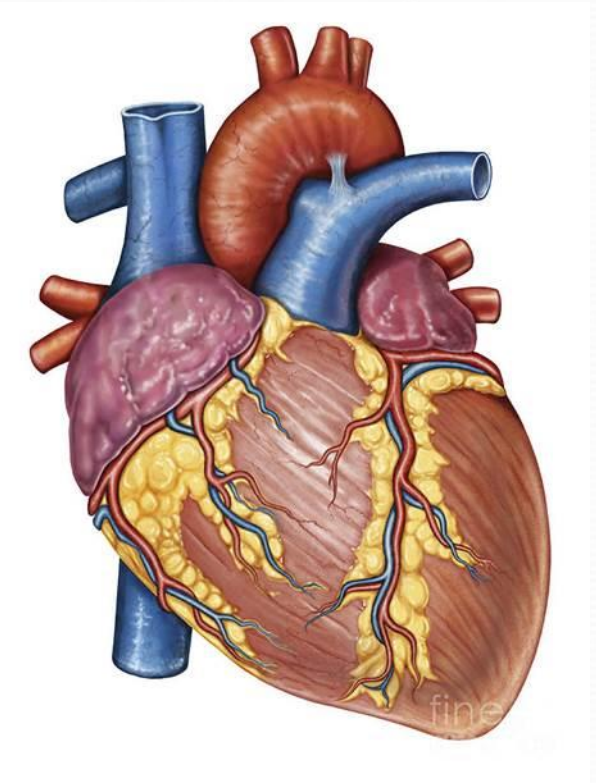
CVS Block
Stroke Volume
Cardiac Output & its Regulation
(Preload, Contractility & Afterload)

(Physiology Lecture: No.6)



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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
- Causes of pathological low or high cardiac output
- Know the method for measurement of CO (2-dimensional echocardiography, ultra-fast computer tomography, Fick's method)

Remember What Are ?

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

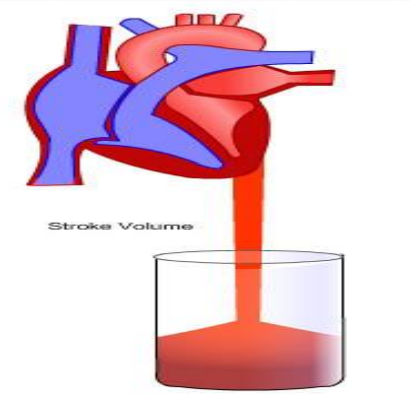
  Volume of blood in ventricles at the end of diastole ≈ **110-130mL**

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

  Volume of blood left in ventricles at the end of systole ≈ **40-60mL**

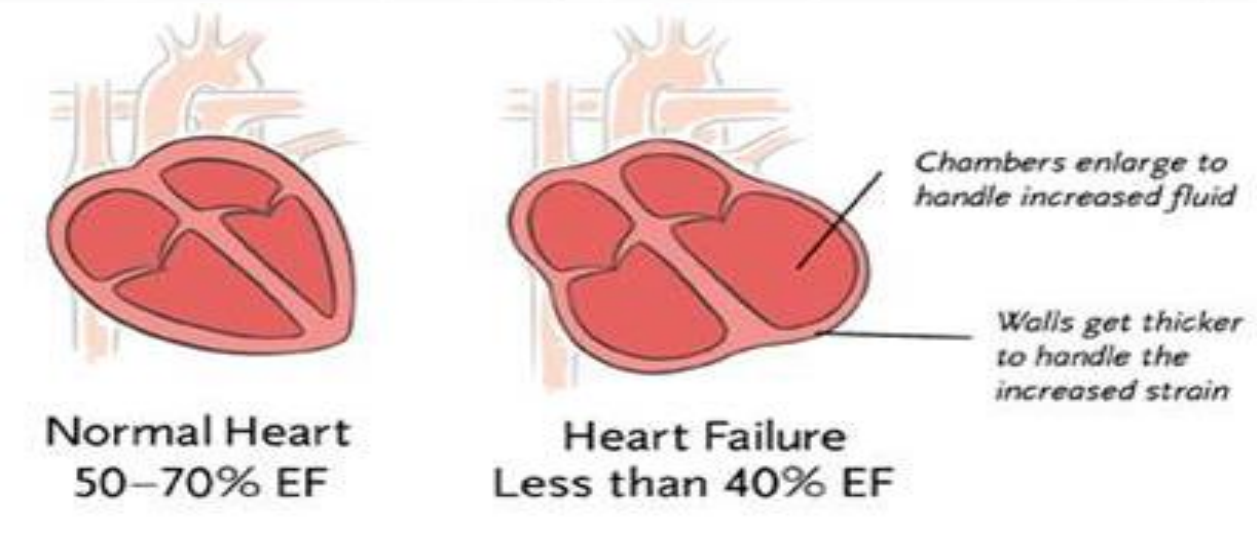
- **Stroke volume (SV):**

  Volume of blood ejected from ventricles during systole ≈ **70-80 mL/beat.**

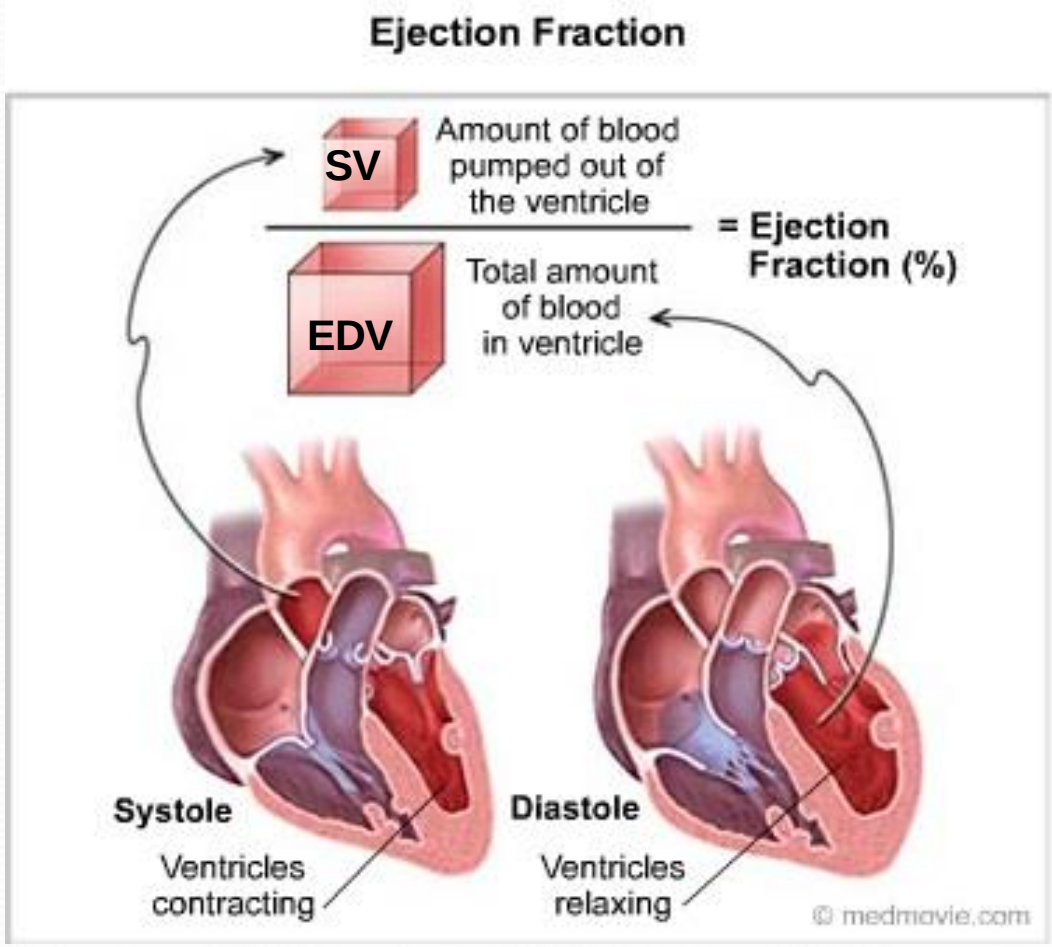


Ejection fraction (EF):

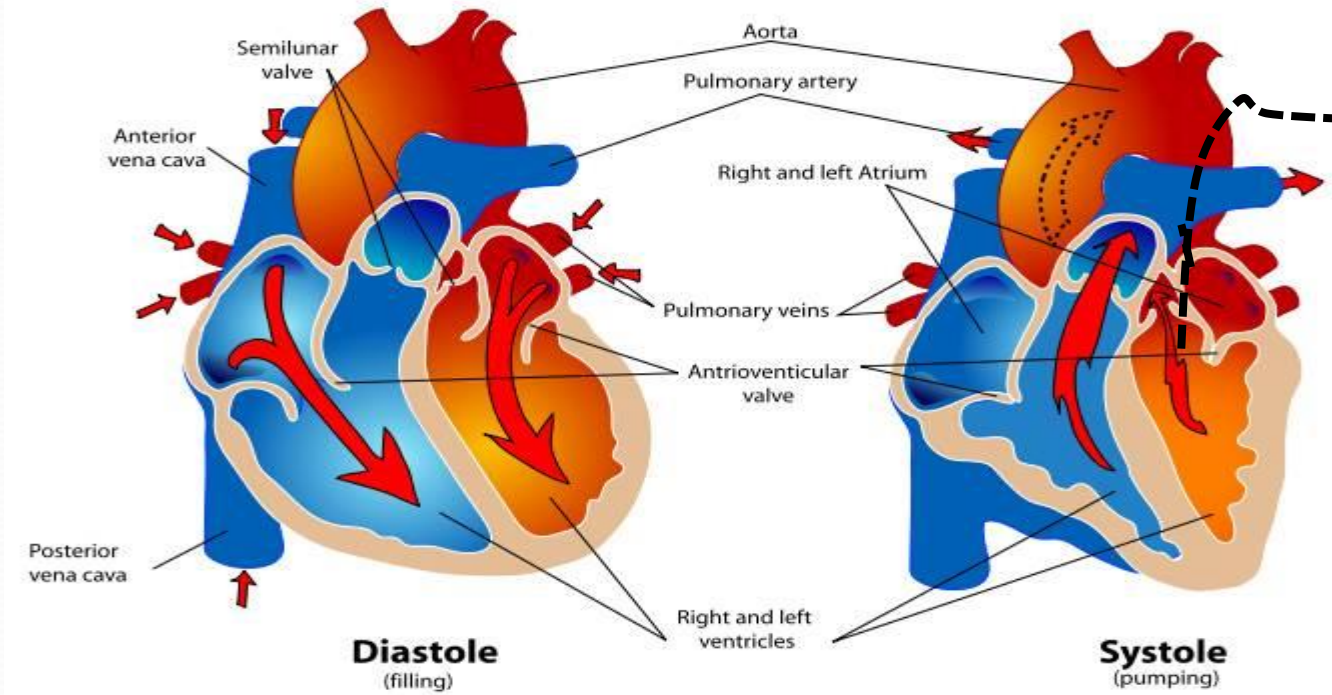
- EF is the percentage of blood that is pumped out of the heart during each beat.
- EF= SV/EDV≈ 60-70%.



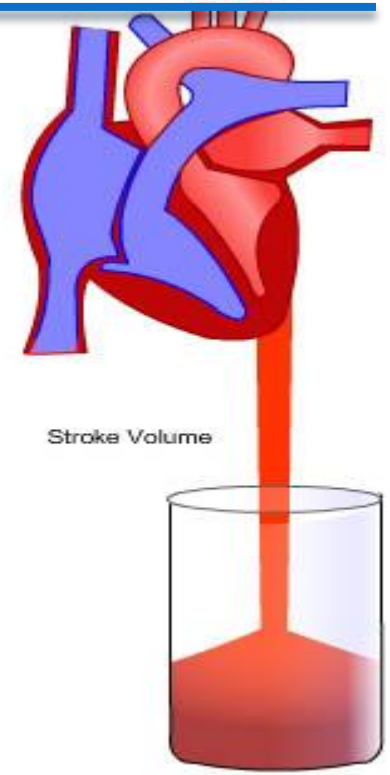
- EF is a key indicator for diagnosing heart failure



The Stroke Volume



Volume 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

−

Volume 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/ ***beat*** = ***stroke volume (≈70ml/beat, in adult at rest).***

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

Cardiac output (CO)

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

≈ 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 CO at Rest

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

- **The factors affecting CO:**
  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 ,↑ CO by ≈ 30% to enhance blood flow in the intestinal circulation.
- Later months of pregnancy ↑ CO by ≈ 30% due to increased uterine blood flow.
- At environmental temperature above 30˚C ,↑ CO due to ↑ skin blood flow .
- Also at low environmental temperature ↑ CO due to shivering that ↑ blood flow to the muscles.
- During anxiety and excitement, sympathetic activity ↑ CO up to 50% - 100%.
- Sitting or standing from the lying position ↓ CO by 20-30%.
- Exercise ?

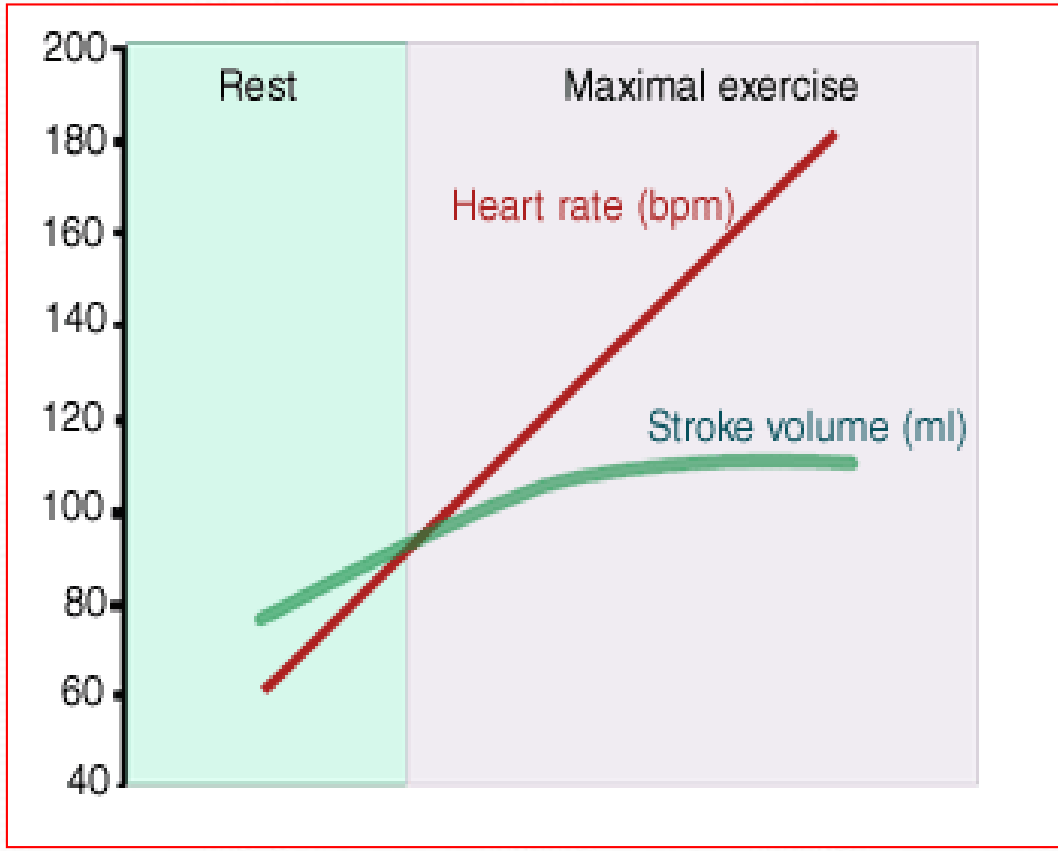
Effects of Exercise on Heart Rate, SV and CO

Moderate Exercise

↑ HR ≈ 200% of resting, (140 beats/min.)

↑ SV ≈ 120% (85 ml)

↑ CO ≈ 240% (12 L)



Severe Exercise

↑ HR ≈ 300% of resting (200 beats/min.)

↑ SV ≈ 175% (125 ml)

↑ CO ≈ 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 ↑ to 125 ml.

What is the Cardiac Index (CI) ?

- Since : CO vary with size of individual, age & gender (e.g: children have smaller CO than adults, women have smaller CO than men).
- Thus it is important to relate heart performance to the size of the individual.

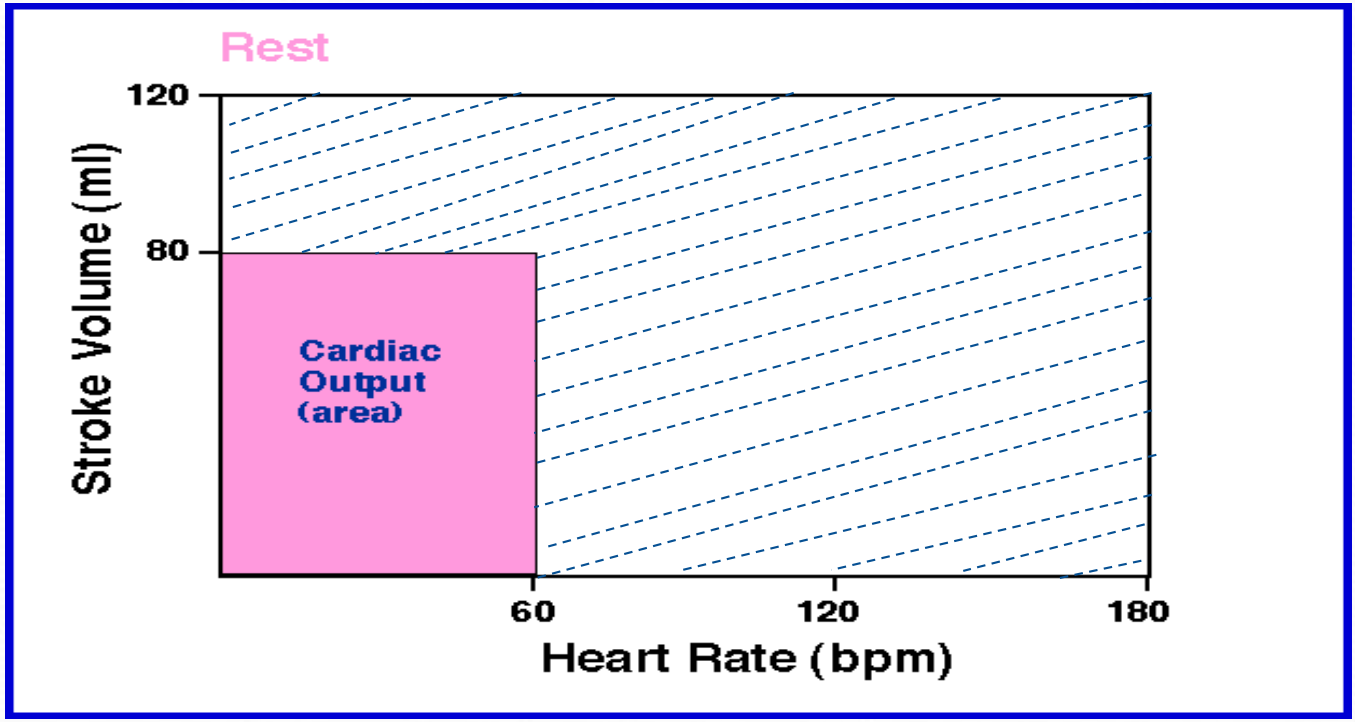
Cardiac index is CO per square meter of body surface area

$$\mathbf{CI = CO/m^2}$$

Normal CI = (3.2 Liters/min/m^2 body surface area)

What is the Cardiac Reserve?

- During exercise, the CO can ↑ to 20-25 L/min.
- In well trained athletes, CO can ↑ as high as 35-40 L/min.



Cardiac reserve = The maximum volume of blood that the heart is capable of pumping/min — The resting CO i.e. at rest

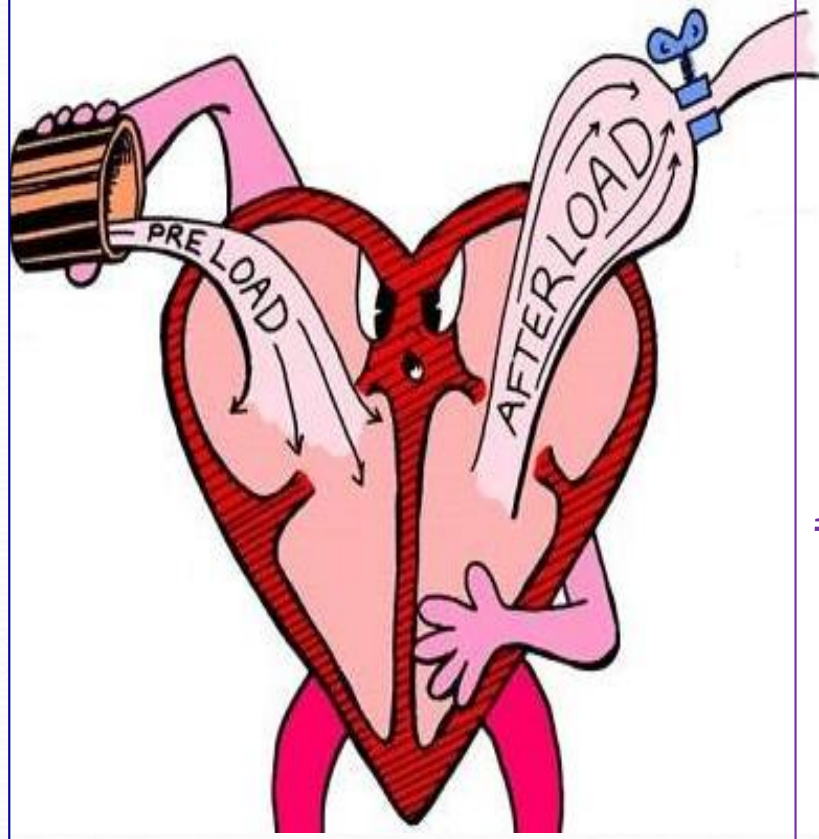
What are the Preload and Afterload

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 ↑ in:

- **Hypervolemia**
- **Heart failure**



Afterload

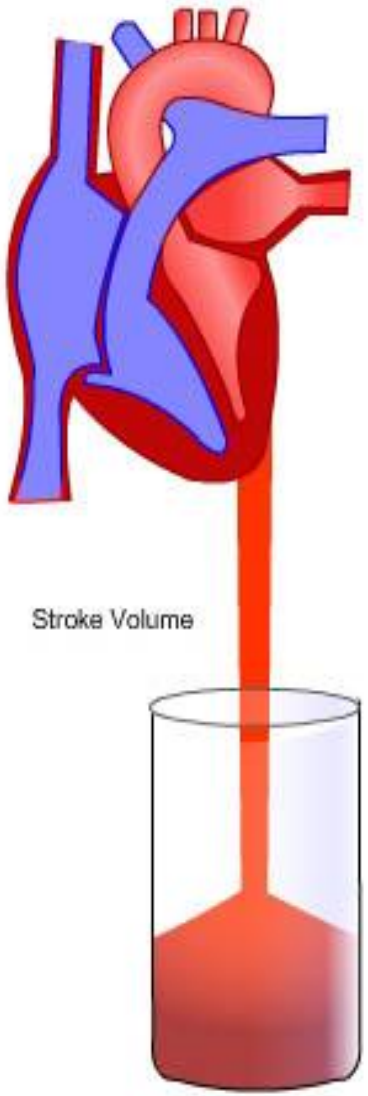
- It is the **resistance** against which the ventricles contract.
- Afterload on the left ventricle, ↑, when aortic pressure ↑
- Afterload on the right ventricle ↑, when pulmonary artery pressure ↑

Afterload ↑ in:

- **Aortic/pulmonary stenosis**
- **Hypertension**
- **Vasoconstriction**

Regulation of CO

- CO is crucial since it is 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.



To increase cardiac output

Increase stroke volume
or

Increase heart rate
or
increase both

Determinants of the CO

CO = SV X HR

EDV – ESV

Venous Return

Preload

Myocardial Contractility (Inotropic state)

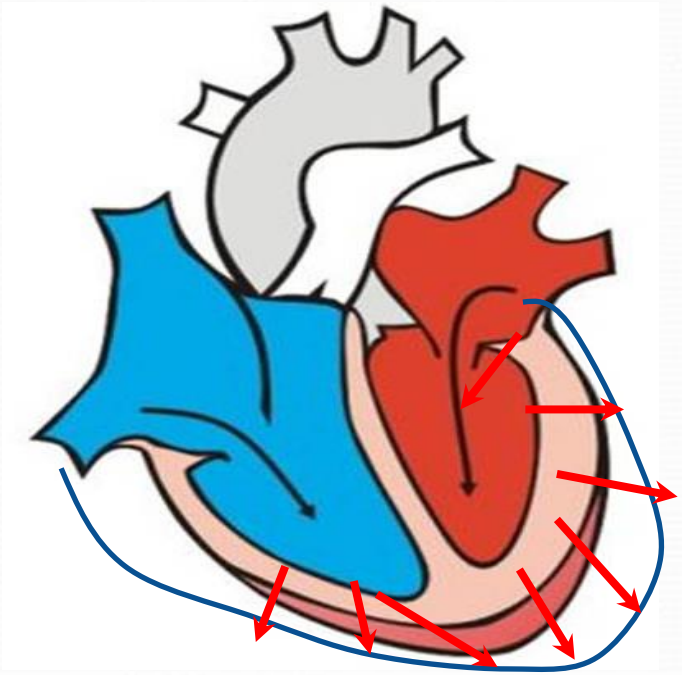
Afterload

?

CO = {EDV-ESV} X HR

Any factor that affects these parameters will affect 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

↓

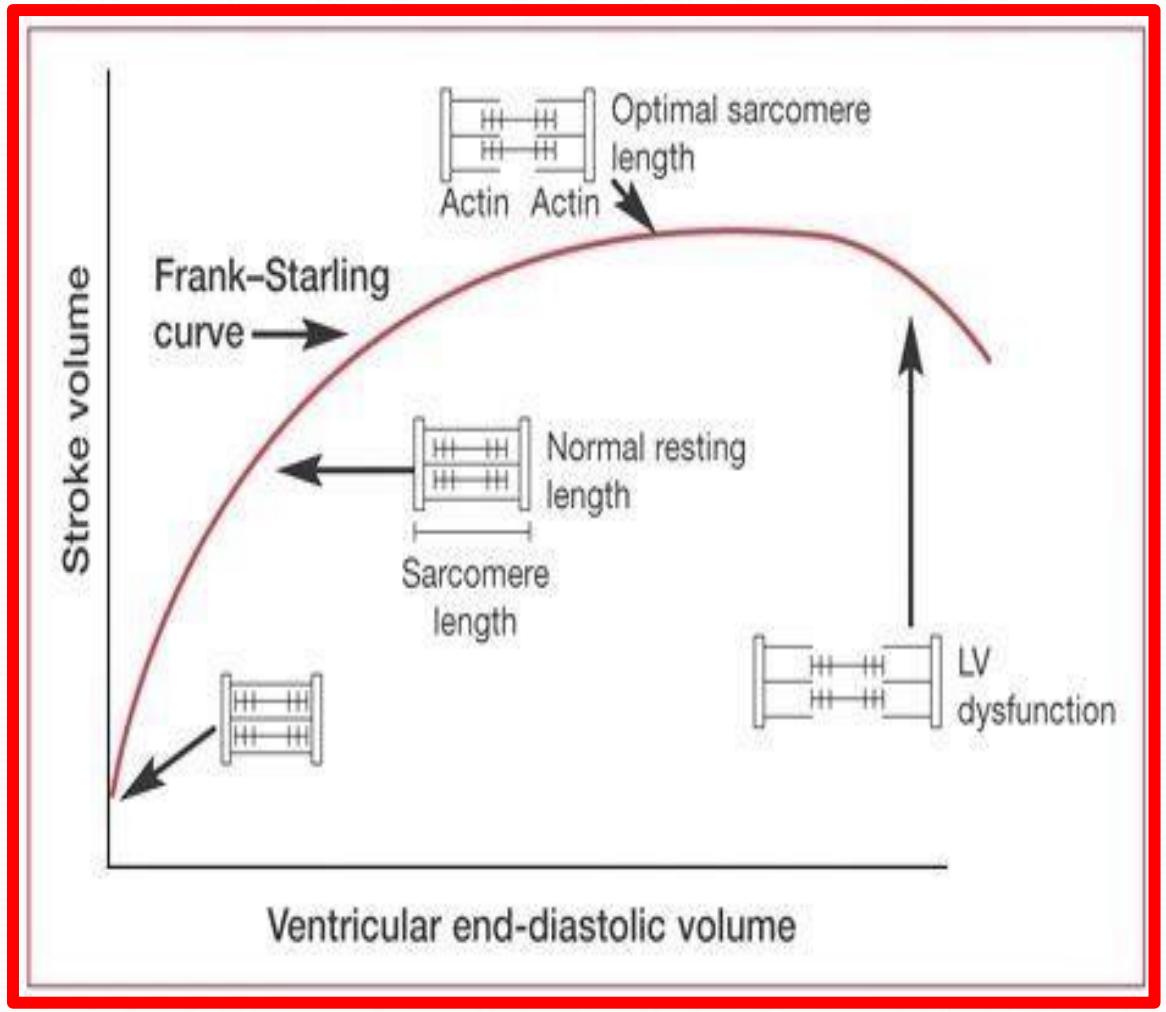
↑↑ The stretch in the myocardium (↑↑ initial fiber length)

↓

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

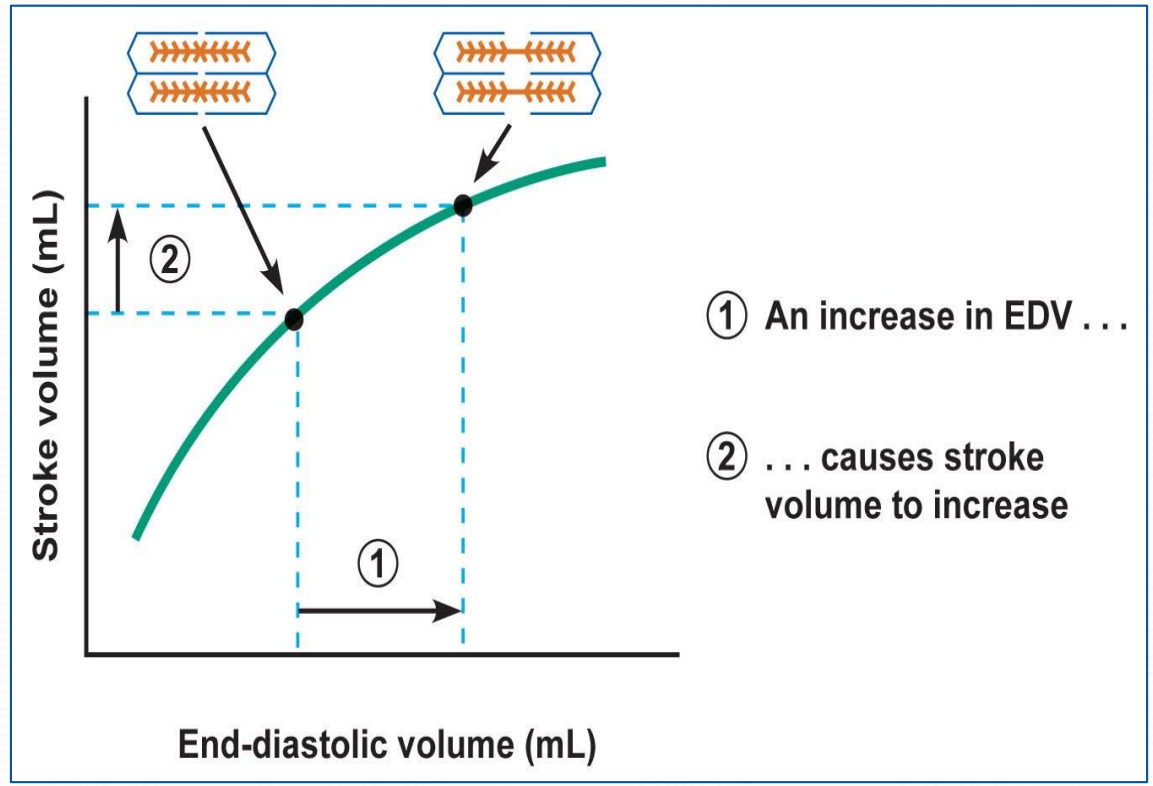
Frank-Starling's Law

- 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).**



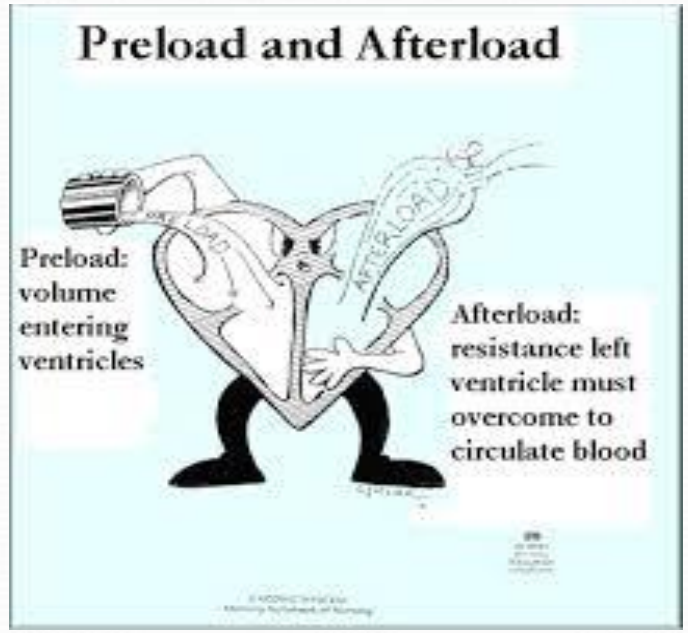
Significance: Frank-Starling's Law

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



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).

Determinants of the CO…..Cont.

CO = SV X HR

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

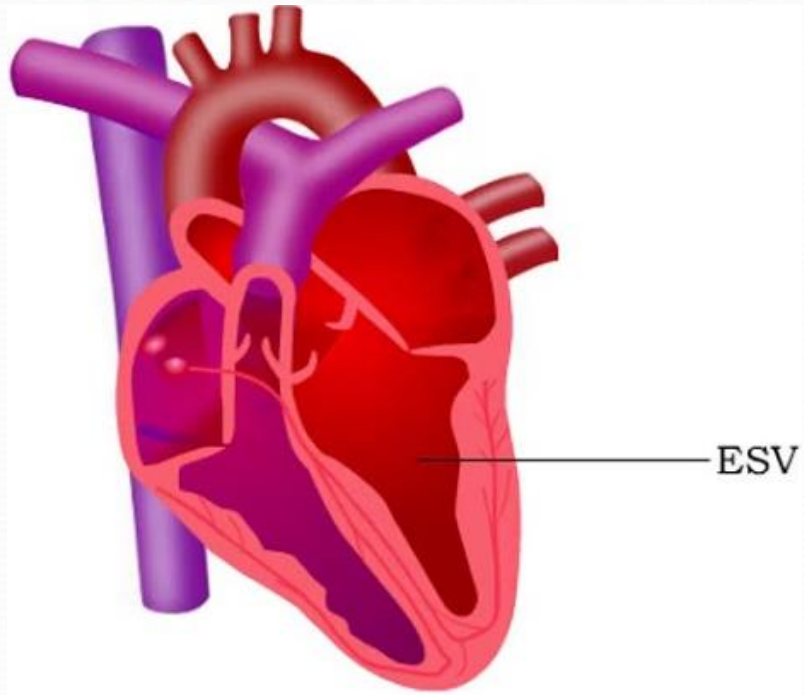
?

CO = {EDV-ESV} X HR

Any factor that affects these parameters will affect the CO

End-Systolic Volume (ESV)

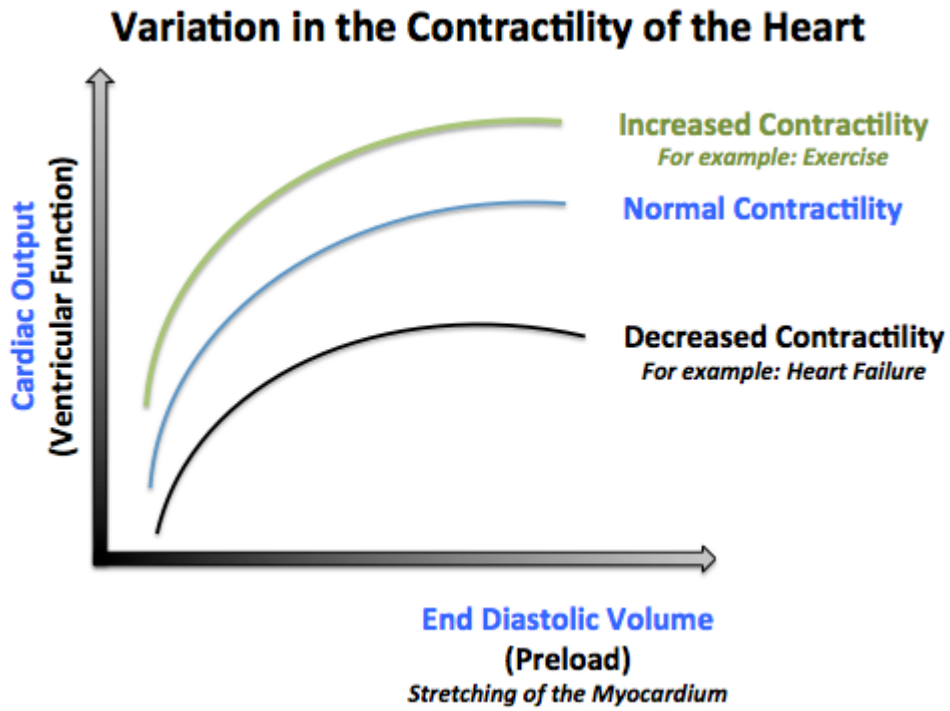
- ***ESV*** = The volume of blood remaining in the ventricle at the end of systole.
- ↑ ESV → ↓ stroke volume
- ↓ ESV → ↑ stroke volume
- ***ESV is determined by:***
  1. **Cardiac contractility**
  2. ***Afterload***



Determinants of ESV

1- Cardiac contractility:

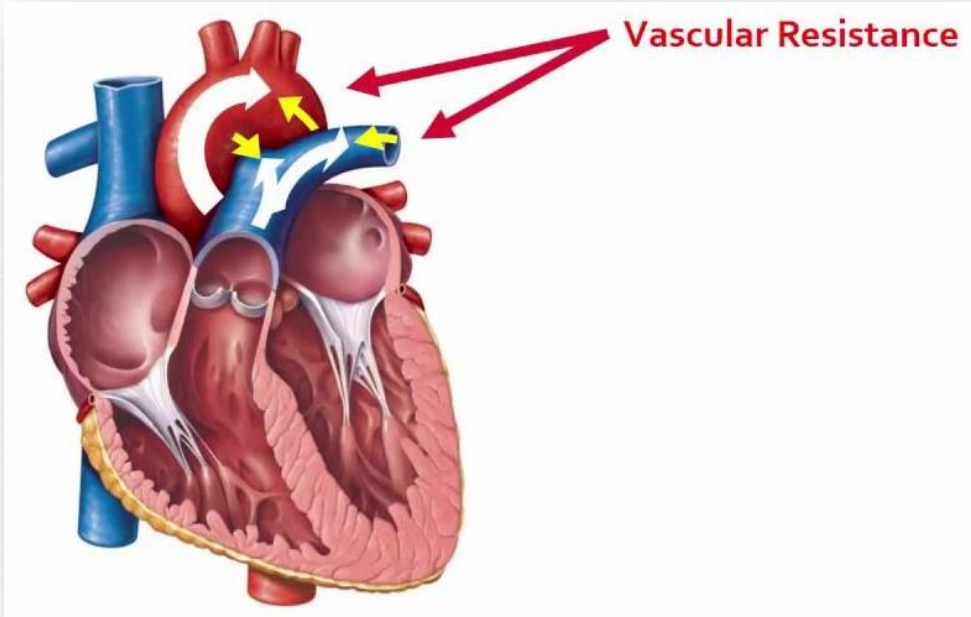
- ↑↑ contractility → ↓↓ ESV → ↑↑ SV & CO
- ↓↓ contractility → ↑↑ ESV → ↓↓ SV & CO



Determinants of ESV….Cont.

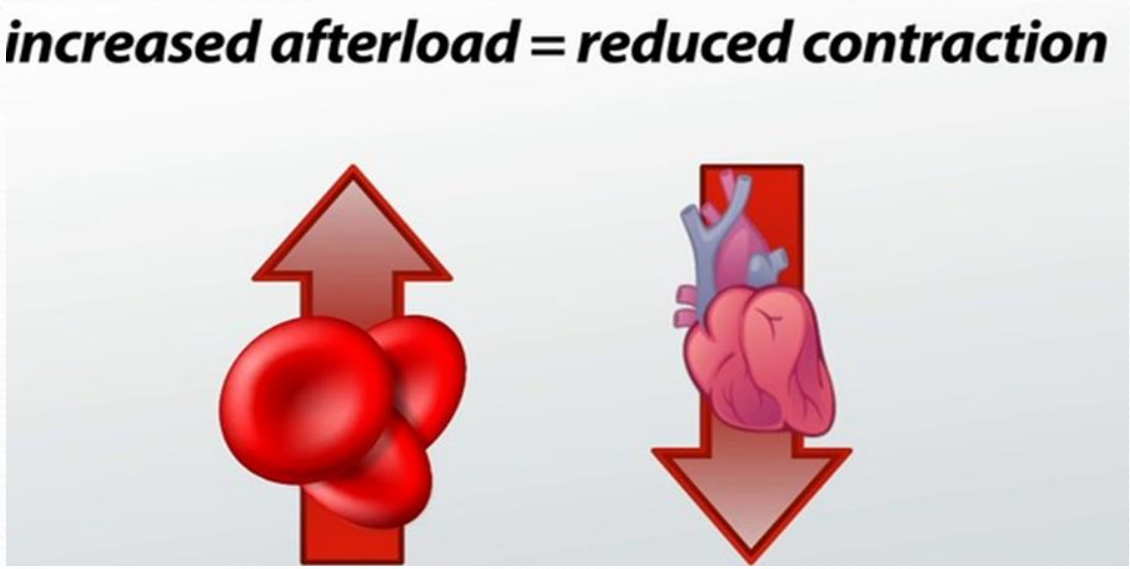
2- Afterload:

- 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.
- Right ventricular afterload represents the force that the muscle must generate to eject the blood into pulmonary artery.



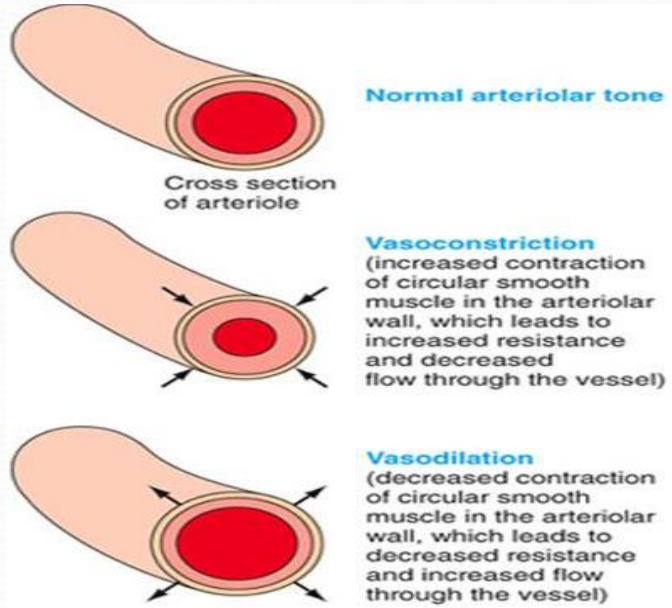
Determinants of ESV….Cont.

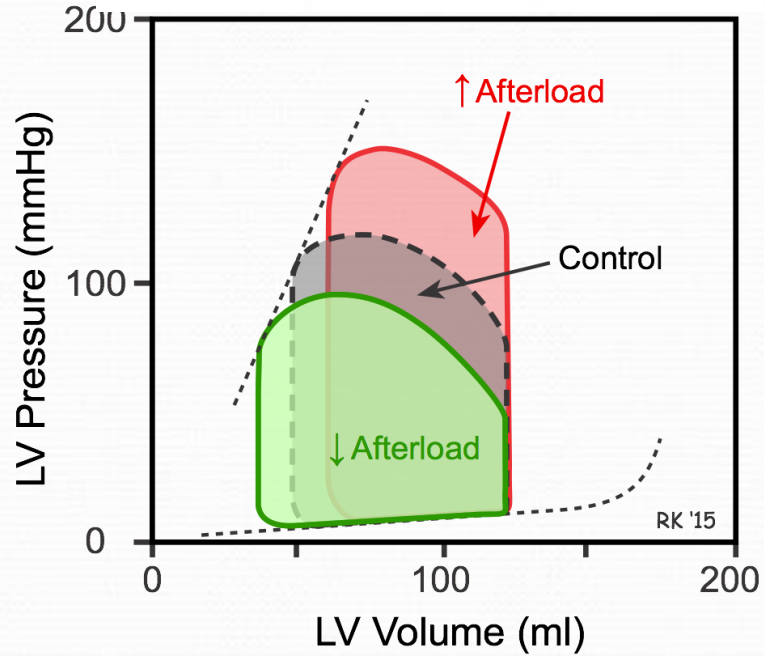
- When the aortic pressure (afterload) increases, the velocity of shortening of the LV myocardial fibers ↓. Hence, the LV ejects less blood → ↓ SV →↑ ESV.
- The opposite is true when LV afterload is reduced.



Factors affecting Afterload

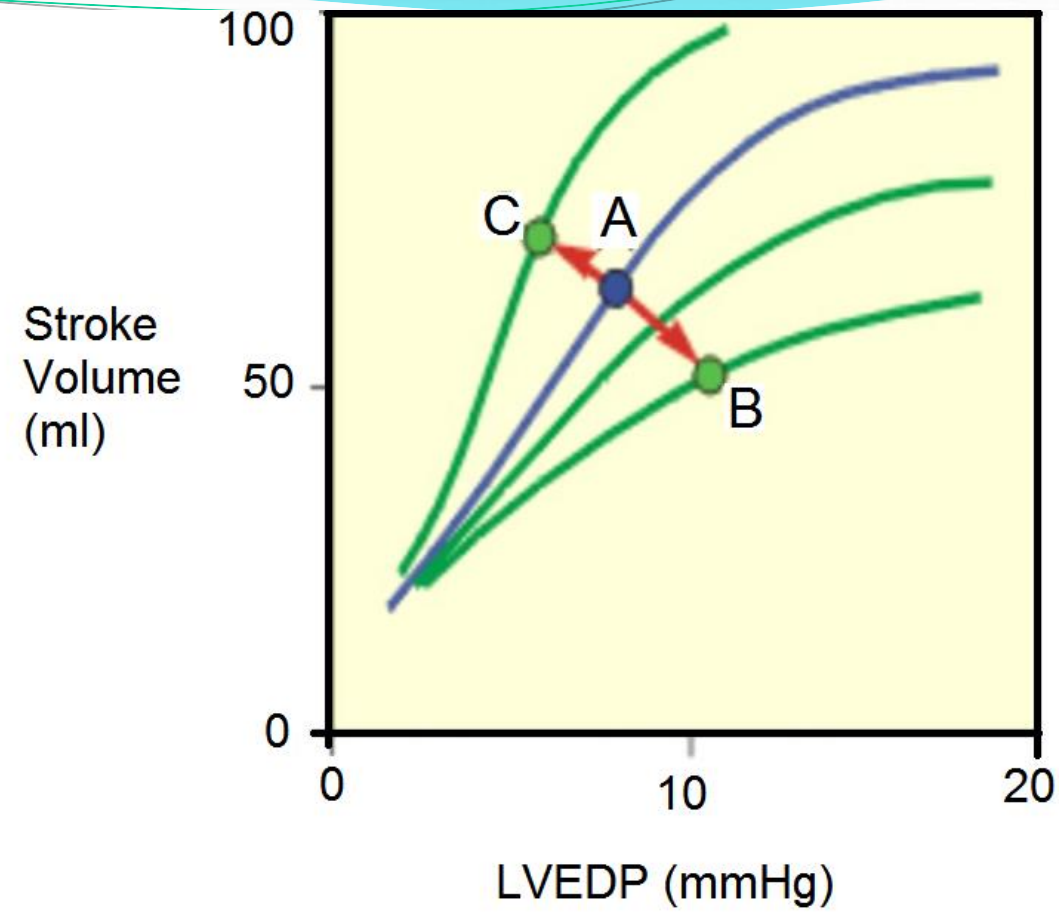
- Afterload ↑ by any factor that restricts blood flow
  - Vasoconstriction ↑↑ the peripheral vascular resistance → ↑↑ ESV → ↓↓ SV & CO
  - Vasodilatation ↓↓ the peripheral vascular resistance → ↓↓ ESV → ↑↑ SV & CO
- **Causes of ↑ left ventricular afterload:**
  1- Aortic valve stenosis
  2- Arterial hypertension.
  3- Vasoconstriction (the peripheral vascular resistance).
- **Causes of ↑ right ventricular afterload:**
  1- Pulmonary valve stenosis
  2- Pulmonary hypertension.
  3- Pulmonary vasoconstriction.





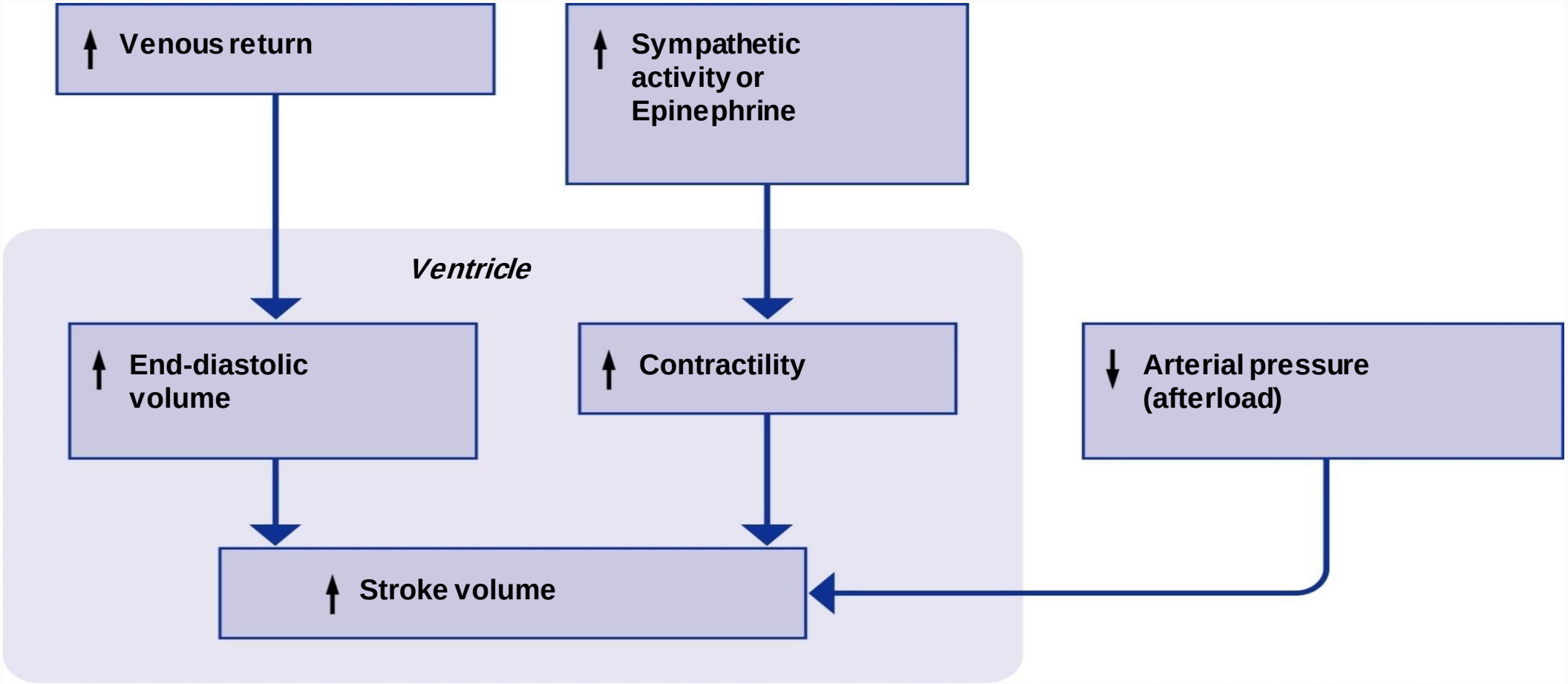
Effect of Afterload on Frank Starling Curve

- ↑ in afterload leads to ↑ ESV and ↓ SV .Thus shifts the Starling's curve down and to the right (from A to B)
- ↓ in afterload ↓ ESV and ↑ SV. Thus shifts Starling's curve up and to the left (from 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 = ↑ in contractility.
- Negative inotropic agent = ↓ in contractility

HEART RATE

- Positive chronotropic effect = ↑ in HR
- Negative chronotropic effect = ↓ in HR

CONDUCTION VELOCITY

- Positive dromotropic effect = ↑ in conduction velocity
- Negative dromotropic effect = ↓ in conduction velocity

The Heart Rate (HR)

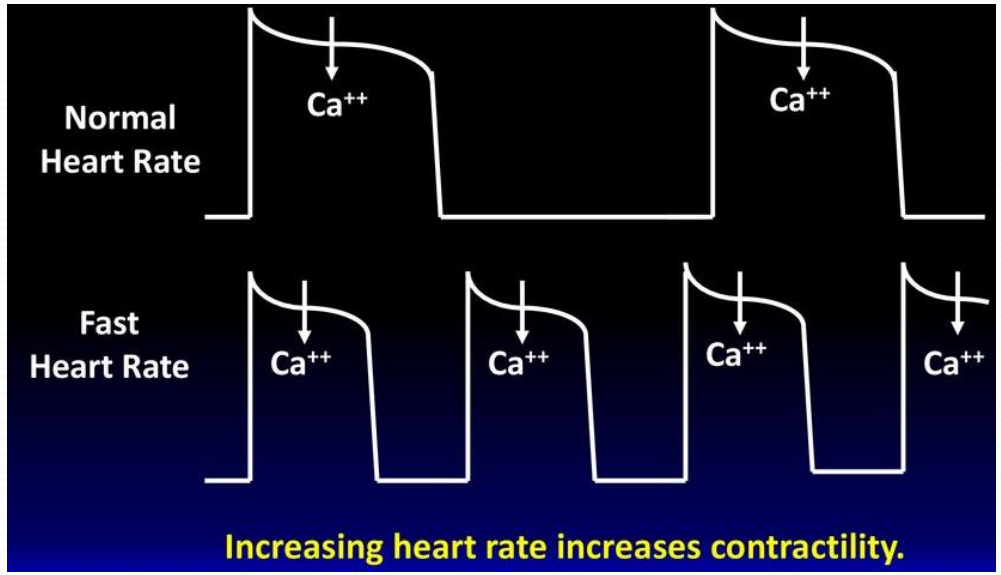
- Normal heart rate is regular sinus rhythm= 60-100 beats/min
- > 100 beats/min → Tachycardia
- < 60 beats/min → Bradycardia
- Since the CO = SV X HR, ↑ heart rate →↑ CO.
- At heart rates up to about 180, ventricular filling is adequate as long as there is enough venous return,
- However, at very high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

Frequency-force relationship

- The heart rate has an influence on cardiac contractility as well (frequency-force relationship).

Increasing heart rate increases contractility.

- This frequency dependency of force generation is probably due to ↑ Ca^{2+} availability to the contractile proteins within cardiac myocytes as a result of:
  - The ↑No. of depolarizations/min → more frequent plateau phases → more Ca^{2+} entry.
  - ↑ The magnitude of Ca^{2+} current → ↑ the intracellular Ca^{2+} stores.
  - Both effects enhance Ca^{2+} release & uptake by the sarcoplasmic reticulum.



Regulation of Heart Rate

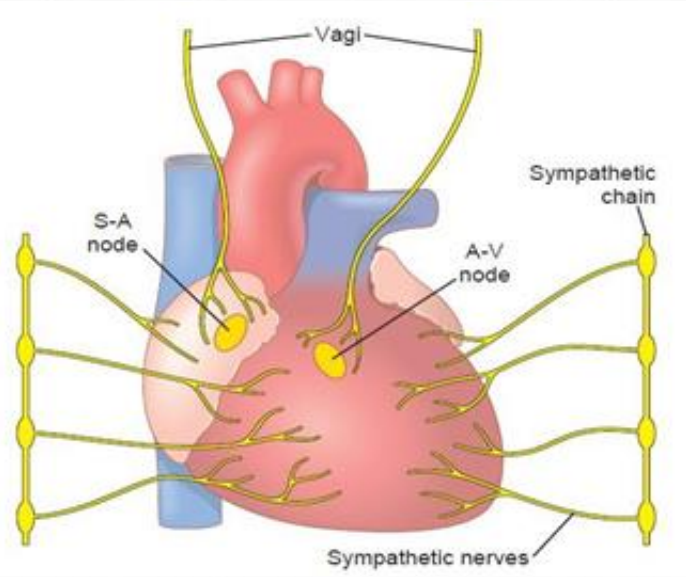
1- Autonomic nervous system

- 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

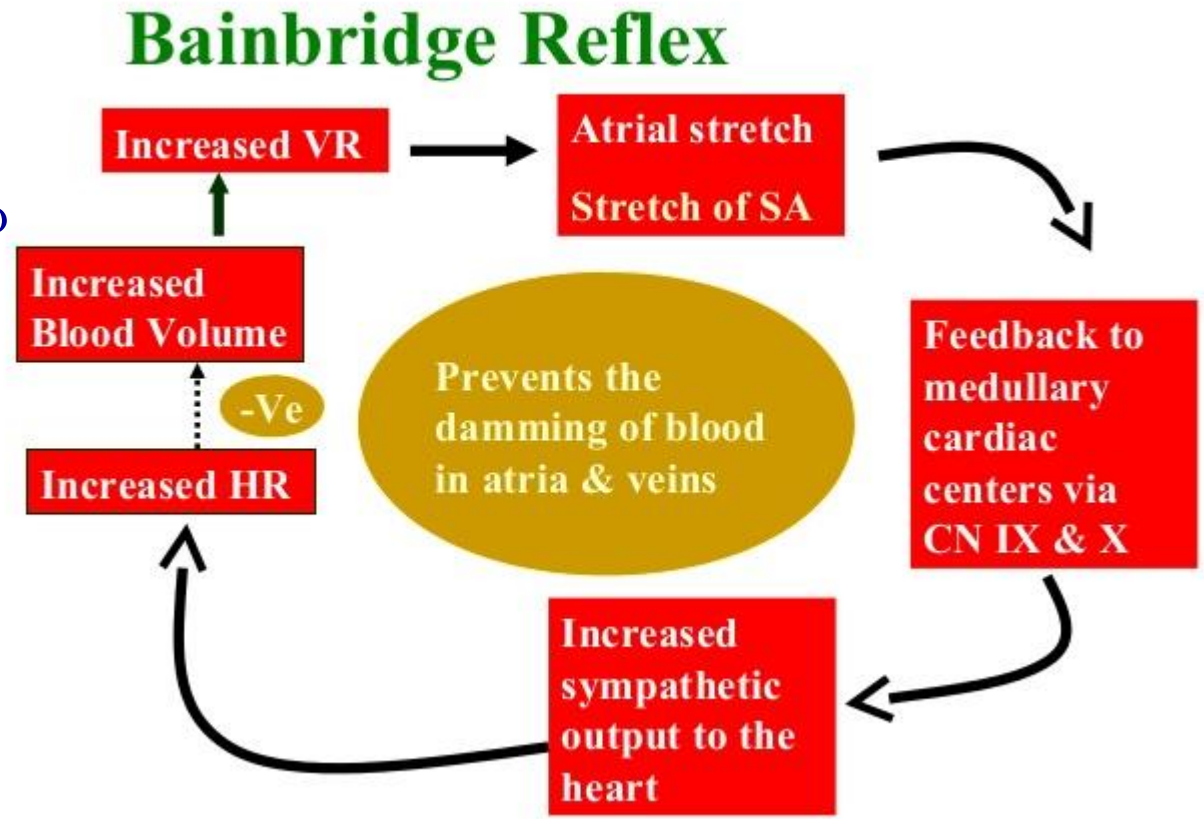
- Epinephrine and thyroxin increase HR.
- Increased Ca^{2+} level in blood causes prolonged contraction
- Reduced Ca^{2+} level in blood depress the heart.

Regulation of Heart Rate…..Cont.

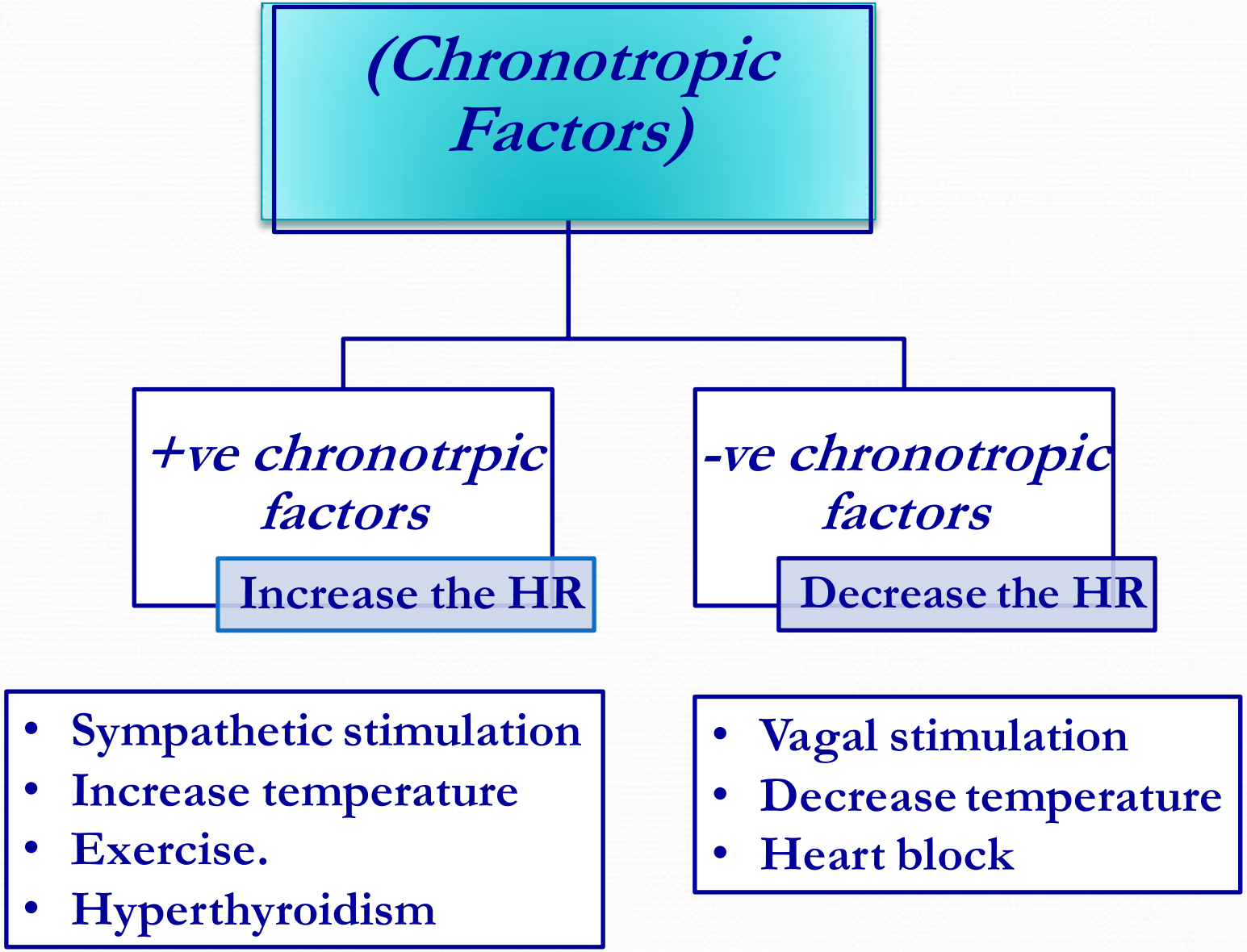
4- Blood volume

Atrial Reflex (Bainbridge reflex)

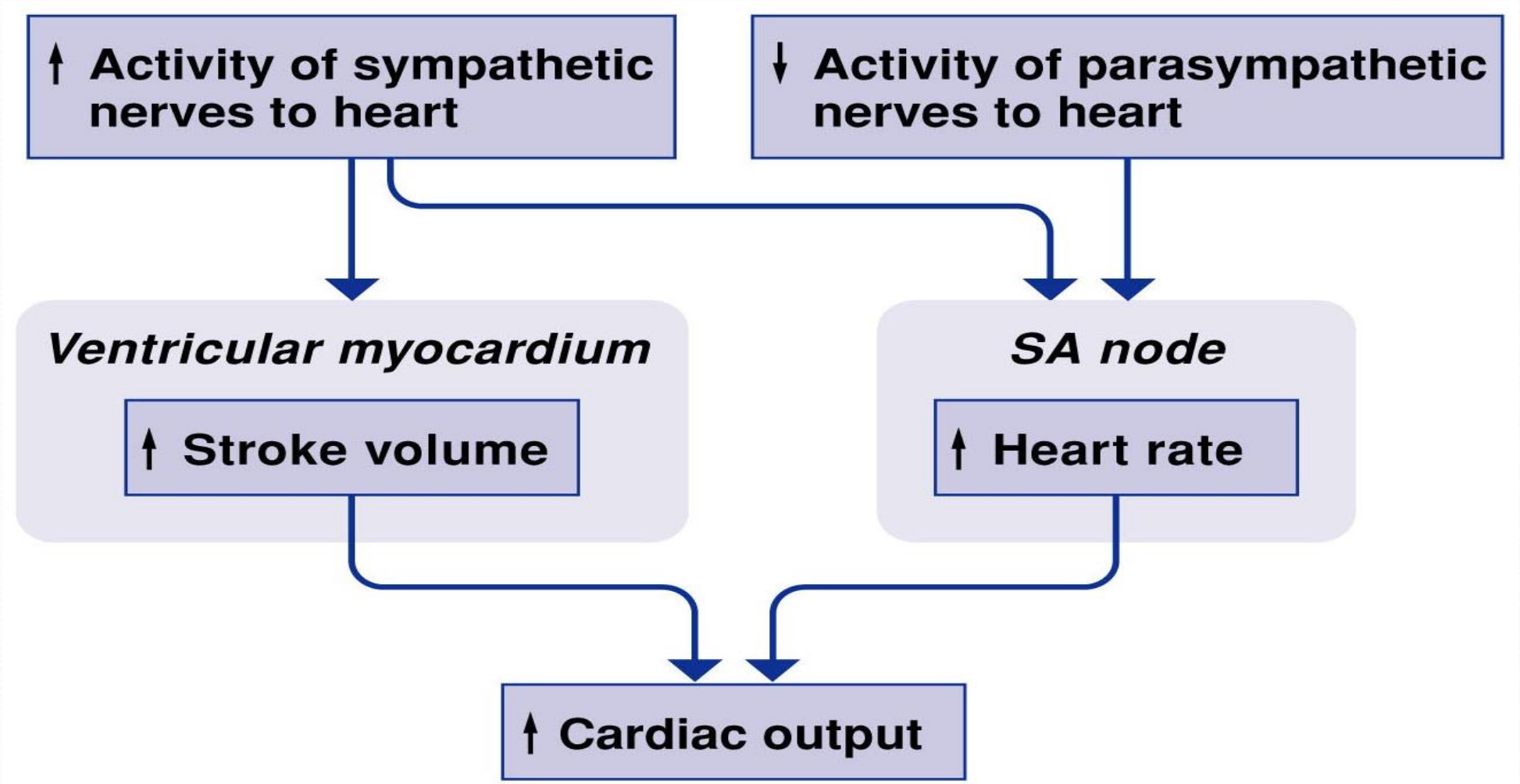
- This reflex adjusts heart rate in response to venous return.
- Increase blood volume, stimulates stretch receptors in right atrium.
- This triggers increase in heart rate through increased sympathetic activity.



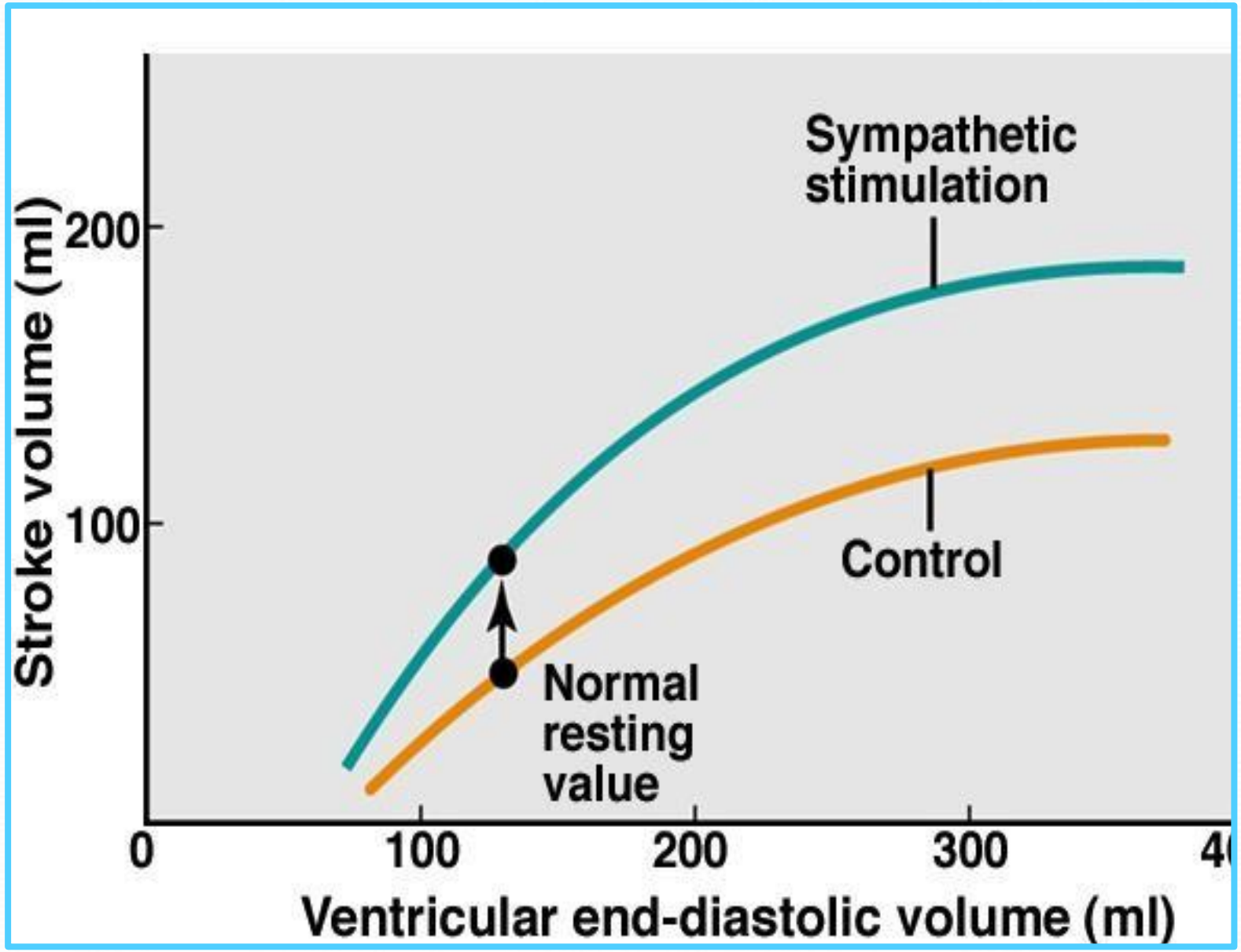
Factors Affecting the HR (Chronotropic Factors)



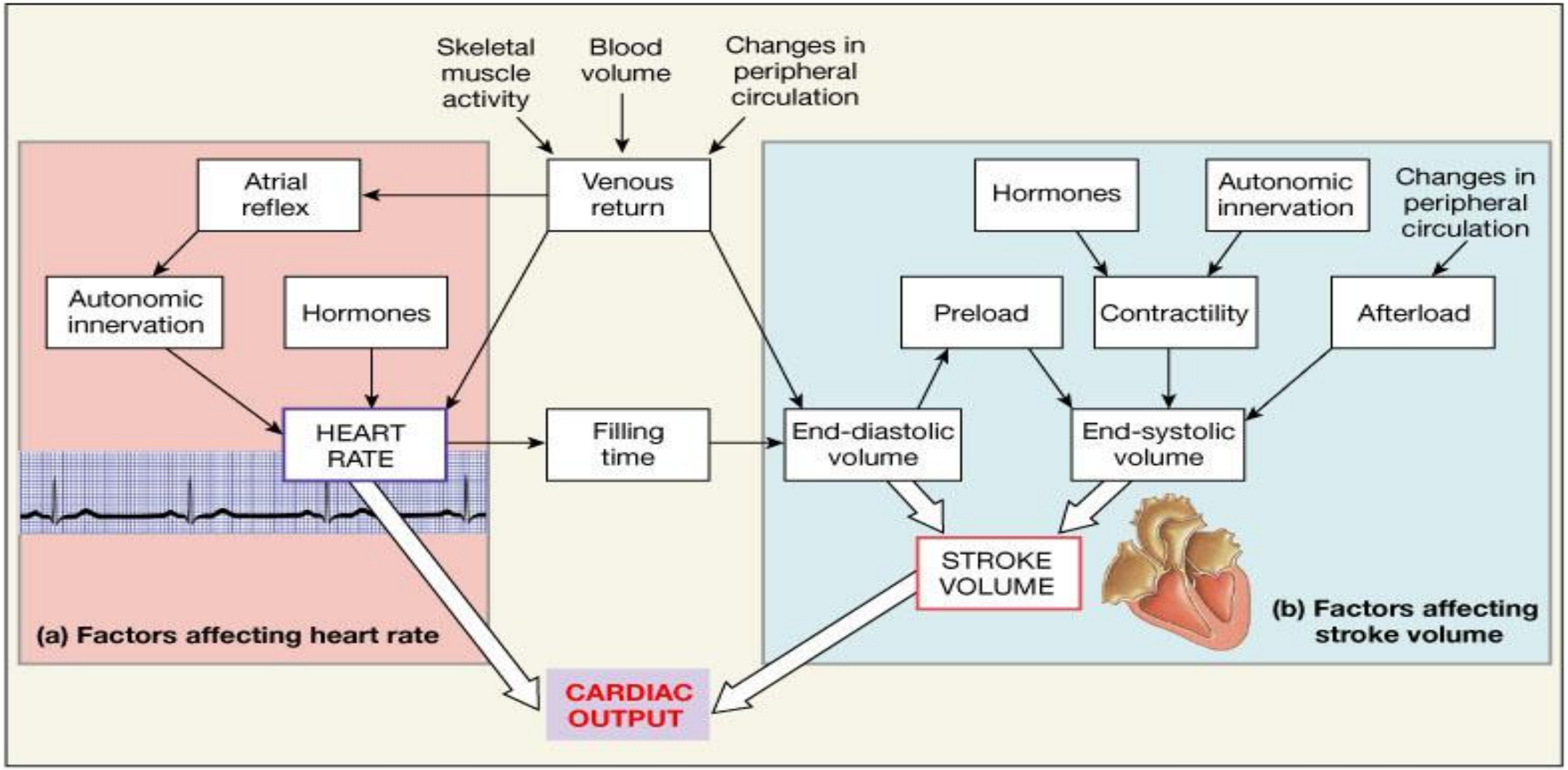
Regulation of Cardiac Output by Autonomic Nerves



Effect of Sympathetic Stimulation on CO



Summary of the Factors Affecting Cardiac Output



Pathological Low Or High Cardiac Output

Causes of low CO:

- Low VR e.g hemorrhage.
- 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:

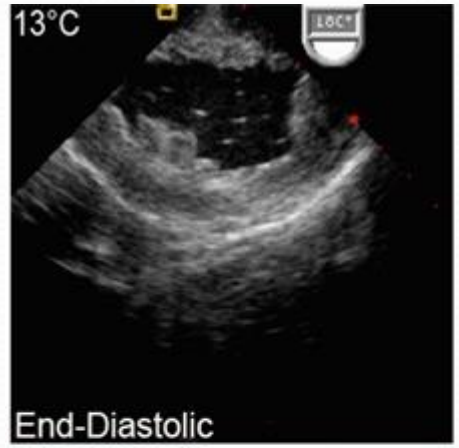
- Hyperthyroidism: the increase in the CO is due to the high metabolic rate → vasodilatation →↑ CO to 50% of control.
- AV fistulas.
- Fever.
- Anaemia.
- Anxiety.

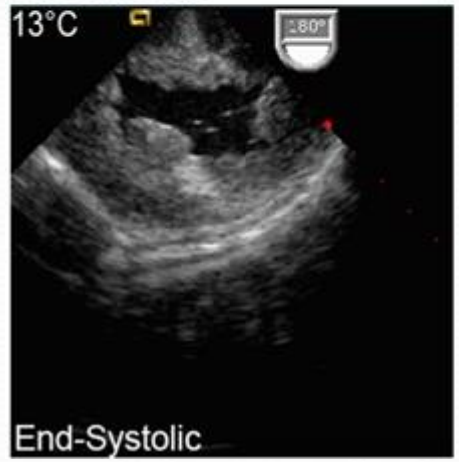
Measurement of Cardiac Output

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

2-Dimensional Echocardiography

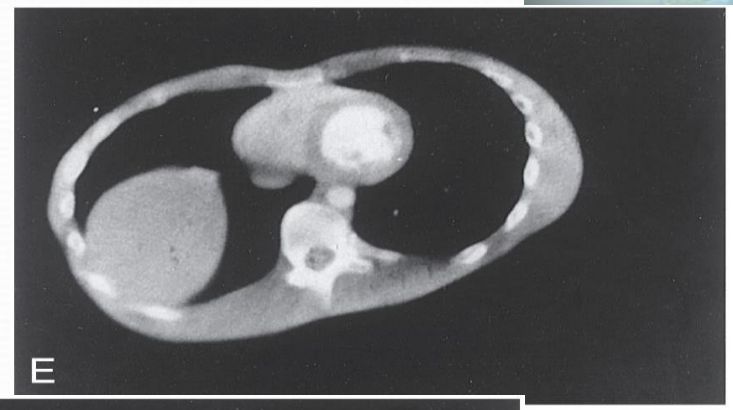
- Records real-time changes in ventricular dimensions during systole and diastole.
- It thus computes the SV, which when multiplied by HR, the CO will be calculated.

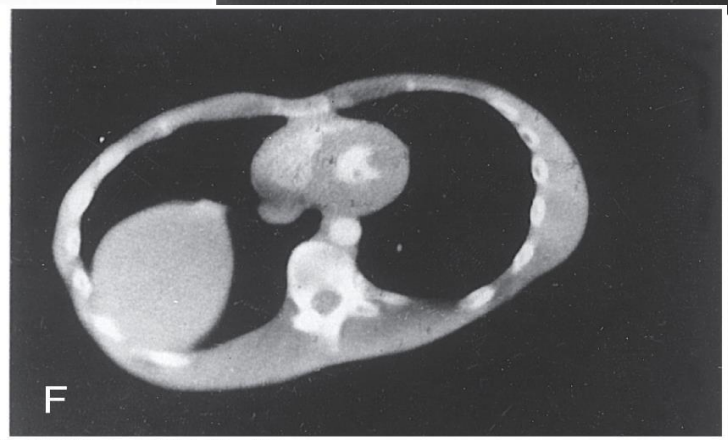




Ultra-fast Computer Tomography

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





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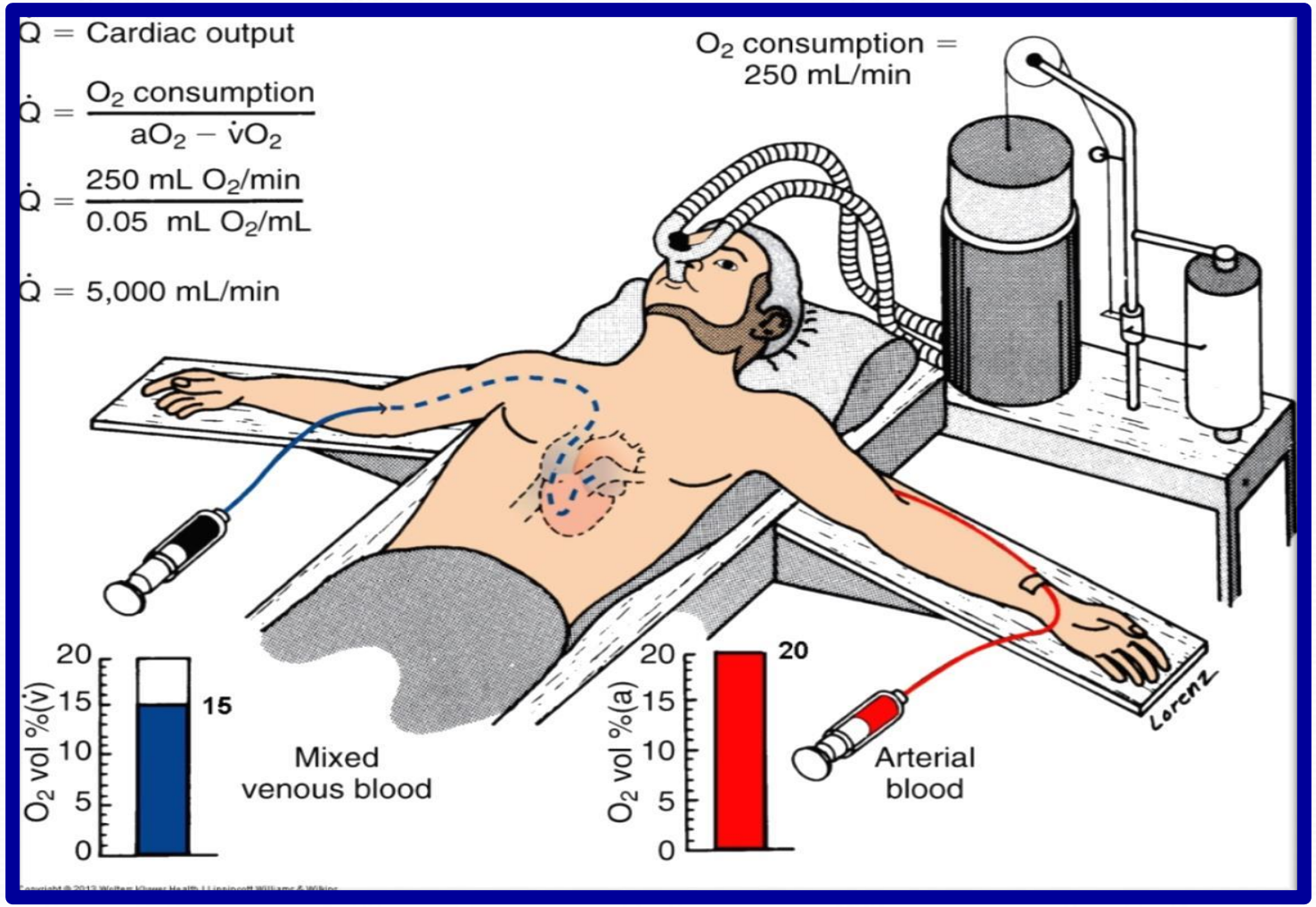
Fick's principle

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.

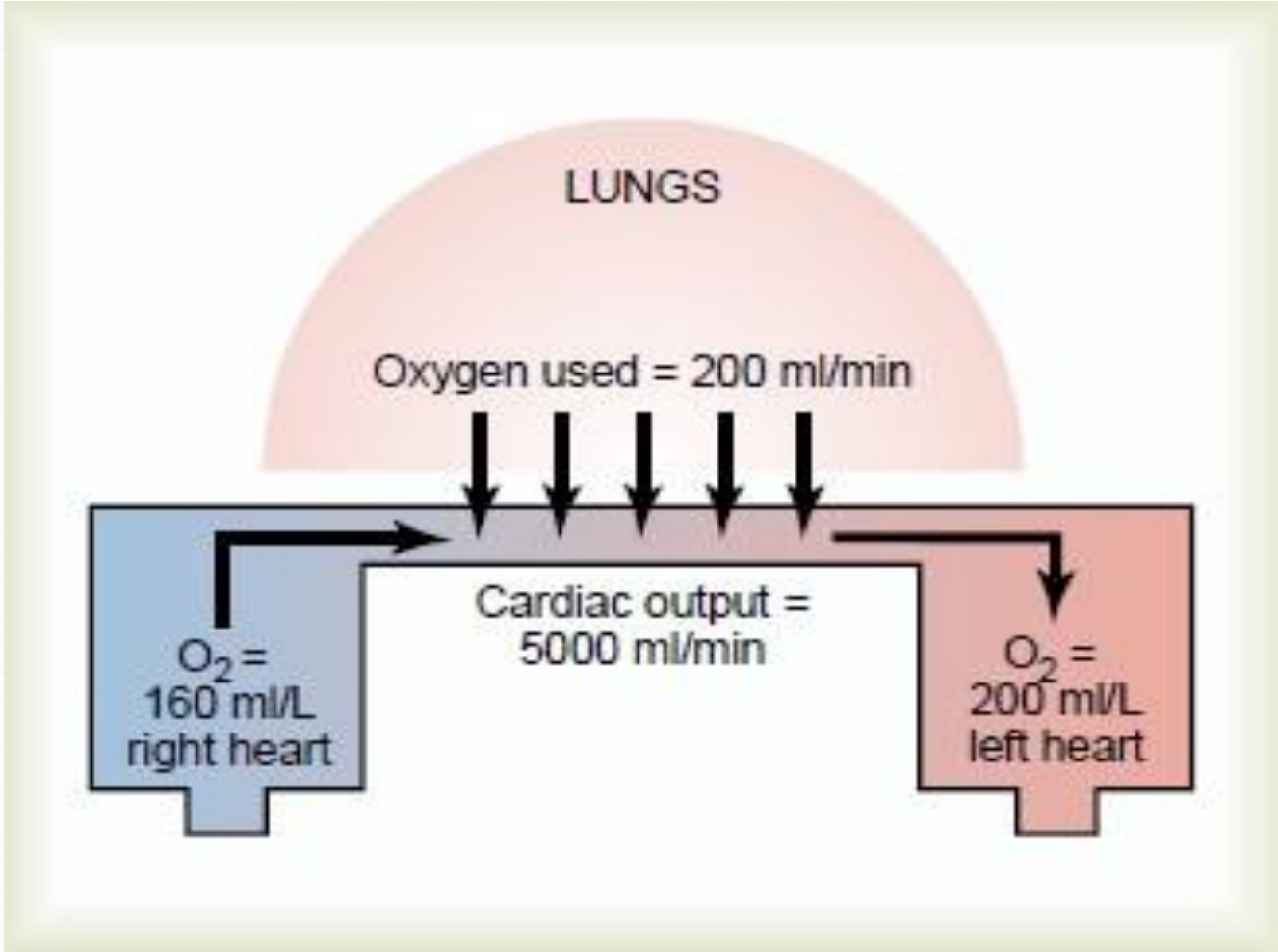


Measurement of Cardiac Output: Fick's method

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

AO_2= Arterial O_2 concentration

VO_2= Mixed O_2 venous concentration

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