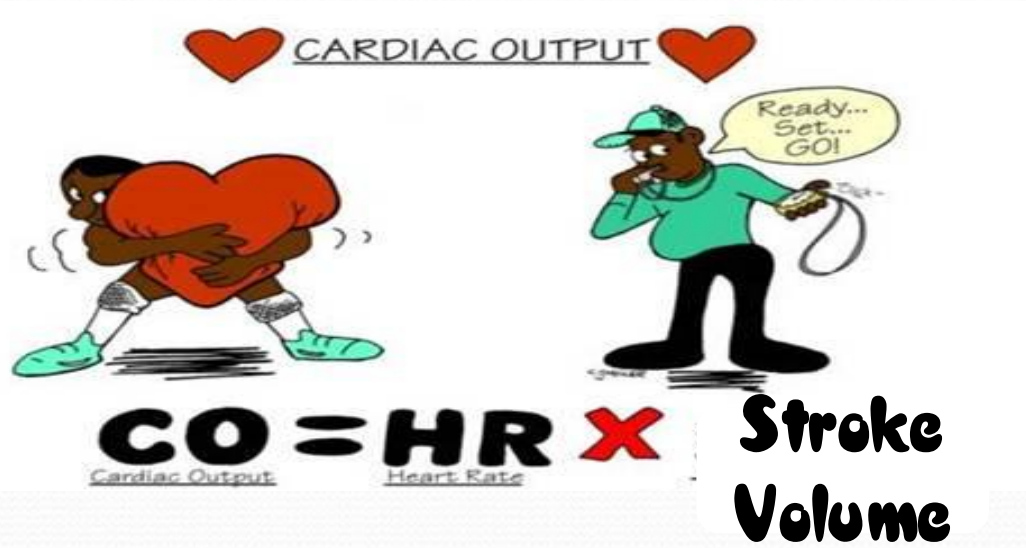
  = Cardiac output (CO)

  ≈ 5L/min. in adult at rest

The Cardiac output (CO)

- It is the volume of blood pumped by each ventricle per minute **≈ 5L/min**.

- Since the normal adult blood volume is about ***5 L***, the entire blood supply passes through the body once each minute.



CO= 70 x 70 ≈ 5L/min.

Normal Values of Cardiac Output at Rest

- **Resting cardiac output:**
  - The average cardiac output for the resting adult is 5L/min.
  - For men, CO ≈ **5.6L/min.**
  - For women, CO ≈ **4.9L/min.**

- **The factors affecting cardiac output are:**
  1. Body metabolism
  2. Pregnancy
  3. Body temperature.
  4. Sympathetic activity
  5. Exercise
  6. Hyperthyroidism

Physiological changes in CO

- During the first 3 hours after meals, the CO increases by ≈ 30% to enhance blood flow in the intestinal circulation.
- Later months of pregnancy are accompanied by 30% increase in CO due to increased uterine blood flow.
- At environmental temperature above 30˚C, the CO is increased due to increased skin blood flow. Also at low environmental temperature CO is increased due to shivering that increases blood flow to the muscles.
- Increased sympathetic activity during anxiety and excitement enhances the CO up to 50% - 100%.
- Sitting or standing from the lying position deceases the CO by 20-30%.
- Exercise?

Effects of Exercise on Heart Rate, SV and CO

Moderate Exercise

HR increases to 200% of resting, (140 beats/min.)

SV increases to 120% (85 ml)

CO increases to 240% (12 L)

Severe Exercise

HR increases to 300% of resting (200 beats/min.)

SV increases to 175% (125 ml)

CO increases to 500% - 700% (25 - 35 L)

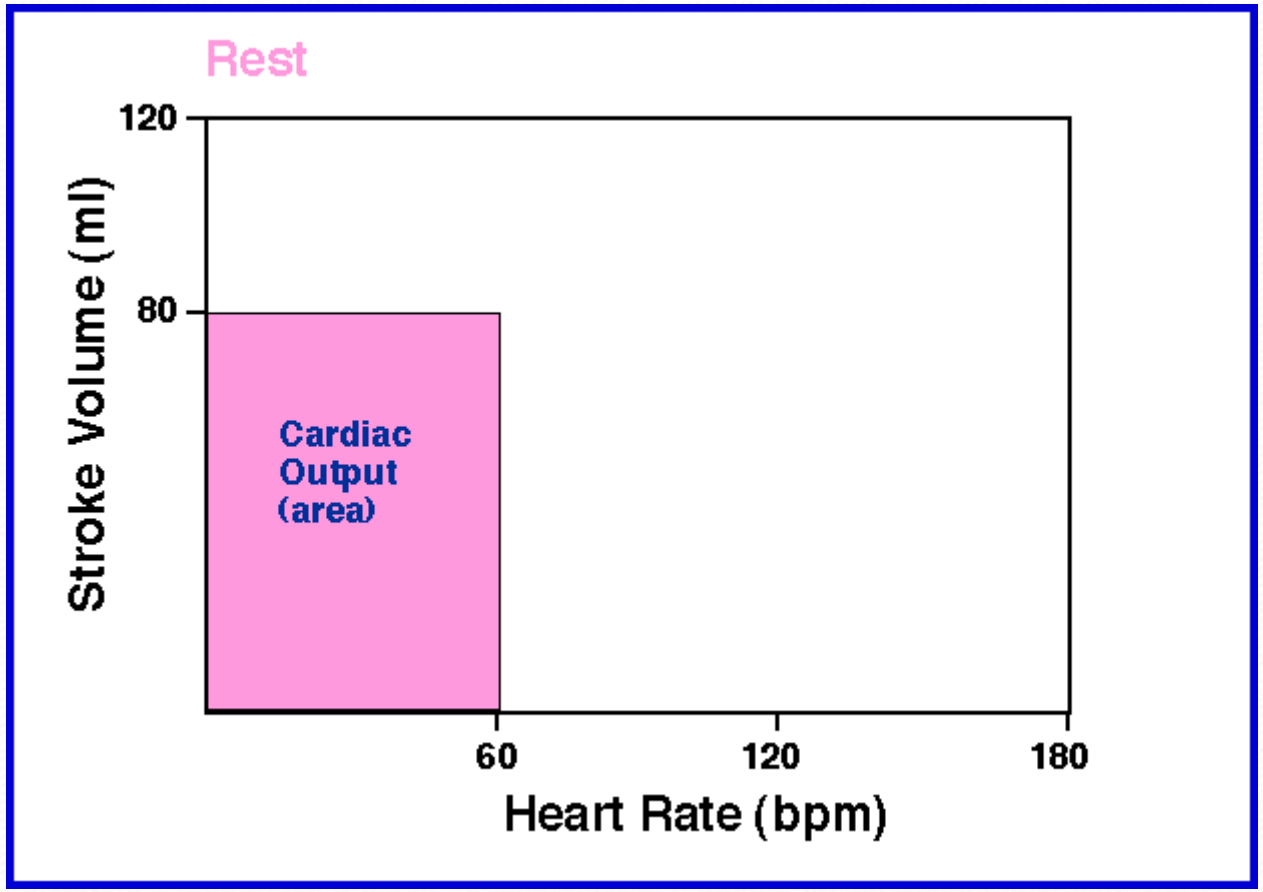
In athletes, maximum CO may be 35L or more - can't increase maximum HR beyond 200 beats/min. Hence, the SV increases to 175 ml.

What is the Cardiac Index?

- Since : CO vary with size of individual, age & gender (For e.g: women have smaller CO than men, children have smaller CO than adults).
- Thus it is important to relate heart performance to the size of the individual.
- Cardiac index is CO per square meter of body surface area.
- CI = CO/m^2
- Normal cardiac index= (3.2 Liters/min/m^2 body surface area).

What is the Cardiac Reserve?

- During exercise, the CO can increase to 20-25 liters/min and to as high as 35 - 40 liters/min in well trained athletes.
- The difference between the resting CO at rest and the maximum volume of blood that the heart is capable of pumping per minute is known as the cardiac reserve.



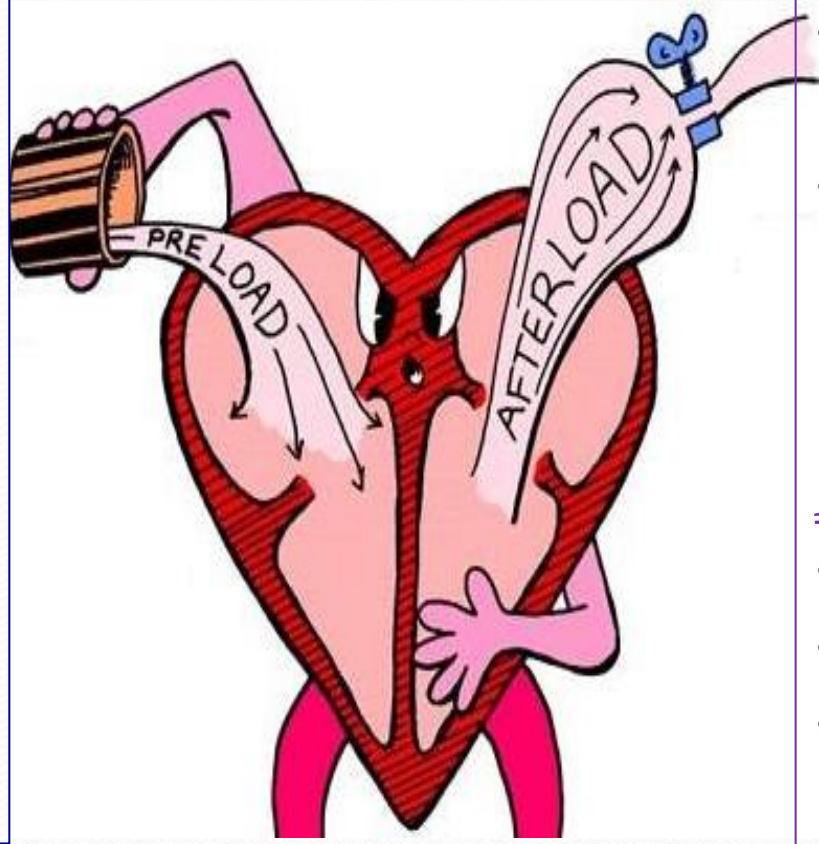
What Are Preload and Afterload

Preload

- It is the amount of blood that returns to the heart from veins (VR).
- It is the load on the muscle in the relaxed state.
- ↑VR→ ↑EDV and stretches or lengthens the ventricular muscle fibers.

Preload increase in:

- Hypervolemia
- Heart failure



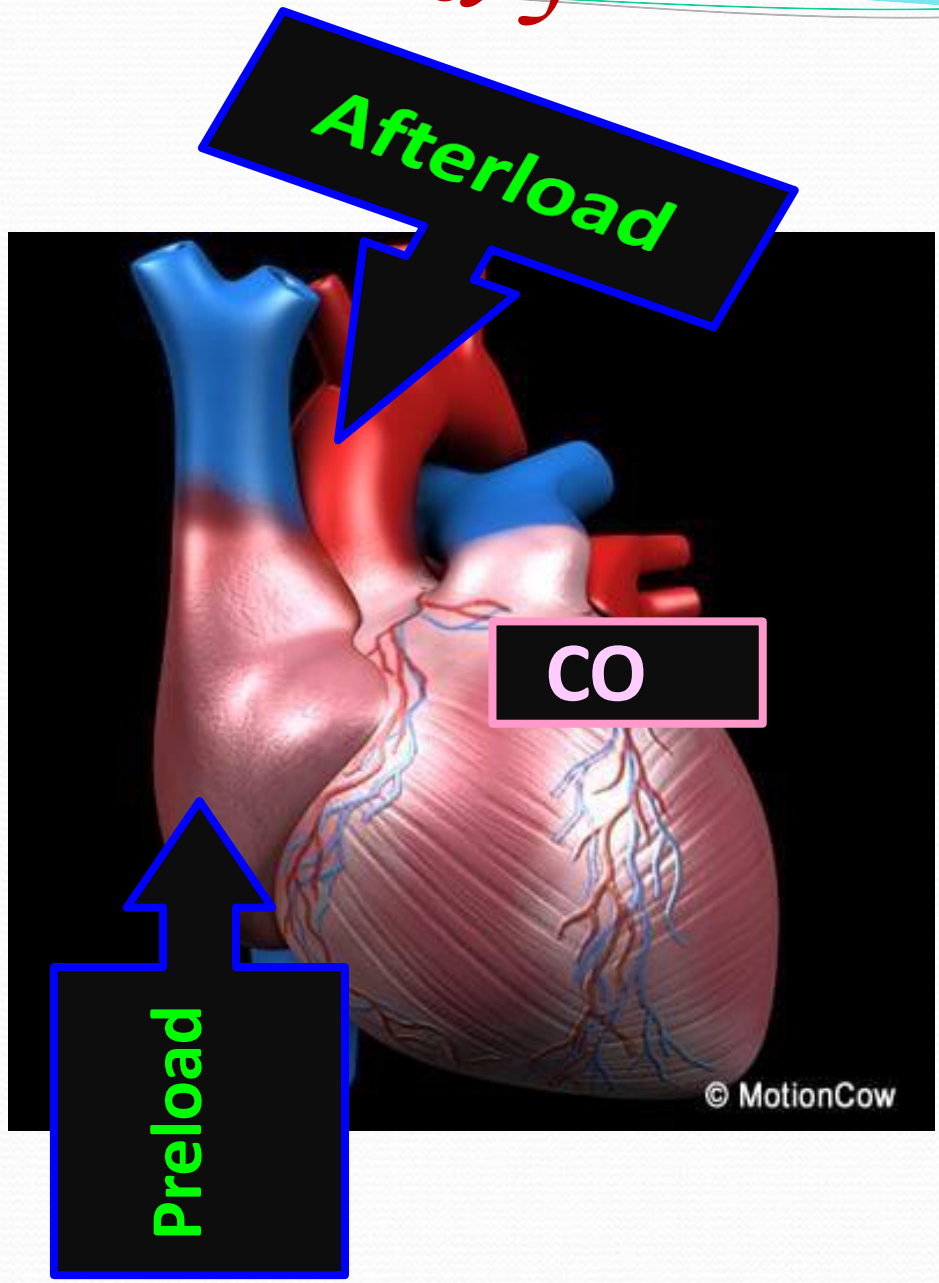
Afterload

- It is the resistance against which the ventricles contract.
- Afterload on the left ventricle, ↑, when aortic pressure ↑
- Afterload on the right ventricle ↑, when pulmonary artery pressure ↑.

Afterload increase in:

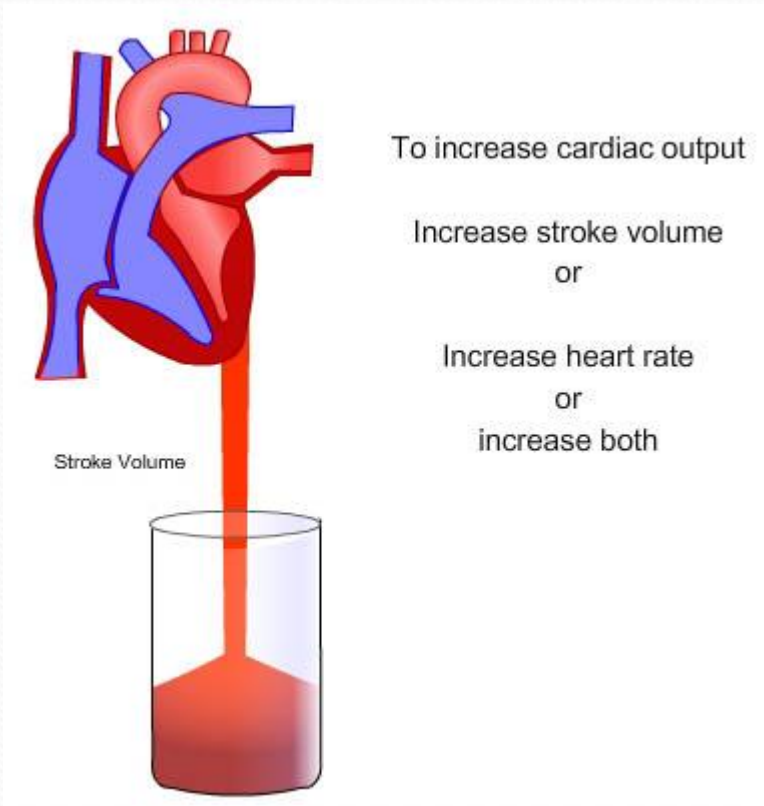
- Aortic/pulmonary stenosis
- Hypertension
- Vasoconstriction

Preload & Afterload

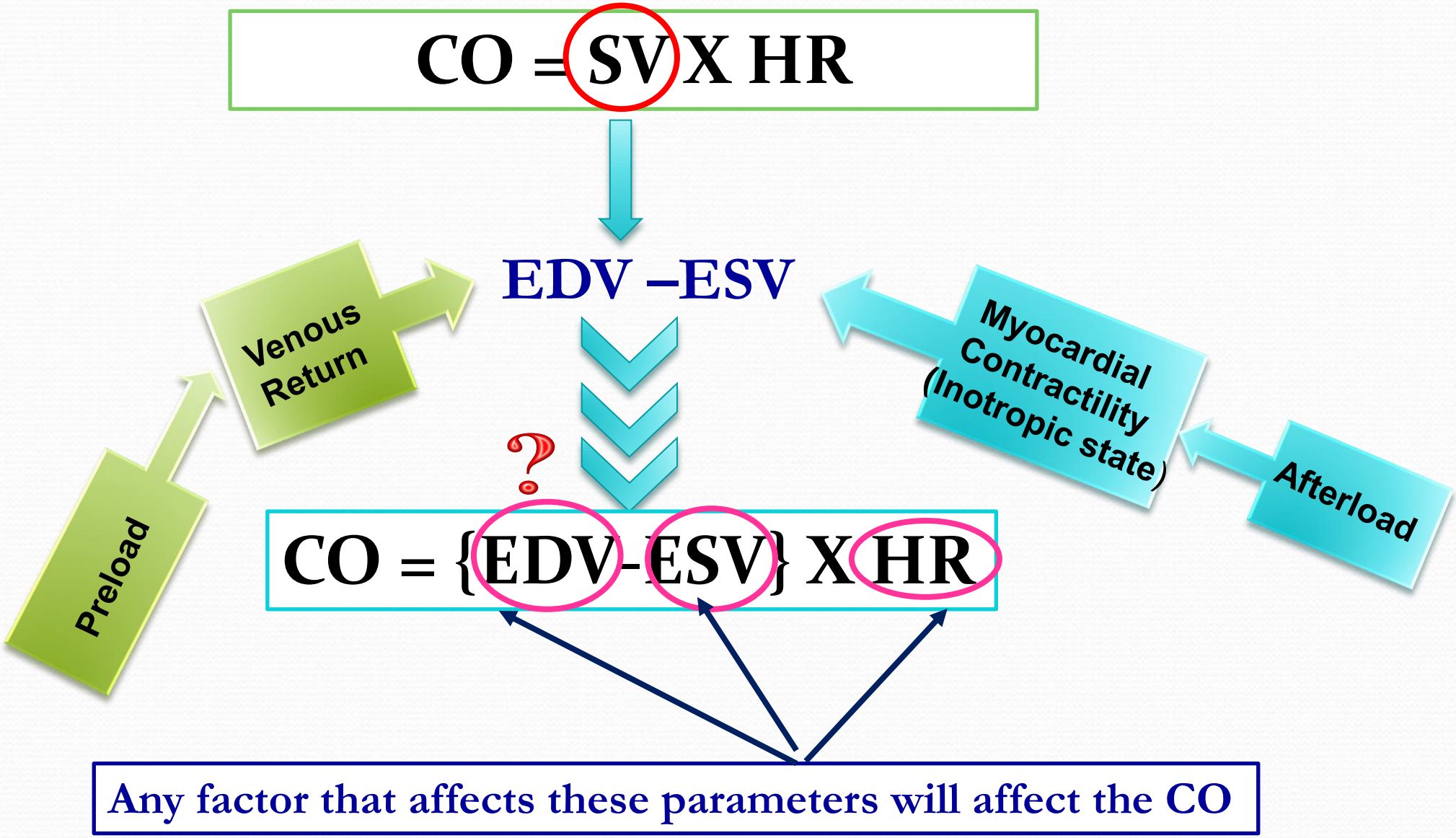


Regulation of CO

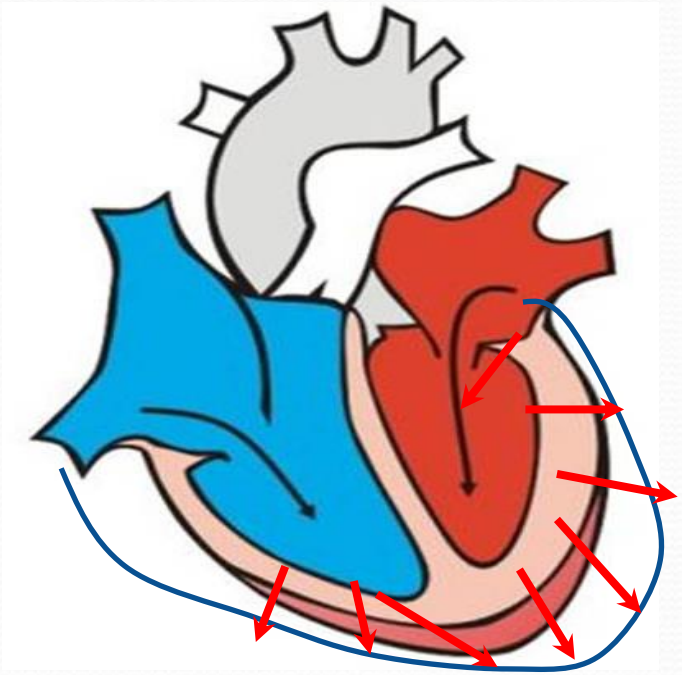
- CO is crucial since it is also the amount of blood that flows into the circulation and is responsible for transporting substances to and from the tissues.
- Thus, the body has strict control mechanisms that maintain adequate CO.
- There are 2 major factors which determine CO.
- These are the SV and HR.



Determinants of the CO



The End-Diastolic Volume (EDV)



- ***EDV*** = is the volume of blood in the ventricles prior to ventricular ejection.
- ***How does the EDV affect the SV and hence the CO?***

↑↑ EDV

↓

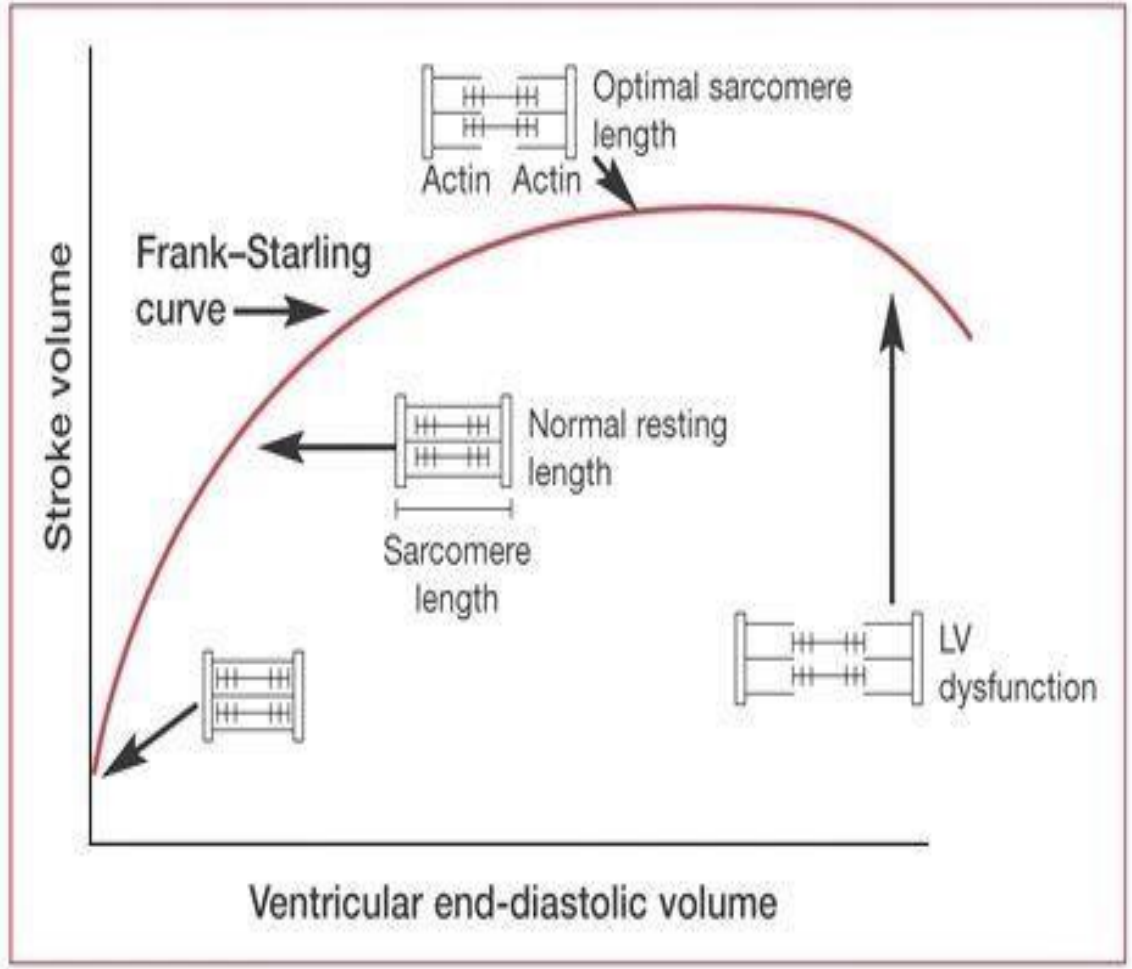
↑↑ The stretch in the myocardium (↑↑ initial fiber length)

↓

↑↑ Myocardial contractility (↑↑ Strength of contraction) Frank-Starling mechanism

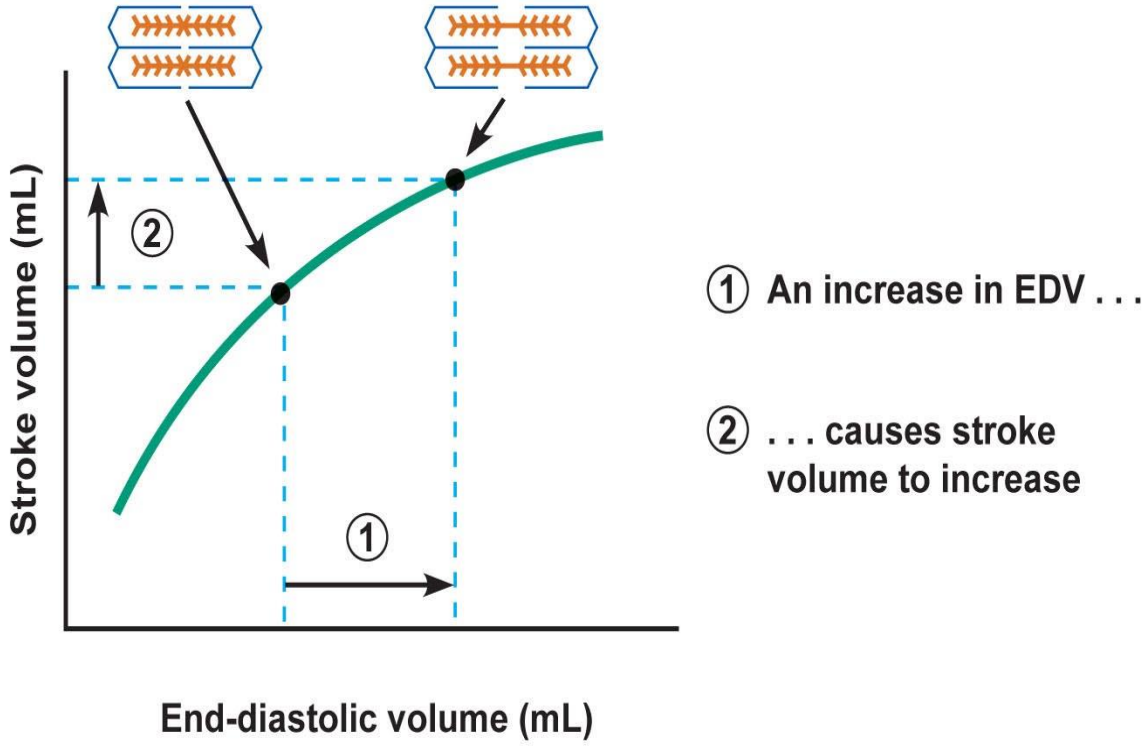
Frank-Starling's Law

- It is the intrinsic relationship between EDV and SV.
- It reflects the ability of the heart to change its force of contraction and therefore SV in response to changes in VR.
- If EDV (preload) is increased, the ventricular fiber length is also increased, resulting in an increased 'tension' of the muscle (i.e **SV increases in response to increase of the EDV).**



Significance: Frank-Starling's Law

- The energy of contraction is proportional to the initial length of the cardiac muscle fibers (the EDV).
- Within physiologic limits, the heart pumps all the blood that returns to it by the way of the veins.
- The greater the stretch of the cardiac muscle the greater would be the force of contraction. Because Actin & Myosin filaments are brought to more optimal degree of sliding, therefore increase force of contraction.



Factors affecting preload (EDV)

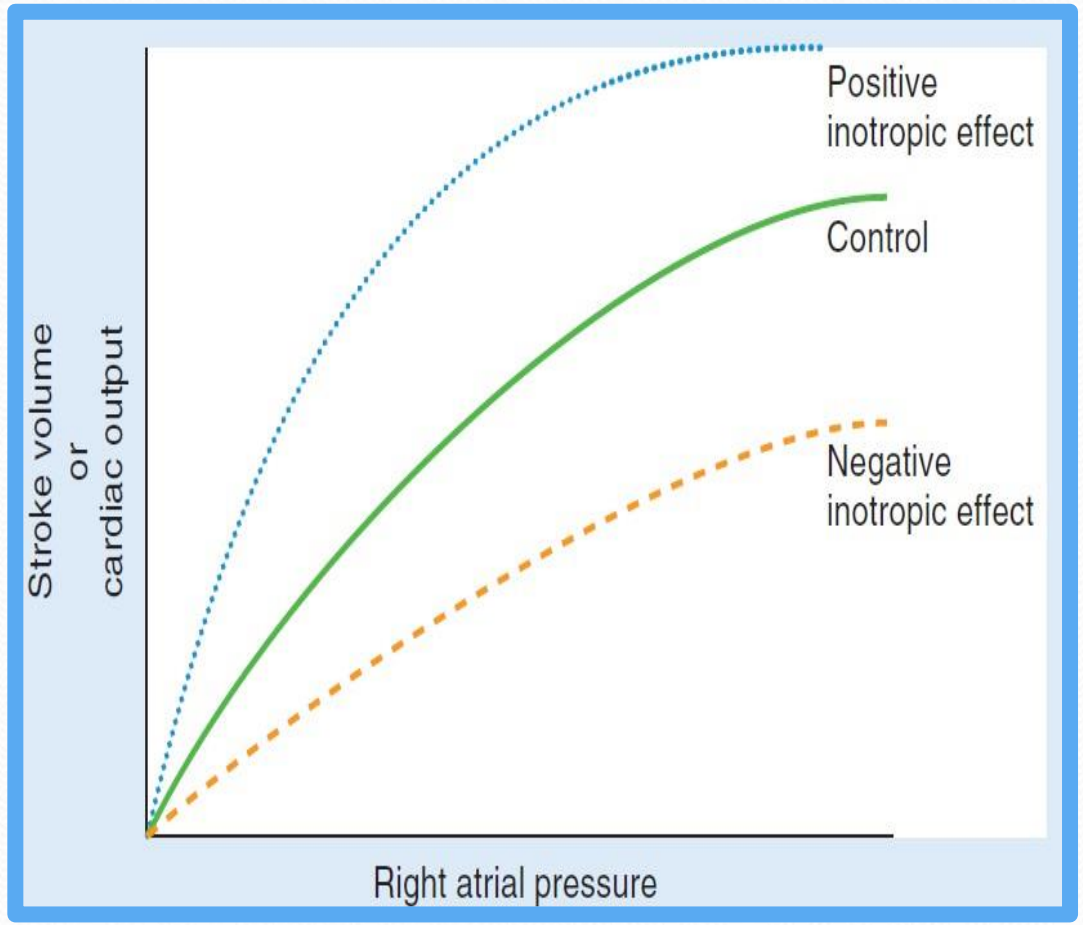
- EDV ↑ with:
  - Increased total blood volume.
  - Increased venous return.
  - Increased venous tone.
    - Increased skeletal muscle pump (exercise).
    - Increased negative intrathoracic pressure.
  - Stronger atrial contraction.
- EDV ↓ with:
  - Standing.
  - Decreased venous return.
  - Increased intrapericardial pressure.
  - Decreased ventricular compliance.

Indices of left ventricular preload:

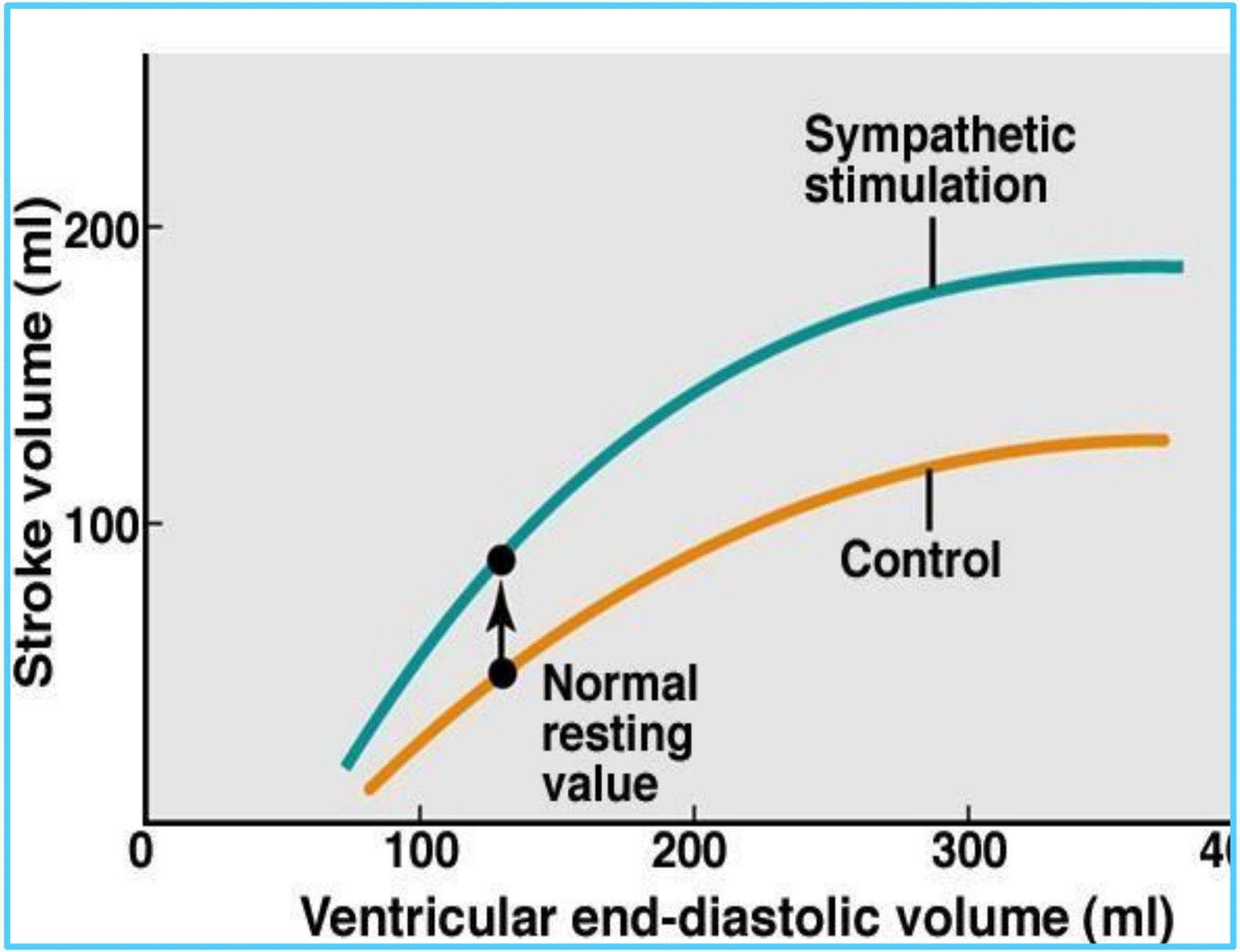
- Left ventricular end-diastolic volume (LVEDV).
- Left ventricular end-diastolic pressure (LVEDP).

Effect of Rt Atrial Pressure on CO

- Normally, Rt atrial pressure (RAP) fluctuates with atrial contraction and respiration.
- When the mean RAP is about 0 mmHg, the CO in an adult is about 5 L/min.
- Because of the steepness of the cardiac function curve, very small changes in RAP (just a few mmHg), can lead to large changes in cardiac output.



Effect of Sympathetic Stimulation on CO



Determinants of the CO…..Cont.

CO = SV X HR

{End-diastolic volume (EDV) – end-systolic volume (ESV)}

CO = {EDV-ESV} X HR

Any factor that affects these parameters will affect the CO

End-Systolic Volume (ESV)

- ***ESV*** = The volume of blood remaining in the ventricle at the end of systole.
- ↑ ESV → ↓ stroke volume
- ↓ ESV → ↑ stroke volume
- ***ESV is determined by:***
  1. **Cardiac contractility**
  2. ***Afterload***

Determinants of ESV

1- Cardiac contractility:

- ↑↑ contractility → ↓↓ ESV → ↑↑ SV
- ↓↓ contractility → ↑↑ ESV → ↓↓ SV

- **N.B** *Revise Regulation Of Heart Pumping (Inotropic Effectors) in the lectures : "Contractile mechanism in cardiac muscle "(Slides 31-35)*

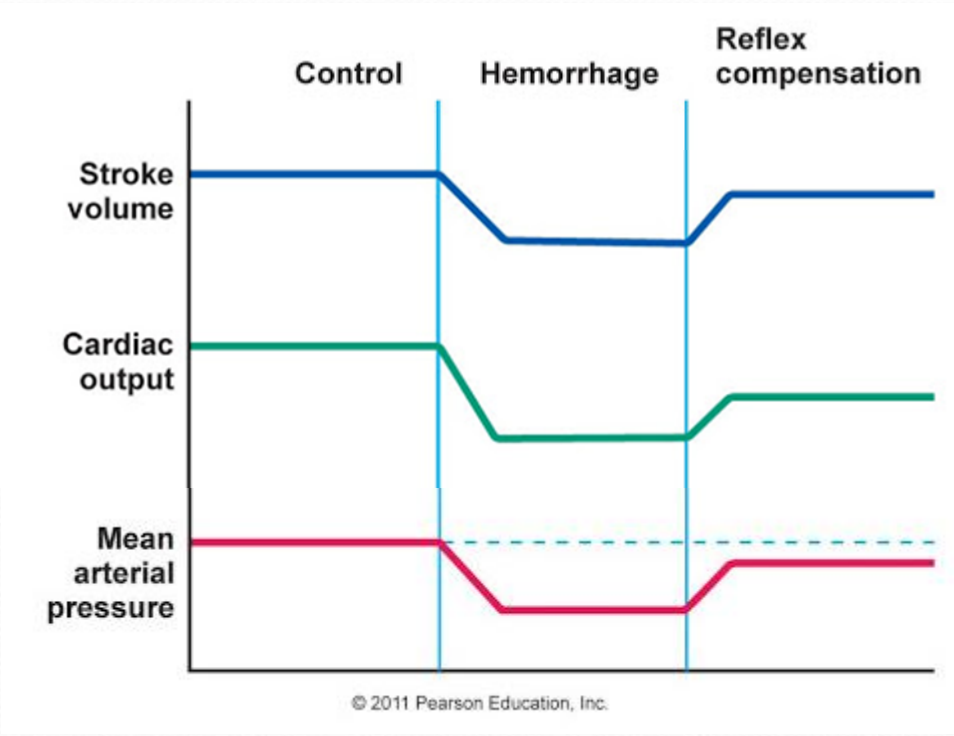
Determinants of ESV….Cont.

2- Afterload:

- It is expressed as tension which must be developed in the wall of ventricles during systole, i.e the load the heart needs to overcome to open the semilunar valves and eject blood to aorta/pulmunary artery.
- Left ventricular afterload represents the force that the muscle must generate to eject the blood into the aorta.
- When the aortic pressure (afterload) is reduced, the velocity of shortening of the LV myocardial fibers increases. Hence, the LV can eject blood more rapidly → ↑ SV → ↓ ESV.
- The opposite is true with increased LV afterload.

Factors affecting Afterload

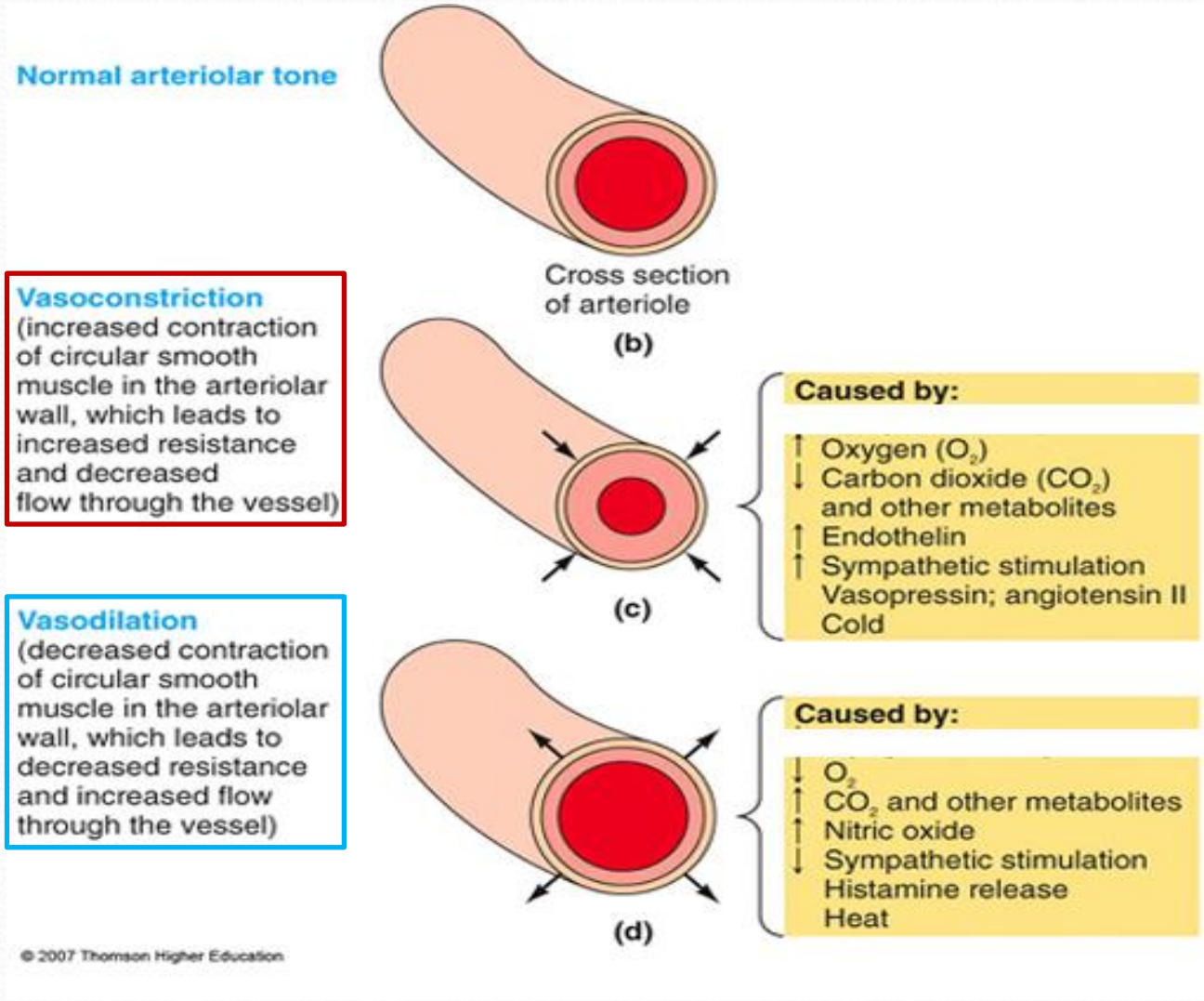
- Left ventricular afterload increases by any factor that restricts arterial blood flow like:
  1- Aortic stenosis
  2- Arterial hypertension.
  3- Vasoconstriction (the peripheral vascular resistance).
  - ↑↑ Resistance → ↑↑ ESV
  - ↓↓ Resistance → ↓↓ ESV



Afterload and Hence ESV is Determined by The Peripheral Vascular Resistance

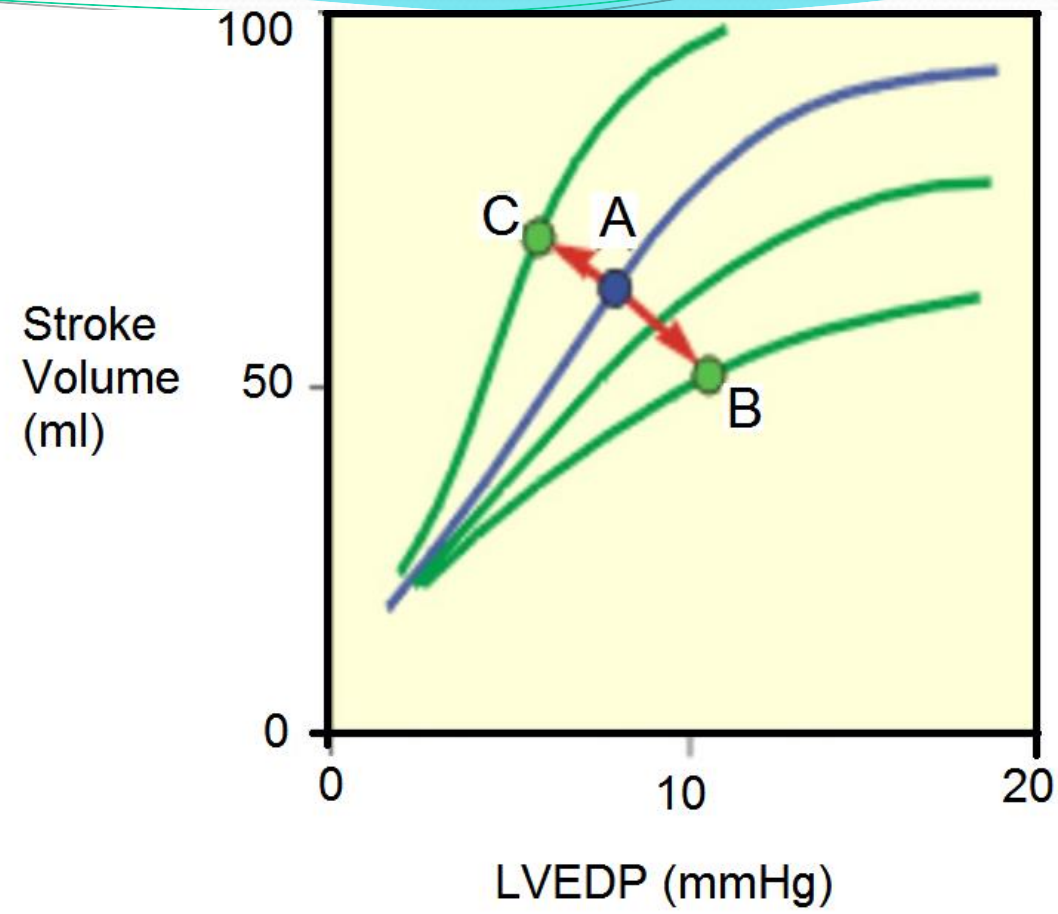
- **Vasoconstriction ↑↑ the peripheral vascular resistance → ↑↑ ESV → ↓↓ SV and CO**

- **Vasodilatation ↓↓ the peripheral vascular resistance → ↓↓ ESV → ↑↑ SV and CO**



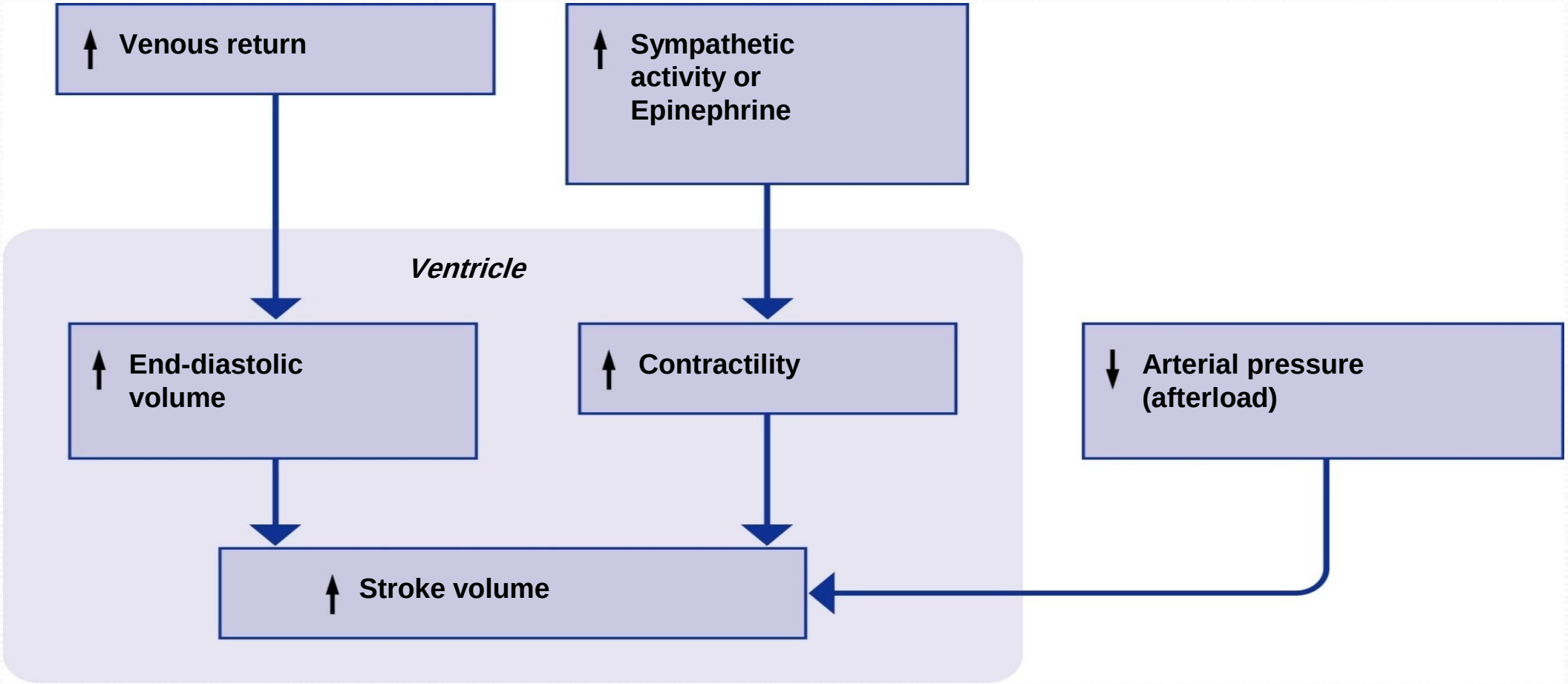
Effect of Afterload on Frank Starling Curve

- An increase in afterload leads to ↑ ESV and ↓ SV .Thus shifts shifts the Starling's curve down and to the right (from A to B)
- A decrease in afterload shifts Starling's curve up and to the left (A to C).



Explanation: an increase in afterload decreases the velocity of fiber shortening. This reduces the rate of volume ejection so that more blood is left within the ventricle at the end of systole → ↑ ESV.

Summary of the Factors Influencing Stroke Volume



Determinants of the CO…..Cont

CO = SV X HR

{End-diastolic volume (EDV) – end-systolic volume (ESV)}

CO = {EDV-ESV} X HR

?

Any factor that affects these parameters will affect the CO

Inotropic, Chronotropic & Dromotropic

CONTRACTILITY

- Positive inotropic agent produces an increase in contractility.
- Negative inotropic agent produces a decrease in contractility

HEART RATE

- Positive chronotropic effect produces an increase in HR
- Negative chronotropic effect produces a decrease in HR

CONDUCTION VELOCITY

- Positive dromotropic effect produces an increase in conduction velocity
- Negative dromotropic effect produces a decrease in conduction velocity

The Heart Rate (HR)

- Normal heart rate is regular sinus rhythm= 60-100 beats/min
- > 100 beats/min → Tachycardia
- < 60 beats/min → Bradycardia
- Since the CO = SV X HR, ↑ heart rate →↑ CO.
- At heart rates up to about 180, ventricular filling is adequate as long as there is enough venous return,
- However, at very high heart rates, filling may be compromised to such a degree that CO falls.
- The heart rate has an influence on cardiac contractility as well (Frequency-force relationship).

Regulation of Heart Rate

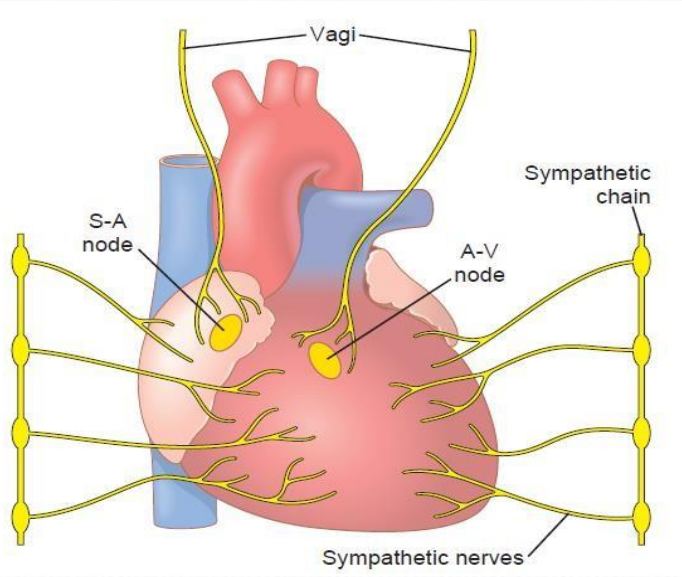
1- **Autonomic nervous system**

- Sympathetic nerves increase HR (and the contractility) through noradrenaline release (or adrenaline), which stimulates heart β1- receptors. E.g during stress, crisis or low blood pressure

- Parasympathetic nerves (vagus nerve) slow HR (but has little inotropic action). Through Ach release that stimulates muscarinic (M2) receptors.

Sympathetic Stimulation

Vagal (Parasympathetic) Stimulation



Under normal conditions the SA node is under continuous vagal tone causing its basal firing rate to decrease (Vagal Tone)

Regulation of Heart Rate…..Cont.

2- **Physical factors:**

- Age: Resting HR is faster in fetus and then gradually decreases throughout life.
- Gender: HR is faster in females (72-80 beats/min) than in males (64-72 beats/min).
- Temperature: Heat increases HR as occurs in high fever. Cold has the opposite effect.
- Exercise: Increases HR through sympathetic nervous system.

3- **Hormones and drugs**

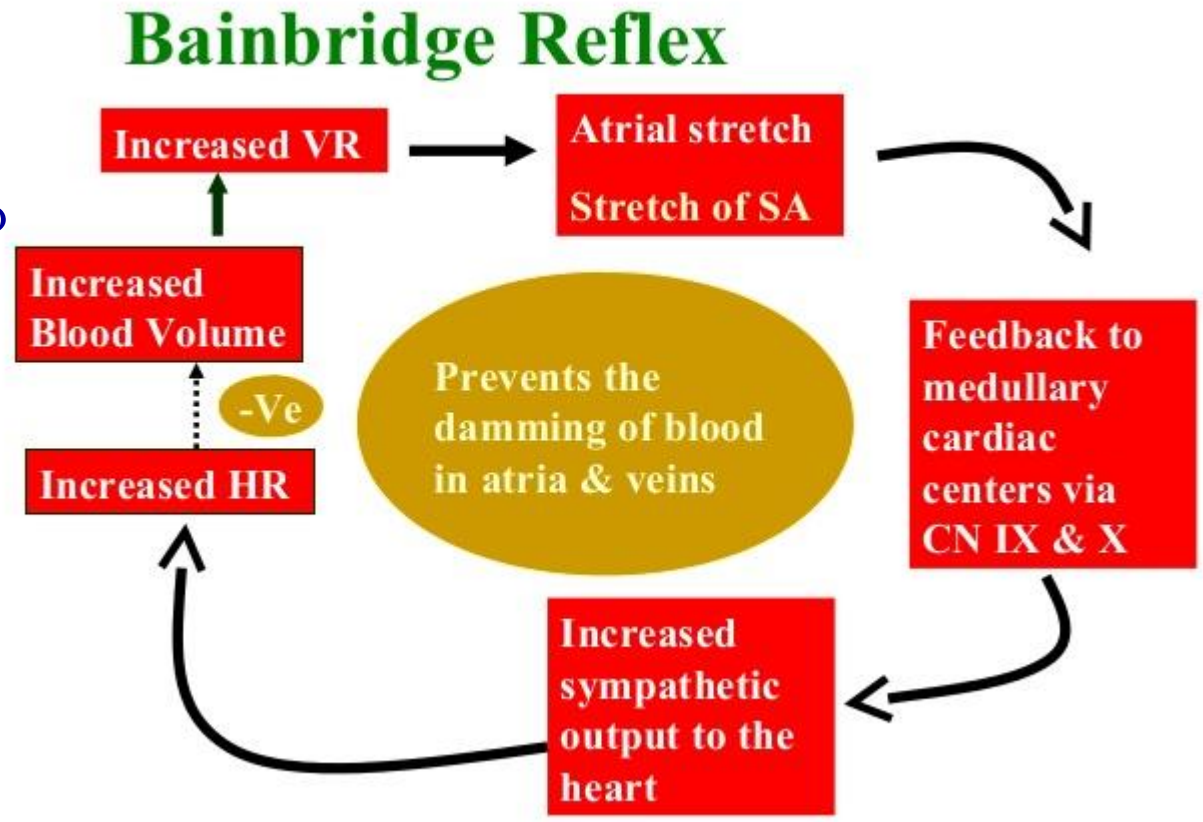
- Epinephrine and thyroxin increase HR.
- Increased calcium level in blood causes prolonged contraction
- Reduced calcium level in blood depress the heart.

Regulation of Heart Rate…..Cont.

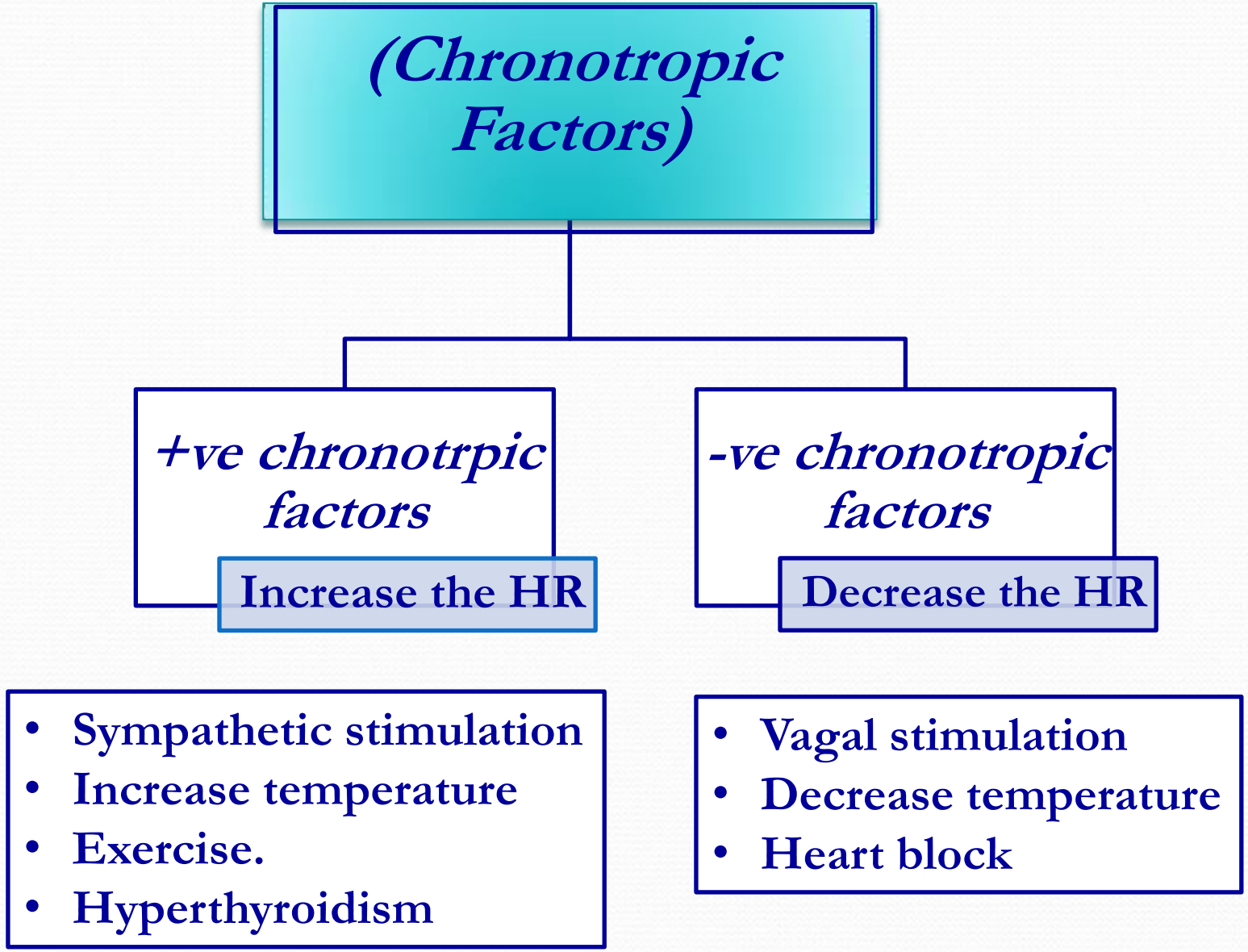
4- Blood volume

Atrial Reflex (Bainbridge reflex)

- This reflex adjusts heart rate in response to venous return.
- Increase blood volume, stimulates stretch receptors in right atrium.
- This triggers increase in heart rate through increased sympathetic activity.



Factors Affecting the HR (Chronotropic Factors)



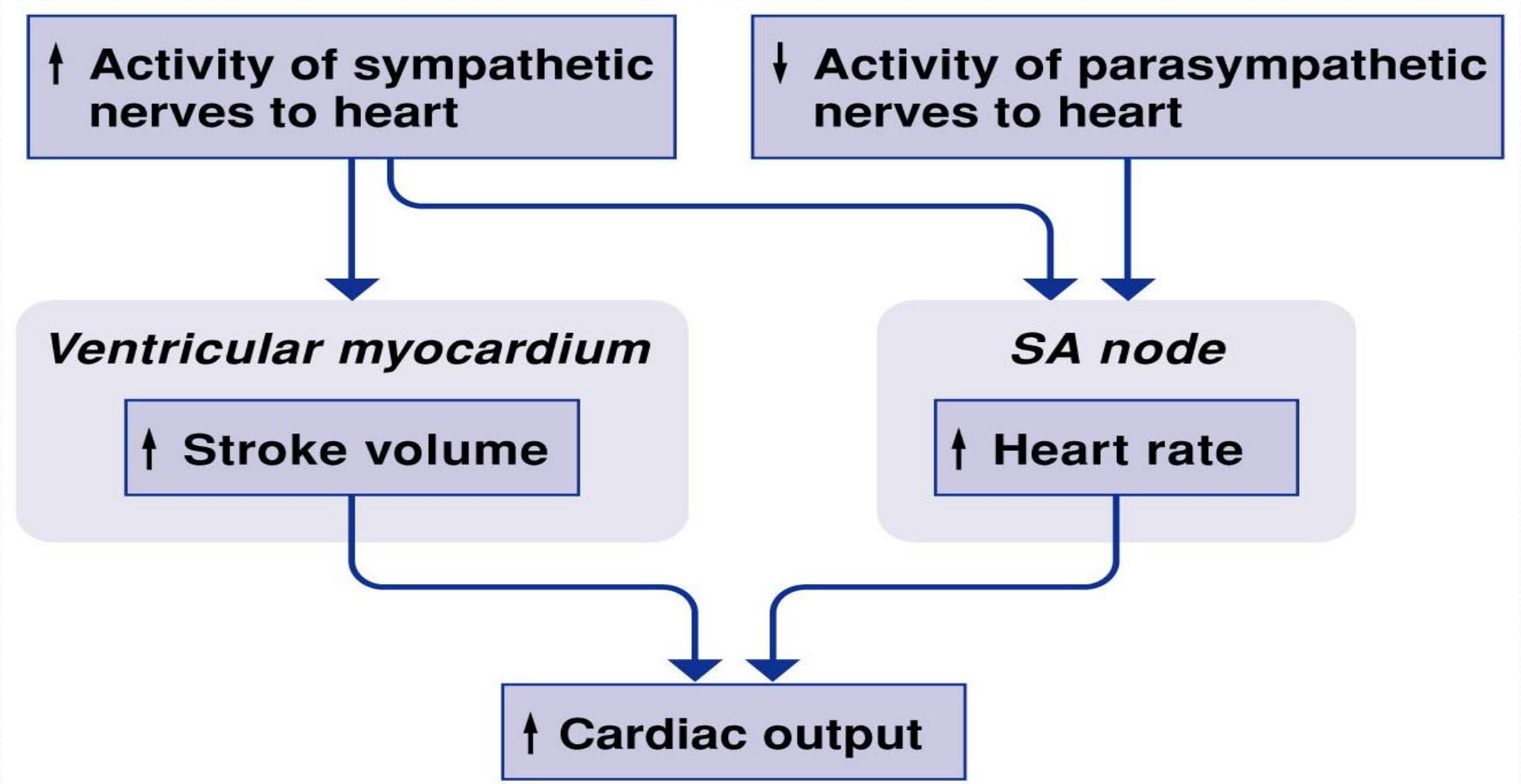
What Is The Influence Of Heart Rate On Myocardial Contractility?

Frequency-force relationship

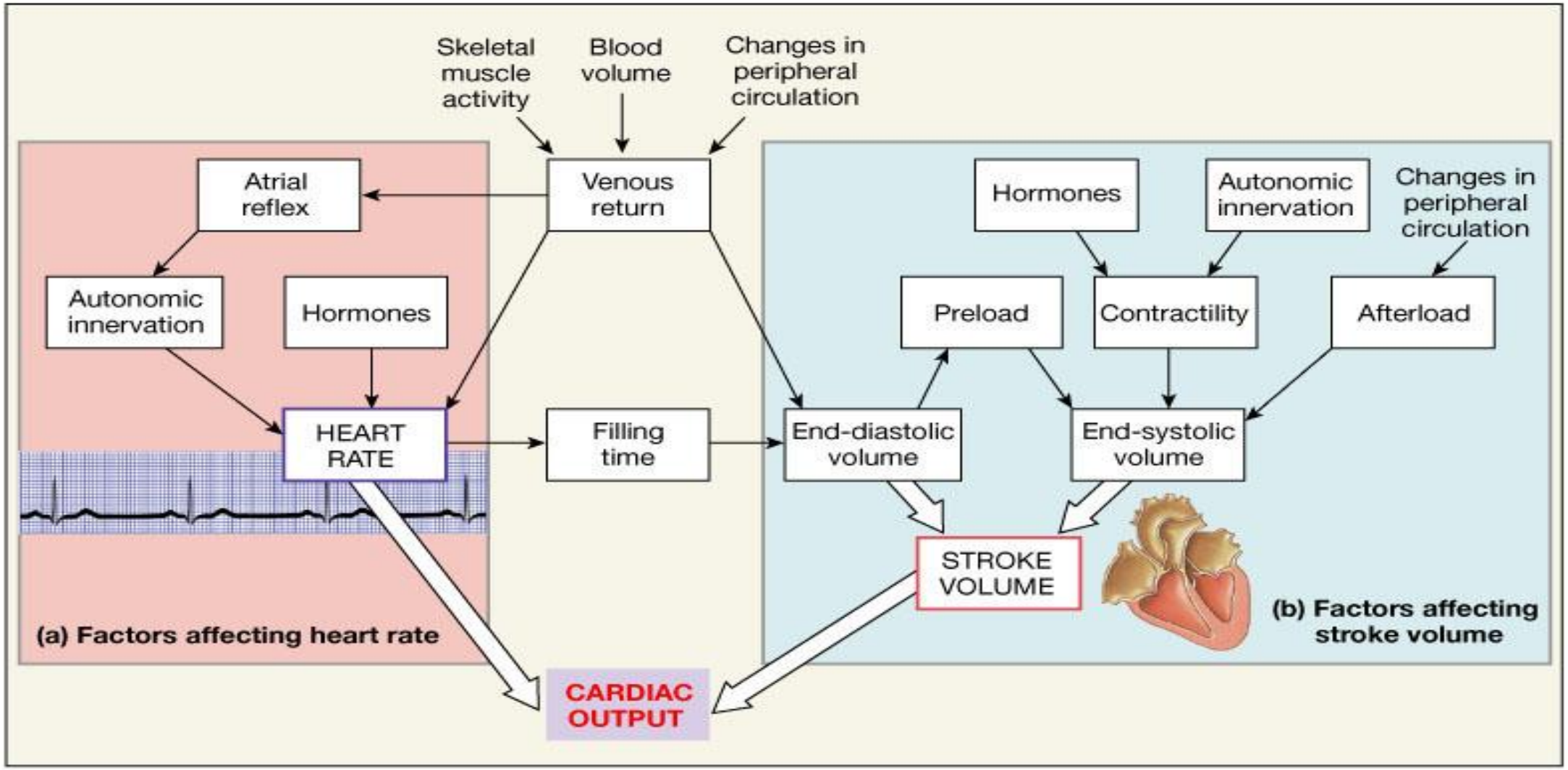
Increasing heart rate increases contractility.

- This frequency dependency of force generation in the heart is probably due to accumulation of Ca^{2+} ions within the myocytes as a result of:
- The increased in number of depolarizations/min → more frequent plateau phases → more Ca^{2+} entry.
- The magnitude of Ca^{2+} current is also increased → increases the intracellular Ca^{2+} stores.
- Both effects enhance the release and uptake of Ca^{2+} by the sarcoplasmic reticulum, thus Ca^{2+} availability to the contractile proteins with more force generation through cross-bridge cycling.

Regulation of Cardiac Output by Autonomic Nerves



Summary of the Factors Affecting Cardiac Output



Pathological Low Or High Cardiac output

Causes of low CO:

- Low VR e.g haemorrhage.
- Reduced contractility e.g. heart failure
- Tachyarrhythmias e.g. atrial fibrillation and ventricular tachycardia
- Marked bradycardia e.g., complete heart block.

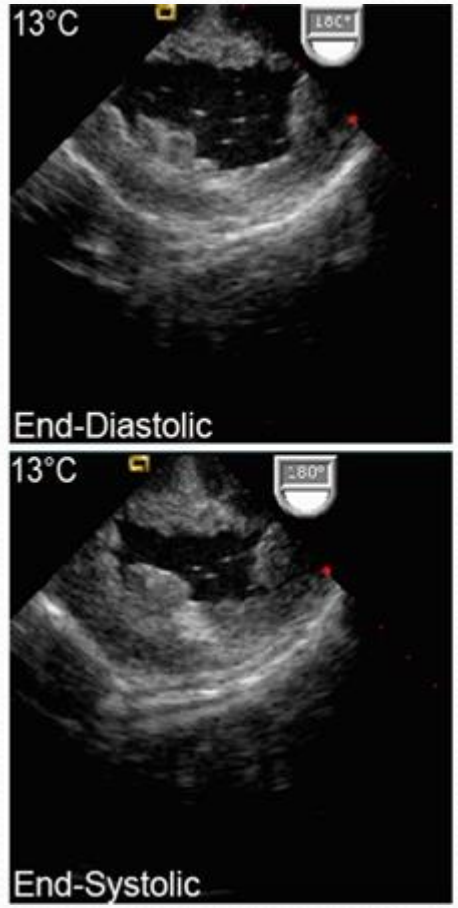
Causes of high CO:

- Hyperthyroidism: the increase in the CO is due to the high metabolic rate → vasodilatation →↑ CO to 50% of control.
- AV fistulas.
- Fever.
- Anaemia.
- Anxiety.

Measurement of Cardiac Output

- 2-Dimensional Echocardiography
- Ultra-fast computer tomography
- Fick's principle

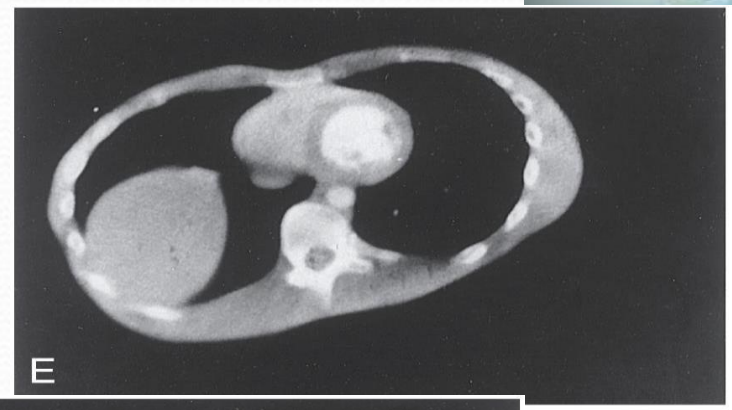
2-Dimensional Echocardiography

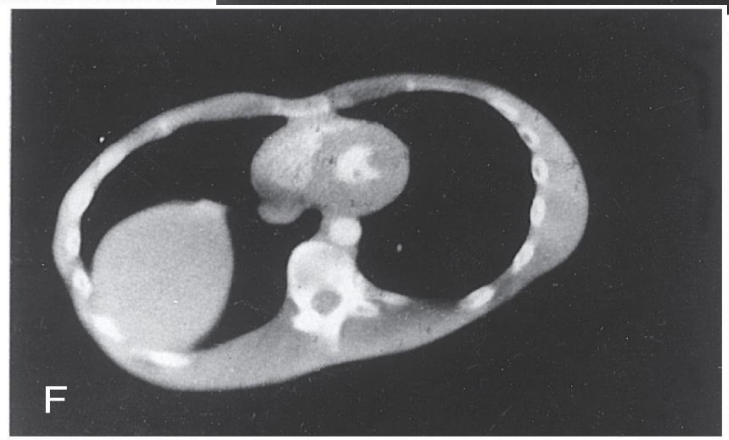


- Records real-time changes in ventricular dimensions during systole and diastole.
- It thus computes the SV ,which when multiplied by HR ,the CO will be calculated.

Measurement of Cardiac Output: Ultra-fast Computer Tomography

Can measure changes in ventricular diameter at several depths to estimate changes in ventricular volume.

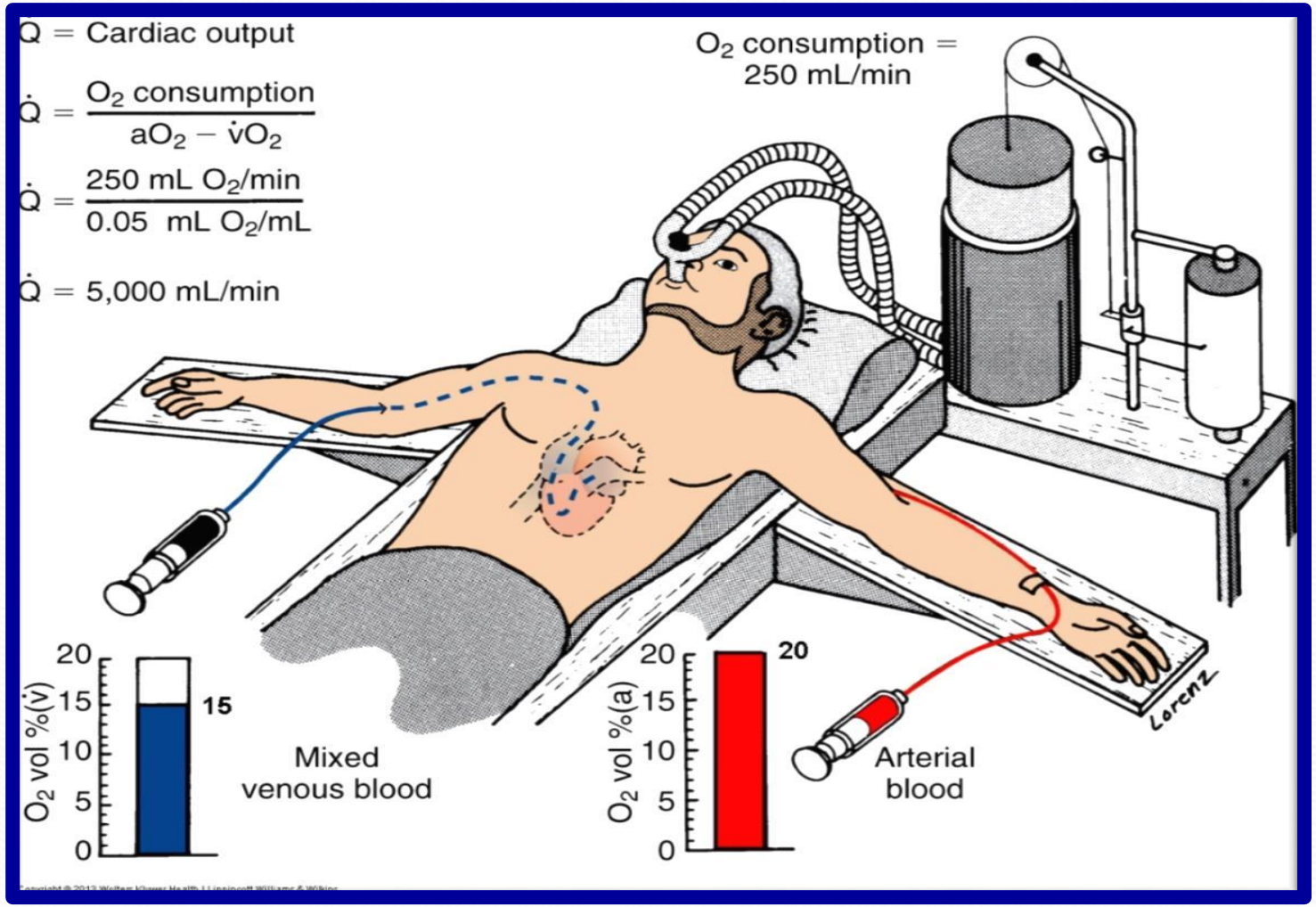




Fick's principle

Fick's principle

It assumes that the amount of oxygen consumed = the amount of oxygen delivered by the arterial blood minus the amount of oxygen in venous blood of the organ.

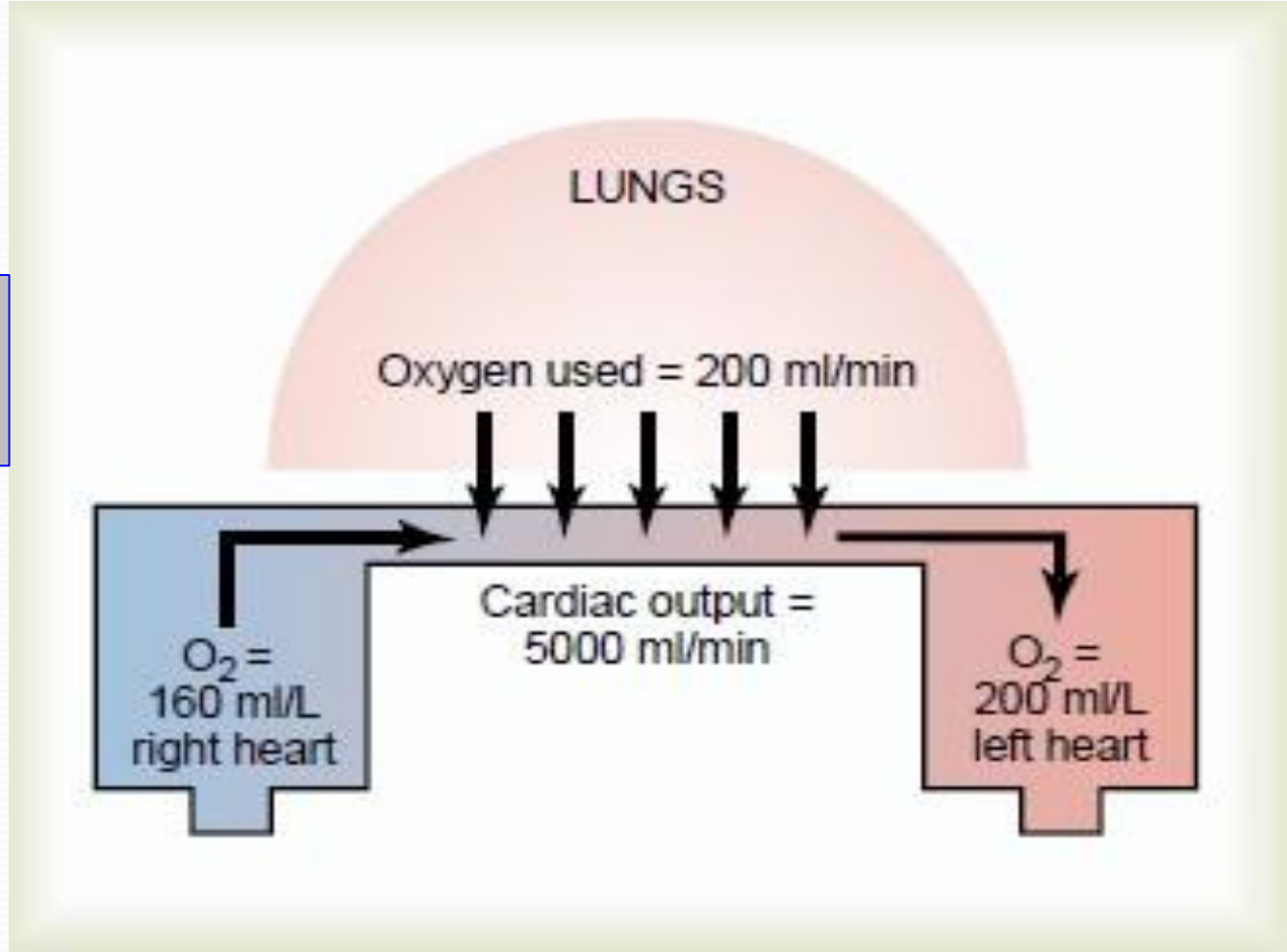


Measurement of Cardiac Output: Fick's method

$$CO\ (L) = \frac{\text{Total } O_2 \text{ consumption}}{AO_2 - VO_2}$$

AO_2= Arterial O_2 concentration

VO_2= Mixed O_2 venous concentration




Thank You!