

## Cardiac Output

Cardiac output can be regulated by SANS/PANS, and it can increase several fold between rest and exercise.

$$\begin{aligned} \text{CO} &= \text{HR} \times \text{SV} \\ \text{SV} &= \text{EDV} - \text{ESV} \end{aligned}$$

Regulation of Cardiac Output can be accomplished by changes in these variables:

- Venous return. Venous return determines EDV, which determines the preload.
- ESV, which depends on contractility and afterload.
- HR, which is influenced by the ANS (PANS slows it down, SANS speeds up)

### Venous Return increases EDV (End Diastolic Volume)

How? When you exercise, you release E/NE which acts as a vasoconstrictor on the venous side of systemic circulation. This increased constriction on the one-way valves of the veins pushes more blood along and this increases Venous Return. Note that this does not increase blood pressure, b/c blood pressure in the veins is low.

You can elevate VR in three ways:

1. Venoconstrict
2. Increase skeletal muscle pump activity
3. Increase respiratory pump activity

} This, in turn, enhances EDV which enhances CO

### Why does increased EDV elevate Stroke Volume?

The fuller the heart is prior to contracting, the stronger it contracts. This is because the fibers are stretched closer and closer to their “optimal length” for optimal contraction. So, you could say that the load is increased right before ventricular contraction. This is called PRELOAD! Increased VR means increased preload!

### The heartrate is influenced by the ANS & associated hormones

SANS enhances contractility

Enhanced contractility elevates SV by lowering ESV

SANS enhances VR through vasoconstriction

Higher EDV (preload) leads to higher SV

Higher ESV leads to lower SV

SANS can lower ESV and that raises SV

PANS decreases heartrate

### Afterload

Afterload is the load the heart is working against to open the aortic semilunar valve. The pressure in the aorta is higher than the pressure in the ventricle, so the heart has to work harder to push that valve open and eject blood.

If you have two cardiac cycles...one with a standard preload and standard ejection, and one with high aortic pressure and the same preload...you will not get the same ejection. It takes longer to open the valve and it doesn't stay open as long. So, ejection goes down, ESV goes up, but EDV stays the same. This means less SV and not enough blood is being ejected.

Note that increases in afterload are typically moderate and easily compensated for by enhanced preload and contractility in people with healthy CV systems. The major problem associated with afterload results from chronic hypertension (>140/90)...the heart attempts to compensate and maintain SV, but this leads to an overworked heart and heart failure. The increased arterial pressure is usually associated with excessive peripheral vasoconstriction and/or arterial blockage.

### **Preload**

Increased preload increases stroke volume. How?

It stretches the heart muscle to its optimal length (recall the Length-Tension relationship of contractile cells). At its optimal length it has optimal tension...any less and it's not optimal, any more and it's also below optimal. The optimal length allows for the most interaction between the thick and thin filaments, so there are more power strokes going on to create more tension! At resting, the myocardium are only at about 20% of optimal length, so there is a lot of room for improvement!

As EDV goes up, you are increasing the length.

As SV goes up, you have more tension.

The two are related!!!

EDV is directly related to SV

If EDV goes up to 40mls, then SV goes up to 40 mls. This is the "Frank Starling Principle of the Heart"

Note that the cellular mechanism for this is the L-T relationship...it enables more cross-bridges to be formed, so you have more tension.

Another difference between skeletal muscle and cardiac muscle is that skeletal muscle is always pretty close to its optimal length (about 80%), while cardiac muscle is closer to 20%...so there is a lot more of a physiological range with cardiac muscle.

Preload does not change ESV...it changes Stroke Volume due to a larger EDV.

$$\begin{array}{l} \text{EDV} - \text{ESV} = \text{SV} \\ 1) 135 - 35 = 100 \\ 2) 175 - 35 = 140 \end{array}$$

Note that the ESV stayed the same, and that SV went up in direct relationship to EDV.

### **EDV(preload) is affected by:**

1. Venous return...a higher VR means a higher preload. Can be enhanced by exercise!
2. Filling time...diastole shortens as HR increase, so increased preload and contractility compensate to increase cardiac output until HR approaches maximum values.

**So, how do you get ESV to go down?** By enhancing contractility, which increases SV, thereby reducing ESV.

### **How do you change SV?**

To change SV you change both contractility and pre-load...they happen together!

### **How does the heart generate extra pressure?**

It is simply that it is closer to optimal length...has nothing to do with EDV or Calcium.

### **A note about intrinsic and extrinsic factors.**

Preload is in intrinsic factor.

- It is not using a chemical messenger to facilitate change
- It is simply a factor of how the myocardium are set up

Contractility is an extrinsic factor.

- Uses a 2<sup>nd</sup> messenger pathway to increase Calcium influx
- E/NE bind to b-receptors to initiate cAMP to act as a 2<sup>nd</sup> messenger.

### **Contractility**

Contractility is defined as increased strength of a contraction. It is independent of fiber length (so not a part of the T-L equation). What causes the greater tension??? Calcium! At rest the amount of Calcium released into the cell is submaximal...again, a lot of room for improvement.

Contractility is increased by the SNS and its release of E/NE.

- There is no change in the EDV (you start with the same amount of blood)
- The increased catecholamines lead to more Calcium leads to more tension
- No change in the length, only a change in tension
- More calcium = stronger contraction (until peak levels)
- More tension = more SV

### **So, how do you get more calcium into the cell???**

The E/NE binds to B-receptors on the cell membrane, initiating a 2<sup>nd</sup> messenger pathway using cAMP. cAMP turns on protein kinase, which phosphorylates proteins. In particular, it phosphorylates L-type Calcium Channels! This increases the chance of the channels being open (increased permeability to calcium), so there is even more calcium-induced calcium-release from the SR. (it also opens more of these channels in the SR.)

They also phosphorylate calcium pumps on the SR, so that it can get the calcium back in that much faster and get ready for the next contraction...which is going to come at a faster rate due to elevated heart rate.

It also phosphorylates myosin ATPase, which energizes the myosin head for more power strokes!

This is all happening in the plateau phase...remember, that is the only time calcium plays a key role in the action potential of a contractile cardiac cell.

So what is the end result? Not only do you get more force, but you shorten the cell at a faster velocity (can eject more in less time).

**Positive inotropic agents** are substances that increase contractility by raising intracellular calcium. Examples are E/NE (which are B-agonists), Glucagon, TH, digitalis, caffeine, hypercalcemia. (recall that TH is permissive for catecholamines!)

**Negative inotropic agents** are substances that decrease contractility by decreasing intracellular calcium. Examples are B-blockers, calcium-channel blockers and hyperkalemia.

**In summary...**

Increased preload and increased contractility happen together to increase stroke volume!  
See slides for the rest...

**EKG**

EKG is a collective recording of electrical activity of the heart over time.

An interval includes at least 1 wave, and a segment is the time between waves.

P wave represents atrial depolarization

QRS represents ventricular depolarization

T wave represents ventricular repolarization