

CIRCULATORY PHYSIOLOGY SECTION 3: CARDIAC MECHANICS – The Control of Cardiac Output*

Summary: In this we will look at the mechanical action of the heart as a pump and how it is able to adjust its stroke volume as a result of the Frank-Starling Phenomenon and the influence of the sympathetic nervous system. We will also see how to find cardiac output using the Fick principle and finally, we will look at the control of cardiac output and work of the heart.

I. The Control of Cardiac Output

A. Obviously there are two general ways to control cardiac output -- changes in stroke volume and/or rate.

1. a change in HR is called a **chronotropic effect**.

(a) Increases in rate are called **tachycardias**

(b) Decreases in rate are called **bradycardias**

2. a change in force of contraction (which is usually accompanied by a change in SV is called an **inotropic effect**.

B. In both cases, the agent causing the change may be either:

1. **intrinsic (myogenic)** in which case the heart responds to some change in the circulation or

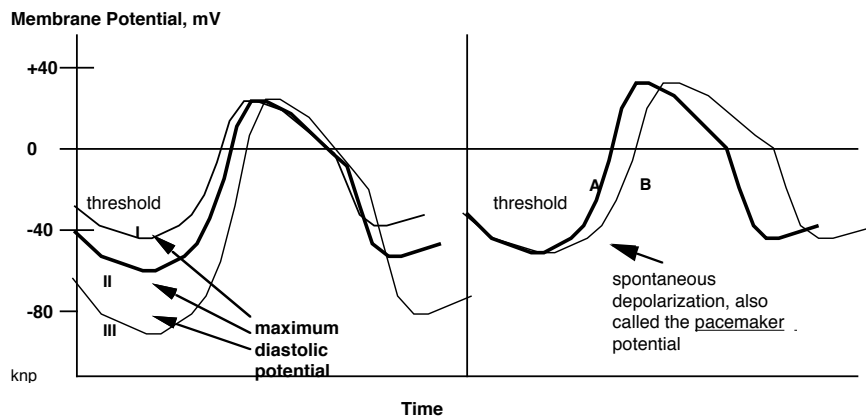
2. **extrinsic** where the heart responds to a neural or endocrine signal

C. **Control of rate:**

1. Generally, rate controls act on the cells of the SA node. There are two general types of things that happen on the cellular level to change rate:

a. Change the rate of depolarization (increasing the pacemaker potential rates).

b. Change the **maximum diastolic potential** (the most negative potential the pacemaker cell reaches) relative to the threshold:



Ways to change heart rate. In the panel on the left, some effect has changed the maximum diastolic potential (MDP). Assume cell II is normal -- in the case of cell #I the MDP has moved closer to threshold and the rate of firing (and therefore heart rate) has increased; in cell #III the cell has a more negative MDP which is further from threshold and therefore the rate decreases. **Right:** Here the rate of spontaneous depolarization (pacemaker potential) changes in A compared to B. A has the faster depolarization rate and therefore is associated with a higher heart rate. In reality both the MDP and pacemaker potential tend to change together; more negative MDPs are associated with slower pacemaker potentials and work together to produce a lower HR and vice versa for higher rates.

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2. **Intrinsic (Myogenic) Control of Rate:** This is a minor factor with respect to rate
a. control is overall genetic and there are differences between individuals and certainly between species.

b. **stretch** of the atria has an important effect but it is mediated through the vagus nerve; see below.

D. **Extrinsic Controls on Rate:** The intrinsic rate of discharge of a myogenic (and neurogenic) heart can be modified by external stimuli. Just considering vertebrates, the avenues involve both branches of the **Autonomic Nervous System** and they are:

1. Neural:

a. **Vagus nerve (Xth Cranial Nerve):** The vagus nerve is part of the **parasympathetic nervous system**. It has endings on a number of tissues, including the SA and AV nodes. Its effect is to slow the heartbeat (inhibit SA node) and slow the rate of transmission through the AV node.

(i) the Vagus releases **acetylcholine** as a neurotransmitter

(ii) It binds to what is called the **muscarinic receptor**; the different action of this receptor in response to its signal, acetylcholine is the reason that the same signal can produce excitation in skeletal muscle and inhibition in cardiac and smooth muscles.

(iii) many effects are mediated through the vagus nerve -- for example, increased stretch on the atria triggers an inhibition in the release of ACH by the vagus and this results in a higher heart rate (Bainbridge effect).

b. **"Accelerator nerve":** This **sympathetic** nerve also ends on the SA and AV nodes. Its effect is to increase the rate of firing of the SA node and increase conduction velocity of the AV node.

(i) The NT released by the accelerator is NE with some E. It has a minor stimulatory effect on rate.

(ii) the NE binds to alpha-receptors in the SA node.

2. **Endocrine: Epinephrine (E) and small amounts of norepinephrine (NE)** are both released by the adrenal medulla in response to sympathetic stimulation.

a. The main effect is via the binding of E on beta receptors of the SA and AV nodes which will cause an increase in SA firing rate by doing both of the things mentioned in the figure above (and perhaps also by lowering the threshold) and AV node transmission rate. E will also have effects on force of contraction (see below).

b. Adrenal release of E is the main means whereby HR is increased via sympathetic stimulation

? In most humans, resting heart rates vary between 60 and 70 b/min at rest, in mice it is 400-500 bpm. When the heart is removed, the rate will increase to about 105 b/min. in humans (referred to as the intrinsic heart rate) and 200-300 bpm in mice. In light of the roles of the two branches of the autonomic nervous system, what do these data tell you about the regulation of heart rate in humans and mice?

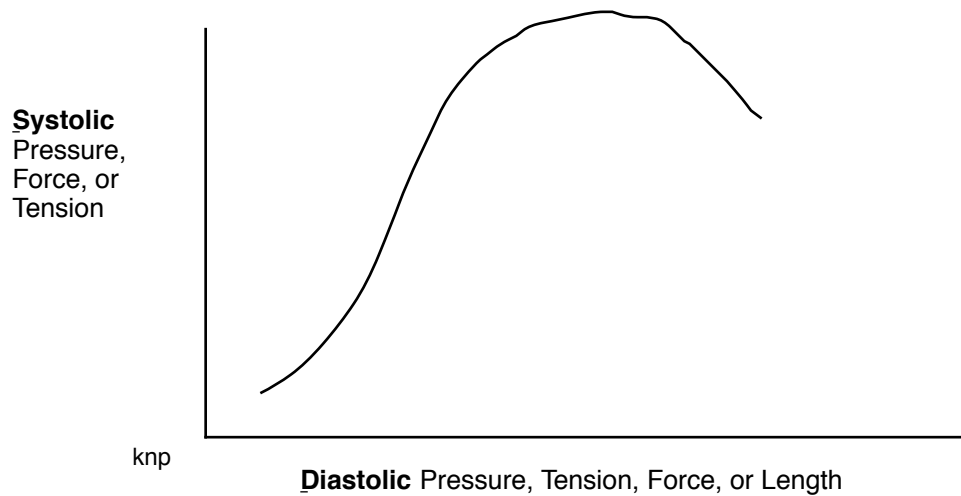
E. **Control of SV:**

1. The fundamental factor within the heart that can change is the rate at which it develops pressure, **dP/dt**. Ultimately, this will be due to changes in force of contraction.

2. **Intrinsic Determinants of Contractile Force -- the Frank-Starling Effect**

a. In cardiac muscle, as in all muscles, **force is a function of the length of the muscle fibers**.

b. Thus, if we plot the **diastolic fiber length (relaxed length) vs. the force developed during systole**, we get the following relationship:



c. The graph above shows that the more the heart is stretched (that is, the more blood that has entered the heart), the greater the force of contraction (in effect meaning the greater the volume of blood that will be pumped).

(i) Stretch on the walls at the end of diastole of the heart as a result of filling is referred to as **Pre-Load**. As the graph above shows, preload is related to a number of different variables:

(a) The most direct is stretch (diastolic tension) or volume of chamber. Clearly, the greater the volume, the longer the fiber (sarcomere length)

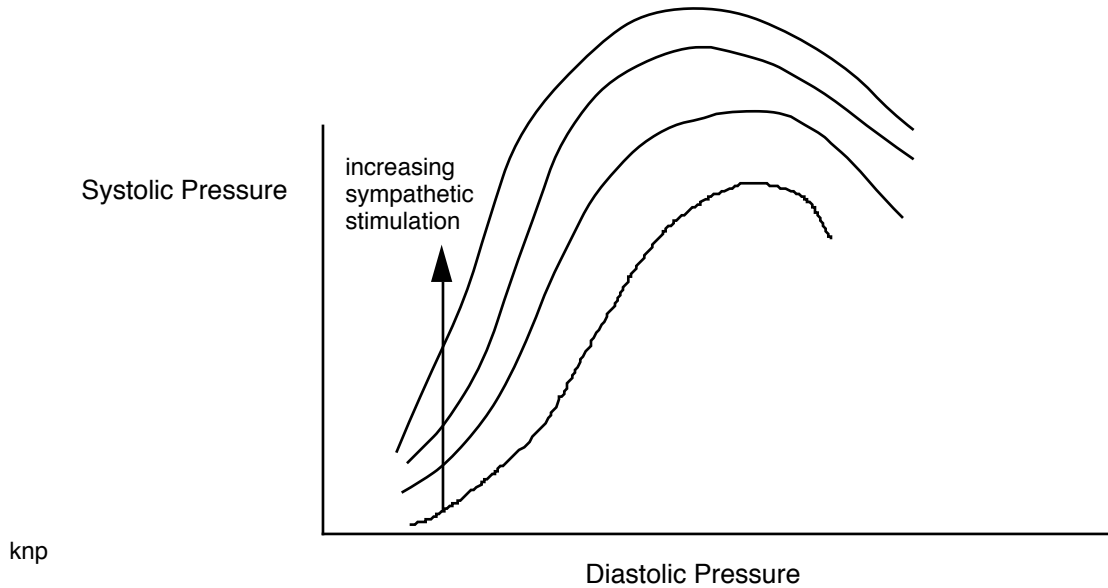
(b) a less direct measure is venous or right atrial pressure. Since pre-load refers to diastole, generally the greater the venous or RA pressure the more blood that has entered the heart and the more distended the heart.

d. This graph is a representation of the **Frank-Starling law of the heart** (or simply **Starling's Law of the Heart**) that states that "**within limits, the heart will pump all blood that comes to it**".

3. **Extrinsic Factors and SV:**

a. **Constant force of contraction but different "afterload"**. The pressure of the blood in the great artery (aorta or pulmonary) is referred to as the **afterload**. For a given artery, it is related to the volume of blood in the artery and the peripheral resistance, as we saw in packet C-2. The greater the afterload, the less blood that can be ejected by a heart producing a certain amount of pressure.

b. **The force of contraction at a given volume (contractility) can also be modified by the effects of epinephrine (E) stimulation on the heart**, such that a whole family of similar curves can be generated, each for different loads of E stimulation: (next page)



- c. The property of the force that the heart can develop at a particular length is called its **contractility**; increases in E increase contractility.
- c. There is no effect of parasympathetic stimulation on contractility.

? When entering into exercise or stressful situations, both venous return and sympathetic stimulation increase at the same time. Make a qualitative diagram that shows the change in stroke volume (blood ejected per beat) as a function of venous return for a real exercise situation. Then sketch in the graph for a situation where there was no increase in sympathetic stimulation even though venous return increased. This should help you view the changes in cardiac output as a result of at least two processes and not as a series of isolated graphs.

? While there is no direct effect of parasympathetic stimulation on SV, there is an indirect effect. What should be the effect of parasympathetic stimulation on stroke volume -- Hint -- it has to do with the parasympathetic chronotropic effect and with Starling's Law.