MUNI MED

Heart as a muscle

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Clinical Case

Setting: *emergency department (ED)*

CC: *"I can't breathe."*

VS: *R: 28 breaths/minute; BP: 150/98 mm Hg; P: 118 beats/minute; T: 97°F*

HPI: *A 63-year-old woman presents to the ED with shortness of breath that started earlier in the day and worsened over several hours. She says the dyspnea is "like swimming a whole pool underwater." It is worsened by exertion and relieved by sitting up.*

She has a history of hypertension and a myocardial infarction 2 years ago. She takes "a bunch of pills" every day, which she cannot remember the name of. Her physician does not have privileges at your hospital, so the record is not available.

ROS:

- *No chest pain*
- *No history of valve disease*

PE:

- *Chest: rales 2/3 up bilaterally*
- *Cardiovascular: jugulovenous distention (JVD), an extra sound on auscultation*
- *Extremities: bilateral pitting edema up to the knees*

Q1

What is the mechanism of the finding on the heart examination?

a. Rapid filling of the ventricle during diastole
b. Rupture of the chordae tendineae
c. Fibrinous exudate in between the heart and the pericardium
d. Aberrant conduction tract at the atrioventricular (AV) node
e. Increased gradient of pressure between the left ventricle (LV) and the aorta

Q2

Edema is found on examination. What is the mechanism?

a. Decreased hydrostatic pressure of the interstitial fluid
b. Decreased oncotic pressure
c. Alteration of the diffusion coefficient (K_F) of the capillary
d. Increased hydrostatic pressure in the peripheral capillaries
e. Increased hydrostatic pressure in the glomerular capillaries

Q3

What is the mechanism of the medication you should try next?

a. Dilation of afferent arteriole of glomerulus
b. Beta-hydroxy-beta-methylglutaryl-coenzyme A (HMG-CoA) reductase inhibition
c. Vasoconstriction of arterioles
d. Positive inotrope and vasodilation
e. Venodilation

CARDIAC MUSCLE CONTRACTION

Key Concepts

✓ *Autorhythmicity* —
Pacemaker cells of the SA node spontaneously depolarize.
Gap junctions allow cell-cell transmission.
- Heart contracts as atrial and ventricular units.

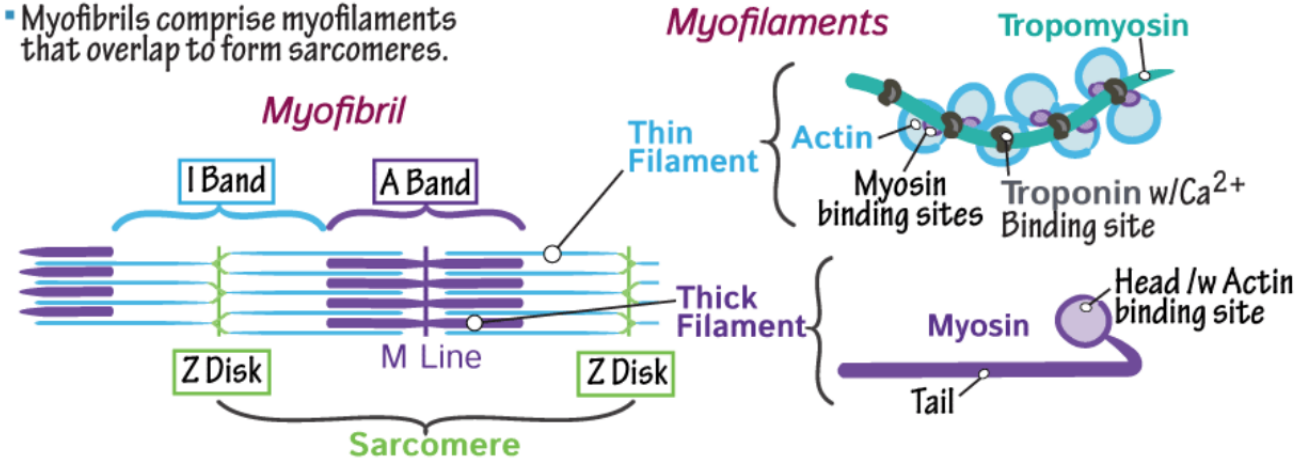
✓ *EC coupling* —
Links action potential to myofibril contraction.
Calcium from ECF *and* SR promotes myofibril contraction.

Calcium

✓ *Contractility* —
The intrinsic ability of cardiac muscle cells to produce force at a given cell length.
- Cardiac glycosides raise ICF calcium and increase contractility.
- Calcium Channel Blockers prohibit calcium influx and reduce contractility.

Cardiac Muscle Myofibrils

- Myofibrils comprise myofilaments that overlap to form sarcomeres.

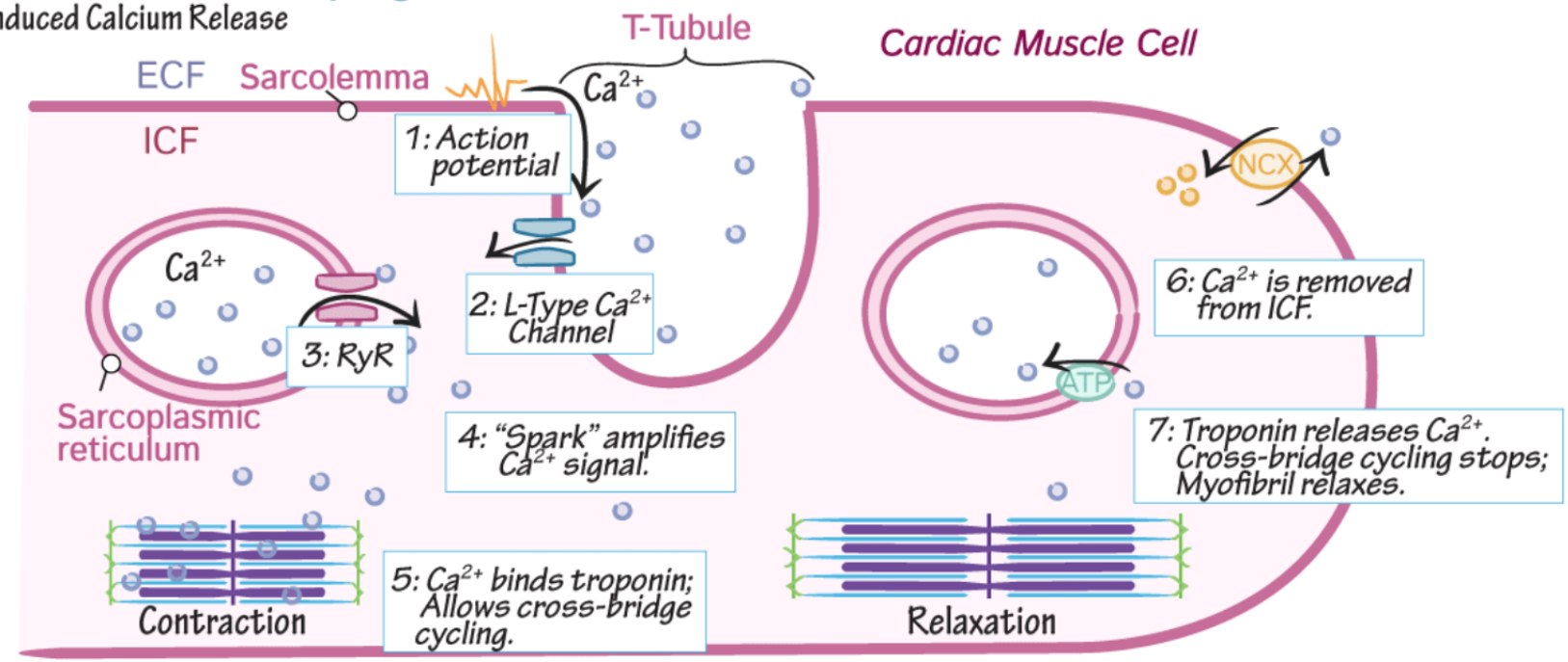


Calcium Allows Cross-Bridge Cycling

1. Troponin binds ICF Ca^{2+}.
2. Tropomyosin moves, exposes myosin-binding sites.
3. Myosin binds actin, cross-bridge cycling contracts myofibrils.

Excitation-Contraction Coupling

- Calcium-Induced Calcium Release



Similarities of myocardial and skeletal muscle contraction

Similarities

- Both have the same functional proteins, i.e., actin, tropomyosin, troponin, myosin, and titin.
- A rise in cytosolic Ca^{2+} initiates cross-bridge cycling thereby producing active tension.
- ATP plays the same role.
- Both have SERCA.
- Both have RyR receptors on the SR and thus show calcium-induced calcium release.

myocardial and skeletal muscle contraction

Differences

- Extracellular Ca^{2+} is involved in cardiac contractions, but not skeletal muscle. This extracellular Ca^{2+} causes calcium-induced calcium release in cardiac cells.
- Magnitude of SR Ca^{2+} release can be altered in cardiac (see section on cardiac mechanics), but not skeletal muscle.
- Cardiac cells are electrically coupled by gap junctions, which do not exist in skeletal muscle.
- Cardiac myocytes remove cytosolic Ca^{2+} by 2 mechanisms: SERCA and a Na^{+}—Ca^{2+} exchanger (3 Na^{+} in, 1 Ca^{2+} out) on the sarcolemmal membrane. Skeletal muscle only utilizes SERCA.

Removal of calcium in cardiomyocytes

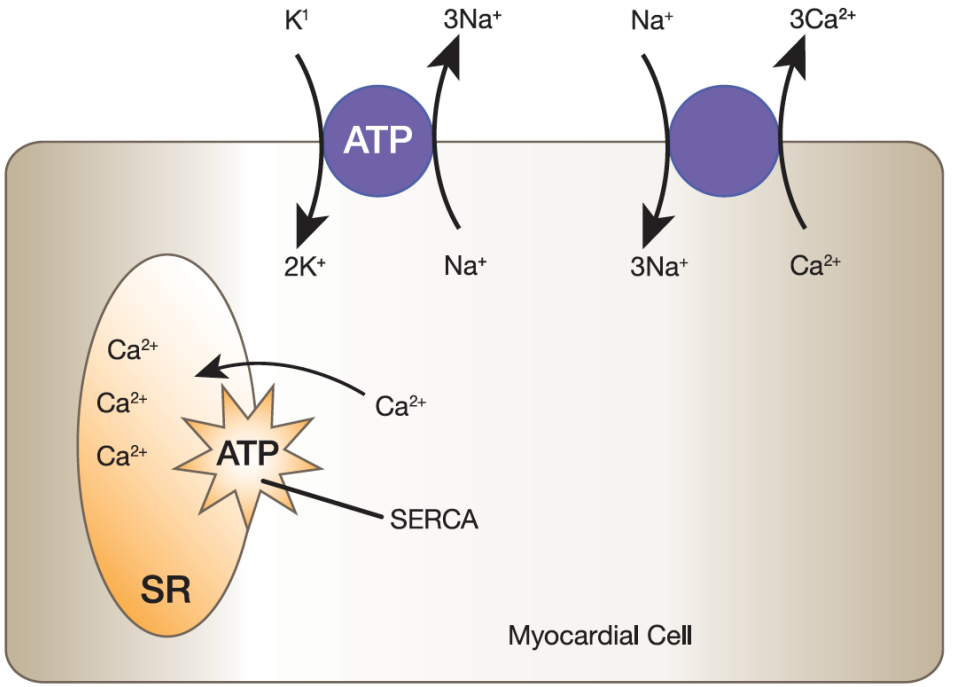
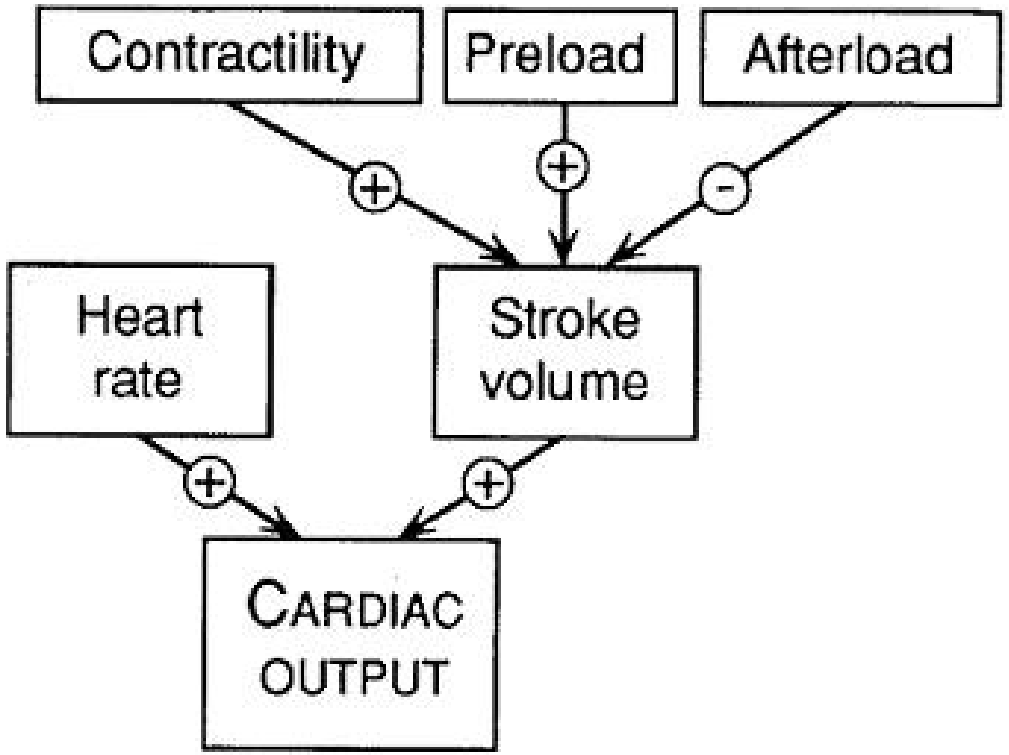


Figure III-1-8. Removal of Cytosolic Calcium in Myocardial Cells

Cardiac output (as a measure of cardiac performance)



SYSTOLIC PERFORMANCE OF THE VENTRICLE

Systolic performance actually means the **overall force generated by the ventricular muscle during systole**.

The heart does 2 things in systole: **pressurizes** and **ejects blood**. An important factor influencing this systolic performance is the **number of cross-bridges cycling during contraction.**

The greater the number of cross-bridges cycling → **the greater the force of contraction**.

Systolic performance is determined by 3 independent variables:

- **Preload**
- **Contractility**
- **Afterload**

PRELOAD

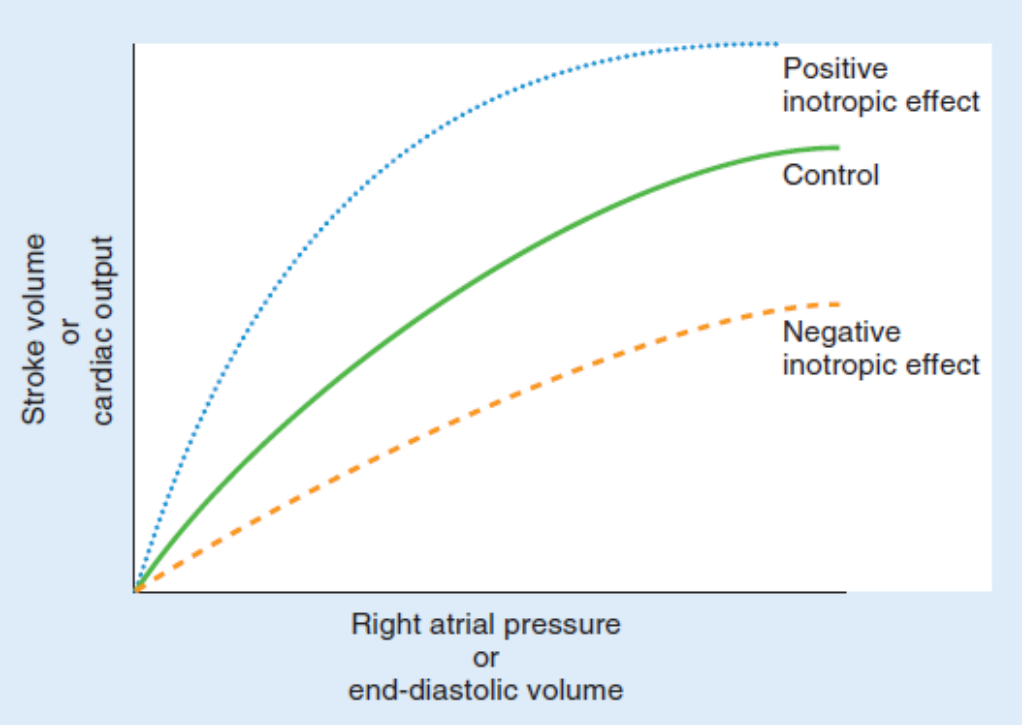
➢ **Preload is the load on the muscle in the relaxed state (before it contracts). More specifically, it is the load or prestretch on ventricular muscle at the end of diastole.**

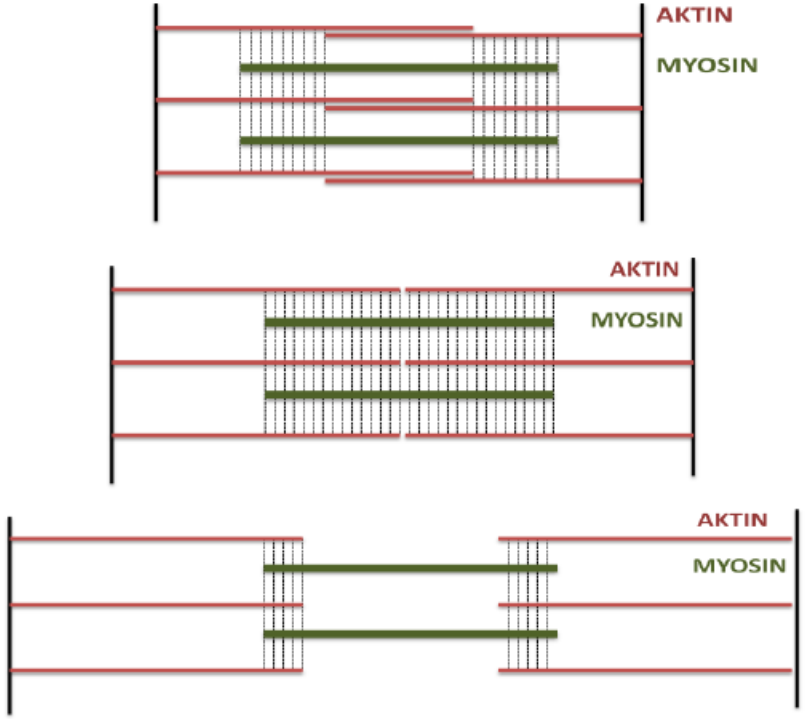
Applying preload to muscle does 2 things ;

1. **Stretches the muscle (sarcomere)** → greater the Preload → greater the stretch of the sarcomere
2. **Generates passive tension in the** muscle (muscle is elastic → resists the stretch like a rubber band !→ resistant is measured as passive tension)

The greater the Preload → the greater the stretch or length of sarcomere → the greater the passive tension →more cross-bridge cycles to be formed → GREATER FORCE OF CONTRACTION! → increase in SV

FRANK-STARLING MECHANISM





Lenght-tension relationship

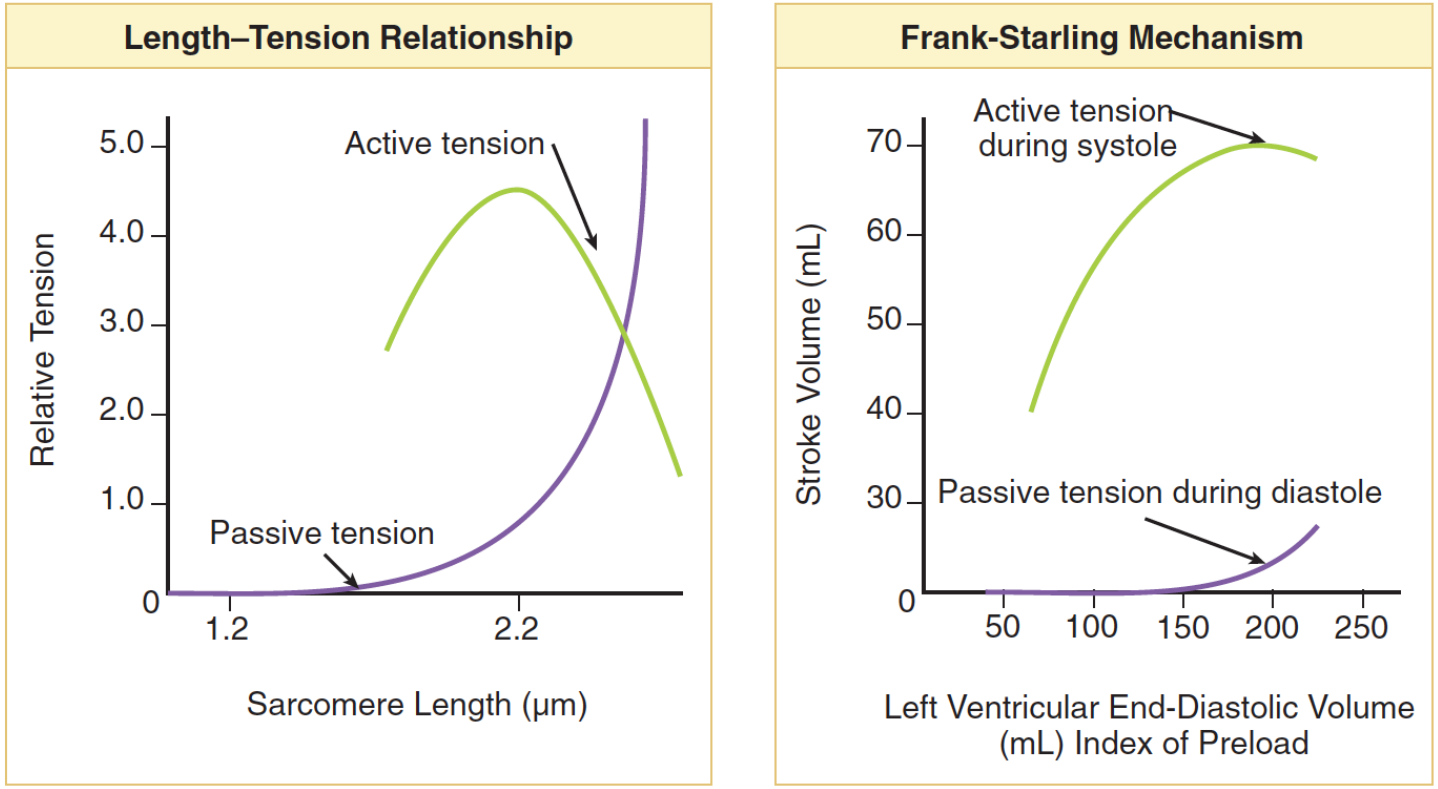


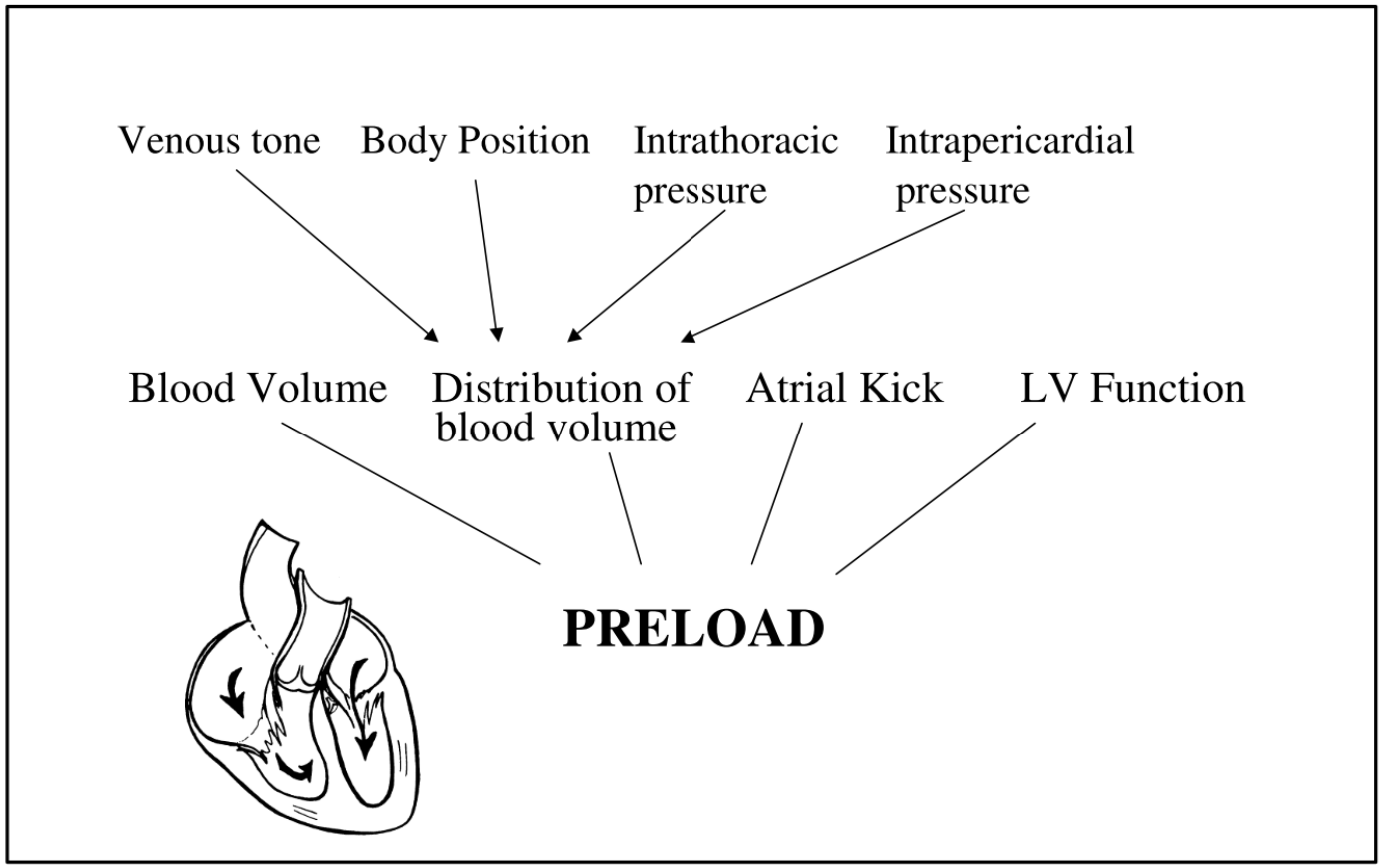
Figure IV-1-1. Length–Tension Relationships in Skeletal and Cardiac Muscle

In summary

Increased stretching (increased preload) of cardiac muscle →

- increases passive tension (prior to contraction)
- Increases total tention (during contraction)
- Increases active tension (during contraction) until a peak response occurs

What determines the **Preload** ?



Conditions that Alter Preload

Hypovolemia

Hemorrhage

Dehydration

Burns

Overdiuresis

Third Spacing

Hypervolemia

Overhydration

CHF

Renal Disease

Altered Size of Vascular Space

Sepsis

Spinal or Epidural Anesthesia

Anaphylaxis

Venous vasodilating drugs

How to measure preload?

Preload on ventricular muscle is not measured directly; rather, indices are utilized.

- **Left ventricular end-diastolic volume (LVEDV)**
- **Left ventricular end-diastolic pressure (LVEDP)**
- Central venous pressure (CVP)
- Pulmonary capillary wedge pressure (PCWP)
- Right atrial pressure (RAP)

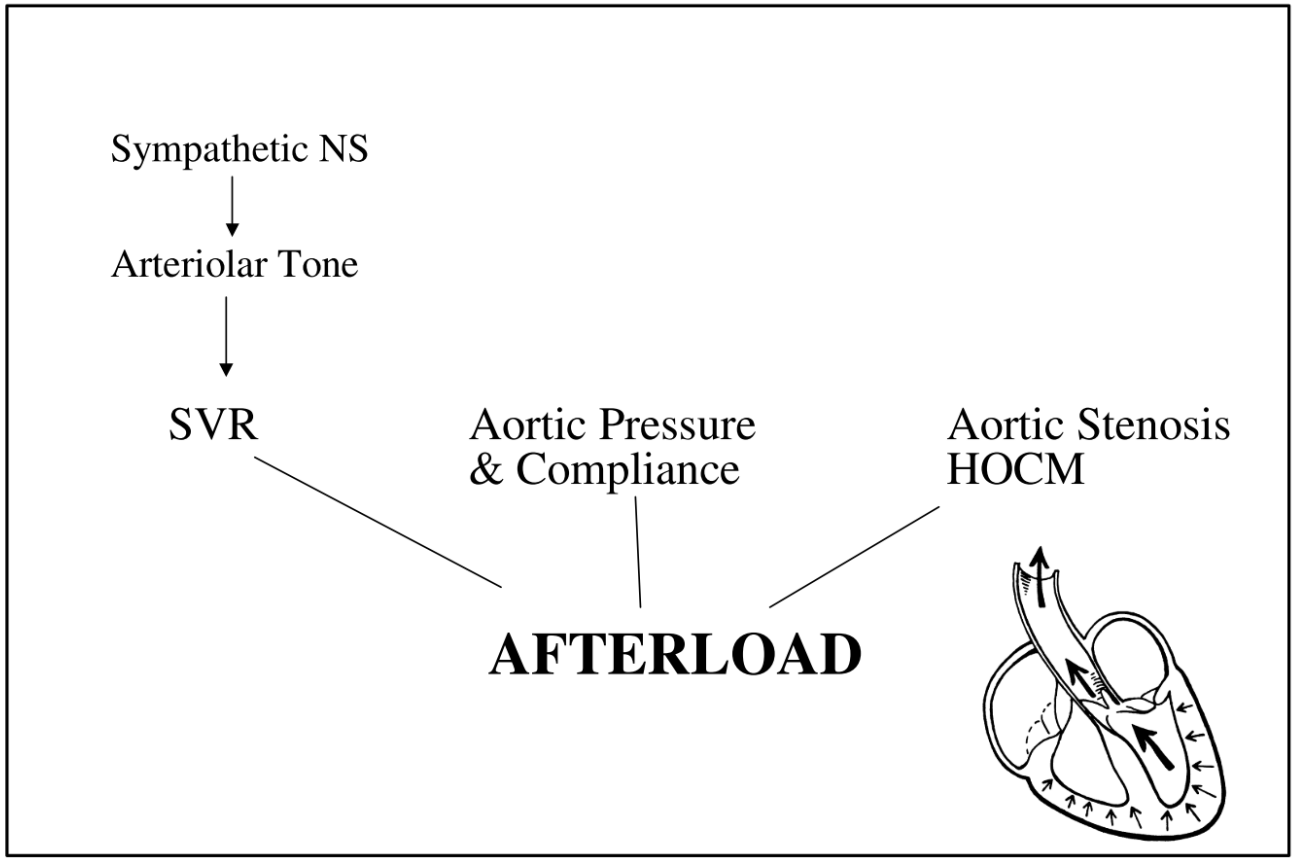
AFTERLOAD

Afterload is defined as the “load” that the heart must eject blood against.

Probably, the best “marker” of afterload is systemic vascular resistance (SVR), also **called total peripheral resistance (TPR).**

However, TPR is not routinely calculated clinically and thus **arterial pressure (diastolic, mean, or systolic)** is often used as the index of afterload.

Afterload



Conditions that Alter Afterload

Vasodilation

Sepsis

Spinal or Epidural Anesthesia

Anaphylaxis

Arterial Vasodilating Drugs

Vasoconstriction

Hypertension

Compensatory vasoconstriction

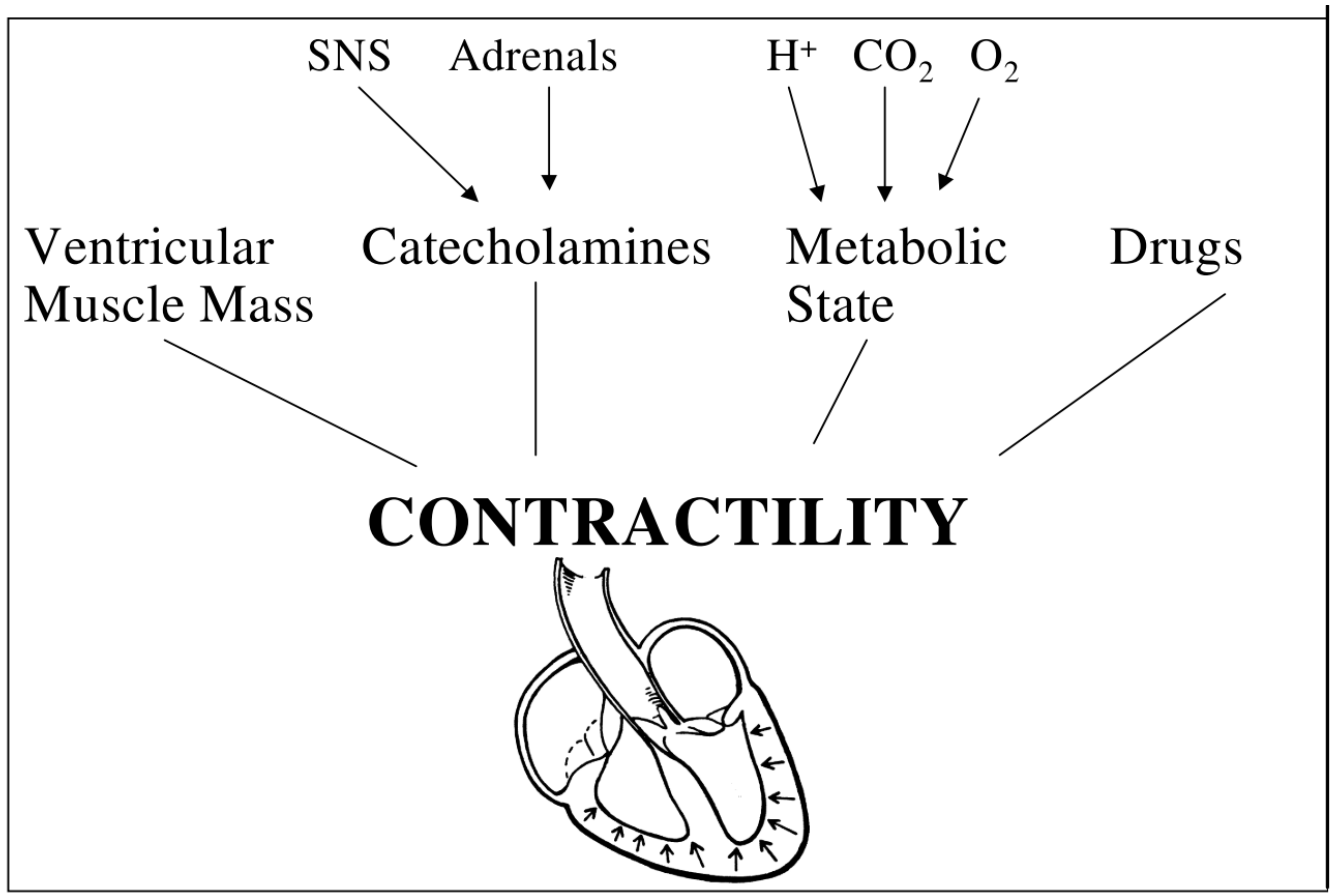
Drugs

CONTRACTILITY (ionotropism)

1. Intrinsic ability of cardiac muscle to develop force at a given muscle length **(inotropism)**.
2. Is related to the **intracellular Ca2+ concentration.**
3. Can be estimated by the **ejection fraction** (stroke volume/end-diastolic volume), which is normally 0.55 (55%).

4. Increased *dp*/*dt* (change in pressure vs. change in time) = rate of pressure development during isovolumetric contraction. Contractility affects the rate at which the ventricular muscle develops active tension, which is expressed as pressure in the ventricle during isovolumetric contraction.

What changes the **Contractility** ?



Conditions that Alter Contractility

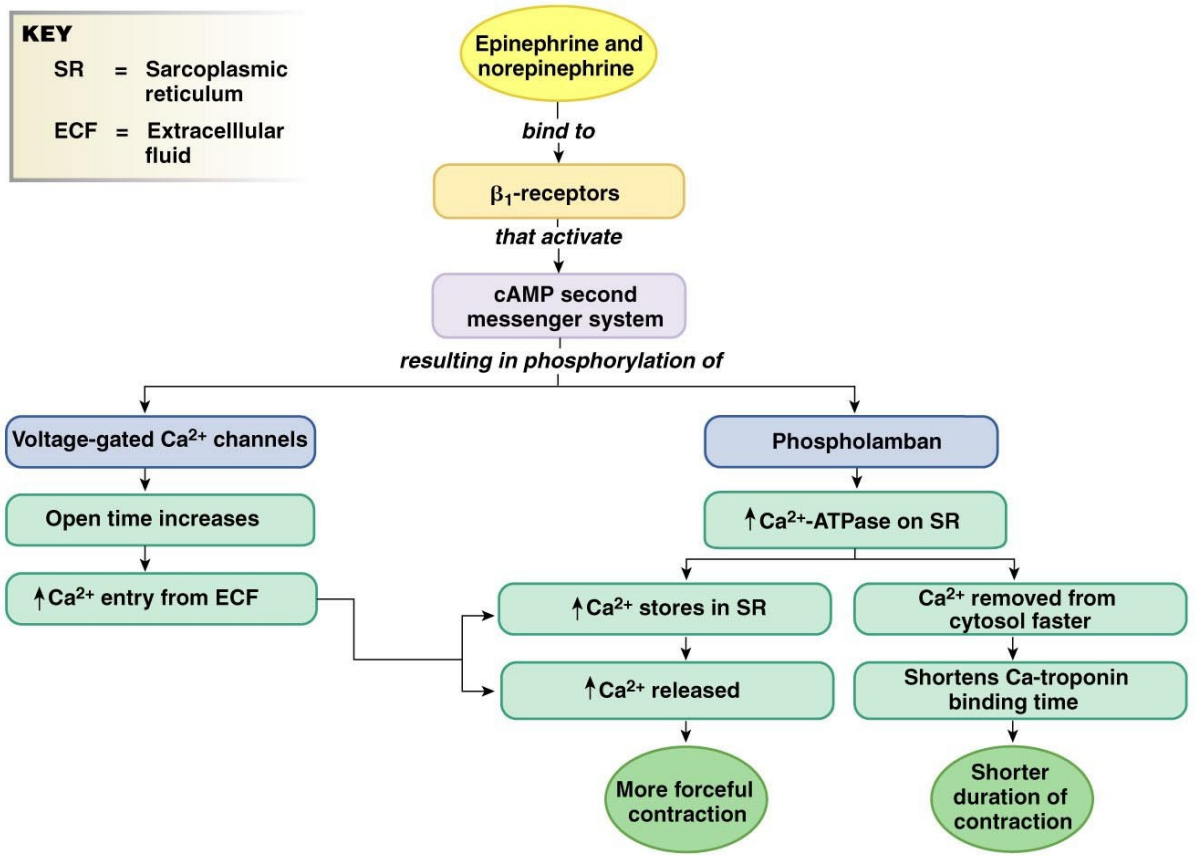
Increase

- Pheocromocytoma
- Hyperthyroidism
- Positive Inotropic Drugs

Decrease

- Myocardial Infarction
- Cardiomyopathy
- Ischemia
- Hypoxia
- Acidosis
- Negative Inotropic Drugs

Modulation of contractility SNS



Effect of increasing contractility

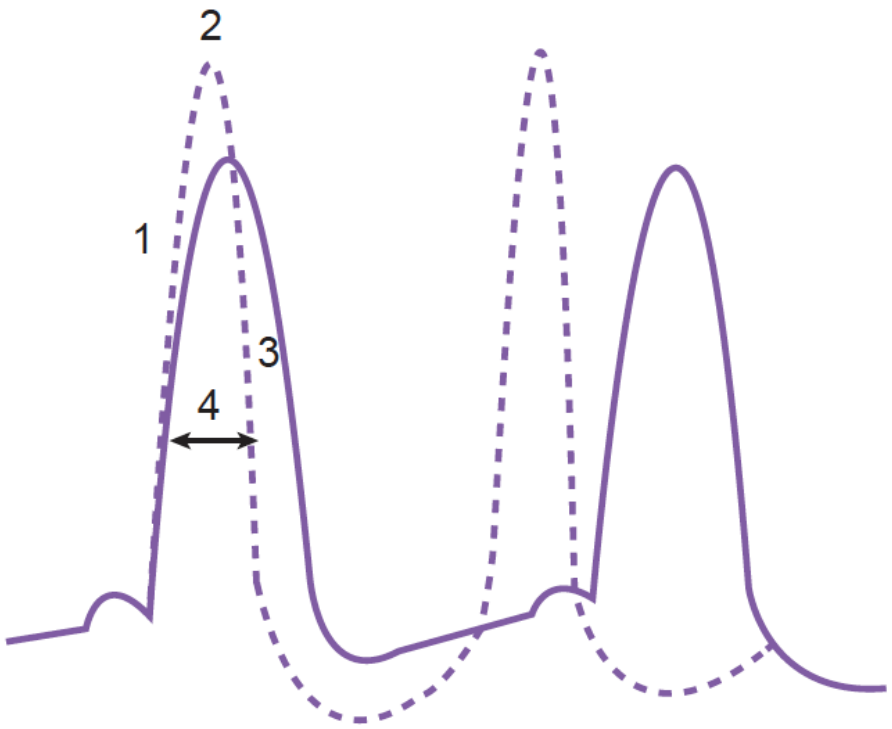
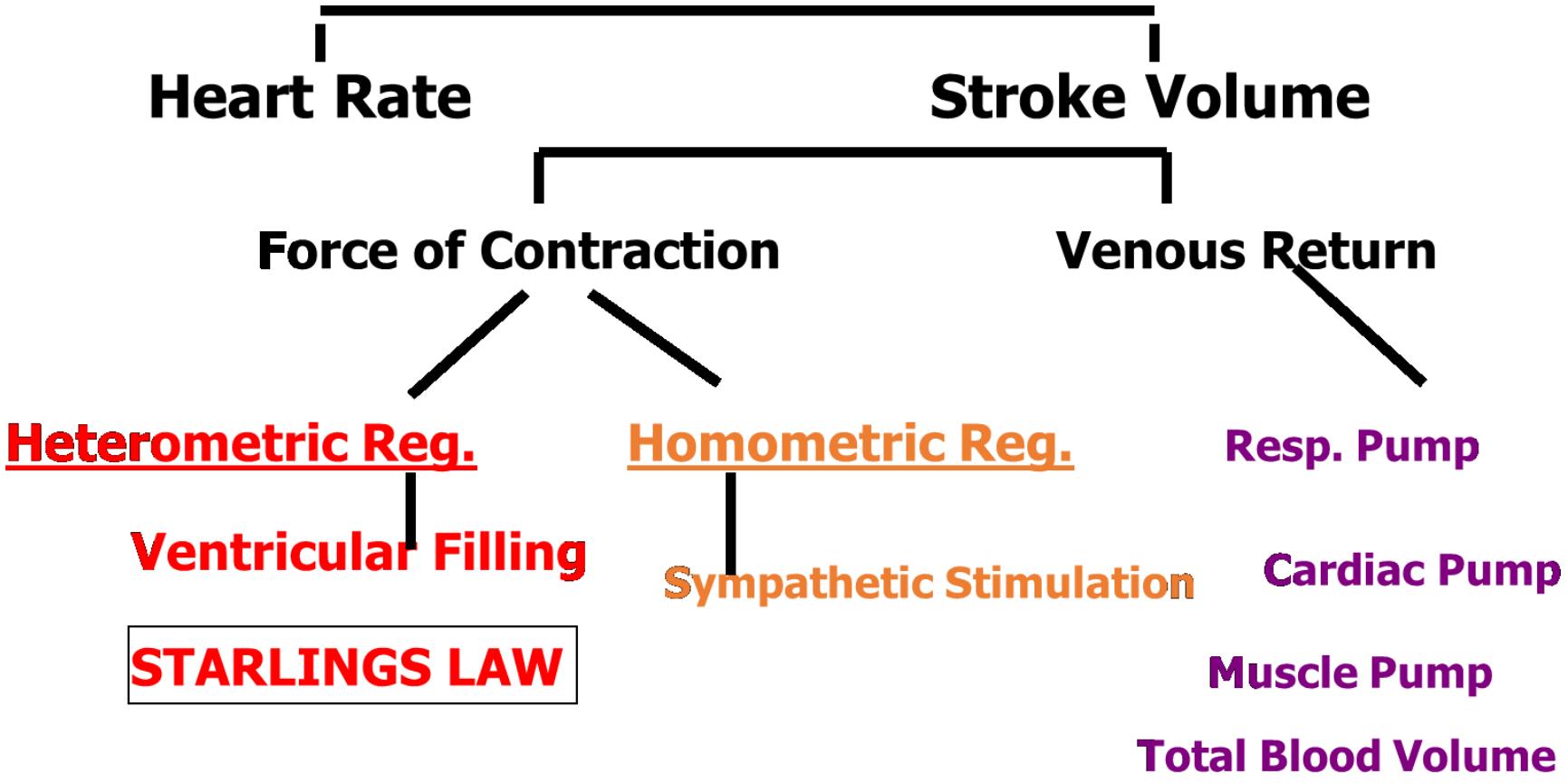
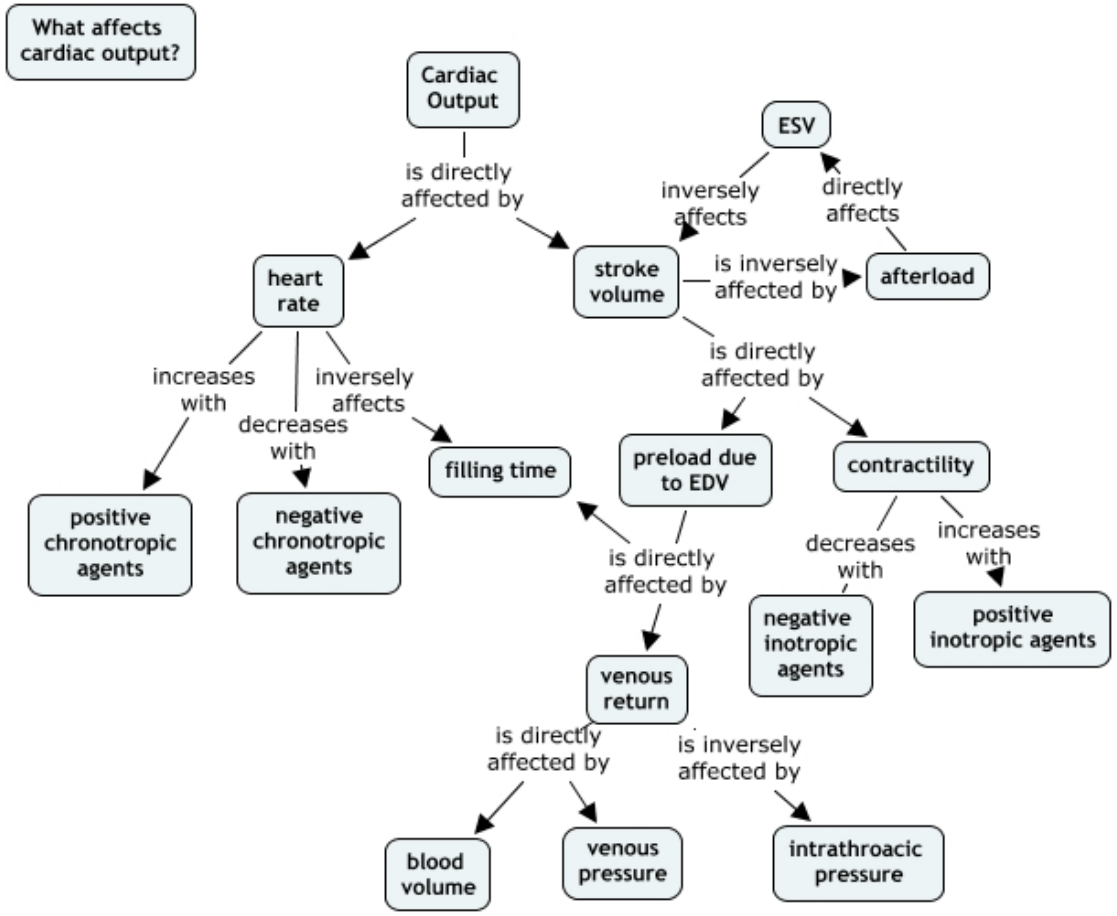


Figure IV-1-2. Effects of Increased Contractility

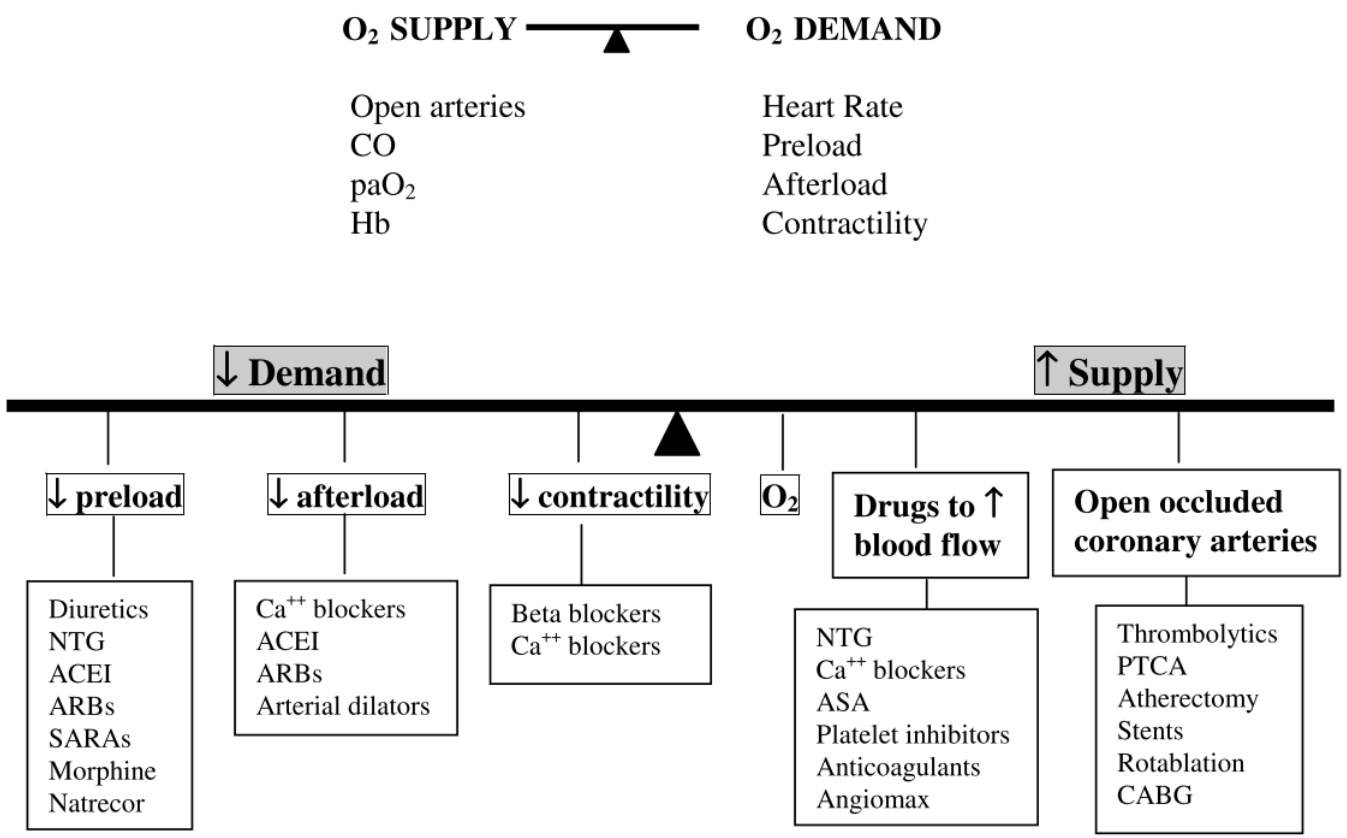
Heterometric and homeometric autoregulation of contractility



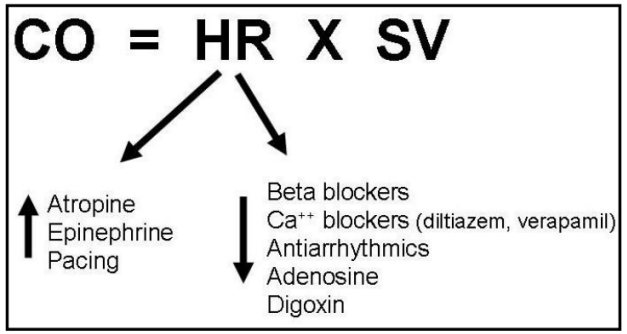
IMPORTANT!

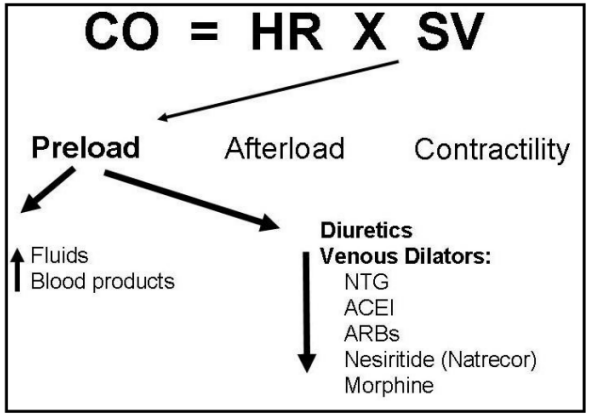

What affects cardiac output?
Cardiac Output
is directly affected by
heart rate
stroke volume
ESV
inversely affects
directly affects
is inversely affected by
afterload
increases with
decreases with
inversely affects
positive chronotropic agents
negative chronotropic agents
filling time
is directly affected by
preload due to EDV
contractility
decreases with
increases with
negative inotropic agents
positive inotropic agents
is directly affected by
venous return
is directly affected by
is inversely affected by
blood volume
venous pressure
intrathroacic pressure

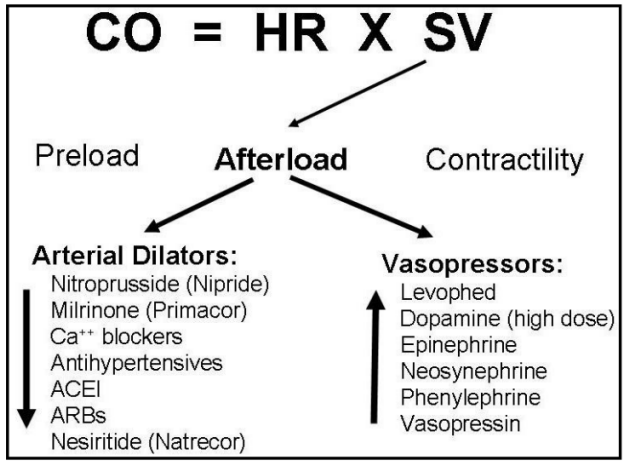
Why are we learning all of these!

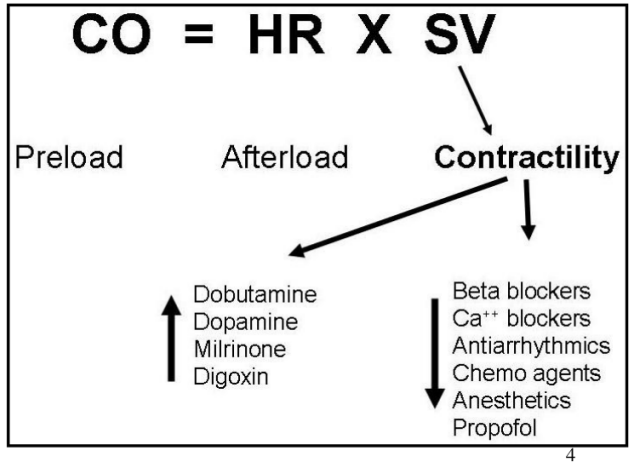


Pharmacological approach

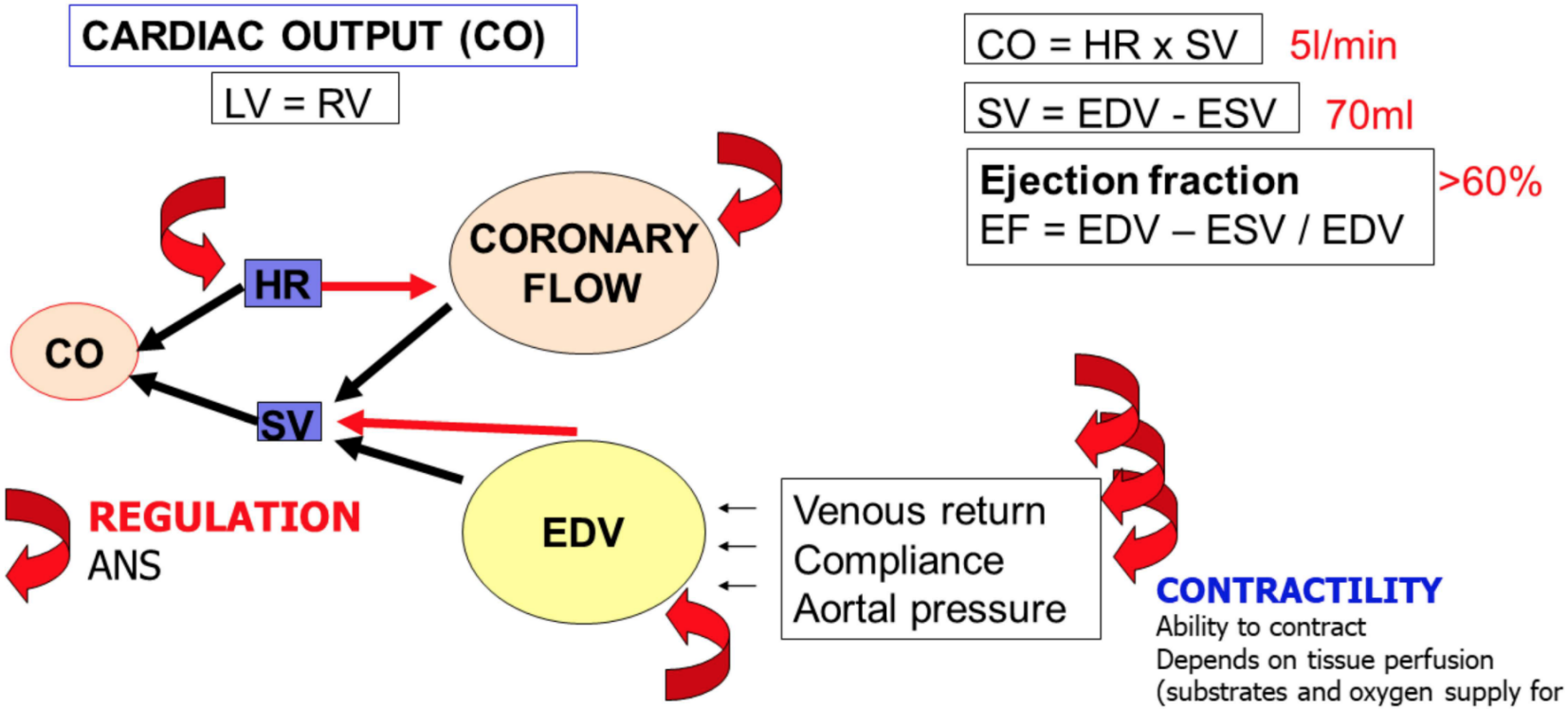








Cardiac Output as the measure of performance (courtesy of Prof. Marie Novakova)



Cardiac Reserve (courtesy of Prof. Marie Novakova)

CARDIAC RESERVE = maximal CO / resting CO	**4 - 7**
CORONARY RESERVE = maximal CF / resting CF	**3,5**
CHRONOTROPIC RESERVE = maximal HR / resting HR	**3 - 5**
VOLUME RESERVE = maximal SV / resting SV	**1,5**

CO = cardiac output
CF = coronary flow
HR = heart rate
SV = stroke volume

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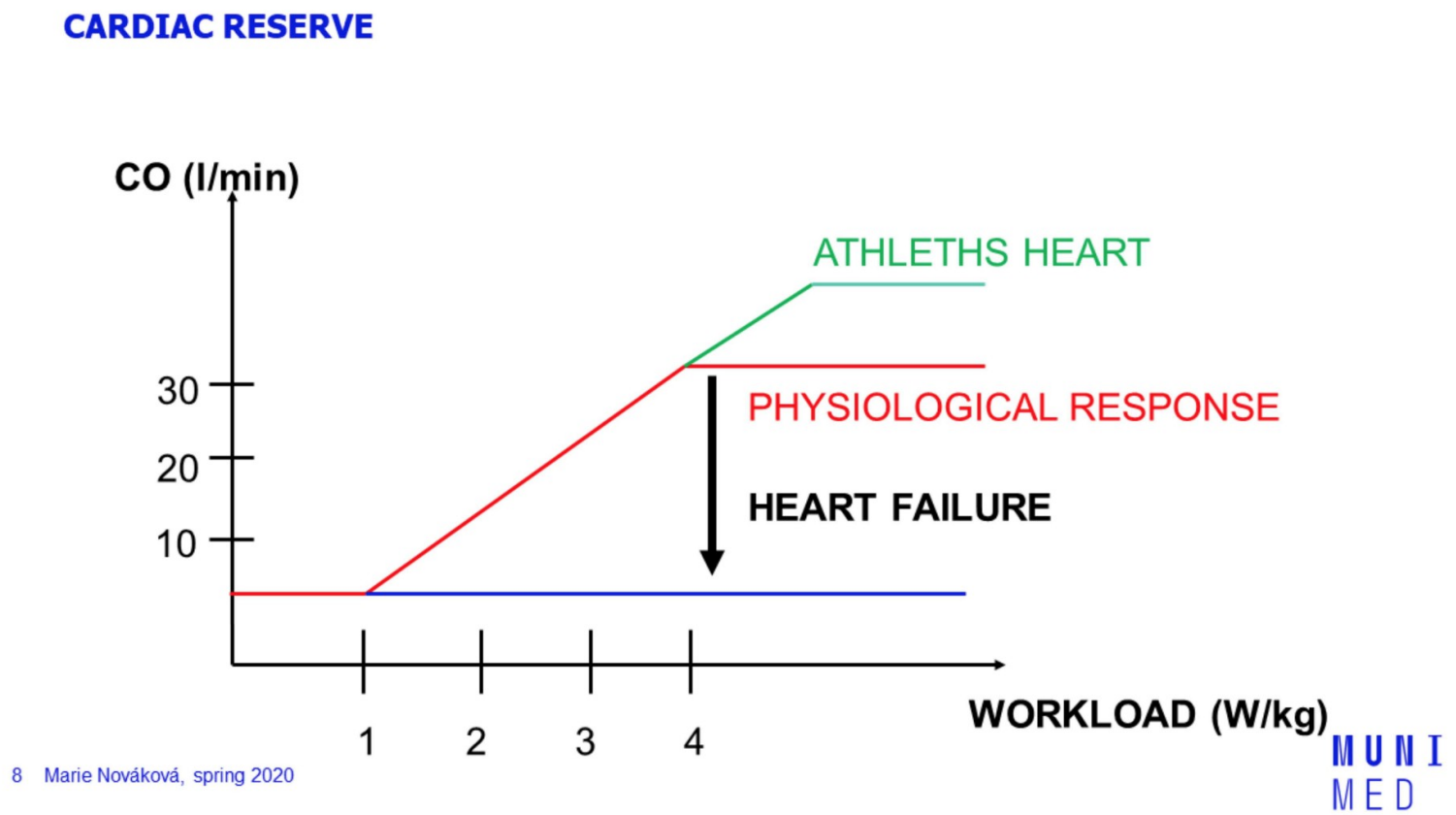
Cardiac Reserve



CARDIAC OXYGEN (O2) CONSUMPTION

Is directly related to the amount of tension developed by the ventricles.

Increased by:

- Increased **afterload** (increased aortic pressure).
- Increased **size of the heart** (Laplace's law states that tension is proportional to the radius of a sphere).
- Increased **contractility**.
- Increased **heart rate**.

Wall tension follows Laplace's law:

$$\text{Wall tension} = \text{pressure} \times \text{radius}$$

$$\text{Wall stress} = \frac{\text{pressure} \times \text{radius}}{2 \times \text{wall thickness}}$$

MEASUREMENT OF CARDIAC OUTPUT BY THE FICK PRINCIPLE

The Fick principle for measuring cardiac output is expressed by the following equation:

$$\text{Cardiac output} = \frac{O_2 \text{ consumption}}{[O_2]_{\text{pulmonary vein}} - [O_2]_{\text{pulmonary artery}}}$$

The equation is solved as follows:

1. O2 consumption for the whole body is measured.
2. Pulmonary vein [O2] is measured in systemic arterial blood.
3. Pulmonary artery [O2] is measured in systemic mixed venous blood.

CARDIAC WORK

- Cardiac Work
- ✓ Measurement of ventricular power.
- ✓ Left ventricular stroke work
- ✓ Cardiac minute work
- ✓ Myocardial hypertrophy
- ✓ Fick principle

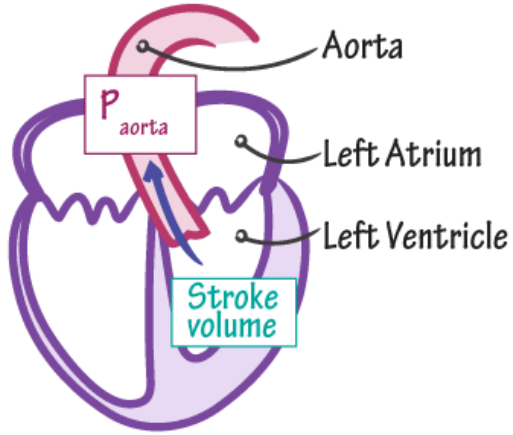
CARDIAC WORK

Stroke Work

Work the heart performs in each beat to eject blood.

Work = Distance * Force

Left Ventricular Stroke Work = Stroke volume * Aortic pressure



Cardiac Minute Work

Cardiac work per unit time.

Cardiac Minute Work = Heart Rate * L. Ventricular Stroke Work = Heart Rate * Stroke Volume * Aortic pressure = Cardiac output * Aortic pressure

(Volume work) (Pressure work)

Stroke volume * Aortic pressure

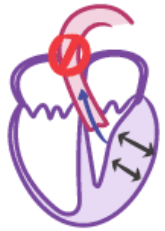
Cardiac output

MYOCARDIAL OXYGEN CONSUMPTION

- ✓ Myocardial O_2 consumption correlates with cardiac minute work.
- ✓ Pressure work is the primary driver (since it is more metabolically costly than volume work).

Cardiac Hypertrophy

↑ Pressure work → ↑ Myocardial O_2 consumption → Myocardial hypertrophy



✓ *Aortic Valve Stenosis & Systemic Hypertension* — Left ventricle hypertrophy

✓ *Pulmonary Hypertension* — Right ventricle hypertrophy

Fick Principle

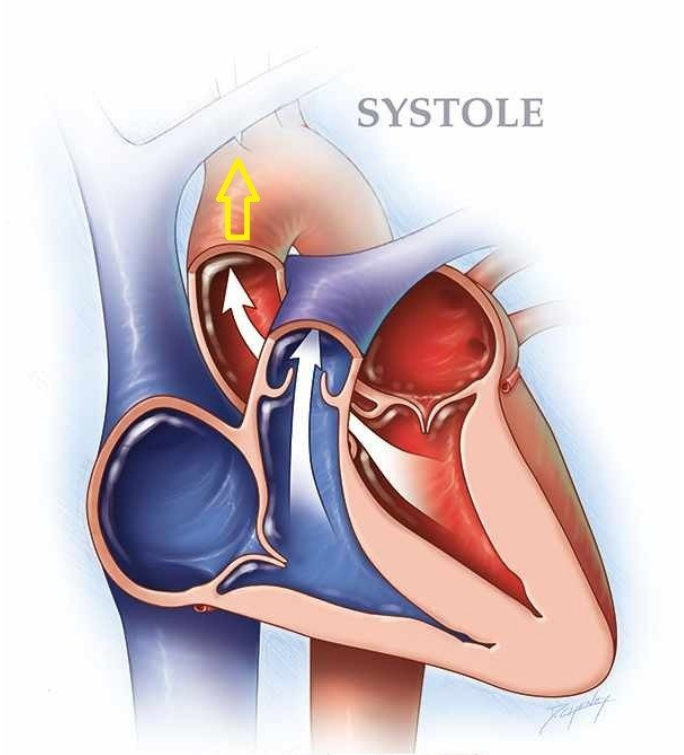
✓ Calculate cardiac output by measuring myocardial oxygen consumption.

$$\text{Cardiac output} = \frac{\text{Total } O_2 \text{ Consumption}}{[O_2]_{\text{pulmonary vein}} - [O_2]_{\text{pulmonary artery}}}$$

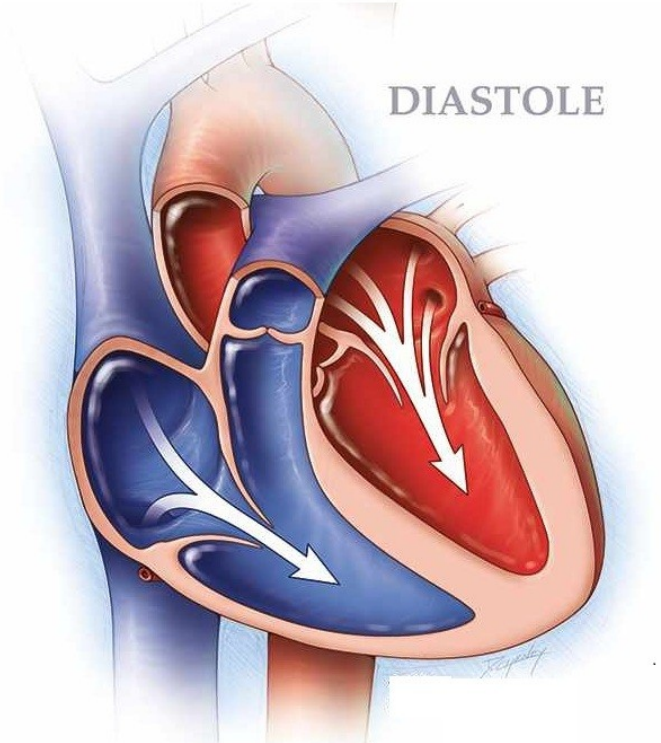
Example:

$$\text{Cardiac output} = \frac{200 \text{ ml } O_2/\text{min}}{0.15 \text{ ml } O_2/\text{ml blood} - 0.1\ O_2/\text{ml blood}} = 4000 \text{ ml/min}$$

3. CARDIAC CYCLE.



Heart muscles
Contract



Heart muscles
Relax

Cardiac cycle

Made of 2 phases :

1) **SYSTOLE**

A. Cardiac contraction(isovolumic contration)

B. Ejection of the blood out of heart (systolic ejection)

2) **DIASTOLE**

A. Cardiac Relaxation (isovolumic relaxation)

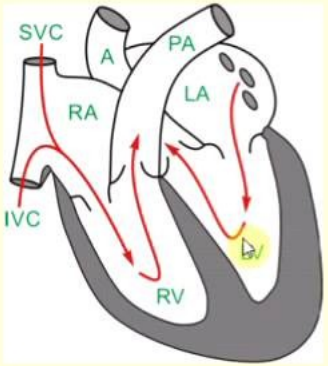
B. Filling of the heart with blood (Ventricular filling)

Intracardiac pressures

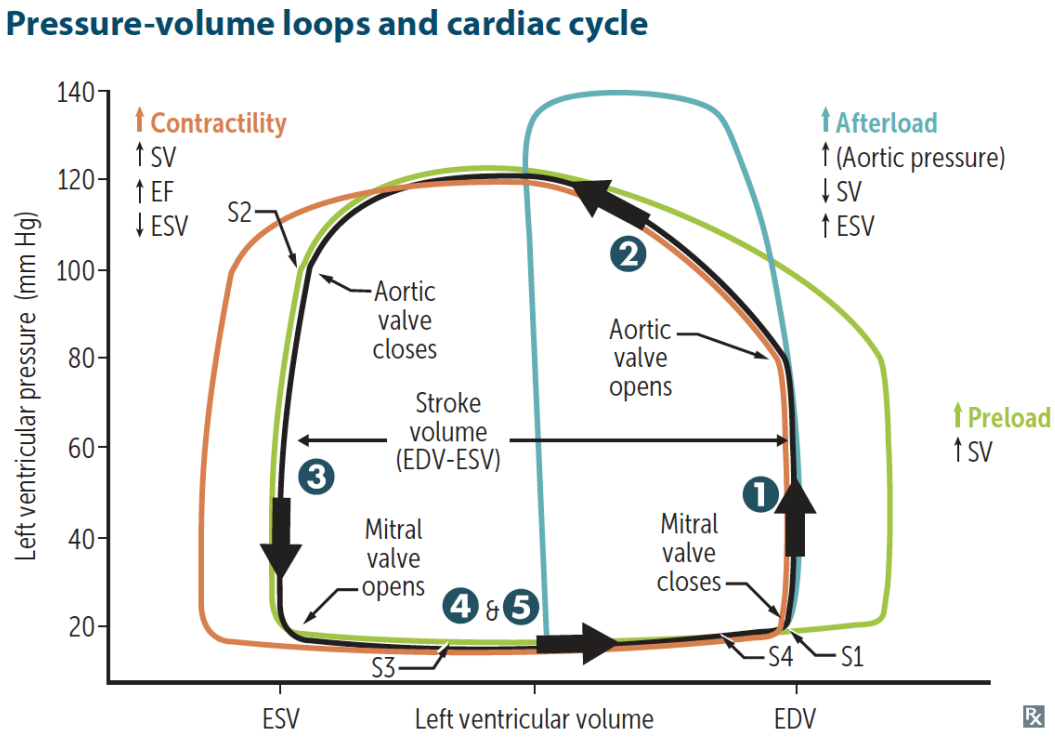
Average, Normal Intracardiac and Vascular Pressures (mmHg)

Right Atrium	0 – 4 (varies with respiration)
Right Ventricle	25 sys/4 dias
Pulmonary Artery	25 sys/10 dias
Left Atrium	8 – 10
Left Ventricle	120 sys/10 dias
Aorta	120 sys/80 dias

dys = systolic; dias = diastolic



LV Pressure-Volume loop

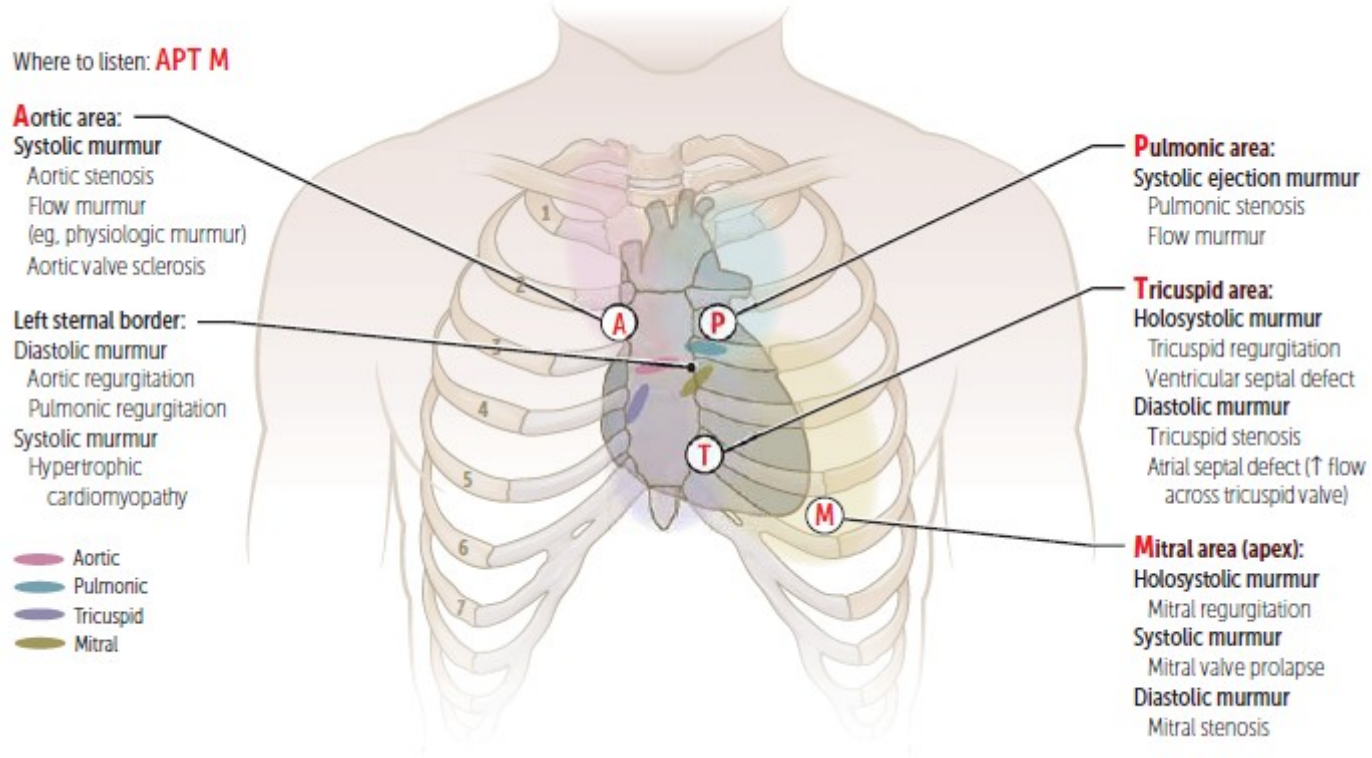


The black loop represents normal cardiac physiology.

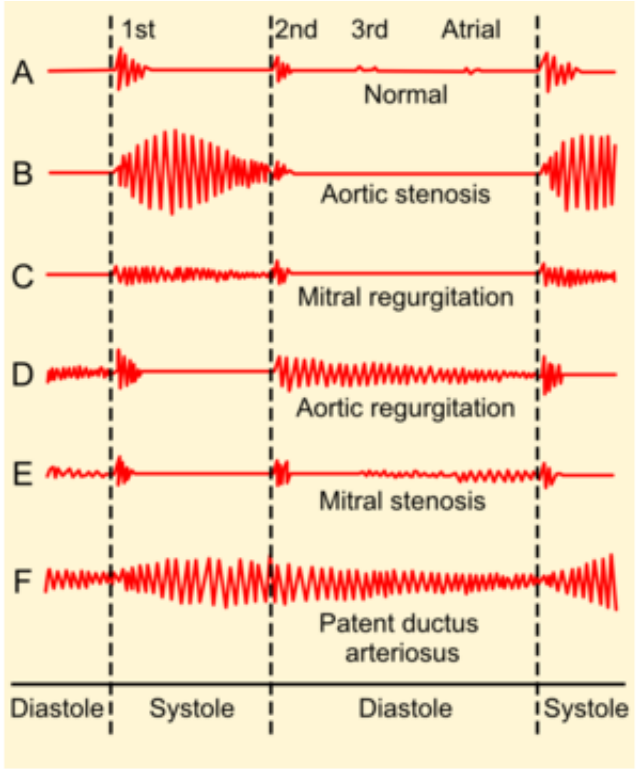
Phases—left ventricle:

1. Isovolumetric contraction—period between mitral valve closing and aortic valve opening; period of highest O_2 consumption
2. Systolic ejection—period between aortic valve opening and closing
3. Isovolumetric relaxation—period between aortic valve closing and mitral valve opening
4. Rapid filling—period just after mitral valve opening
5. Reduced filling—period just before mitral valve closing

AUSCULTATION OF HEART

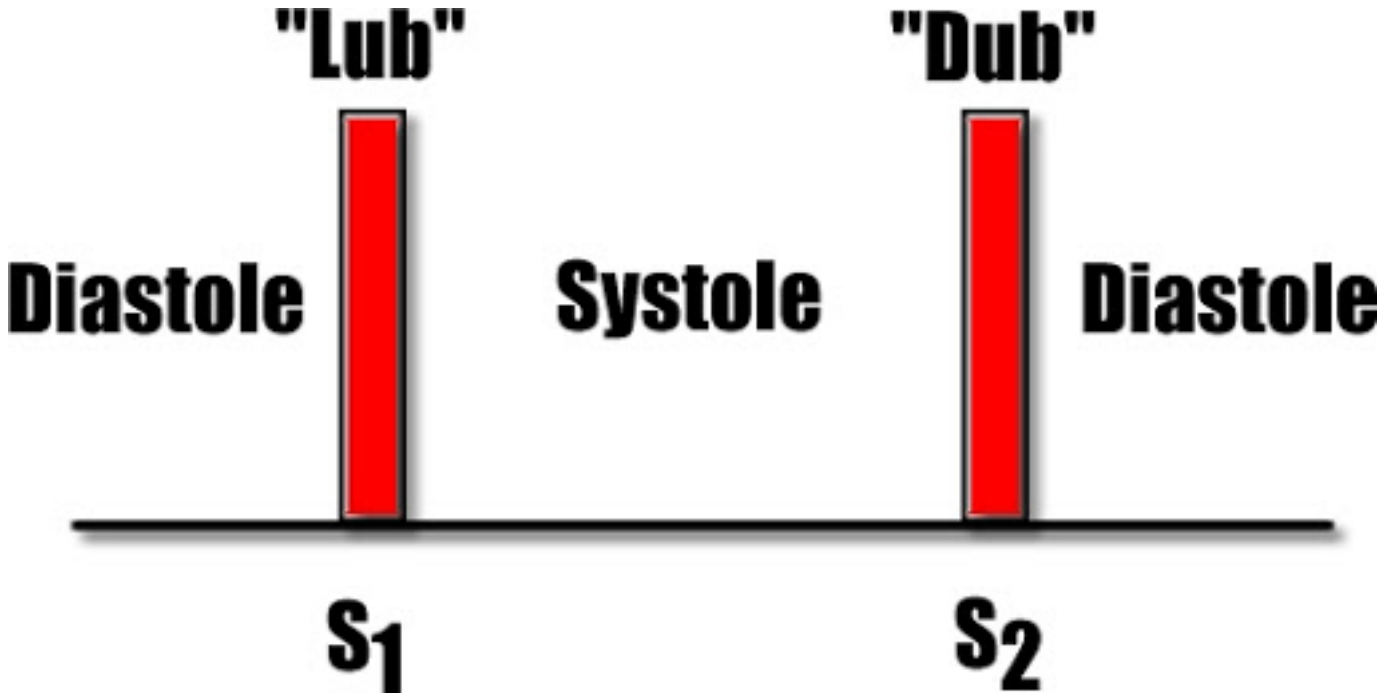


phonocardiography

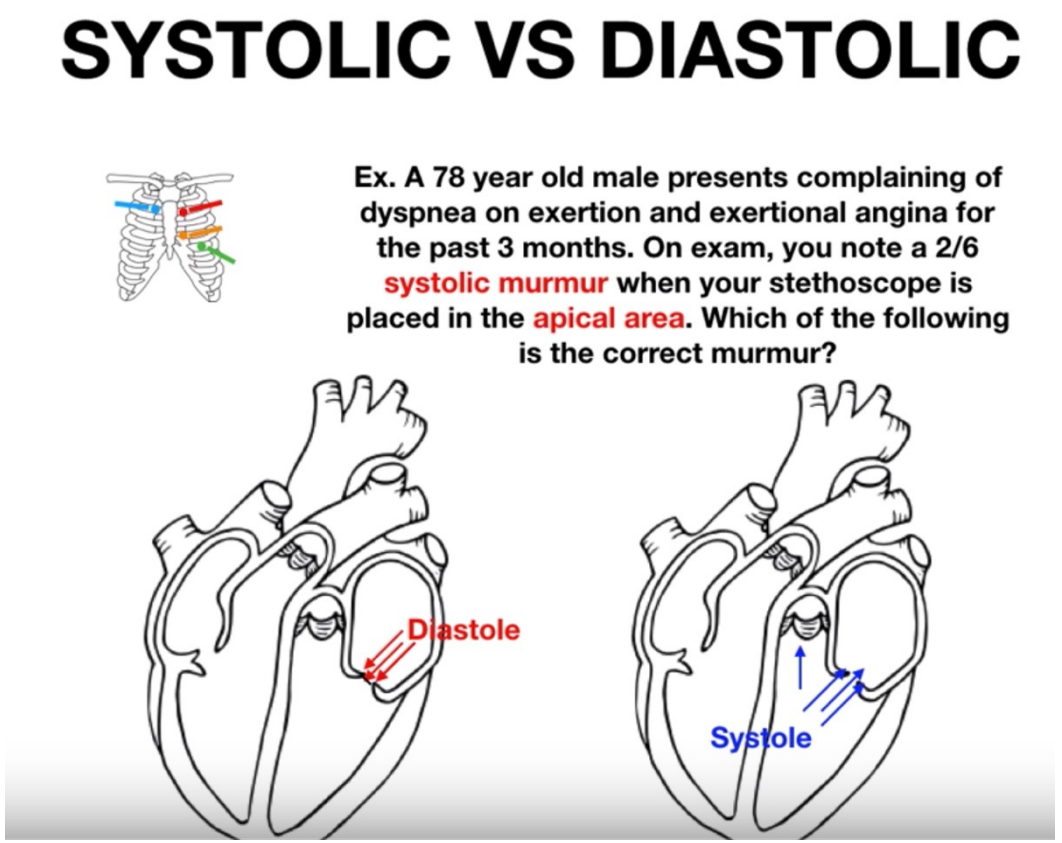


Phonocardiograms from normal and abnormal heart sounds

Physiological heart sounds



Question ?


SYSTOLIC VS DIASTOLIC
Ex. A 78 year old male presents complaining of dyspnea on exertion and exertional angina for the past 3 months. On exam, you note a 2/6 systolic murmur when your stethoscope is placed in the apical area. Which of the following is the correct murmur?
Diastole
Systole

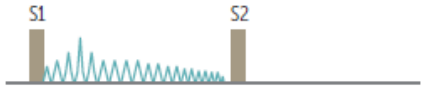
murmurs

SYSTOLIC	DIASTOLIC
Aortic Stenosis	Aortic Regurgitation
Pulmonic Stenosis	Pulmonic Regurgitation
Tricuspid Regurgitation	Tricuspid Stenosis
Mitral Regurgitation	Mitral Stenosis

Heart murmurs

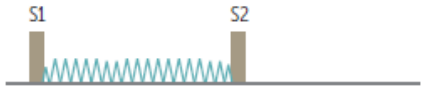
Systolic

Aortic stenosis



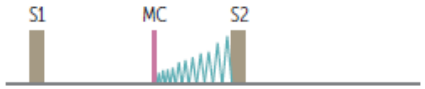
Crescendo-decrescendo systolic ejection murmur (ejection click may be present). LV >> aortic pressure during systole. Loudest at heart base; radiates to carotids. "Pulsus parvus et tardus"—pulses are weak with a delayed peak. Can lead to Syncope, Angina, and Dyspnea on exertion (SAD). Most commonly due to age-related calcification in older patients (> 60 years old) or in younger patients with early-onset calcification of bicuspid aortic valve.

Mitral/tricuspid regurgitation



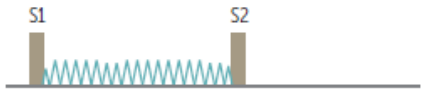
Holosystolic, high-pitched "blowing murmur."
Mitral—loudest at apex and radiates toward axilla. MR is often due to ischemic heart disease (post-MI), MVP, LV dilatation.
Tricuspid—loudest at tricuspid area. TR commonly caused by RV dilatation.
Rheumatic fever and infective endocarditis can cause either MR or TR.

Mitral valve prolapse



Late systolic crescendo murmur with midsystolic click (MC; due to sudden tensing of chordae tendineae). Most frequent valvular lesion. Best heard over apex. Loudest just before S2. Usually benign. Can predispose to infective endocarditis. Can be caused by myxomatous degeneration (1° or 2° to connective tissue disease such as Marfan or Ehlers-Danlos syndrome), rheumatic fever, chordae rupture.

Ventricular septal defect



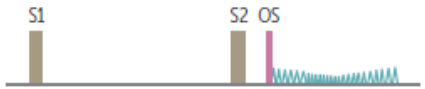
Holosystolic, harsh-sounding murmur. Loudest at tricuspid area.

Diastolic

Aortic regurgitation

High-pitched "blowing" early diastolic decrescendo murmur. Long diastolic murmur, hyperdynamic pulse, and head bobbing when severe and chronic. Wide pulse pressure. Often due to aortic root dilation, bicuspid aortic valve, endocarditis, rheumatic fever. Progresses to left HF.

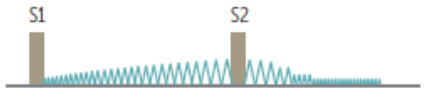
Mitral stenosis



Follows opening snap (OS; due to abrupt halt in leaflet motion in diastole, after rapid opening due to fusion at leaflet tips). Delayed rumbling mid-to-late diastolic murmur (↓ interval between S2 and OS correlates with ↑ severity). LA >> LV pressure during diastole. Often a late (and highly specific) sequela of rheumatic fever. Chronic MS can result in LA dilatation.

Continuous

Patent ductus arteriosus



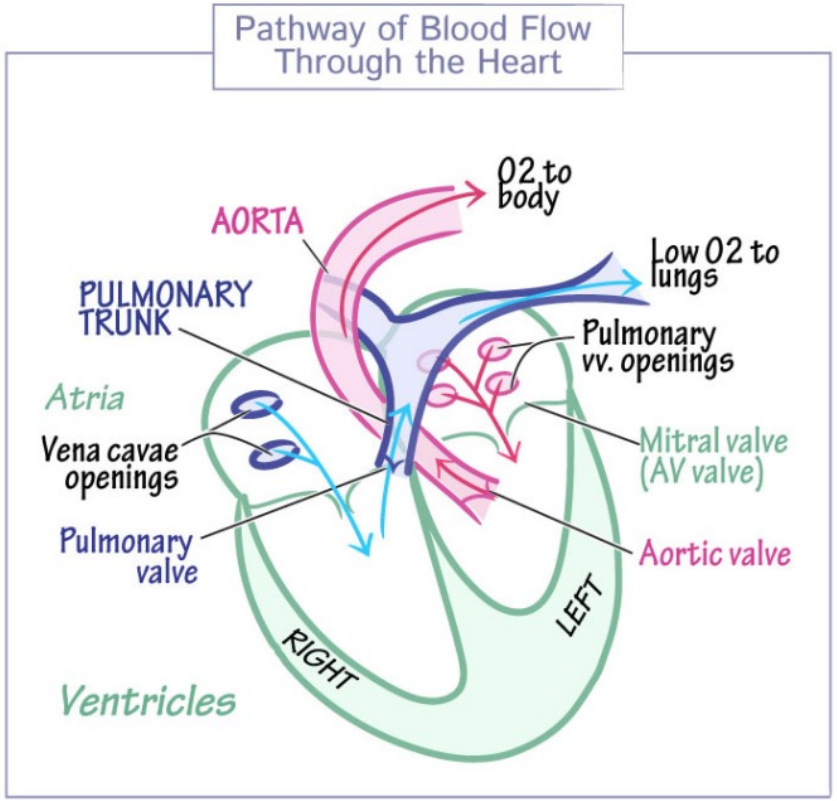
Continuous machine-like murmur. Loudest at S2. Often due to congenital rubella or prematurity. Best heard at left infraclavicular area.

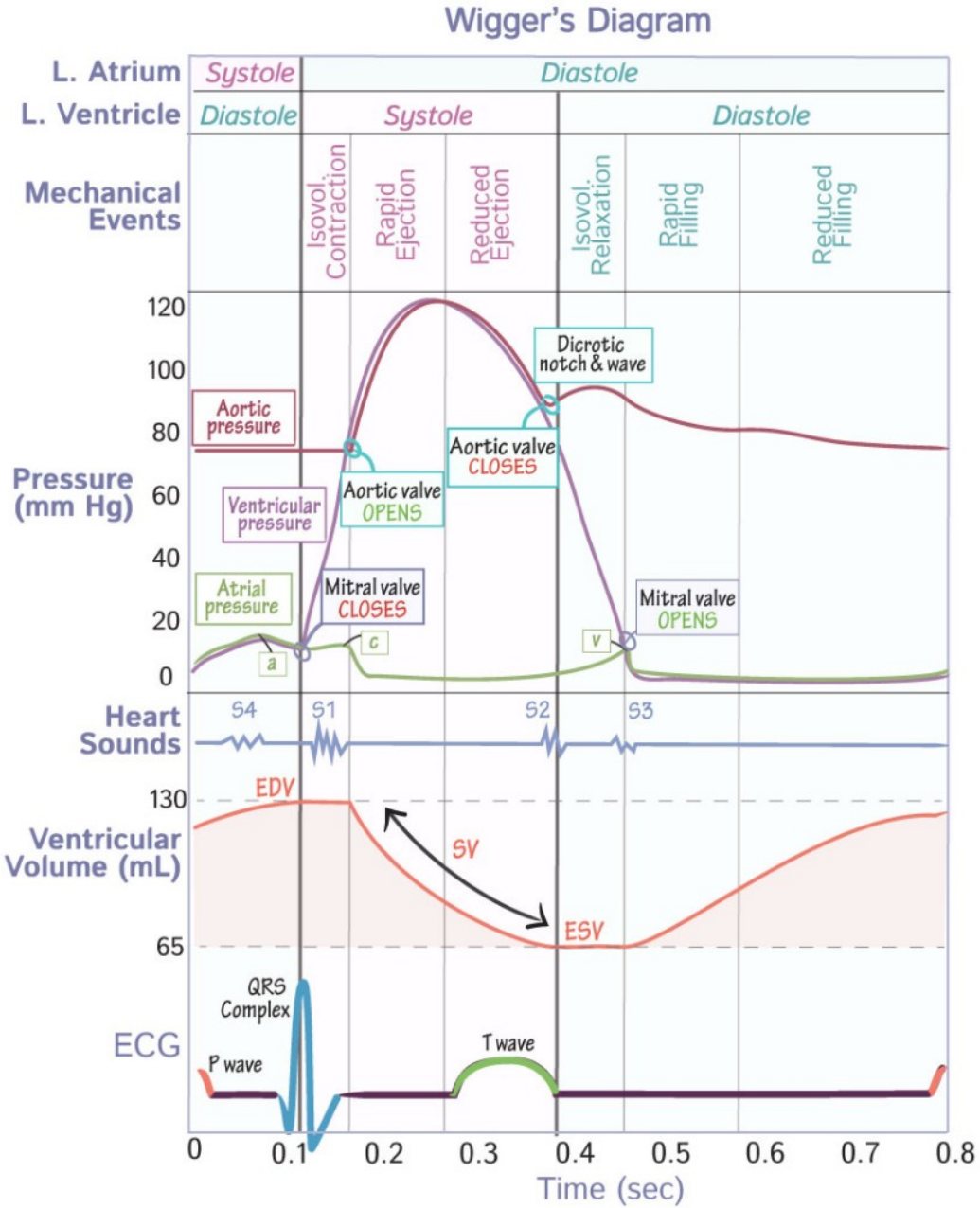
4. POLYGRAPHY

GRAPHING THE CARDIAC CYCLE

Wigger's Diagram

✓ Shows multiple parameters of cardiac flow and volume simultaneously.





THANKS FOR YOUR ATTENTION!