1ST YEAR MEDICAL STUDENTS
GENERAL PHYSIOLOGY
STARLING LAW OF THE HEART

BY

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4. CONTRACTILITY

Definition:
It is the ability of the cardiac muscle to contract (i.e. to change the chemical energy into mechanical work; contraction).

The effect of various factors on contractility is called inotropism:

- **A positive (+ve) inotropic effect means an increase in contractility.**
- **A negative (-ve) inotropic effect means a decrease in contractility.**

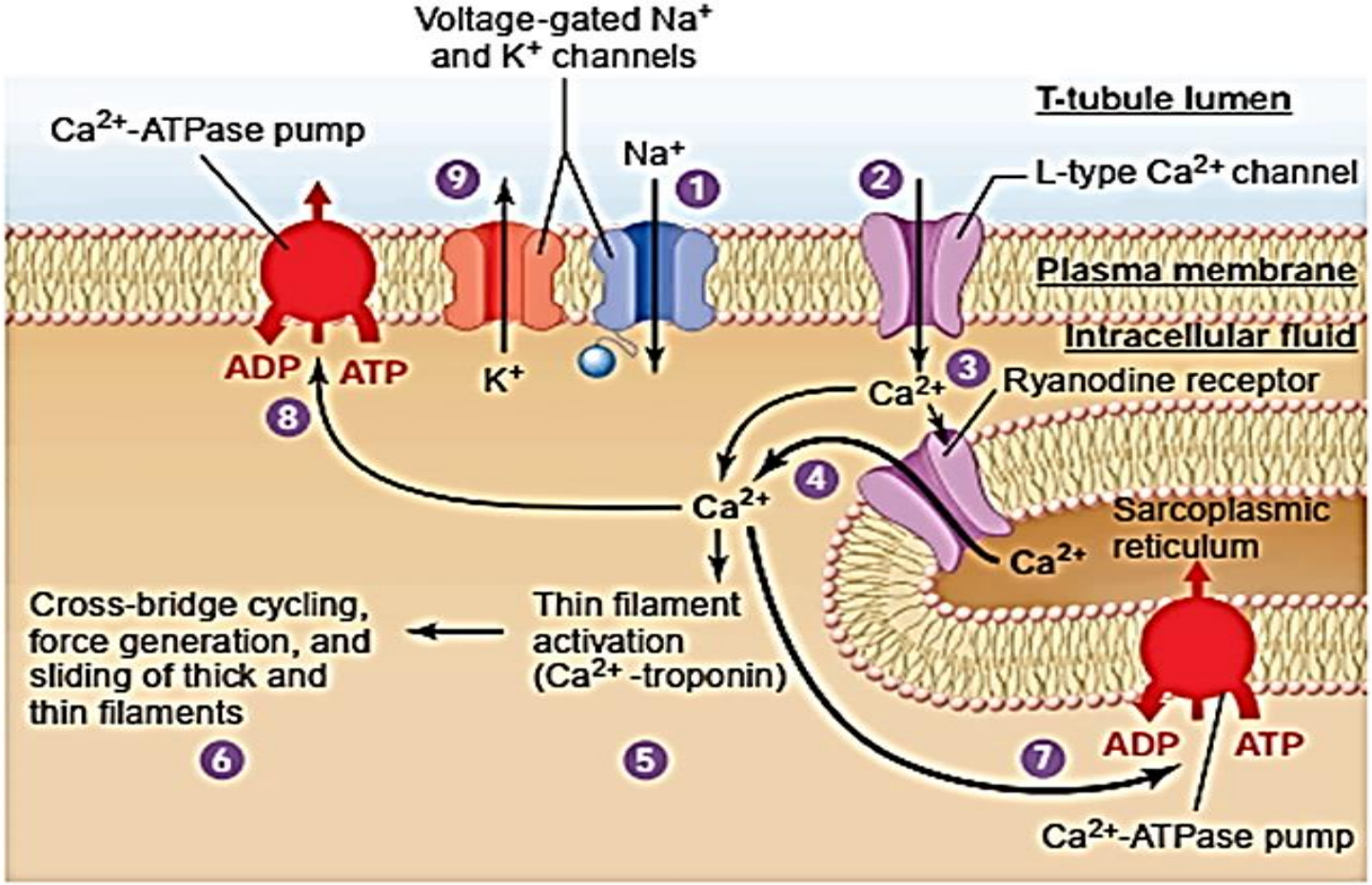
Myocardial Excitation-Contraction Coupling (ECC)

Membrane depolarization initiates the process of excitation contraction coupling (ECC) as follows:

- ✓ Opening of the long lasting (L-type) Ca^{2+} channels present in the sarcolemma and T-tubules→ Ca^{2+} influx from ECF into cardiac muscle fibers.
- ✓ This Ca^{2+} is called **depolarizing Ca^{2+}**. Although its amount is normally very small, it is important.
- ✓ This Ca^{2+} is sensed by the Ca^{2+} release channel in the terminal cisterns of the sarcoplasmic reticulum (SR) → this triggers the release of large amount of Ca^{2+} from the sarcoplasmic reticulum (**activator Ca^{2+}**).
- ✓ Calcium binds to troponin C → allows sliding of actin over myosin → muscle contraction.

Muscle relaxation occurs by

- Active reuptake of Ca^{2+} back to the SR (by Ca^{2+} ATPase pump; SERCA)
- Extrusion of Ca^{2+} from the cell by Na^{+} /Ca^{2+} exchanger and Ca^{2+} ATPase pump.


Voltage-gated Na+ and K+ channels
T-tubule lumen
Ca2+-ATPase pump
Na+
L-type Ca2+ channel
Plasma membrane
Intracellular fluid
ADP
ATP
K+
Ca2+
Ryanodine receptor
Sarcoplasmic reticulum
Cross-bridge cycling, force generation, and sliding of thick and thin filaments
Thin filament activation (Ca2+ -troponin)
ADP
ATP
Ca2+-ATPase pump
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In the cardiac muscle, the Ca^{+2} required for contraction comes from TWO sources;

Intracellular;

From the **SR (major** source called **activator** Ca^{2+}).

Extracellular,

via voltage gated **(L-type) Ca^{2+} channels** called **depolarizing** Ca^{2+} **(although limited** source, but it is very **important** as it **promotes** more Ca^{2+} release from the SR).

- ✓ **Cardiac output (CO): The volume of blood each ventricle pumps /minute.** It is usually expressed in **liters per minute**. It is **about 5 L/minute**.
- ✓ **CO= HR X SV.**
- ✓ **HR : is the number of beats/minute.**
- ✓ **Stroke volume (SV): The volume of blood pumped by each ventricle/beat.**

SV = the difference between ventricular end diastolic volume (EDV) and ventricular end systolic volume (ESV).

= EDV - ESV

= 140 ml– 70 ml = 70 ml/beat.

- ✓ **Ejection fraction (EF):**

It is the ratio of SV to EDV.

EF = 70 ml/140 ml X 100= about 50 %

It is directly proportional to the pumping capacity of the ventricles (to the SV).

Factors that affect cardiac contractility

These include : **Mechanical, cardiac and extra-cardiac factors.**

(A) Mechanical Factors

I. The Preload:

- ✓ In the intact heart, the level of preload is represented by the end-diastolic volume (EDV) (the volume of blood in the ventricles just before contraction).
- ✓ The preload determines the initial length of the resting muscle before contraction.
- ✓ It affects the tension developed in the muscle as well as the velocity of shortening and its extent.
- ✓ All these **increase when EDV increases**, resulting in a stronger ventricular contraction and a rise of intraventricular pressure which **increases the stroke volume (SV).**
- ✓ However, this occurs only up to a certain limit after which the peak ventricular performance is decreased.

Frank-Starling Mechanism of the Heart

- It **describes** the relation **between** the initial length of the muscle and the force (i.e. tension) generated in that muscle (i.e. **Length-Tension Relationship**).
- In the **cardiac** muscle: **Within limits, the force of cardiac muscle contraction is directly proportional to the initial length of the muscle fibers.**
- (i.e. the greater the initial length of cardiac muscle fiber, the greater is the force of contraction).
- The **initial length** of the cardiac muscle is determined by the **degree of diastolic filling** or **preload** (i.e. **EDV**) which in turn **depends on the amount of venous return (VR) to the heart**.
- This **relationship between stroke volume and EDV** is known as the **Frank–Starling mechanism** (also called ***Starling's law of the heart***).
- **Due to this law**, the heart is able to **pump any amount** of blood that it receives. But **overstretching** of cardiac muscle fibers → marked decrease in contractility.

Starling's Law of the heart

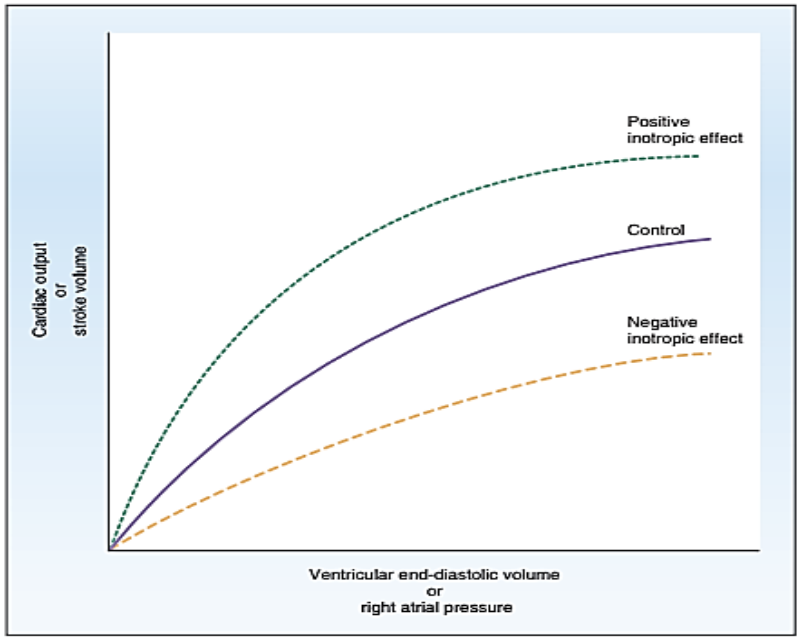
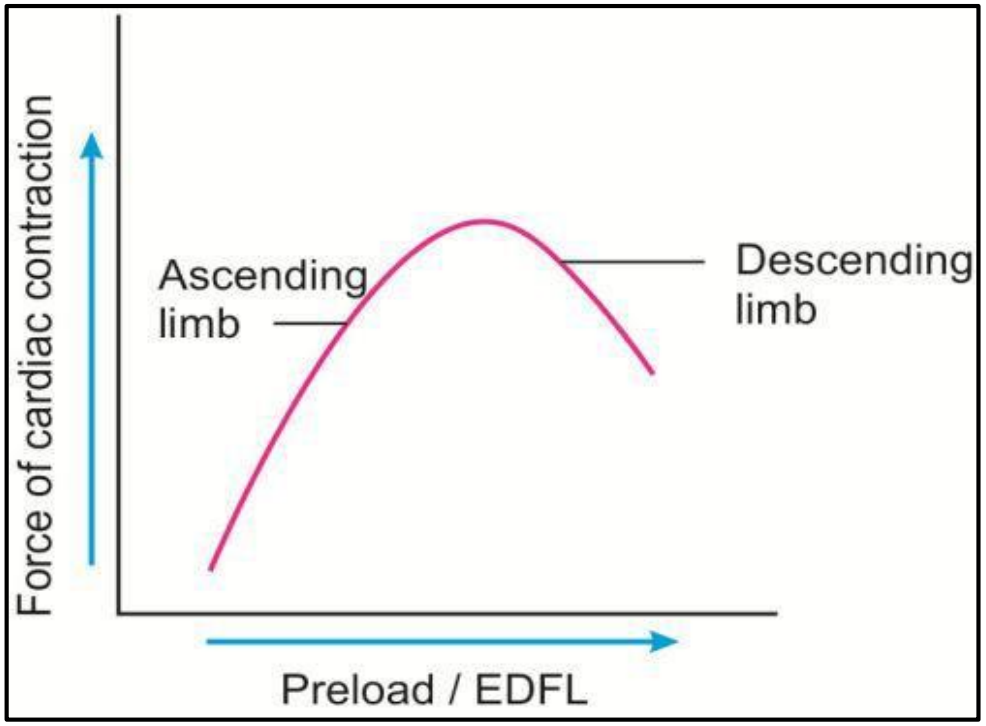
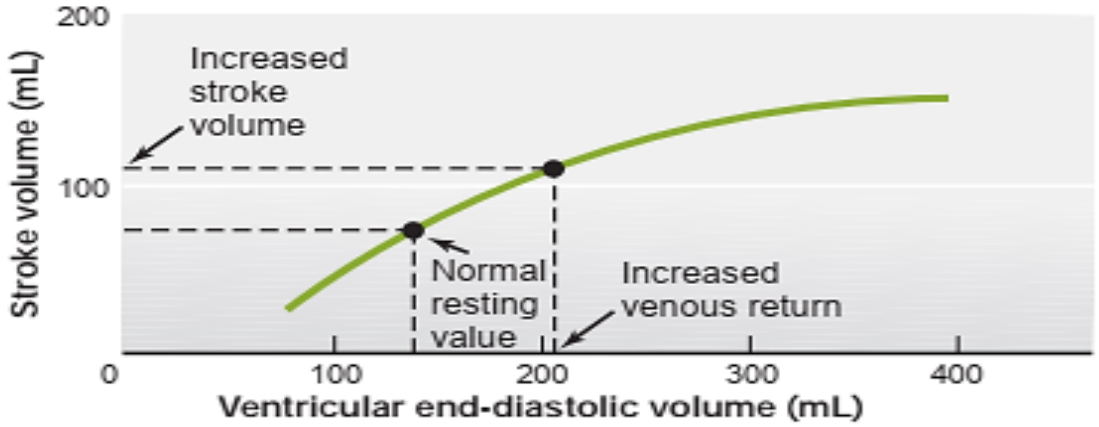


Fig. 4.22 Frank-Starling relationship in the heart. The effects of positive and negative inotropic agents are shown with respect to the normal Frank-Starling relationship.





Significance of Starling's law of the heart

Starling's law allows heterometric autoregulation of myocardial contractility (= regulation of contractility by changing the length of the muscle fibers), which occurs in the following conditions:

1. **In normal hearts** → Allows the heart to pump excess blood returning to it from veins (i.e. matches the ventricular output to the changes in VR). e.g. **during muscular exercise**. Thus, prevents stagnation of blood in the heart and veins.

2. **In denervated (i.e. transplanted) heart** → it is considered the main mechanism to adjust the pumping capacity of the heart.

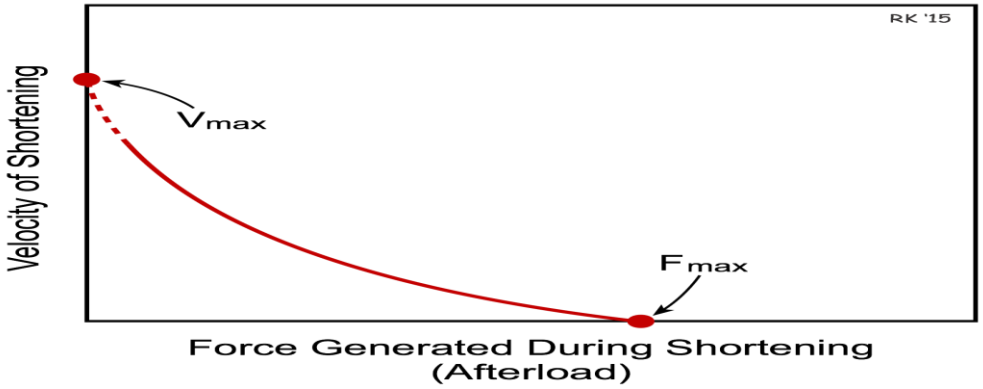
II. The Afterload

- The **afterload is the load that the muscle faces when it begins to contract**.
- It is the **arterial pressures against which the ventricles pump**.
- Changes in afterload affect mainly the velocity of shortening of the cardiac muscle.
- **Effect of afterload on velocity of shortening (Force-Velocity curve):**

✓ **The initial velocity of shortening is inversely proportional to the magnitude of afterload.**

✓ **At zero afterload, maximal velocity of shortening (V max) is achieved.**

✓ **While, at critical afterload, the velocity of shortening becomes zero and the muscle contracts isometrically.**



(B) Cardiac (or intrinsic) Factors

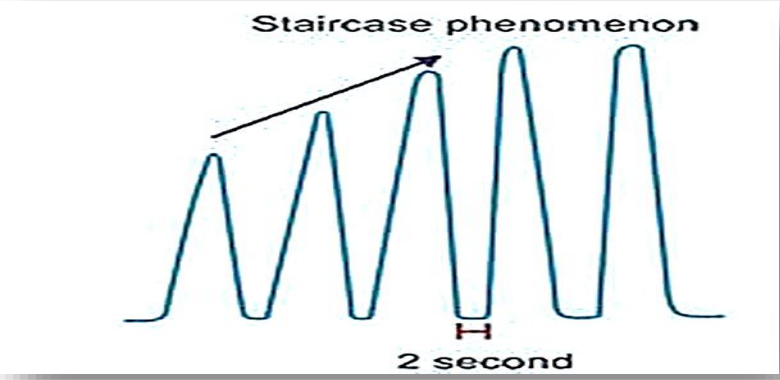
(1) The myocardial mass:

A significant injury (or loss) of the functioning ventricular mass (e.g. due to ischemia or necrosis) decreases the force of myocardial contractility. This also occurs in cases of heart failure.

(2) The heart rate:

Normally, there is a **Force-Frequency relationship** in the heart. i.e. the force of cardiac contractility is affected by the frequency of stimulation (heart rate).

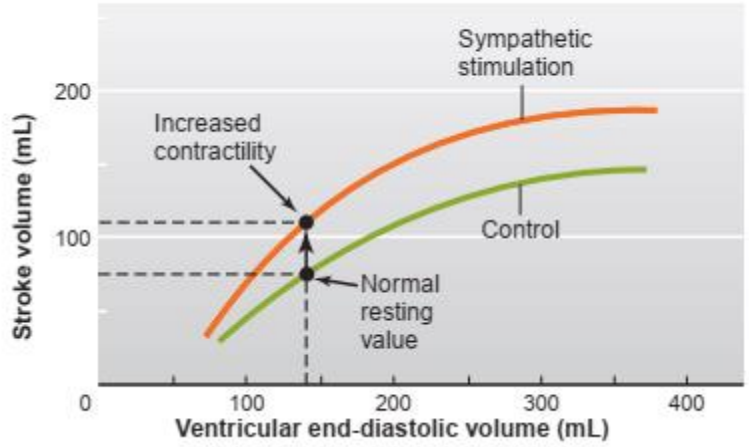
An increase in the frequency of stimulation causes a proportional increase in the force of contraction (like the staircase or treppe phenomenon) and vice versa.



(C) Extra-cardiac (Extrinsic) Factors

(1) Nervous Factors:

- Sympathetic Stimulation → ↑ contractility (positive inotropic effect).
- Vagal Stimulation (on atria ONLY): → ↓ contractility (negative inotropic effect).



(2) Chemical Factors

(A) Hormones:

Catecholamines, glucagon and thyroid hormones all exert a +ve inotropic effect.

(B) Blood gases:

- Moderate hypoxia (O_2 lack) and hypercapnia (CO_2 excess) increase the cardiac contractility through stimulating the chemoreceptors.
- Severe hypoxia and hypercapnia directly depress the cardiac muscle and decrease the contractility. This is usually due to insufficient blood supply → inhibits ATP production which is the source of energy of muscle contraction.

(C) Effect of ions: Ca^{2+}

Excess Ca^{2+} (i.e. Hypercalcemia) →↑ contractility (a +ve inotropic effect) as a result of more calcium influx into the cardiac muscle fibers. It prolongs the systole on the expense of diastole and the heart may stop in systole (Ca^{2+} rigor). So, I.V. Ca^{2+} injections should be given very slowly.

(D) Acetylcholine → ↓ contractility (–ve inotropic effect).

(3) Physical Factors:

- Moderate rise of body temperature → ↑ contractility.

(Due to increased metabolism and decreased viscosity of myocardial structures and increased Ca^{2+} influx).

- Hypothermia→ ↓ contractility.


Thank
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