

PHYSIOLOGY

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ



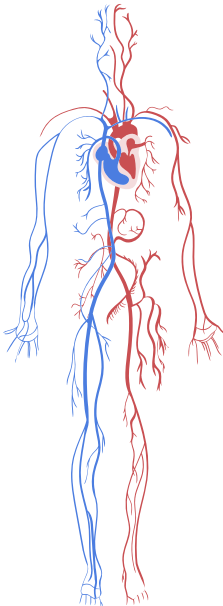
MID | Lecture 8

Heart Pump & Cardiac Cycle Pt. II

وَلَقَدْ خَلَقْنَا الْإِنْسَانَ وَنَعْلَمُ مَا تُوَسْوِسُ بِهِ نَفْسُهُ وَنَحْنُ أَقْرَبُ إِلَيْهِ مِنْ حَبْلِ الْوَرِيدِ
اللهم إنا نعوذ بك من شرور أنفسنا ومن سيئات أعمالنا

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Heart Pump and Cardiac Cycle

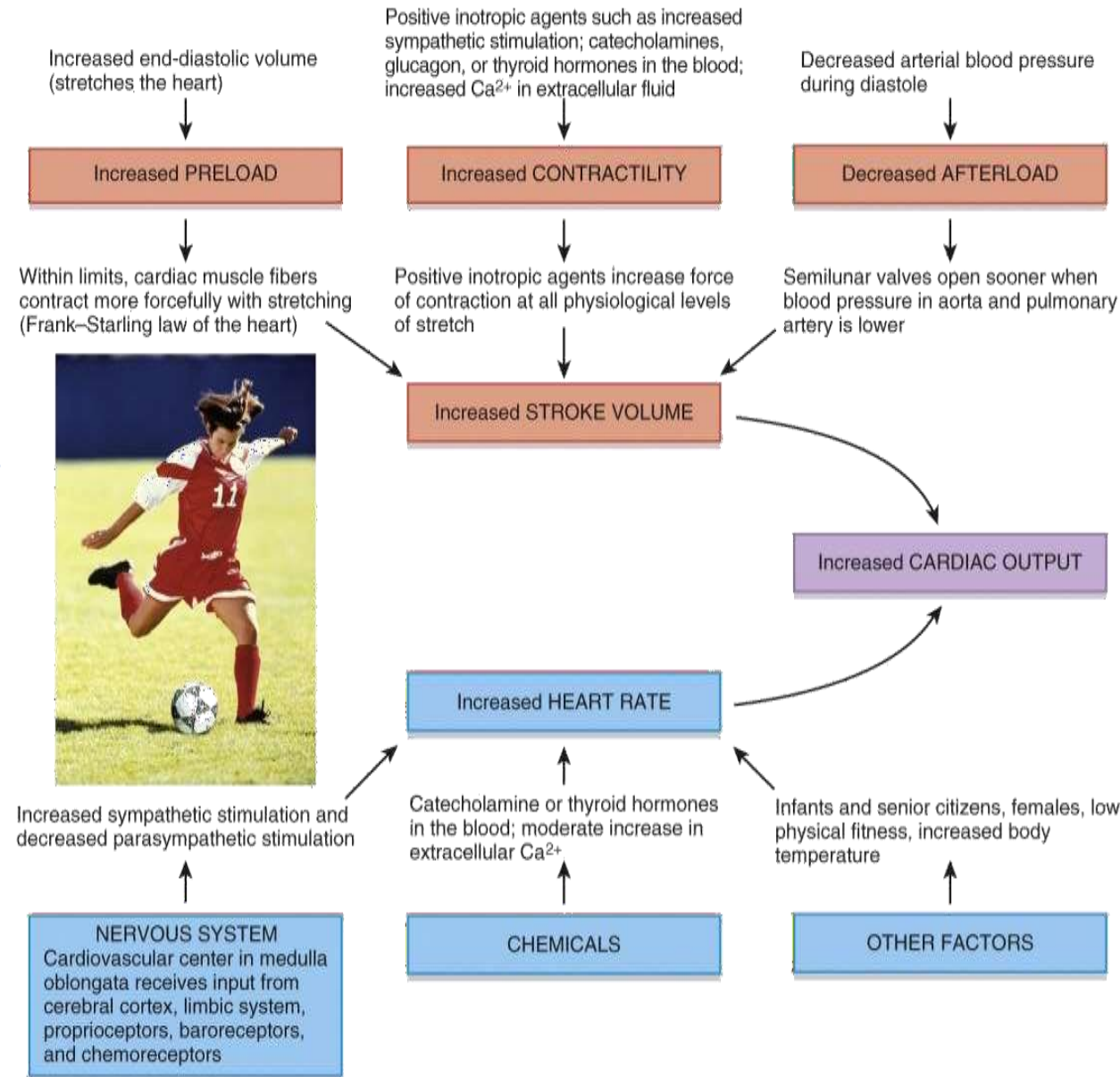
Faisal I. Mohammed, MD, PhD

Cardiac Output

Recall:

Cardiac Output (CO) = Stroke Volume (SV) x Heart Rate (HR).

Changes that increase the **stroke volume**, **heart rate**, or **both** will increase the cardiac output. Let's visit physiological mechanisms we can target to increase both the stroke volume and/or the heart rate, which will consequently increase the cardiac output.



Stroke Volume & Cardiac Output

To increase the **stroke volume**, we can target several physiological mechanisms:

1. Increase the **preload**:

Preload is the end-diastolic volume, which is the degree of tension or stress present in the ventricular walls before contraction. According to the Frank-Starling Law, within physiological limits, an increase in the EDV leads to greater myocardial fiber stretch and therefore a larger stroke volume.

2. Increase **contractility**:

Contractility is the heart's intrinsic ability to generate force at a given EDV. Increasing the contractility raises stroke volume **without** changing the preload, resulting in a higher ejection fraction– also known as a **positive inotropic effect**. **Sympathetic stimulation** increases contractility as the SNS innervates the entire heart (unlike the PSNS, which primarily innervates the atria, SA, and AV nodes). Parasympathetic (vagal) stimulation reduces heart rate but has little effect on ventricular contractility. Other positive inotropes include **norepinephrine, epinephrine, and thyroid hormones**, which are growth hormone-like hormones that upregulate the β -adrenergic receptors enhancing sensitivity and the heart's responsiveness to catecholamines. **Glucagon** also increases contractility, although, **without** increasing the heart rate and can be used clinically when enhanced contractility is needed without inducing tachycardia.

3. Decrease the **afterload**:

Afterload is the amount of tension that the ventricles must overcome to open the semilunar valve and eject blood. This can also be recognized as the pressure in the pulmonary artery and the aorta during diastole. **Reducing the afterload increases the stroke volume** because the semilunar valves open earlier and the ventricle ejects blood more efficiently. On the other hand, increased afterload, like in patients with hypertension, forces the heart to generate greater pressure to overcome the high aortic arterial pressure, which increases myocardial oxygen demand. If coronary blood flow is limited, such as in cases of coronary artery stenosis, this imbalance may result in a myocardial infarction.

Heart Rate & Cardiac Output

1. Sympathetic & Parasympathetic Nervous System stimulation:

The **sympathetic** predominates in controlling contractility, while the **parasympathetic** predominated in controlling **decreasing** the heart rate. If both are cut off, contractility will decrease while the heart rate increases.

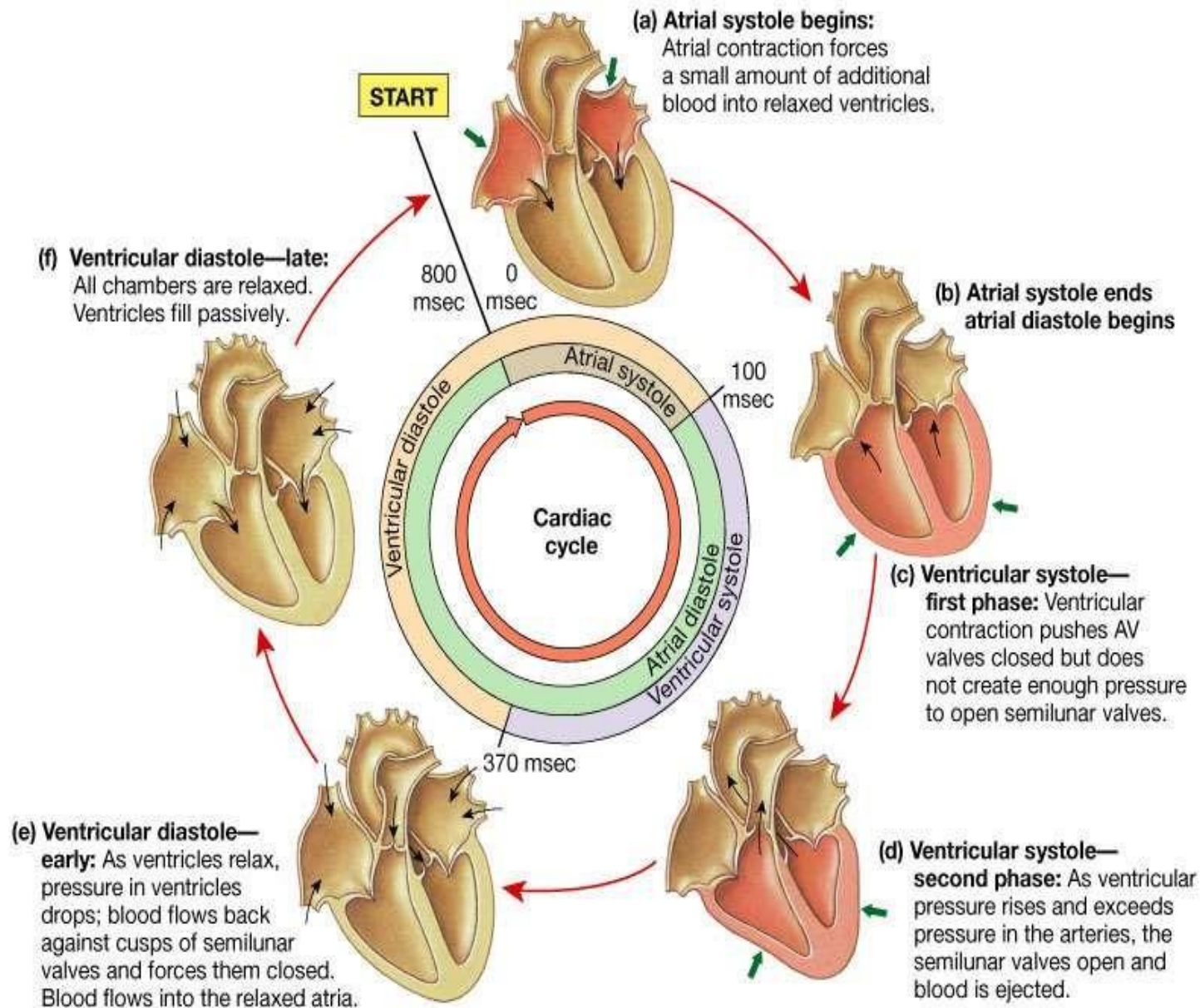
2. Thyroid Hormones & Calcium

3. Other factors, such as high temperatures, physical fitness, and infants.

As previously discussed, high fever in children can be dangerous because it significantly increases heart rate. An elevated heart rate shortens the duration of the cardiac cycle. For example, if the normal cardiac cycle is 0.8 seconds, diastole occupies 0.5 seconds and systole 0.3 seconds. If the heart rate increases to 100 beats/minutes, the cardiac cycle shortens to 0.6 seconds, with systole lasting 0.29 seconds and diastole about 0.31 seconds. The most important change is the marked reduction in diastolic duration, which is critical because diastole is when the ventricles fill with blood. If this time were to decrease, EDV decreases, lowering SV and the CO ultimately. Although the stroke volume decreases as heart rate rises; the increased heart rate compensates for that decrease, thus, normally, an increase in the heart rate (within physiological limits) increases cardiac output.

For instance, if the heart rate is 70 beats/minute with a stroke volume of 70 mL/beat, cardiac output is about 4.9 L/minute. If the heart rate increases to 100 beat/minute and stroke volume decreases to 60 mL/beat, cardiac output rises to approximately 6L/minute. However, this compensatory effect has limits, as once the heart rate exceeds ~80% of the individual's physiological limit ($210 - \text{age in years}$), stroke volume falls so significantly that the cardiac output also begins to decline.

Phases of the Cardiac Cycle



Extrinsic Factors Influencing Stroke Volume

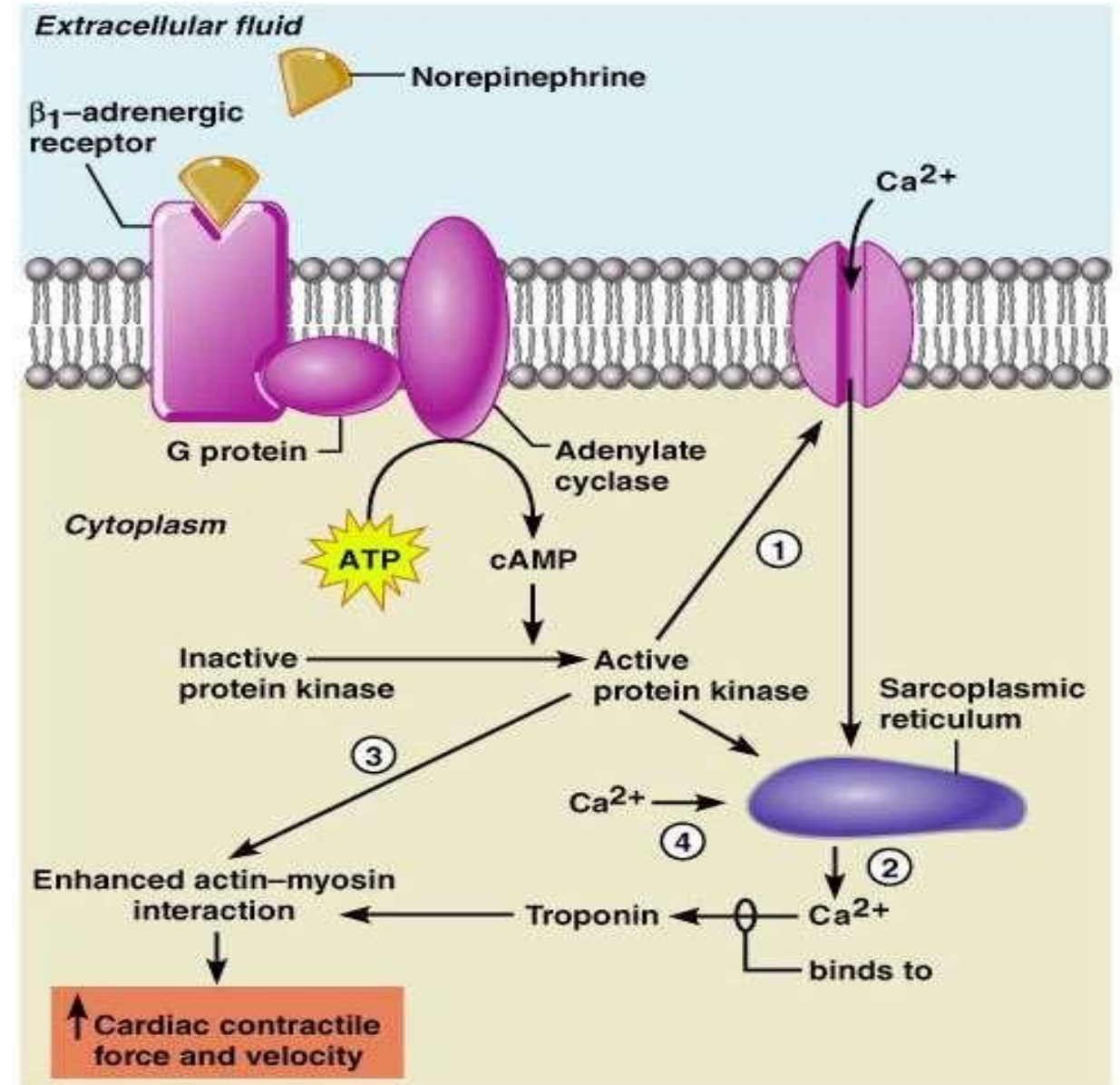
- Contractility is the increase in contractile strength, independent of stretch and EDV
 - ✓ If the EDV were to increase or decrease, **Frank-Starling law** would apply.
- Increase in contractility comes from:
 - Increased sympathetic stimuli
 - Certain hormones
 - ✓ Catecholamines (EP & NE), thyroid hormones, & glucagon.
 - Ca^{2+} and some drugs

Extrinsic Factors Influencing Stroke Volume

- Agents/factors that decrease contractility include:
 - Acidosis ✓ Acidosis disturbs the intracellular metabolism and enzymes.
 - Increased extracellular K^+
 - Calcium channel blockers Decreased actin-myosin bridge formation.

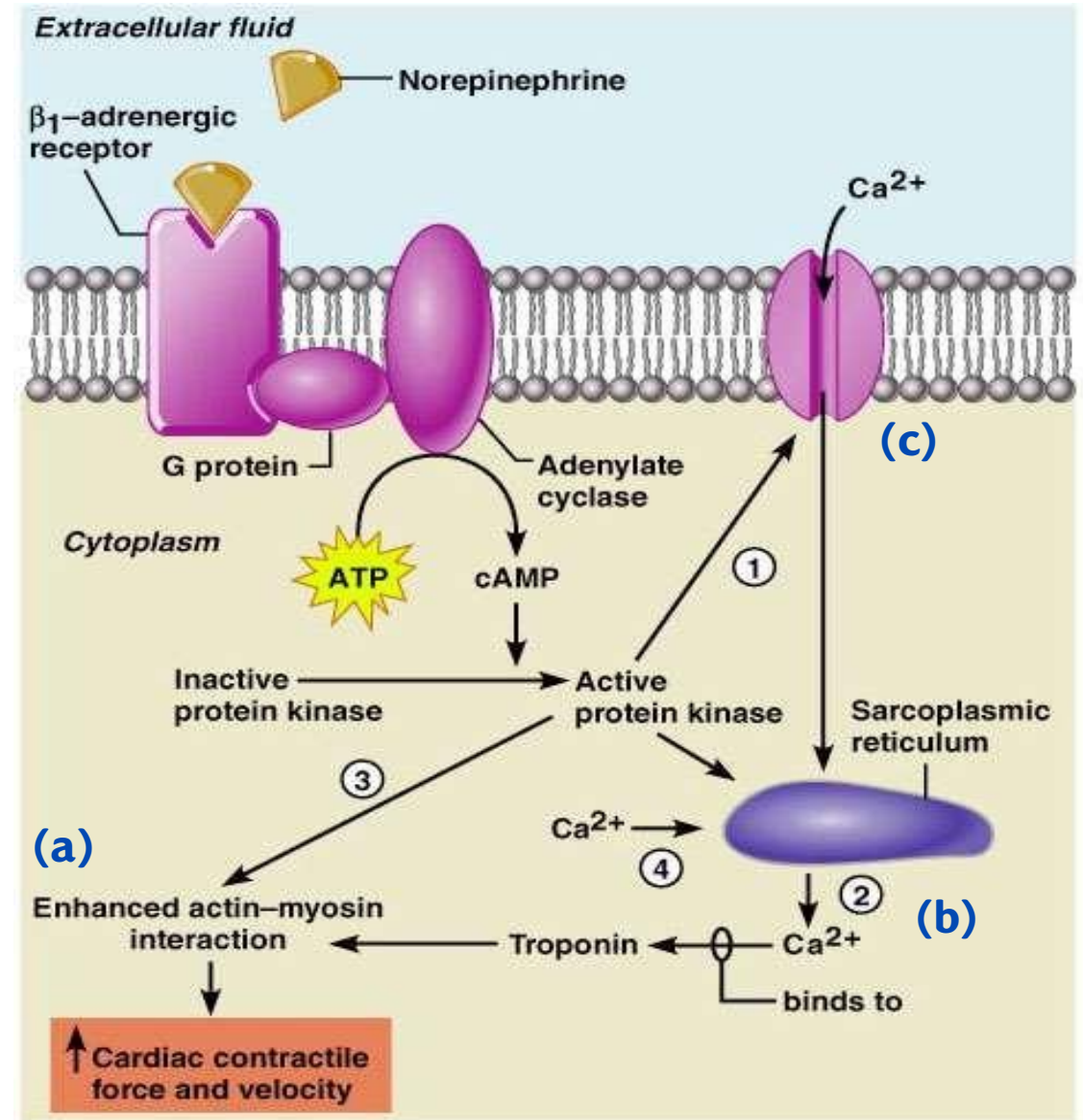
Contractility and Norepinephrine

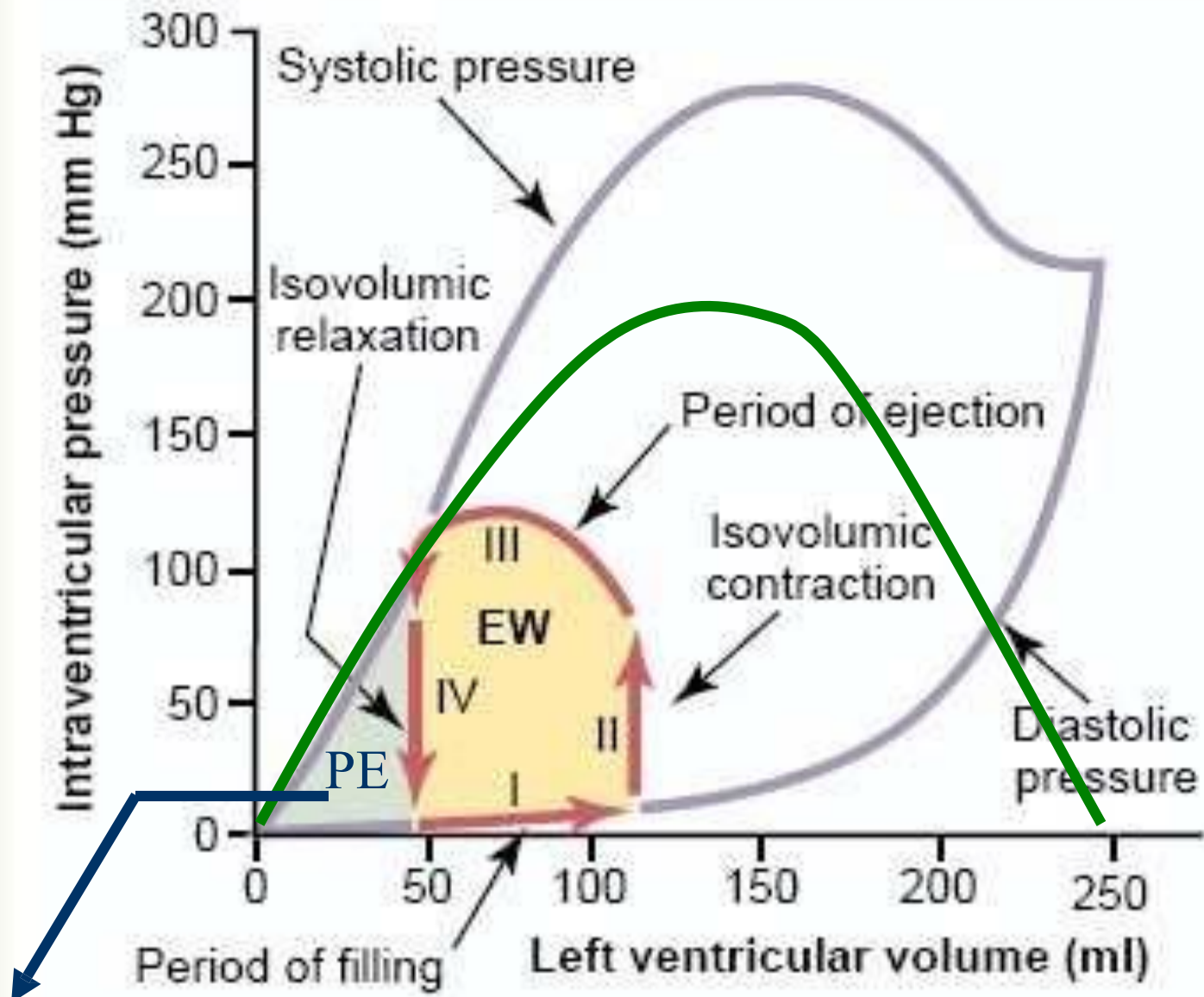
- Sympathetic stimulation releases norepinephrine and initiates a cyclic AMP second-messenger system



Contractility and Norepinephrine

- ✓ Catecholamines bind to their β -adrenergic receptors on the cardiac cells (the diagram indicates β_1 , but Dr. Faisal specifies β_2). Activation of the G-protein-coupled receptor causes the Gs alpha-subunit to dissociate and stimulate adenylyl cyclase, which converts ATP to cAMP. Elevated cAMP activates protein kinase A (PKA), which (a) enhances actin-myosin interactions by phosphorylating certain proteins. It will also (b) phosphorylate proteins in the sarcoplasmic reticulum (SR), activating the calcium pump causing it to efflux calcium from the SR. (c) PKA can also phosphorylate the calcium channel on the sarcolemma and increase the calcium influx, thus increasing contractility.

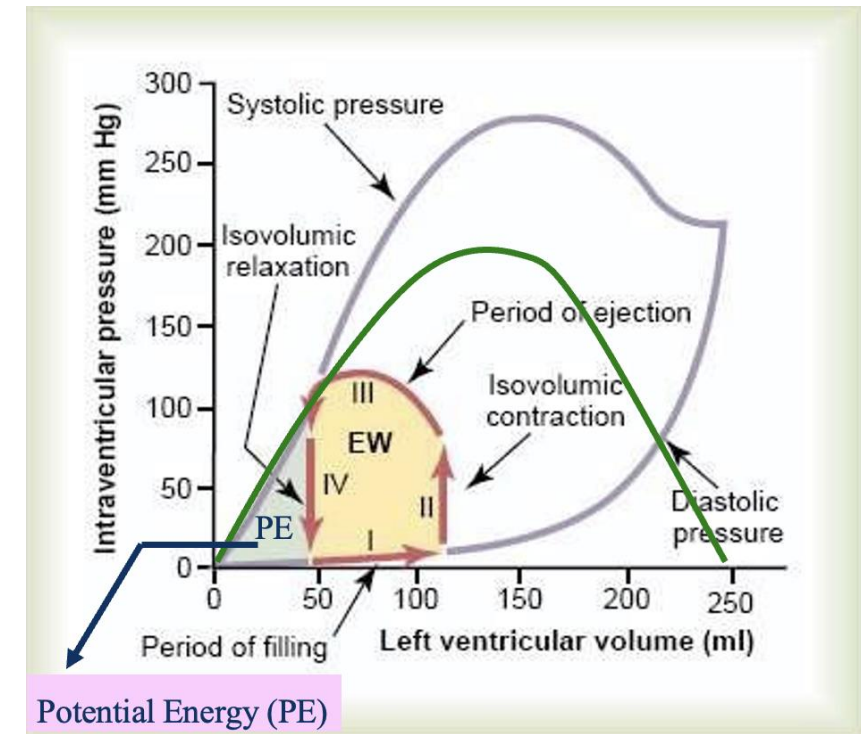




Potential Energy (PE)

Pressure-Volume Loop Explained

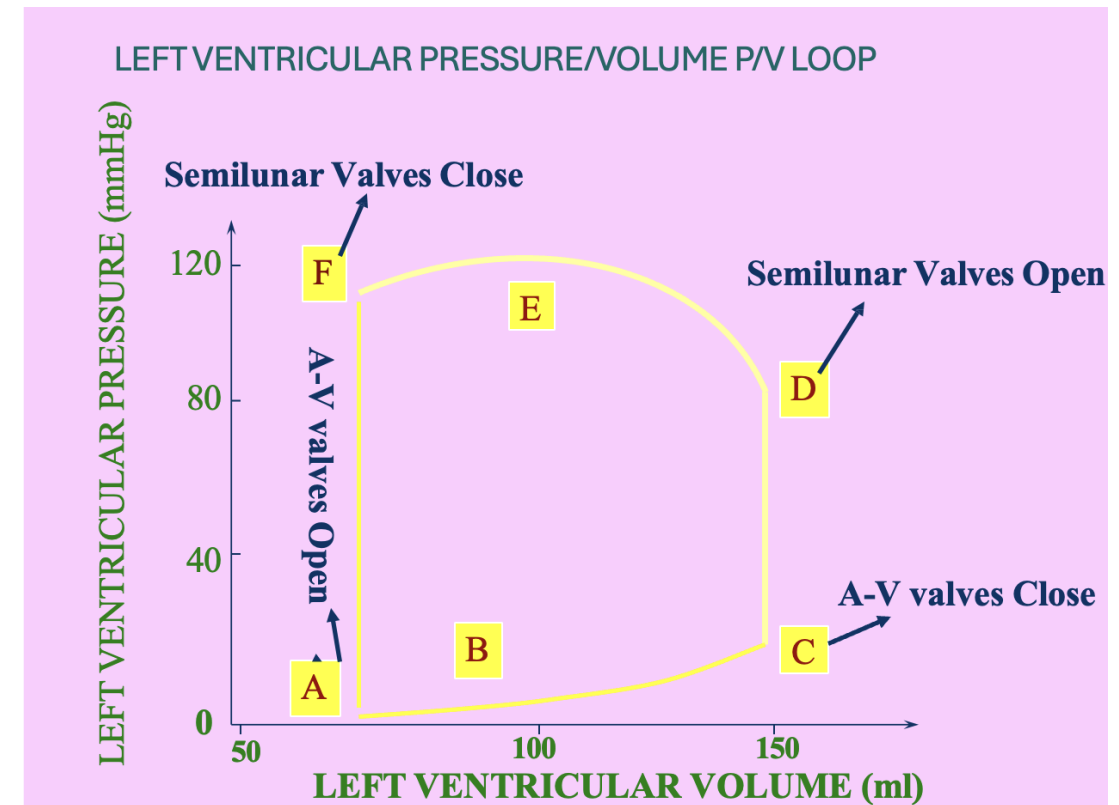
- ✓ In a **pressure-volume loop**, the **volume** in the left ventricle is presented on the **x-axis**, while the **intraventricular pressure** is presented on the **y-axis**.
- ✓ At the 50 mL mark (end-systolic volume), the **AV valve opens** and the ventricles begin filling up with blood. The ventricles are **compliant**, meaning additions in the ventricular blood volume is met with a small increase in pressure. Similarly, although through different mechanisms, the lung is also compliant. It can be inflated with air while the pressure only very slightly increases.
- ✓ Blowing up a balloon requires 100x more effort than is needed to inflate the lungs.



Pressure-Volume Loops Explained II

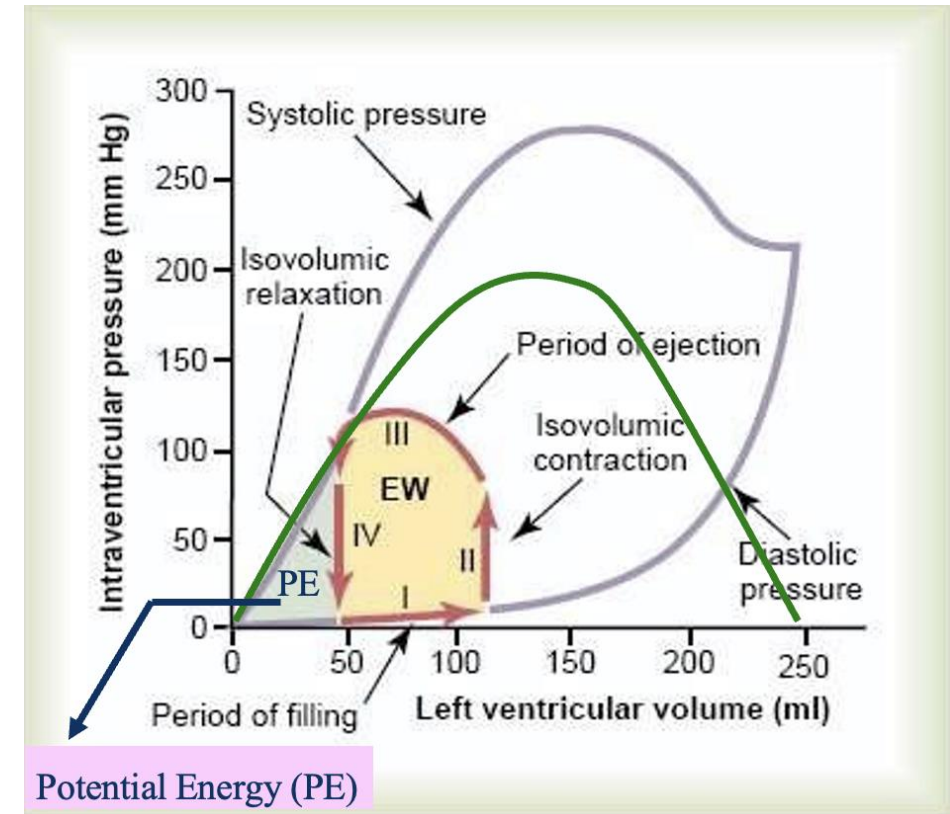
- ✓ Point B represents the ventricles filling up with blood (notice the pressure slightly increasing with volume). As this pressure builds up inside the left ventricle, the AV valve closes (C) recall that AV valves, both **mitral** and tricuspid, close when the pressure in the ventricles is greater than the pressure in the atria to **prevent backflow** of blood.
- ✓ In the period between AV valve closing and the semilunar valves opening, the ventricle undergoes **isovolumic contraction**. The pressure will increase greatly until the semilunar valve opens (D), when the aortic pressure is lower than the ventricular pressure, and the blood is ejected into the aorta. Consequently, the volume decreases (shifts from right → left).
- ✓ At the end of ejection, diastole (relaxation) begins. Diastole begins by **isovolumic relaxation**, where the volume is fixed but the pressure is decreasing. Once the pressure decreases in the ventricles, the AV valve opens, ventricular filling, systole begins, and the cycle goes on.

Remember, the PVL measure **left ventricular** pressure/volume, so keep in mind all the terminology specific to the left ventricle (mitral valve, aortic valve, etc.).



Pressure-Volume Loops Explained III

- ✓ The toast-shaped area under the curve represents the **external work**, which is the energy needed to move the blood through the circulation. The blue line on the graph shows the **passive or diastolic tension**, reflecting the tension generated by ventricular filling during diastole. As more blood enters the ventricle, the pressure rises gradually.
- ✓ In cases of excessive cardiomegaly, total tension and systolic pressure barely overcome the diastolic pressure. In these cases, the active pressure is zero, meaning no cardiac output. Even in cases of severe heart failure, the ventricles usually generate some active pressure, so the cardiac output will be very low, but not necessarily zero.



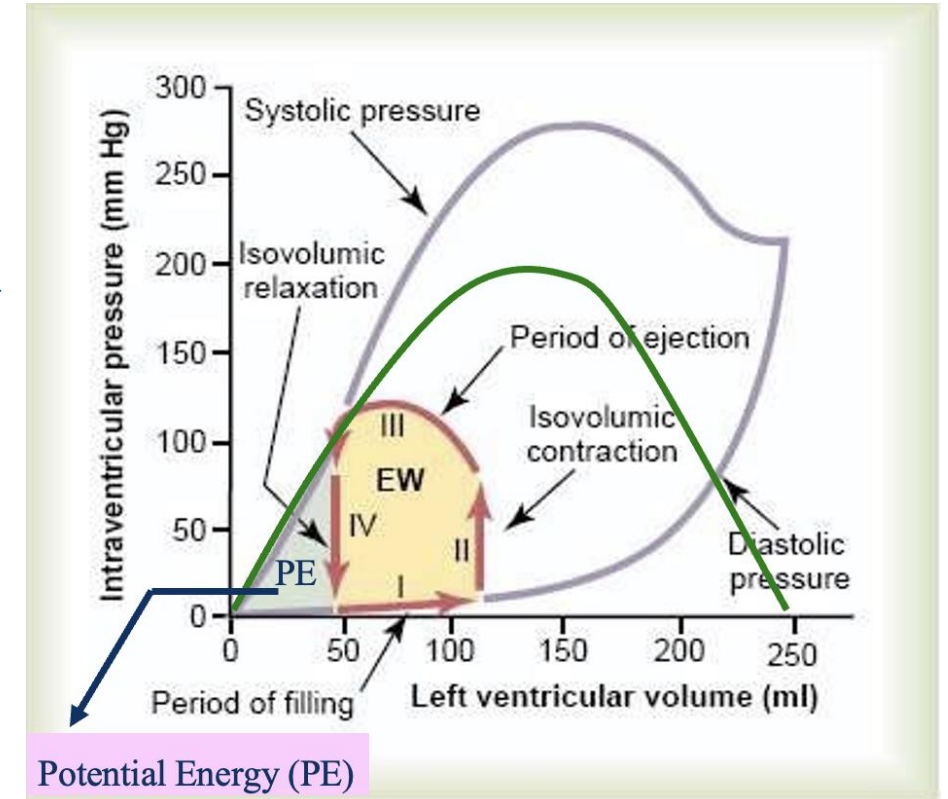
Pressure-Volume Loops Explained IV (last one fast one)

Total energy = External Work + Kinetic Energy

To increase the ejection fraction, the **end-systolic volume** must be lowered (shift to the left). This shift will be at the expense of the **potential energy**, which is the energy stored in the system that can be utilized to increase the ejection fraction. The potential energy is shown on the graph as the area extending from 0-50mL under the diastolic pressure curve.

$$\text{Kinetic Energy} = \frac{1}{2} \text{ Mass} \times \text{Velocity}^2$$

Under normal conditions, **kinetic energy** does not constitute more than 1% of the total energy. This is because when the semilunar valve opens, the velocity is very low, and the mass stays the same. However, in **aortic stenosis**, the blood moves with a **high velocity** through the **narrowed** stenosed valve, thus increasing the KE value. Now, the kinetic energy becomes significant as it may constitute up to 50% of the total energy. This increased workload emphasizes the importance of timely management of severe stenosis.



Valvular Function

- To prevent back-flow.
- Chordae tendineae are attached to A-V valves.
- Papillary muscle, attached to chordae tendineae, contract during systole and help prevent back-flow.
- Because of smaller opening, velocity through aortic and pulmonary valves exceed that through the A-V valves.

Valvular Function (cont'd)

- ❑ Most work is external work or pressure-volume work.
- ❑ A small amount of work is required to impart kinetic energy to the heart ($1/2 mV^2$).
- ❑ What is stroke-volume in previous figure?

Remember: $SV = EDV - ESV$

So it's the **width of the loop** between :

- (largest volume of blood in ventricles $\rightarrow$ EDV)
- (smallest volume after ejection $\rightarrow$ ESV)

- ❑ External work is area of Pressure-Volume curve.

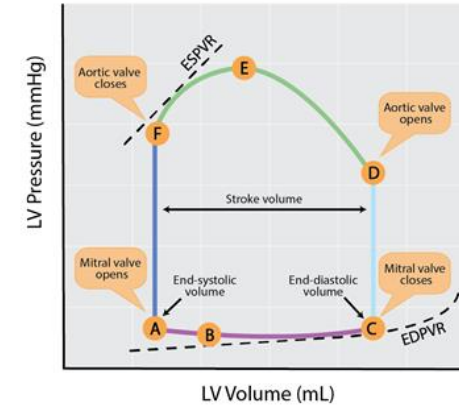
Work = area under the PV loop, often approximated it as : $\text{work} = \text{width} * \text{MAP}$

- Width = stroke volume
- MAP = mean arterial pressure during ejection

But “mean pressure” here **does NOT** mean $(EDP + ESP) / 2$, because systole and diastole are **not equal in duration**. In a normal cardiac cycle, systole lasts about 0.3 seconds, while diastole lasts about 0.5 seconds, so diastole occupies a **longer fraction** of the cycle. Therefore, the contribution of each phase to the mean pressure must be **weighted by time**.

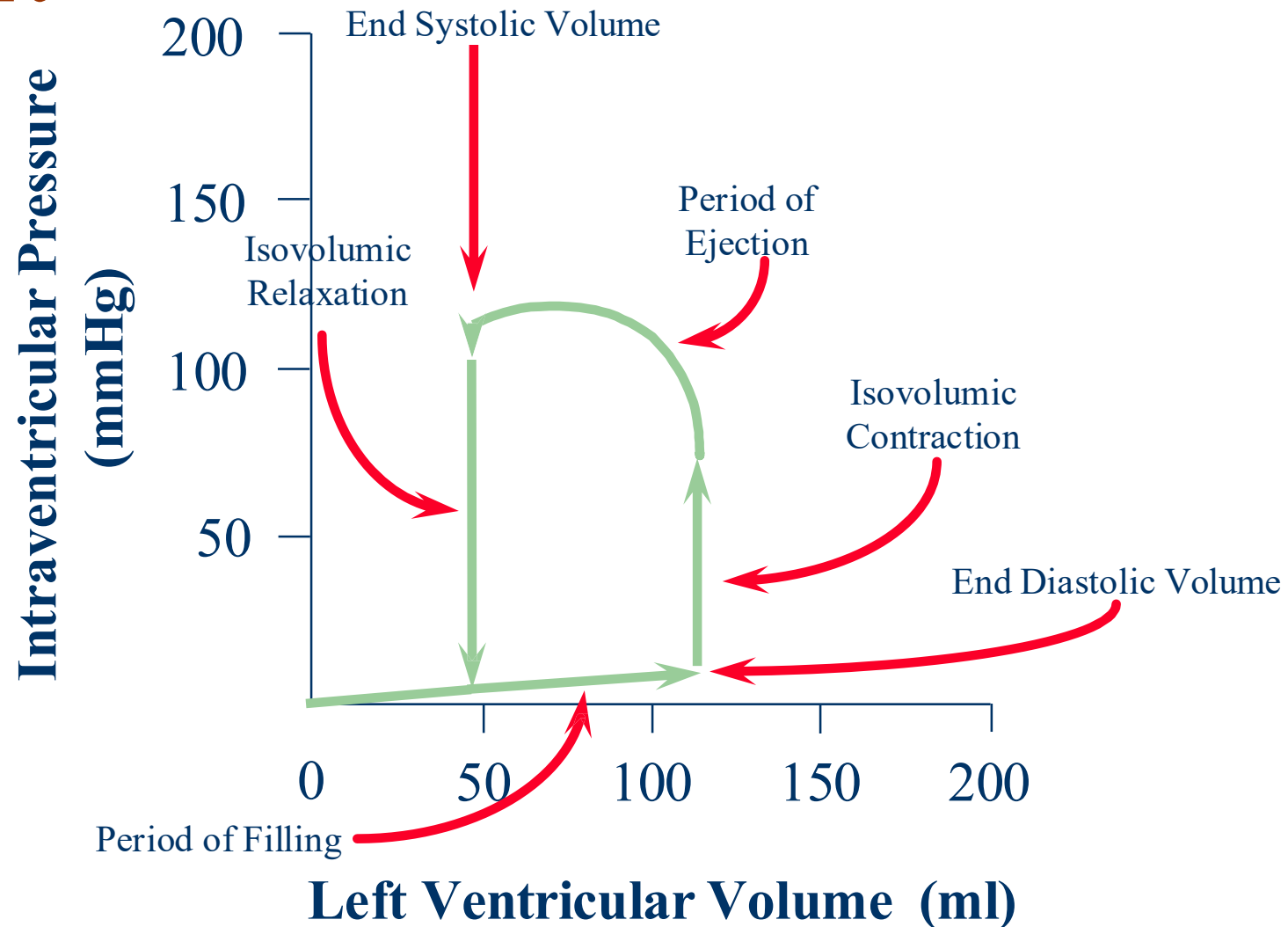
MAP $\approx$ 1/3 systolic pressure + 2/3 diastolic pressure.

- ❑ Work output is affected by “preload” (end-diastolic pressure) and “afterload” (aortic pressure).



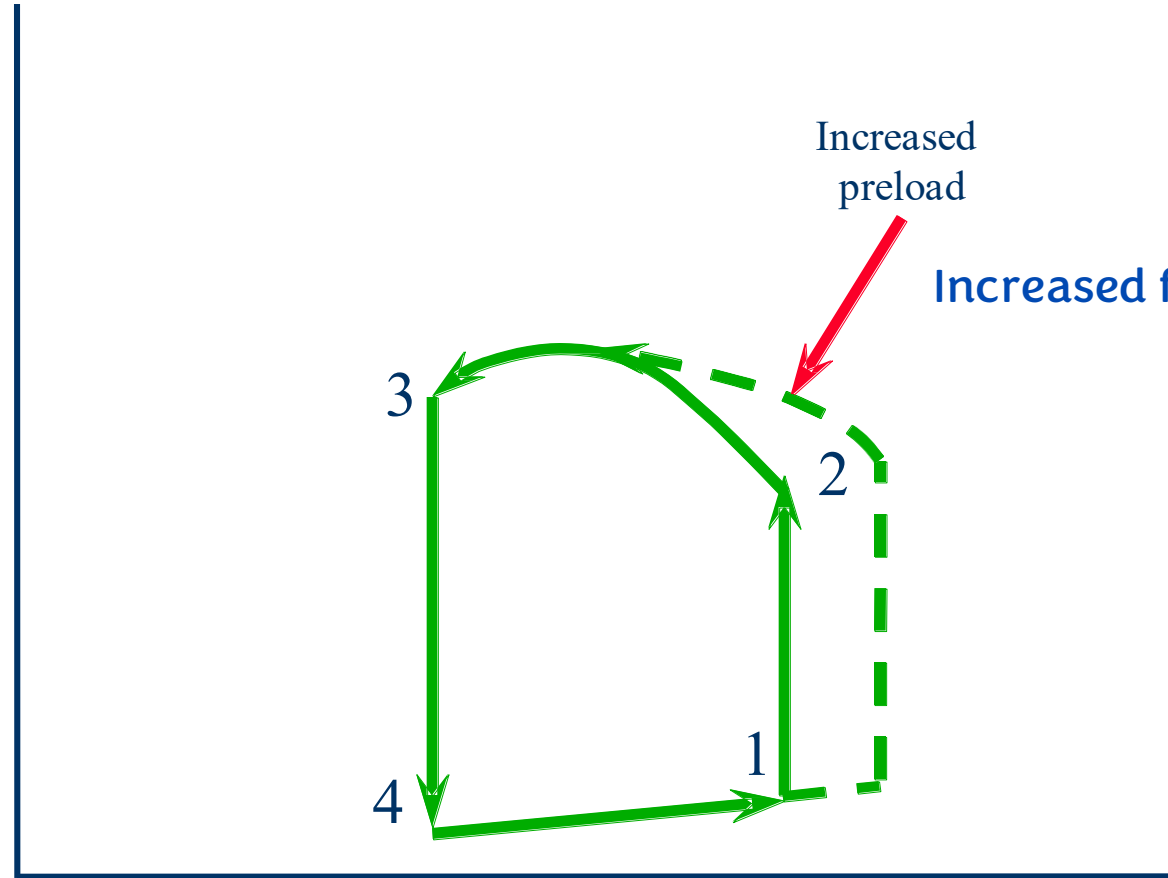
Additional photo shows width/stroke volume

Work Output of the Heart



A

Left Ventricular Pressure

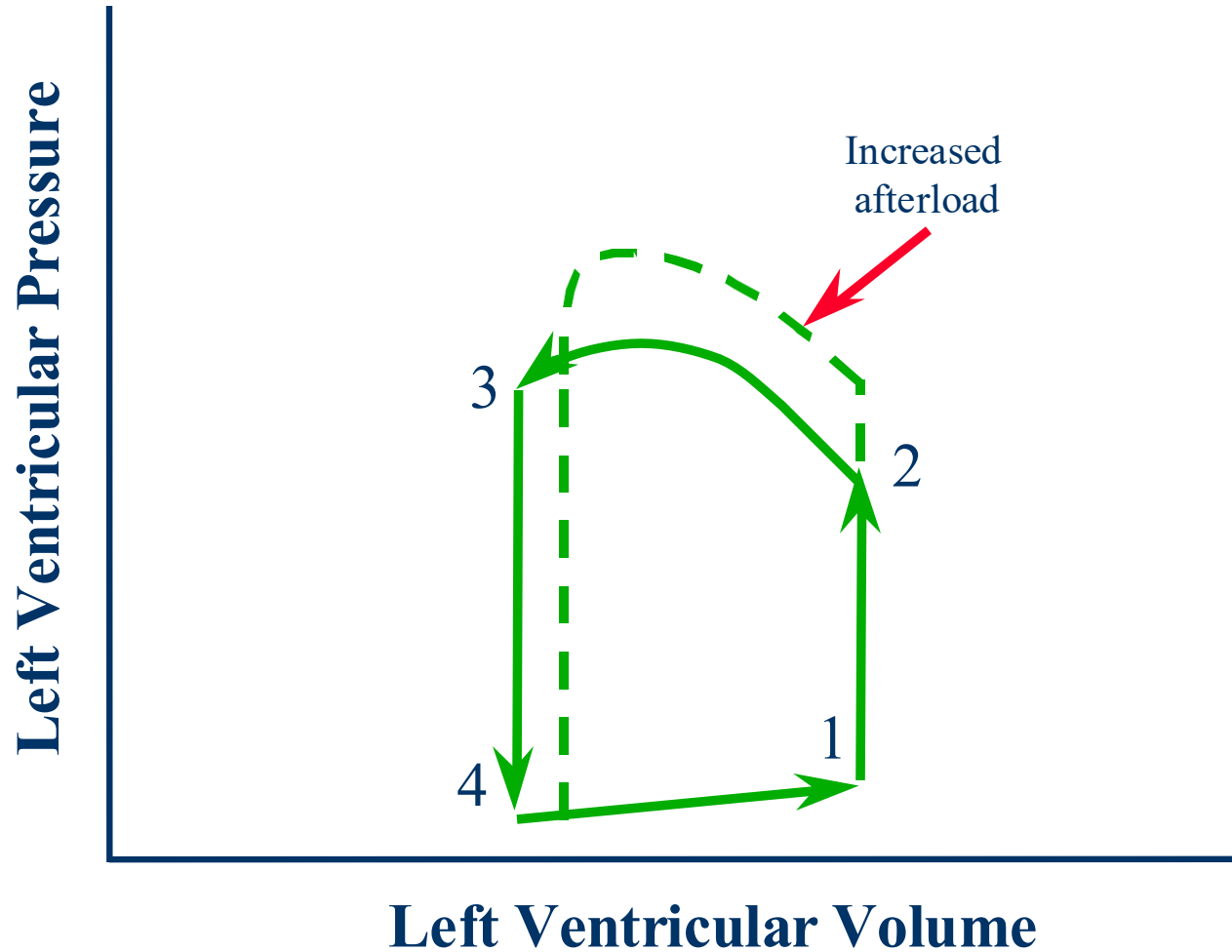


Increased
preload

Increased frank-starling load

Left Ventricular Volume

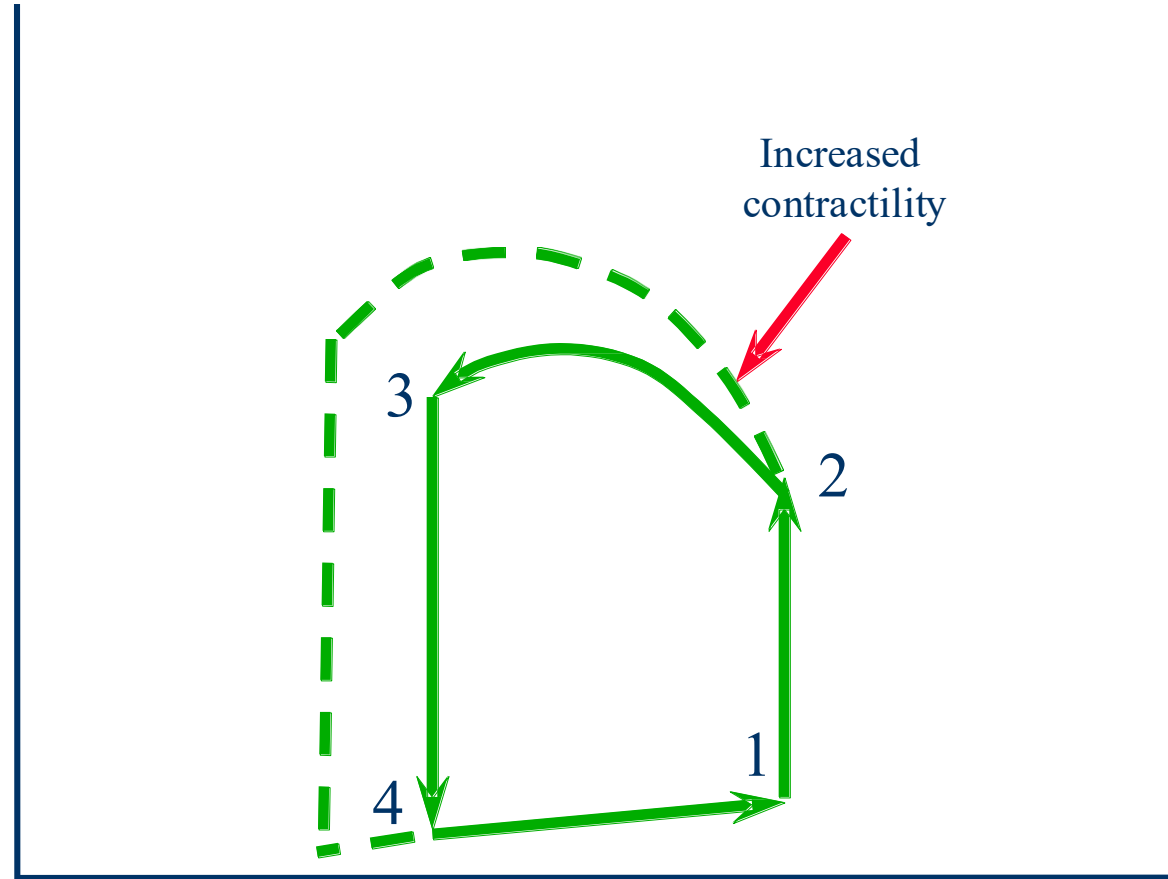
B



- ✓ Increased afterload decreases stroke volume.
- ✓ If the same stroke volume to be maintained, higher energy should be exerted by the left ventricle to overcome the high pressure of the aorta.

C

Left Ventricular Pressure



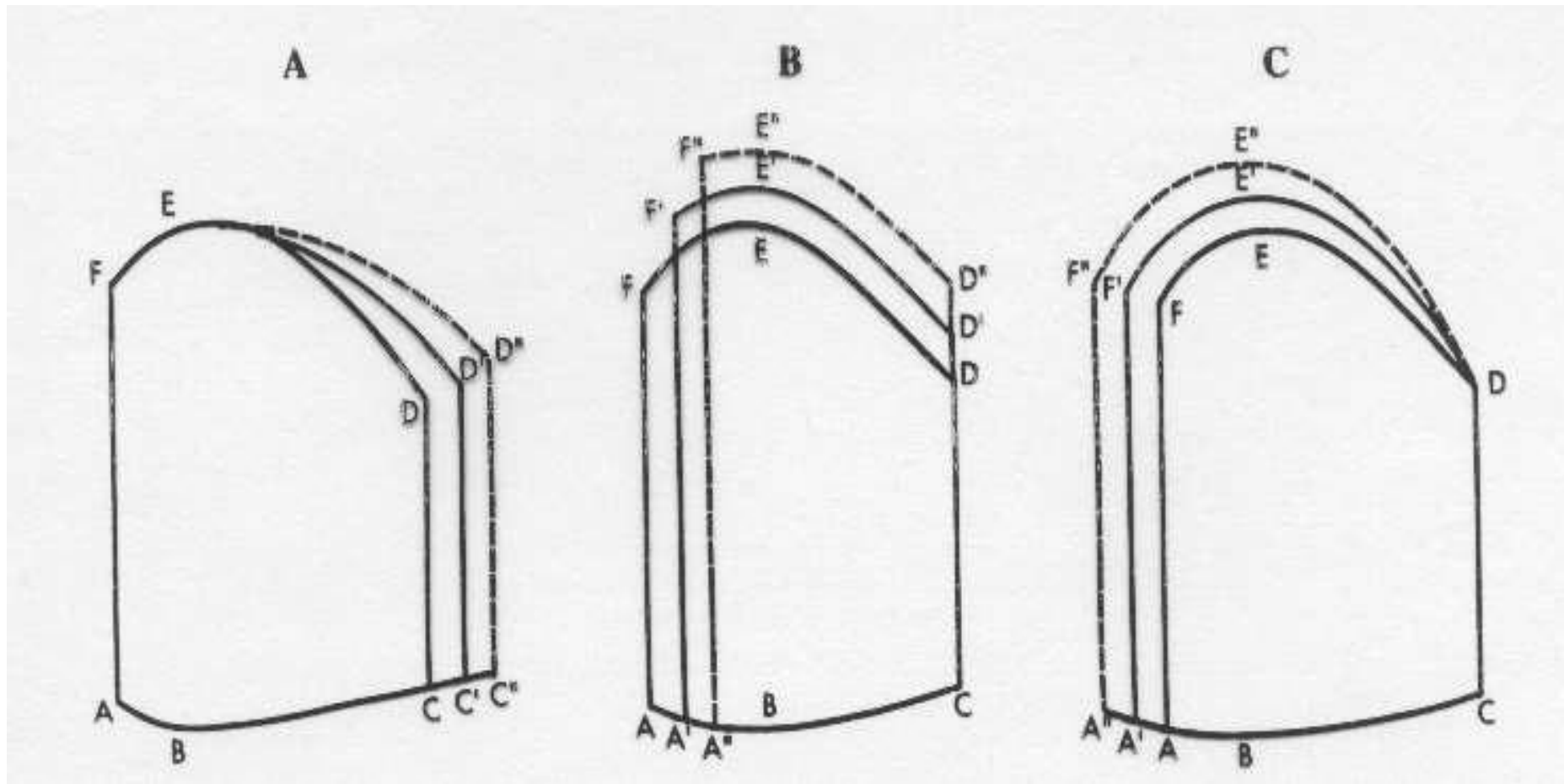
Increased
contractility

Left Ventricular Volume

Curve c

- ✓ positive inotropy, increased contractility while the EDV is fixed; the ESV is decreased.
- ✓ $\uparrow$ **Contractility** $\rightarrow$ $\uparrow$ **stroke work**, $\downarrow$ **potential energy**
- ✓ contractility = slope of (changed pressure over time) = dP/dt , not easy to be calculated manually and requires computerized methods.
- ✓ More of the ventricle's total mechanical energy is **converted into ejection**.

PRESSURE/VOLUME RELATIONSHIPS UNDER DIFFERENT CONDITIONS



PRELOAD



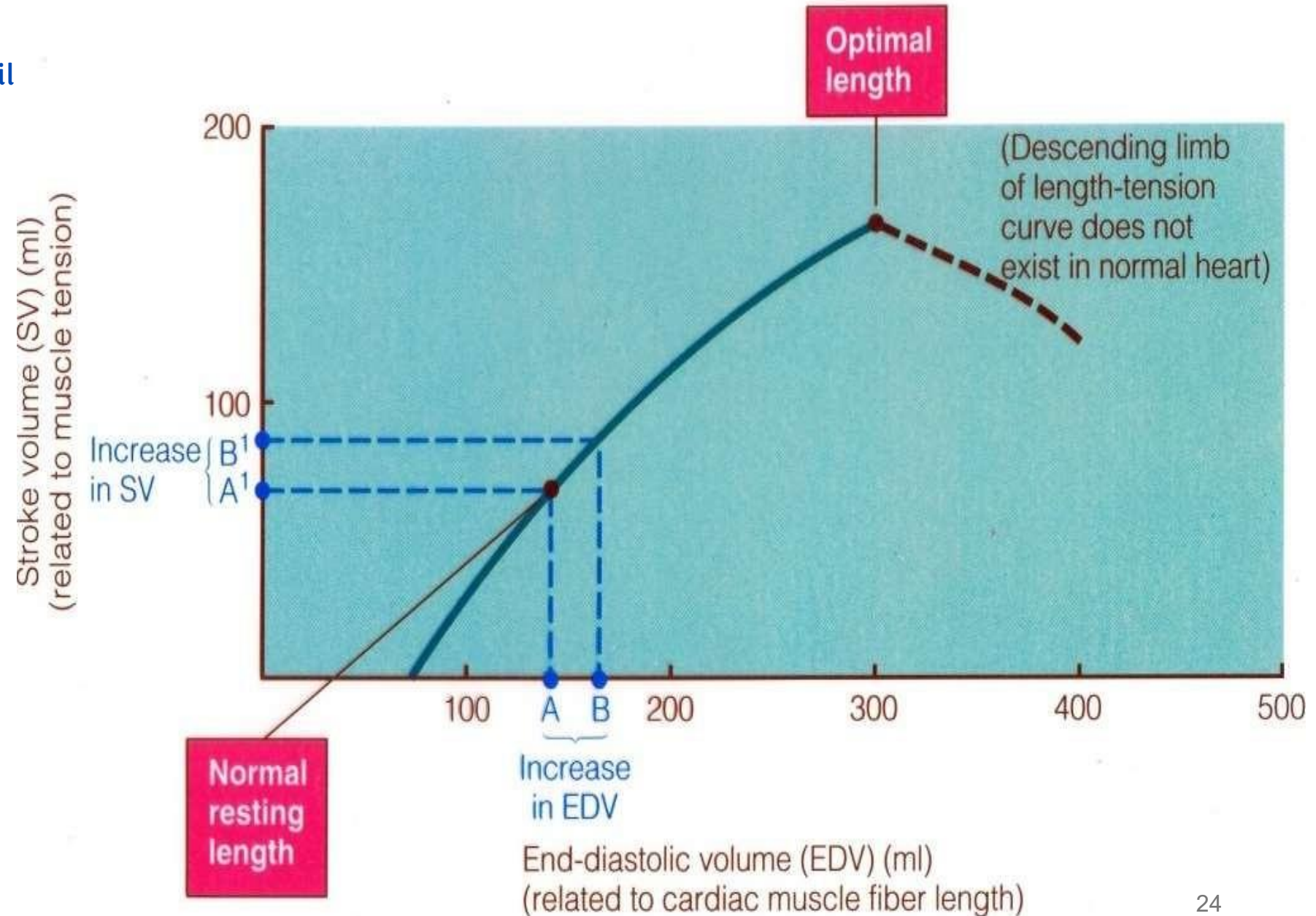
AFTERLOAD



CONTRACTILITY

Intrinsic Control of Stroke Volume (Frank-Starling Curve)

- Within physiological limits (until the muscle reaches the optimal length), an increase in passive tension increases total tension (**SV increases**).
- **exceeding** optimal limit $\Rightarrow$ decreases total tension $\Rightarrow$ SV decreases $\Rightarrow$ **Heart Failure**.



Regulation of Heart Rate

- Positive chronotropic factors increase heart rate
- Negative chronotropic factors decrease heart rate

Regulation of Heart Rate: Autonomic Nervous System

- Again: if both are cut, increased heart rate and decreased contractility.
- Sympathetic nervous system (SNS) stimulation is activated by stress, anxiety, excitement, or exercise
- Parasympathetic nervous system (PNS) stimulation is mediated by acetylcholine and opposes the SNS
- PNS dominates the autonomic stimulation, slowing heart rate and causing vagal tone

Atrial (Bainbridge) Reflex

- Atrial (Bainbridge) reflex – a sympathetic reflex initiated by increased blood in the atria
 - Causes stimulation of the SA node
 - Stimulates **baroreceptors** in the atria, causing **increased SNS stimulation**

- The **atria are very compliant but small**, so even a small **increase or decrease in volume** changes the **atrial pressure**.
- When atrial pressure rises:
 - 1) **SA node stimulation** increasing the heart rate.
 - 2) **Atrial baroreceptors** detect the pressure and trigger increased sympathetic nervous system activity, further increasing the heart rate.
- This reflex ensures that the extra venous return is pumped out efficiently, **preventing blood from pooling in the atria**.

Chemical Regulation of the Heart

- The hormones epinephrine and thyroxine increase heart rate
- Intra- and extracellular ion concentrations must be maintained for normal heart function

Important Concepts about Cardiac Output (CO) Control

- Cardiac output represents the total flow of blood pumped by the heart (to the pulmonary circulation and the systemic circulation, as the amount of blood returns to the heart is the same that goes to the pulmonary circulation, gets oxygenated, to the heart again, to the systemic circulation).
- Variations in CO between individuals are often adjusted for body surface area (BSA), which accounts for age and weight differences. Then the Cardiac output is measured by (L/min/m²).
- Cardiac output is proportional to tissue blood flow, and tissue blood flow is in turn proportional to oxygen consumption. Conceptually, CO can be treated like an electrical current controlled by Ohm's law:
flow = pressure difference / resistance.
- Flow of CO = the **pressure difference** (between the aorta and the right atrium)/**resistance** (the total peripheral resistance of the systemic circulation).
- ✓ The aortic pressure is calculated as the mean arterial pressure (MAP), which is again, 1/3 systolic pressure+ 2/3 diastolic pressure, while the right atrium pressure is nearly zero, so its neglected.
- ✓ Therefore, Cardiac output can be expressed as: **CO= MAP/PVR**, [CO]= liter /min.

Important Concepts about Cardiac Output (CO) Control

- Cardiac Output is the sum of all tissue flows and is affected by their regulation (CO = 5L/min, cardiac index = 3L/min/m² (surface area in m²)).
- CO is proportional to tissue O₂ use.
- CO is proportional to 1/TPR when AP is constant.
- **$CO = (MAP - RAP) / TPR$**

Cardiac output curves

1. Right atrial pressure and right ventricular volume:

The right atrium receives blood from all the systemic veins, so the pressure in the atrium (**central venous pressure, CVP**) reflects the volume of blood returning to the heart. When right ventricular volume increases, the right atrium must push harder to fill the ventricle, which raises right atrial pressure and consequently leads to increase in right ventricular volume.

2. Cardiac output vs right atrial pressure (Frank-Starling curve):

If you plot **cardiac output (CO)** on the y-axis and **Rt. Atrial pressure** on the x-axis, you get a curve that shows:

At **Rt. Atrial pressure = 0**, CO is about **5 L/min** (resting CO).

As **right atrial pressure** increases, EDV increases. According to the **Frank-Starling law**, even without external stimulation, this mechanism alone can raise cardiac output (CO) up to **15 L/min**.

The difference between (15L/min) and the resting CO is called cardiac reserve, and it equals 10 L/min.

3. Effect of inotropic changes:

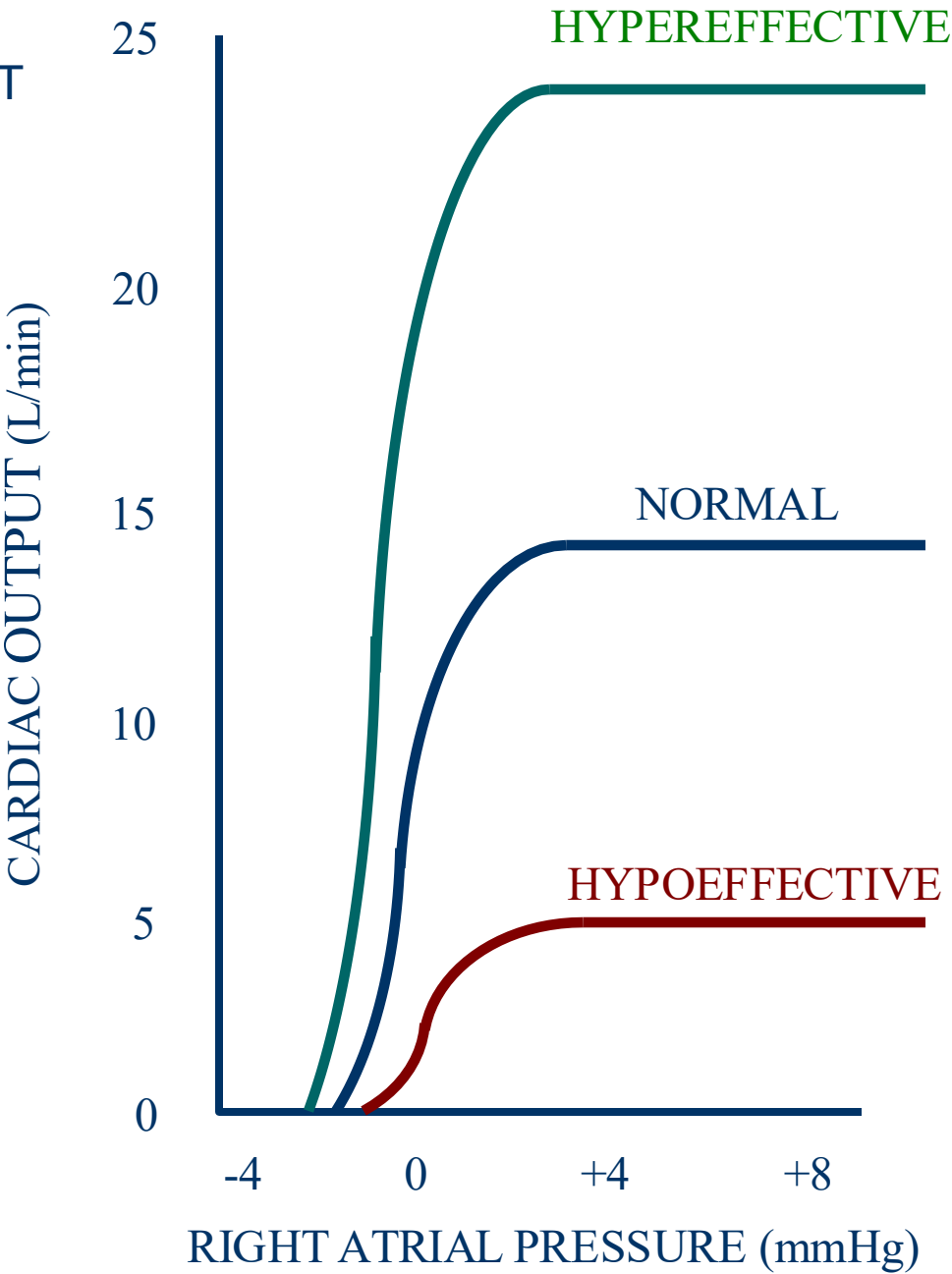
Positive inotropy (sympathetic stimulation) makes the heart **more effective at the same EDV**, lifting the curve upwards, **HYPEREFFECTIVE heart** (in the next slide).

- Normal hyper-effective heart: CO ~25 L/min.

- Athletes: CO ~35 L/min.

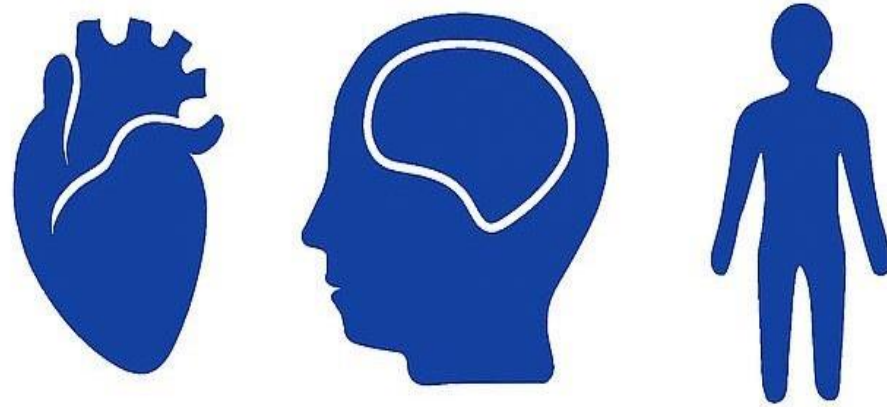
- **Negative inotropy** (sympathetic inhibition) makes the heart **less effective**, **HYPOEFFECTIVE heart** (in the next slide).

CARDIAC OUTPUT
CURVES



Thank You





**PHYSIOLOGY
QUIZ
LECTURE 8**

Resources:

Doctor Faisal's lecture.

Additional resources:

Gyuton and Hall

Chapter 3

Pages 120-126

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Corrections from previous versions:

Versions	Slide # and Place of Error	Before Correction	After Correction
V0 → V1			
V1 → V2			