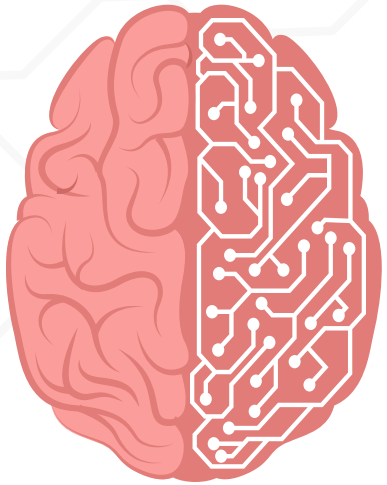


Physiology - CVS

Done By

Dana Alkhateeb, Raneem Al-Zoubi,
Hani Titi, Dana Tarawneh

Corrected By

Dana Alkhateeb

Heart Pump and Cardiac Cycle 2

Quick reminder

Last time we discussed the control of stroke volume and cardiac output.

Three factors control the stroke volume:

1.Preload, or the degree of the stretch ,of cardiac muscle cells before they contract

- The Frank-Starling Law states that, within physiological limits, the higher the preload the higher the stroke volume. in another way: within physiological limit an increase in the length of the muscle before it contracts (resting length, Resting tension , passive tension) increases the force of contraction. However, we cannot measure the length in the heart, but we can measure the volume /pressure of the ventricle before it contracts and this is what we refer to as the preload.
- Preload is affected by the heart rate and the blood volume

2.Contractility

3.Afterload

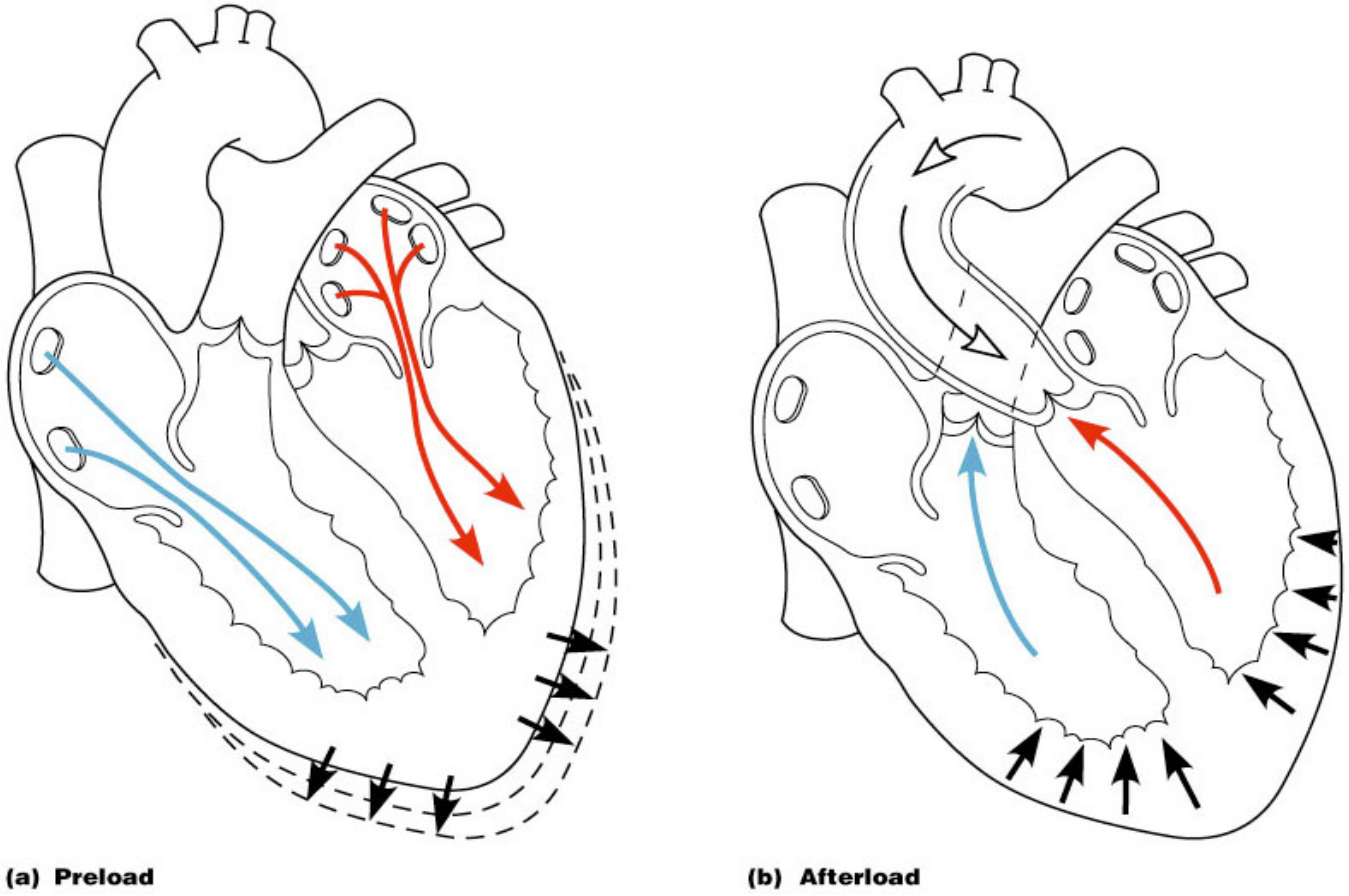
Frank-Starling Law of the Heart

- Preload, or degree of stretch, of cardiac muscle cells before they contract is the critical factor controlling stroke volume
- Slow heartbeat and exercise increase venous return to the heart, increasing SV
- Blood loss and extremely rapid heartbeat decrease SV

Frank-Starling Mechanism

- Within physiological limits the heart pumps all the blood that comes to it without excessive damming in the veins.
- Extra stretch on cardiac myocytes makes actin and myosin filaments interdigitate to a more optimal degree for force generation.

Preload and Afterload



(a) Preload

(b) Afterload

The left figure indicates the preload, the amount of blood found in the ventricle before it contracts. The ventricles are dilated and full of blood.

The right figure indicates the afterload, the force that the ventricle has to exert to open the semilunar valves.

To do this, the force that has to develop in the right and left ventricles should be higher than the diastolic pressure in the pulmonary artery and aorta, respectively

Cardiac Output

Few notes

Increased end-diastolic volume (stretches the heart)

Increased PRELOAD

Within limits, cardiac muscle fibers contract more forcefully with stretching (Frank–Starling law of the heart)

Positive inotropic agents such as increased sympathetic stimulation; catecholamines, glucagon, or thyroid hormones in the blood; increased Ca^{2+} in extracellular fluid

Increased CONTRACTILITY

Positive inotropic agents increase force of contraction at all physiological levels of stretch

Decreased arterial blood pressure during diastole

Decreased AFTERLOAD

Semilunar valves open sooner when blood pressure in aorta and pulmonary artery is lower

Increased STROKE VOLUME

The cardiac output increases with increasing stroke volume, heart rate, or both.

Increased CARDIAC OUTPUT

Increased HEART RATE

Increased sympathetic stimulation and decreased parasympathetic stimulation

Catecholamine or thyroid hormones in the blood; moderate increase in extracellular Ca^{2+}

Infants and senior citizens, females, low physical fitness, increased body temperature

NERVOUS SYSTEM
Cardiovascular center in medulla oblongata receives input from cerebral cortex, limbic system, proprioceptors, baroreceptors, and chemoreceptors

CHEMICALS

OTHER FACTORS

when you multiply heart rate and stroke volume you get the cardiac output.

catecholamines:Epinephrine and NE (postganglionic neurotransmitters in the Sympathetic NS)

glucagon (an endocrine hormone secreted by the pancreas)

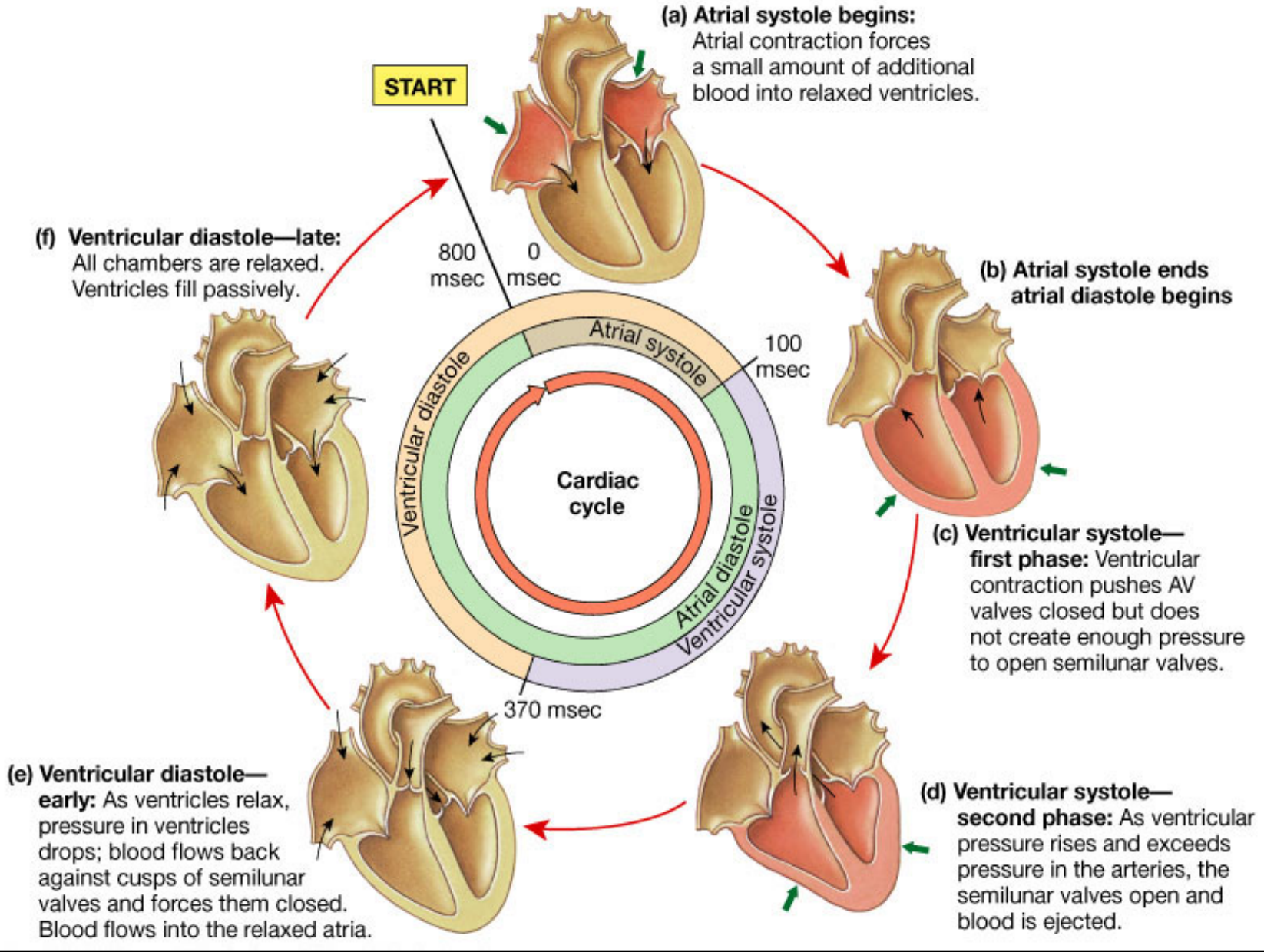
thyroid hormones in the blood (T3 and T4)

Patients with hyperthyroidism have tachycardia.

patients with fever have higher heart rate, which sometimes may lead to lower stroke volume

Patients who are nervous (=increased sympathetic stimulation) also have increased heart rate.

Phases of the Cardiac Cycle



The atrial systole only imparts less than 25% of the ventricular volume .

This is because the AV valves remain open before the atrial contraction, so even if the atria do not contract , a large amount of blood still passes from the atria into the ventricles. In fact, atrial systole is not essential for the normal functioning of the heart.

Extrinsic Factors Influencing Stroke Volume

- Contractility is the increase in contractile strength, independent of stretch and EDV
- Increase in contractility comes from:
  - Increased sympathetic stimuli

    You know sympathetic stimulation has positive inotropic and positive chronotropic effects
  - Certain hormones

    Like glucagon and thyroid hormones (positive chronotropic agents)
  - Ca^{2+} and some drugs

    such as digoxin, a positive inotropic agent

Extrinsic Factors Influencing Stroke Volume

- Agents/factors that decrease contractility include:
  - Acidosis

    Decreased pH inhibits cellular enzymes and this will cause a depression in cellular activities
  - Increased extracellular K^+

    hyperkalemia
  - Calcium channel blockers

    By blocking calcium influx through the slow calcium channels, , intracellular calcium levels will decrease ,so the force of contraction will be lower

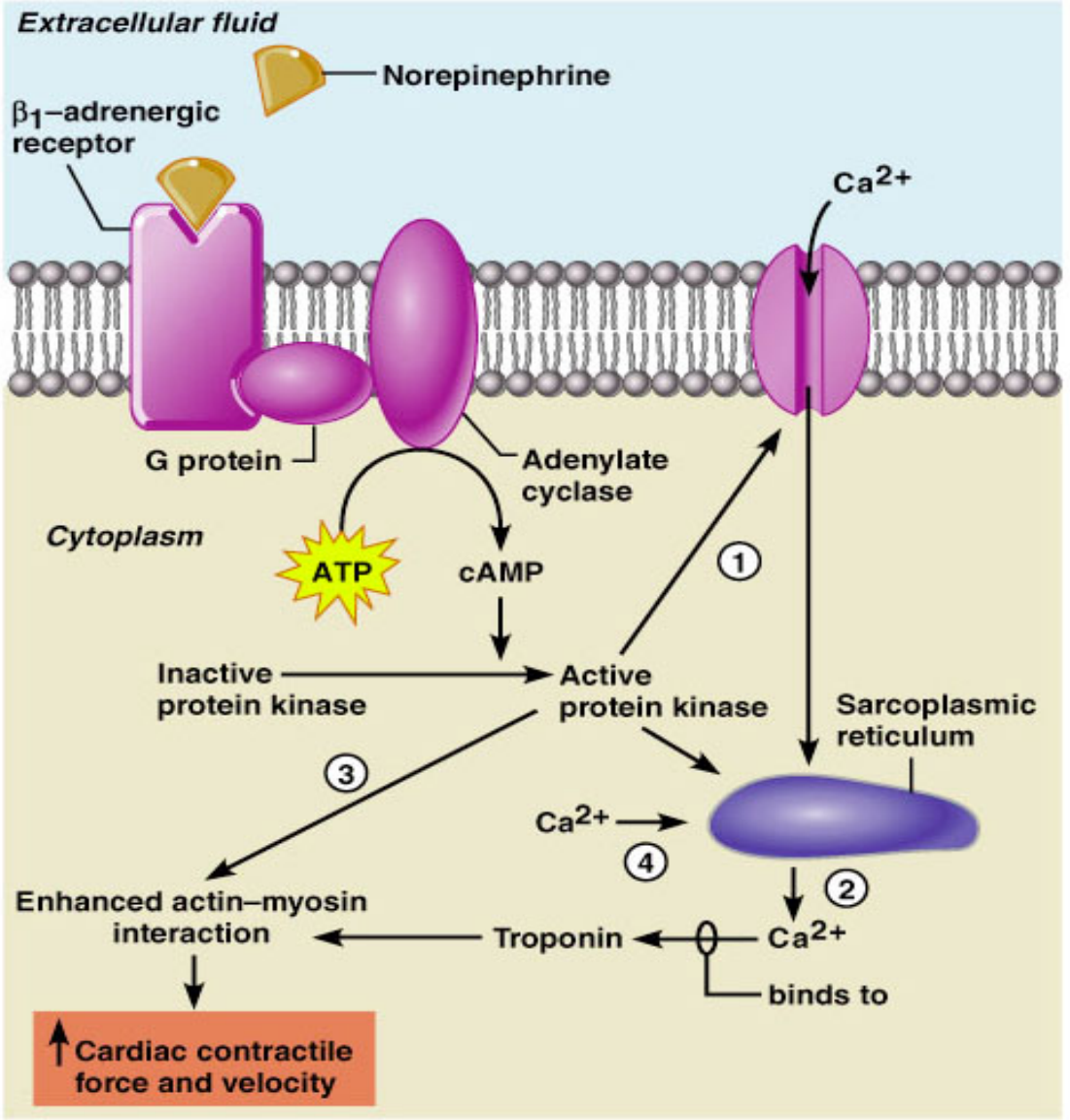
Contractility and Norepinephrine

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

Catecholamines are inotropic agents
β1 receptors in the heart bind catecholamines (Epi , NE) These receptors are G-protein coupled receptors, and when bound by norepinephrine, the alpha subunit of the G protein dissociates. The alpha subunit then activates adenylate cyclase (a membrane enzyme), which converts ATP to cAMP. cAMP activates PKA, a cAMP-dependent protein kinase.

Active PKA activates calcium channels to increase influx of Ca2+. More Ca2+ influx leads to higher force of contraction . Also It enhance the interaction between actin and myosin ,which increases cardiac contractility . More Ca2+ influx means more Ca2+ release from the sarcoplasmic reticulum , which leads to a higher force of contraction

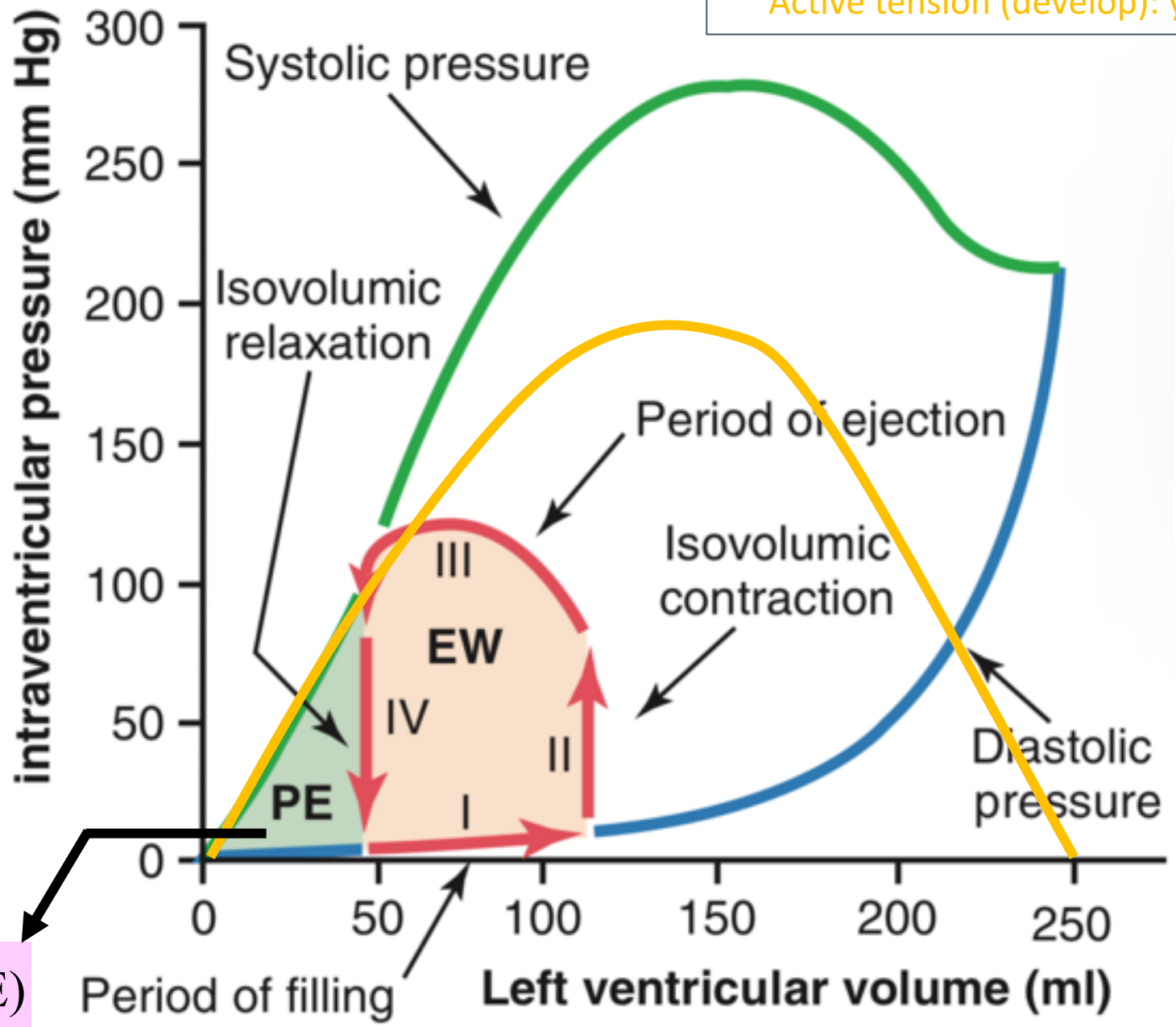
Activated PKA phosphorylates phospholamban, a sarcoplasmic reticulum protein. This speeds up the uptake of Ca2+ through the SR Ca2+ pump. This shortens the time for relaxation, which increases the heart rate.



The control of the cardiac cycle in a mathematical representation

Passive tension (Resting tension) blue curve
Total tension (Systolic tension): green curve
Active tension (develop): yellow curve

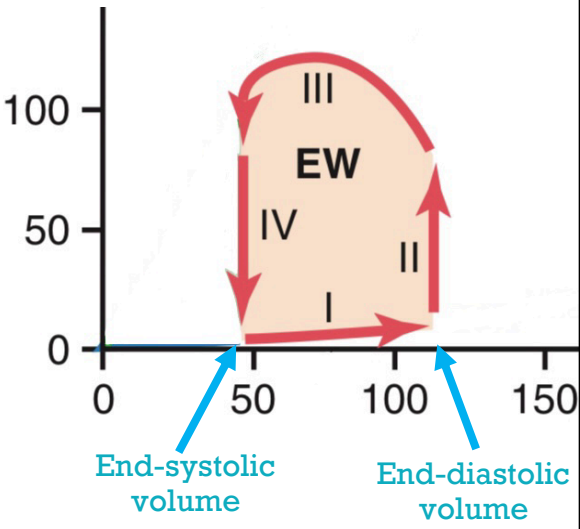
It represents:
the left ventricular volume (or the length of the muscle) on the x-axis
intraventricular pressure (or the tension) on the y-axis
(volume-pressure diagram)



Potential Energy (PE)

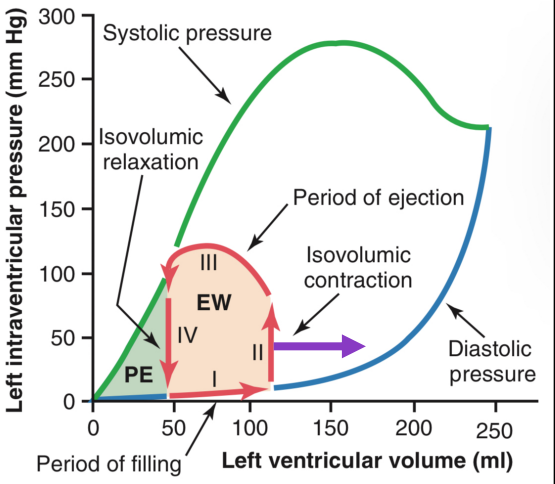
One cardiac cycle:

- **Phase I: filling**: starts from the end systolic volume and then when an AV valve opens, there is filling of the blood to the ventricle. there isn't a big increase in the pressure until reaching the end diastolic volume
- **Phase II: isovolumic contraction**: now the first phase of of contraction is isovolumic contraction, the volume of the ventricle does not change but there is change in the pressure until the semilunar valve opens and there is ejection of blood .
- **Phase III: ejection**: during ejection, the pressure increases and the volume of the ventricle decreases
- **Phase IV: isovolumic relaxation**: the volume doesn't change but the pressure decreases



The cycle continues from phase I, phase II, phase III, reaching phase IV

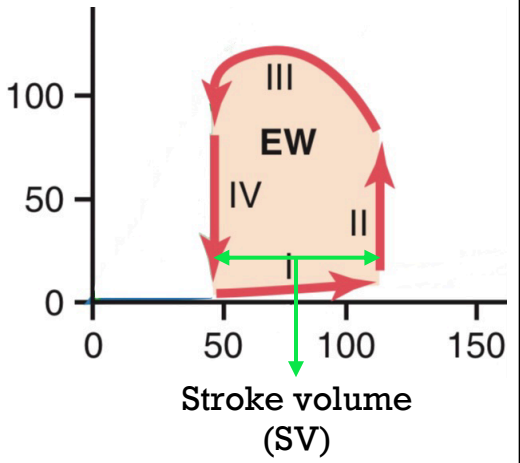
This is one cardiac cycle but still this cardiac cycle can go up (extend to the right in the diagram) (purple arrow)
the whole diagram is drawn to represent the ability of the heart to change its resting tension, total tension and active tension.
so there might be an increase the in diastolic volume and the curve follows the changes in the resting tension or the diastolic pressure and accordingly these are the changes in the total tension (systolic pressure) that can occur and active tension = total tension - passive tension (resting tension) AT = TT - PT



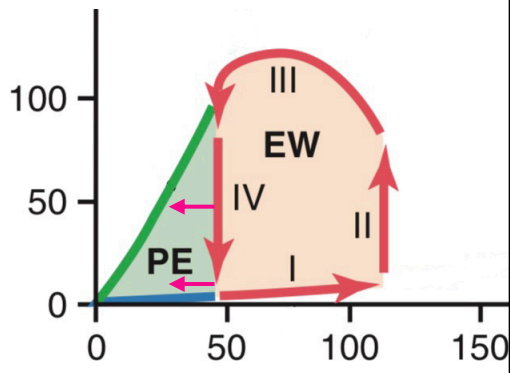
The area under the curve: is the energy that can be spent to move the blood inside the circulation which is called the external work (Ew) so the external work is the energy that can be used to move the blood inside the circulation and it equals volume multiplied by pressure

Ew = V*P

- Volume (V): is the stroke volume (green arrow)
- Pressure (P) = the mean change in systolic - the mean change in diastolic



PE (potential energy): the energy that is stored in the system and it can be used to increase the stroke volume without increasing the end diastolic volume, how?
By taking a part of this potential energy (moving to the left) (pink arrow)
so what do we mean if the end diastolic volume is fixed but the stroke volume is increased? this means that there is an increase in the contractility, this is increase in the ejection fraction
so an increase in the contracting is to use part of the potential energy that is stored in the system



This is one cardiac cycle

A: The AV valve opens
- When it opens, the filling phase starts

B: The filling phase

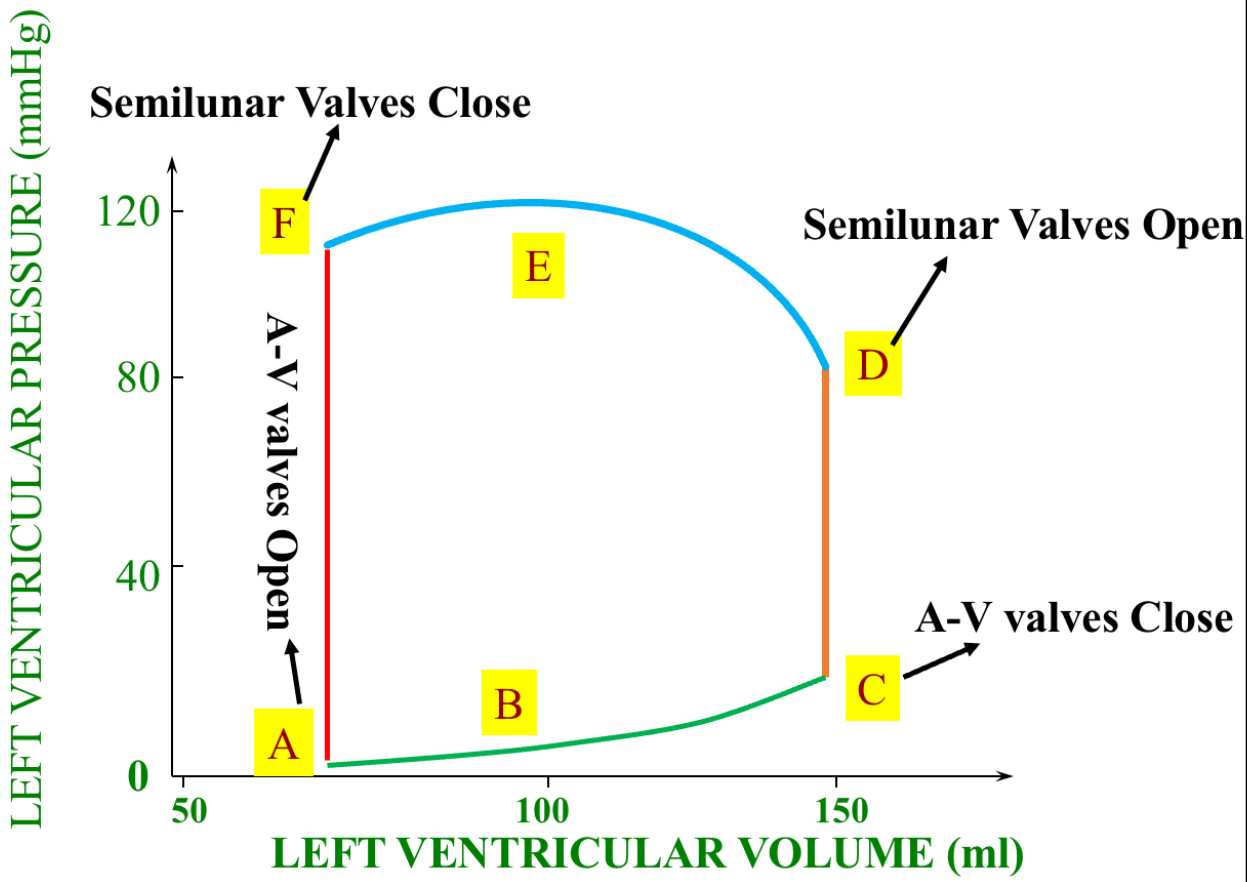
C: The AV valve closes
- When it closes, the isovolumic contraction starts
- When the AV valve closes, we have heart sound number one (S1)

D: The semilunar valve opens
- When it opens, ejection of blood starts and the decrease in the volume of the ventricle

E: The ejection phase
- here there is increase in pressure and decrease in volume

F: the semilunar valve closes
- when the semilunar valve closes, we have S2

LEFT VENTRICULAR PRESSURE/VOLUME P/V LOOP



Valvular Function

- To prevent back-flow.

What prevents the backflow of the AV valves to the atria?

- 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).
  1/2 Mass*Velocity^2
  - Normally, this kinetic energy is negligible, but this velocity and this kinetic energy can be important when there is **aortic stenosis**
  - Sometimes this kinetic energy might form around 50% of the total energy because in aortic stenosis, the aortic valve is narrowed so to move the same amount of blood through a narrow orifice of aortic valve, you need very large amount of kinetic energy.
  - That's why aortic stenosis can be very dangerous sometimes if the orifice is so narrow because the left ventricle of the heart has to spend a lot of energy to move the blood through the orifice and have the same stroke volume.
- What is stroke-volume in previous figure? (remember the green double-sided arrow)
- External work is area of Pressure-Volume curve.
- Work output is affected by "preload" (end-diastolic pressure) and "afterload" (aortic pressure).

Work Output of the Heart

Area under the curve represents external work (EW)

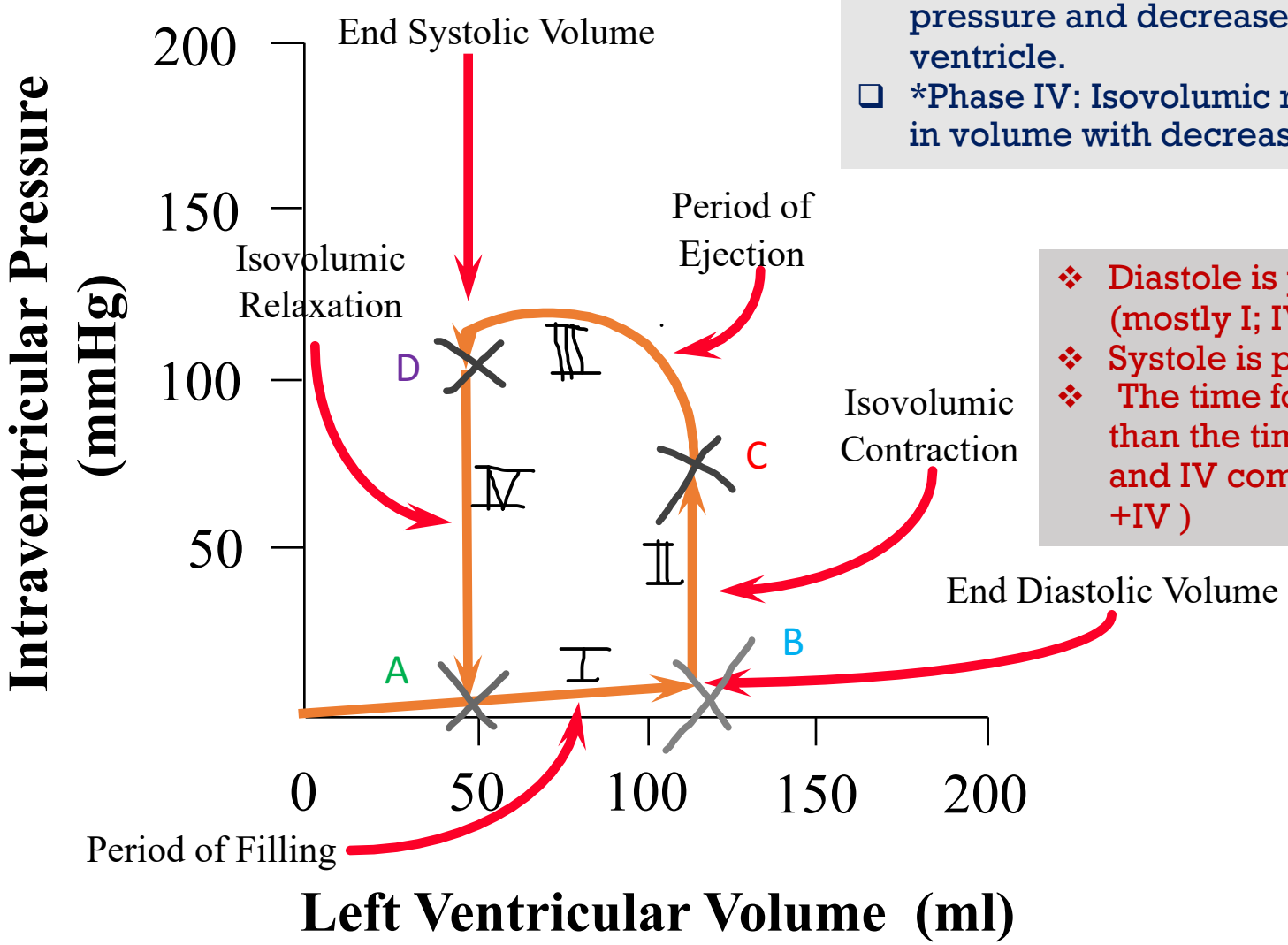
A - Green X : the point at which AV valve opens .

B - EDV : the point at which AV valve closes. Where we hear S1.

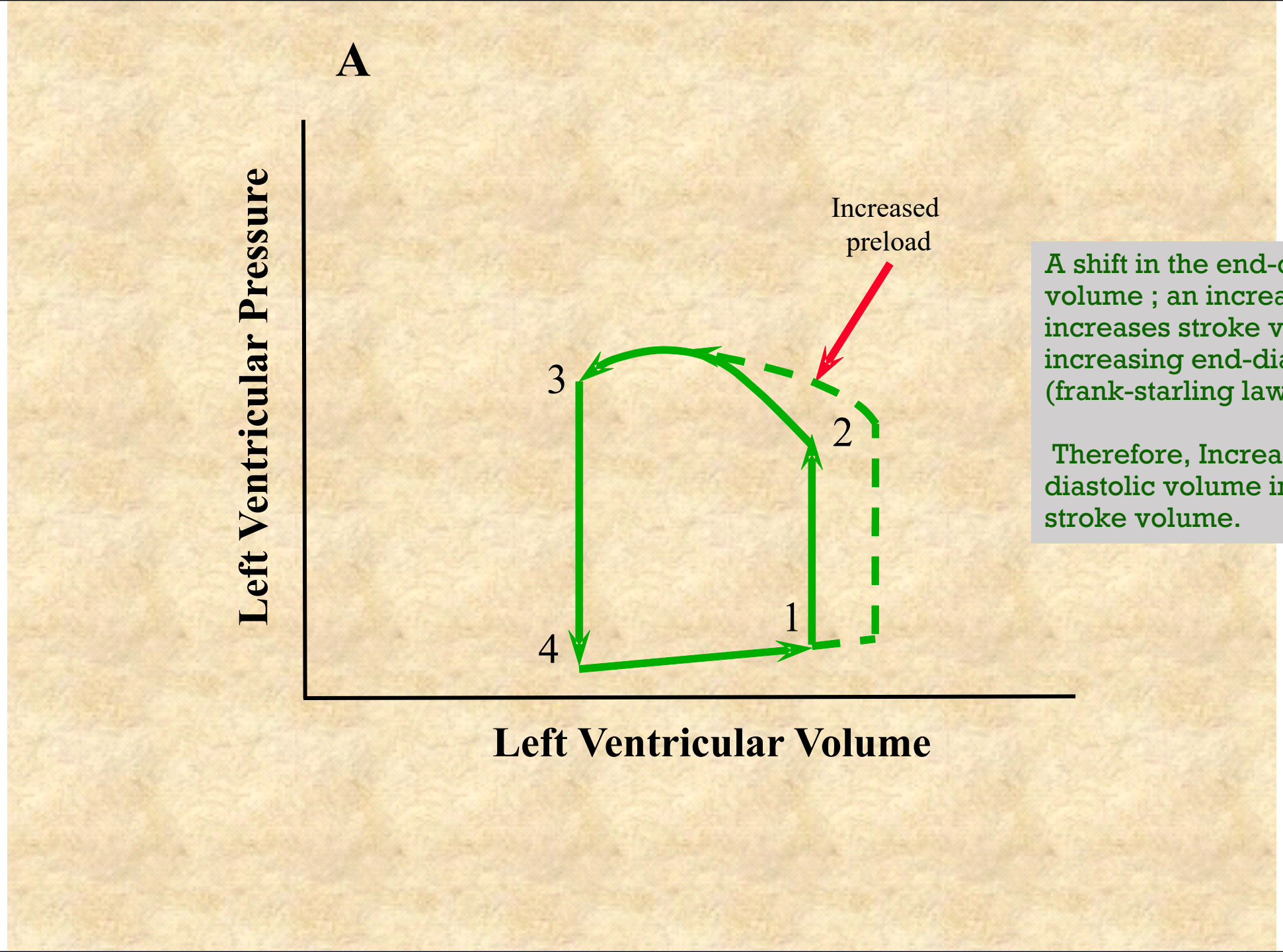
C - Red X : the point at which the semilunar valve opens.

D - Purple X : the point at which semilunar valve closes . Where we hear S2.

- *Phase I: Period of blood filling in the ventricle. There is little increase of pressure.
- *Phase II: Isovolumic contraction; no change in volume, only change in pressure.
- *Phase III: Period of ejection; increased pressure and decrease in volume of the ventricle.
- *Phase IV: Isovolumic relaxation; no change in volume with decreased pressure.



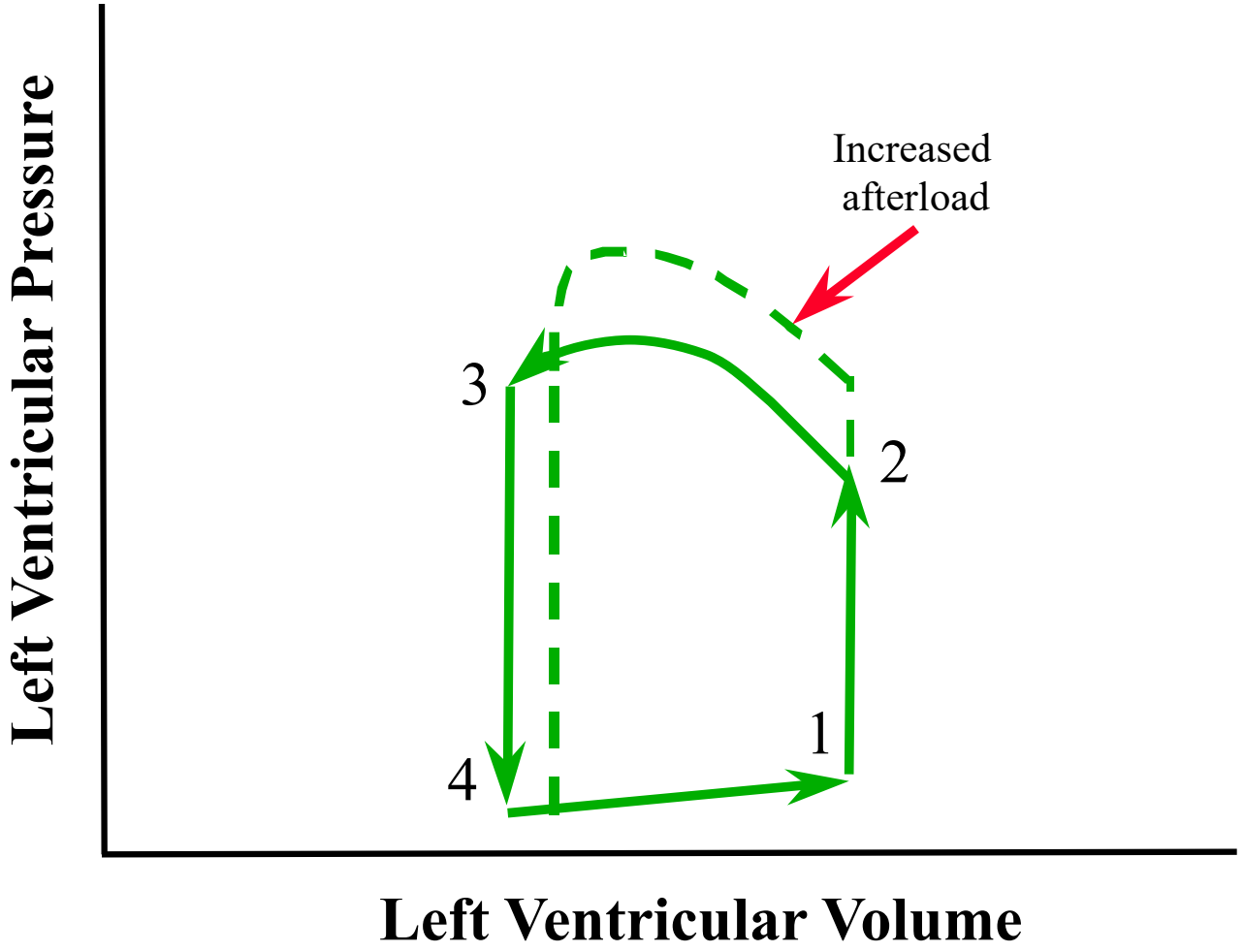
- Diastole is phases I and IV (mostly I; IV is short).
- Systole is phases II and III.
- The time for phase I is greater than the times of phases II, III, and IV combined.(time I >II +III +IV)



A shift in the end-diastolic volume ; an increase in preload increases stroke volume by increasing end-diastolic volume (frank-starling law).

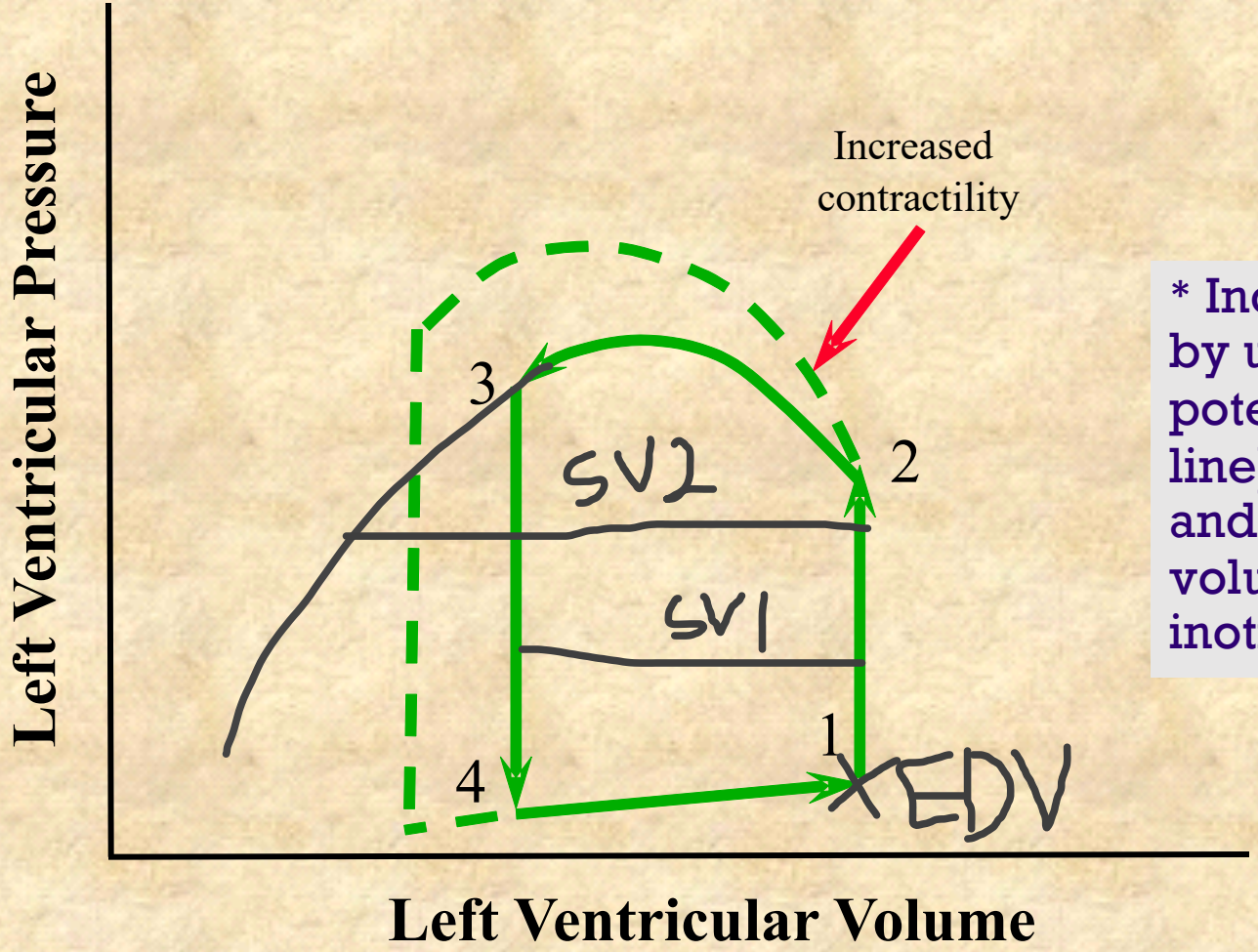
Therefore, Increasing the end-diastolic volume increases stroke volume.

B


Left Ventricular Pressure
Increased
afterload
3
2
1
4
Left Ventricular Volume

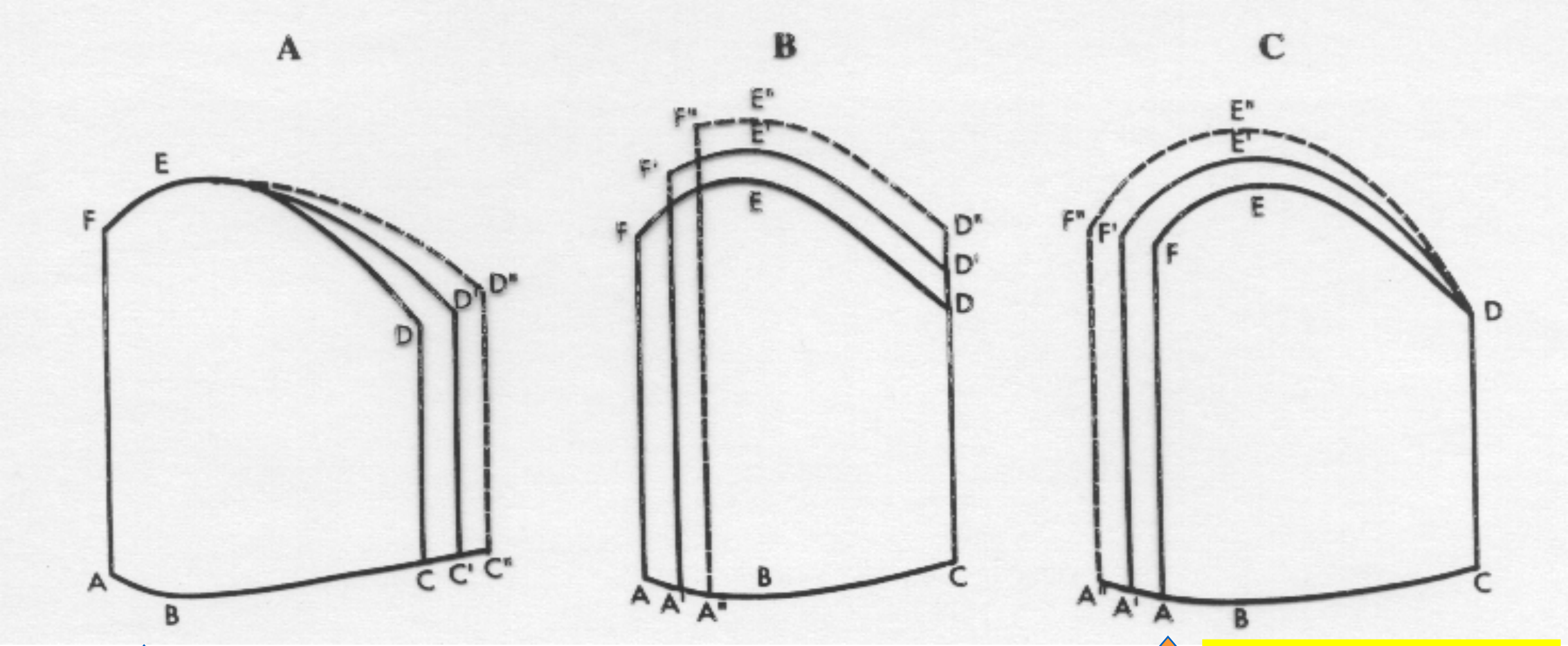
- A shift in the pressure curve upwards ; increased diastolic pressure due to increasing afterload .
- In order to keep the energy (external work) the same ; stroke volume would decrese.
- Stroke volume can be maintained if EW is increased.
- The dangers of an increased afterload is that with arterial hypertension, there is increased diastolic and systolic pressure. If you increase the arterial diastolic pressure, the heart has to spend more energy (EW) than before to keep the stroke volume the same; more energy is needed to overcome the pressure in aorta that keeps the aortic valve closed and pump the same amount of blood.
- Otherwise , stroke volume decreases, cardiac output decreases and the amount of blood pumped might not be enough to supply the tissue.

C



* Increased contractility by using a portion of the potential energy (blue line), a constant EDV, and increased stroke volume (SV2). Positive inotropic agents.

PRESSURE/VOLUME RELATIONSHIPS UNDER DIFFERENT CONDITIONS



PRELOAD

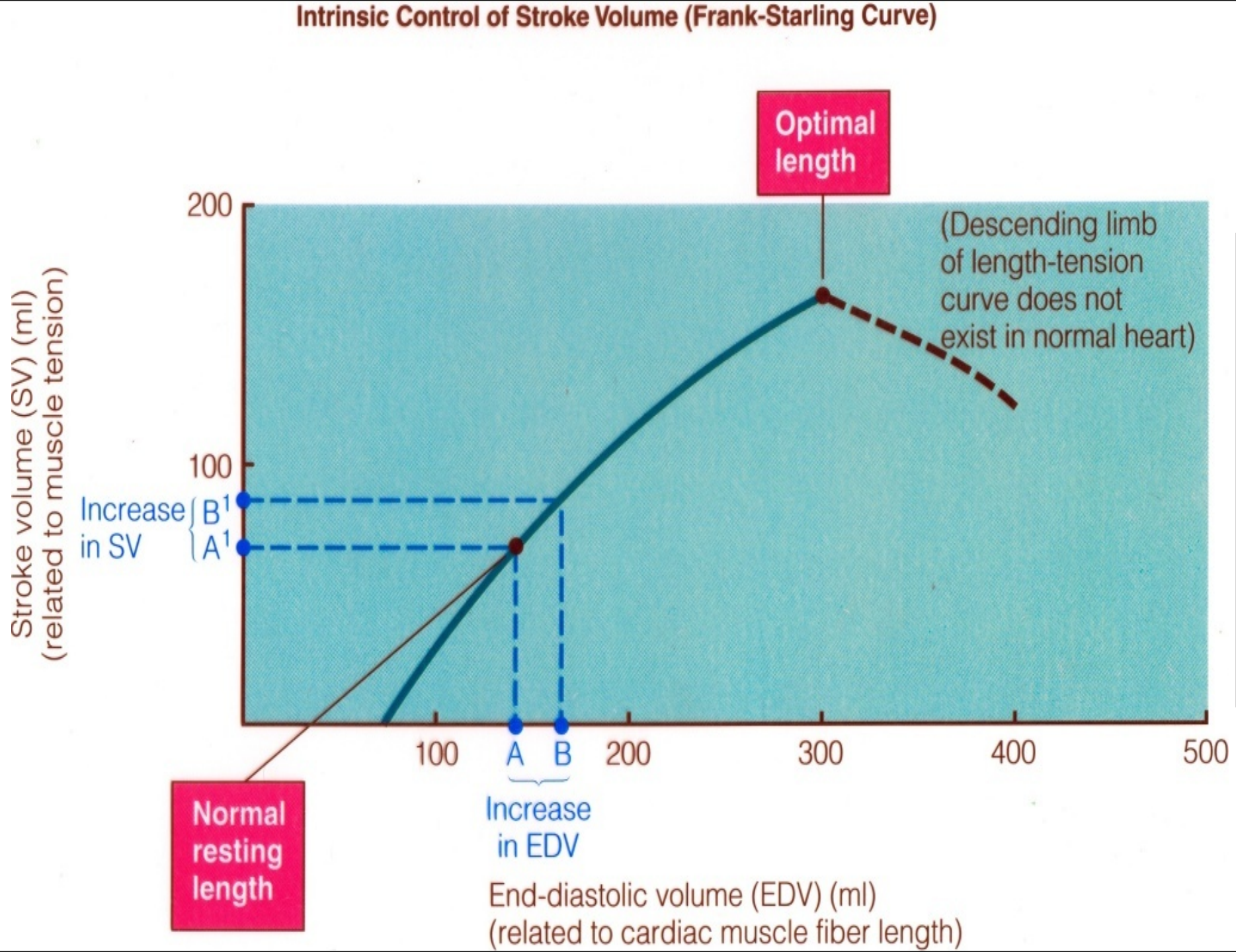
Leads to increased stroke volume

AFTERLOAD

SV decreases , keeping in mind that the energy that has to be spent stays the same

CONTRACTILITY

EDV remains the same. Increasing SV indicates increasing contractility, positive inotropic action



A representation of the Frank-Starling Law. The higher the EDV the higher the SV up to the physiological limit (the optimal length). If you exceed the optimal length, it means more EDV but a deacreased SV (heart failure).

Regulation of Heart Rate

- Positive chronotropic factors increase heart rate
  (sympathetic increases the heart rate)
- Negative chronotropic factors decrease heart rate
  (parasympathetic decreases the heart rate)

❑ Positive inotropic —>higher aortic systolic pressure (numerator)

Regulation of Heart Rate: Autonomic Nervous System

- Sympathetic nervous system (SNS) stimulation is activated by stress, anxiety, excitement, or exercise **(it dominates contractility)**
- Parasympathetic nervous system (PNS) stimulation is mediated by acetylcholine and opposes the SNS **(it dominates the heart rate)**
- PNS dominates the autonomic stimulation, slowing heart rate and causing vagal tone.
- **If you have both sympathetic & parasympathetic innervation to the heart cut, you'll notice an increase in the heart rate (due to the parasympathetic cut) & a decreases in contractility (due to the sympathetic cut)**

Atrial (Bainbridge) Reflex Bainbridge after the Australian scientist who discovered it

- Atrial (Bainbridge) reflex – a sympathetic reflex initiated by increased blood in the atria (increased atrial pressure especially in the right atria thus increasing the heart rate).
  - Causes stimulation of the SA node (increasing the atrial pressure presses on the SA node thus increasing the permeability to sodium & calcium. Remember that increasing the permeability to sodium and calcium lowers the resting membrane potential [less negative] and the slope for the slow repolarization is going to be faster).
  - Stimulates baroreceptors in the atria, causing increased SNS stimulation

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
- An increase in calcium also might increase the heart rate (a case of hypercalcemia)

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/m^2 (surface area in m^2).
- CO is proportional to tissue O_2 use. (during exercise, the more intense it is, the more is the Oxygen consumption & the more is the cardiac output [they go side by side & parallel to each other]).
- CO is proportional to 1/TPR when AP is constant. (the cardiac output is flowing from the aorta to the right atrium, so it equals → (the mean arterial pressure – right atrial pressure) / total peripheral resistance (TPR)
- ***CO = (MAP - RAP) / TPR*** since RAP is zero, CO = MAP / TPR
- CO = SV x Heart rate.
- Remember that cardiac output is the amount of blood that goes from the aorta/pulmonary artery through different arteries to reach the tissues so the sum of blood flow to these tissues will equal the cardiac output.
- Cardiac output varies between humans due to different factors like sex, size, etc..
- Cardiac index = cardiac output /Surface area (in meters ^{2}) → L/min/m^2
- It's better to compare people in terms of cardiac index than comparing people using their cardiac output.

❑ MAP(mean arterial pressure) =

1) 3/5 systolic blood pressure+5/8 diastolic blood pressure

OR

2) 1/3 systolic BP+2/3 diastolic BP (for simplification)

❑ (Normally diastole is longer than systole)

Thank You