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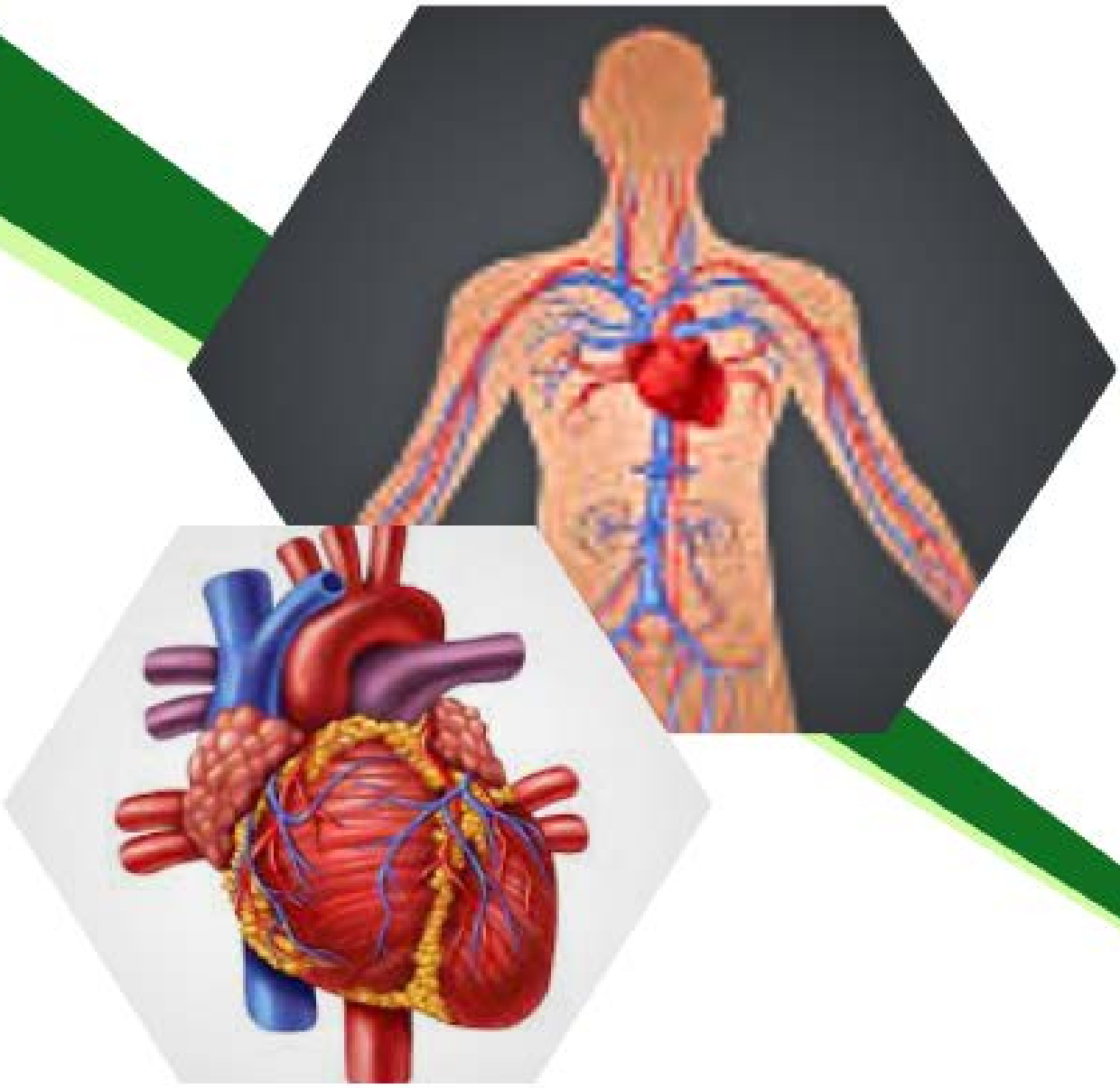
no. 9

CVS
PHYSIOLOGY



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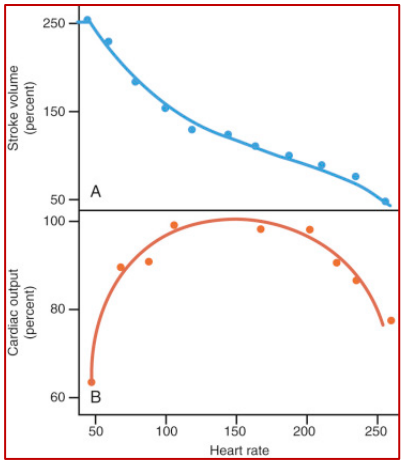
Cardiac Output (CO) and Reserve

- CO is the amount of blood pumped by each ventricle in one minute
- CO is the product of heart rate (HR) and stroke volume (SV)
  - Q= HR*SV
  - HR is the number of heart beats per minute
  - SV is the amount of blood pumped out by a ventricle with each beat
  - For ex: CO (ml/min) = HR (75 beats/min) x SV (70 ml/beat) →CO = 5250 ml/min (5.25 L/min)



  - From this equation we may conclude that there is a linear relationship between CO and HR, however, this is only true up to a certain point (maximal CO point) beyond which this relation deviates into a more bell-shaped as the curve starts to decline.
  - Let's assume a HR of 200 bpm then each cardiac cycle will take 0.3 secs, systole 0.19 secs and diastole 0.11 secs which is shorter than the systole; no enough time for filling, therefore, no enough blood for ejection.
  - An increased heart rate occurs at the expense of diastolic time which leads to a decrease in stroke volume.
  - We are concerned about exceeding the heart rate (HR) corresponding to maximal cardiac output (CO) in patients with ischemic heart disease (IHD). An elevated heart rate increases oxygen demand, ultimately leading to ischemic propagation.
  - Hypoxia impairs the function of Na-K-ATPase, membranes become more permeable to both Na and K which leads to cationic intracellular overload; reaching the threshold easily and generating an ectopic pacemaker, we finally reach ventricular fibrillation and death as the ischemic tissue propagates more and more.

- In short, decreased CO is mostly feared when it generates an ischemic focus which may become an ectopic pacemaker that increases the HR more and more (positive feedback) and finally leading to ventricular fibrillation and death.
- We can calculate the maximal HR that we should not exceed by this simple equation:
  HR_{Max}= (220-age)*75% (normal individuals)
  HR_{Max}= (220-age)*85% (athletes)
  HR_{Max}= (220-age)*65% (>60 yrs old or with coronary heart disease)
- Again, sympathetic stimulation increases HR by increasing I_f (increasing Ca entry through t-type channels→ increasing the slope of phase 4) while parasympathetic stimulation works by the contrary and Ach may increase K outflow (further away from the threshold→ decreasing the slope) and all drugs acting by same mechanisms are called positive/negative chronotropes.

- Cardiac reserve is the difference between resting and maximal CO

Regulation of Stroke Volume

- SV = end diastolic volume (EDV) minus end systolic volume (ESV)
- EDV = amount of blood collected in a ventricle during diastole
- ESV = amount of blood remaining in a ventricle after contraction.
- End systolic or end diastolic (volume or pressure) is time-point.

Factors Affecting Stroke Volume

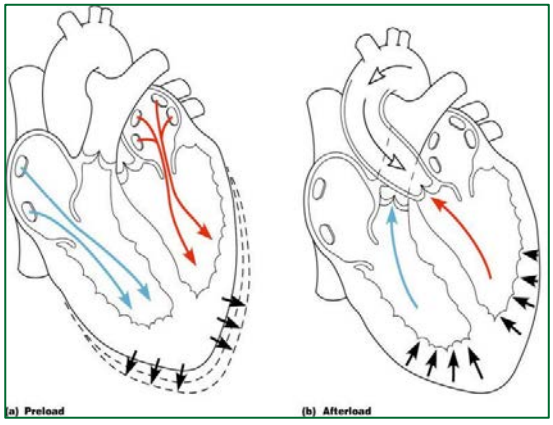
- Preload (EDV)– amount ventricles are stretched by contained blood (increases SV).
- Contractility – cardiac cell contractile force due to factors other than EDV (increases SV).
- Afterload – back pressure exerted by blood in the large arteries (aortic) leaving the heart after contraction (decreases SV).

Quick recap

- Cardiac output (ml/min)=heart rate per minute* stroke volume per beat.
- Q=72 (beat/min) * 70 (ml/beat)=5000 (ml/min).
- Heart rate is under the effect of ANS (sympathetic and parasympathetic).
- Factors affecting SV:
  - Preload (EDV).
  - Contractility.
  - 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.



- Sarcomere is located between two adjacent Z-lines, a relaxed sarcomere of the heart, in normal physiological conditions, is 2.2 µm in length (the optimal length).
- Within physiological limits, the force of contraction of the muscle fiber is influenced by the length of the sarcomere which enhances the sliding movement, known as the length-tension relationship.
  Frank-starling law: within physiological limits, the longer the sarcomere, the stronger the force of contraction.
- Overly stretched sarcomere (beyond the L-max) hinder the sliding movement of actin and myosin filaments, this is due to reduced overlap and fewer cross bridges formed, which diminishes the force of contraction.

- L-max→ the length of sarcomere at which maximum tension develops.
- Skeletal muscle: L-rest= L-max, so upon giving the skeletal muscle stimulus it will produce the maximum response.
- Cardiac muscle: L rest< L max, which acts as a CO reserve, giving a spared output.
  i.e. in cases of weak cardiac fibers with an ejection fraction (EF) less than 50%, often associated with cardiomyopathy; by increasing the end-diastolic volume (preload), we enhance the ejection fraction, this ability is attributed to the cardiac muscle overstretch before reaching the maximin length (L max).
- Increased preload results in an increased sarcomere length.
- As preload increases, contractility (tension generated by the cardiac myocyte) increases.

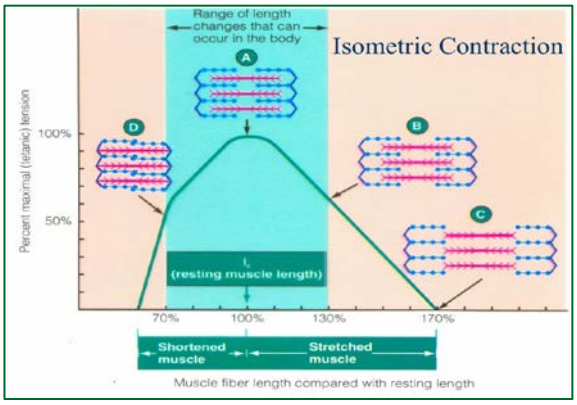
- *Cardiac reserve*: The maximum percentage that the cardiac output can increase above normal. If cardiac output rises to 25 l/min, this corresponds to 400% cardiac reserve.
- Diagnosis of Cardiac reserve: Exercise Test: Symptoms of HF such as 1. Dyspnea, 2. muscle fatigue, and 3. Excessive increase in HR because the nervous system is trying to compensate for the decrease Q.

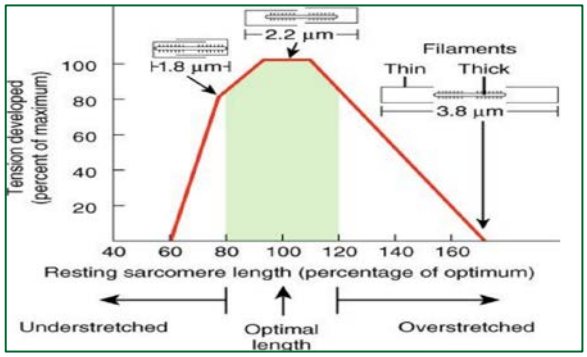
Normal cardiac reserve	400%
Athlete	600%
Moderate coronary disease	200%
Severe coronary disease	Zero
Severe valvular disease	Zero

- A helpful reminder in case you've forgotten the physiology of muscles:

- Resting length (L-rest): maximizes the ability of the muscle to contract when stimulated.
- *Length-tension relationship*: effect of resting fiber length on muscular contraction.

- In skeletal muscle maximal active force is generated at length close to the resting length of the muscle.
- In cardiac muscle there's an optimal ability to increase the L max, hence, increasing preload and force of contraction.
- Passive force (tension) results from the stretching of muscle fibers, arising from its elastic properties.
- Active force is generated during muscle contraction in response to a neural stimulus due to sliding phenomenon of actin and myosin.

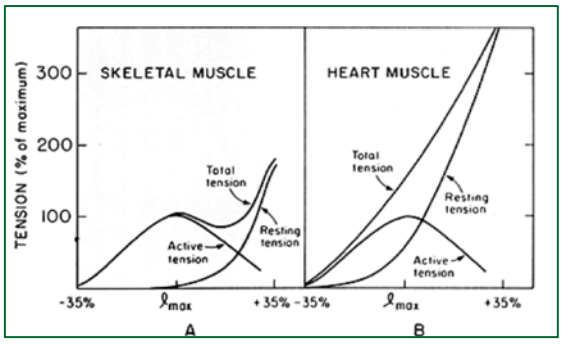


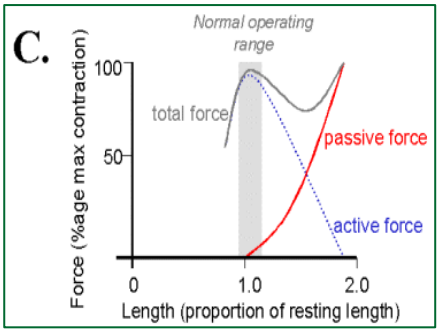


Length-Tension Relation for Skeletal Muscle

- Active tension cannot be measured directly, what can be measured?
  1. passive tension - tension required to extend a resting muscle
  2. total tension - active tension and passive combined
- Active is calculated from 1 & 2
- (AT = TT – PT)
- Note that active tension falls away linearly with increasing length.

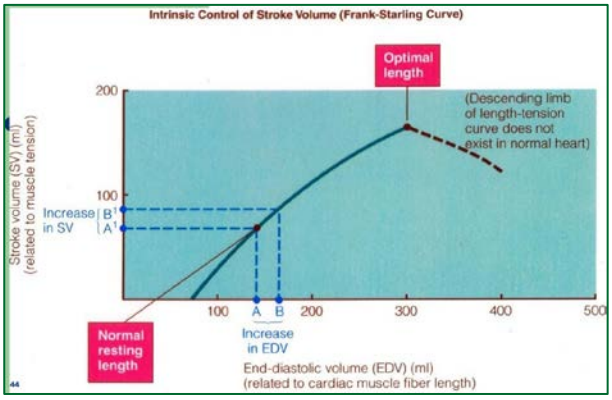
The Dr didn't mention these calculations, so just grasp the concept.





Cardiac Muscle length-tension relationship

- Cardiac muscle works at much less than its maximum length in contrast to skeletal.
- Total, Active and Passive length-tension relationship differ
- Frank-Starling law of the heart



- As a protective mechanism, the pericardium is formed from collagen instead of elastic fibers, to prevent the overstretching of the cardiac muscle beyond its maximum length.

اللهم إنّا إليك راغبون، إليك تائبون، فاستعملنا ولا تستبدلنا، وكن لإخواننا عونًا ونصيرًا.