CIRCULATORY PHYSIOLOGY SECTION 3: CARDIAC MECHANICS*

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 found cardiac output using the Fick principle and finally, we will look at the control of cardiac output and work of the heart.

I. PUMPS and Cardiac Anatomy

A. GENERAL PRINCIPALS: There are two basic types of pumps used in the circulations of all animals: **positive and negative pressure pumps**. They can be distinguished based on **whether they move blood by pushing it along (+ pressure) or by pulling it into a low-pressure area (- pressure).** Both types of pumps are used in humans**.** In all cases, **valves** are required to make the resulting **flow move in only one direction**.

1. Positive Pressure Pumps: these are anything that squeezes on blood and thereby increases the pressure in it compared to the pressure of the pressure of adjacent blood. The result is movement.

a. A primary example that will be considered in much more detail several pages below is the heart. Muscular contraction by the walls of the heart increases the pressure of the blood within it. The blood would tend to be expelled in two different directions, just like if you squeezed on the middle of a sausage. However, a system of valves allows blood to move in one direction only.

b. A secondary but important type of pump is the skeletal muscle - venous pumps that exist in various regions of the body, especially the legs. Their operation will be considered now:

i. At rest the pressure decreases steadily throughout the venous system (as we saw in packet C-1).

(a) The result is that any location upstream (closer to the capillaries on venous side) would have a higher pressure than downstream points and the valves would be opened. This is shown on the left in the figure below. Blood flows down its pressure gradient.

(b) Valves are present in these veins.

(i) Valves are flaps of connective tissue that are pushed one way or another by pressures and flows of the blood.

(ii) Valves are set up so that flow or pressure gradients in one direction will cause them to deform in such a way that they largely open the vessel -- the flaps or **leaves** of the valves are pushed to the wall of the vessel.

(iii) On the other hand, flow or pressure gradients working in the other direction push the valves backwards, but instead of their being blown to flush with the walls their leaves increasingly resist being deformed and eventually slap together to form a basket-like structure that closes off the vessel. They are constructed so that it the resist further deformation once they have been forced together -- only very large forces would cause them to blow through and point in the opposite direction from normal flow:

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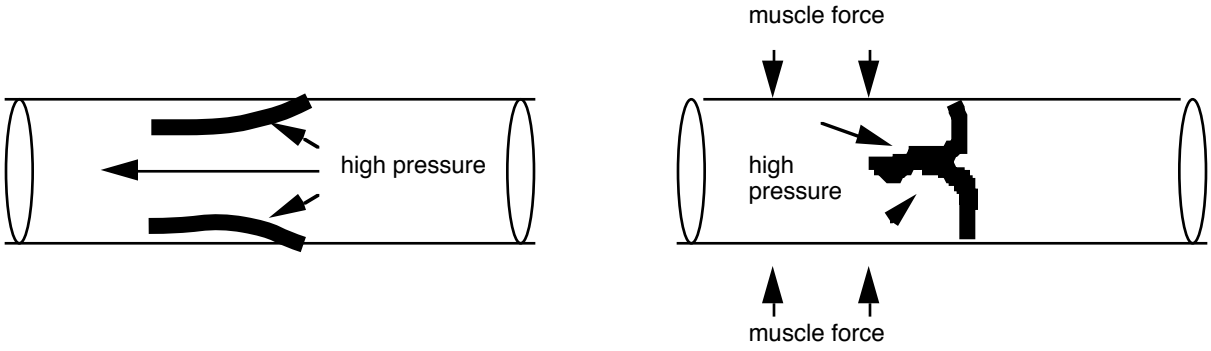


Valve Opened Due to Higher Upstream Pressure

Valve Closed Due To Higher Downstream Pressure

c. When exercising, **muscles that surround many veins contract and press on the veins**. As a result, the pressure increases locally to levels that are greater than pressures in adjacent up- and down-stream areas. These pressures propel the fluid forward as permitted by the valves; as we have just seen the valves prohibit reverse flow and also tend to isolate the earlier parts of the circulation somewhat from some of the effects of muscle contraction.

2. Negative/Positive Pressure Pump: the foremost of these is the THORACIC-ABDOMINAL PUMP; its pumping action is a consequence of alternating negative and positive thoracic pressures.

a. During inspirations, primarily during exercise, the pressures throughout the thorax become more negative than at rest.

b. The negative pressure causes the vein to distend outwardly, thus creating a **suction that draws blood upward into the thorax**.

c. Expirations are accompanied by a rise in pressure however,

d. Valves at the about the level of the diaphragm prevent back-flow during the expiration when the pressure become less negative and would tend to force blood back to the abdomen.

This pump is of major significance to the return of venous blood to the heart from the lower extremities.

? What is the relationship between the degree of thoracic pumping and the demand for O_2? HINT: think about what the lungs are doing at different levels of O_2 demand.

3. Heart Chambers as Negative Pressure Pumps: One other example of a negative pressure pump is the **rebound of the atria and ventricles after a contraction**. After the heart chambers contract and then relax, they rebound elastically back towards a preferred resting length and chamber volume (this should sound familiar). The result is that suction is created that helps pump blood into the chamber from the veins or from the other chambers.

B. The HEART:

1. The heart is constructed of tissues that are either
   a. derived from muscular tissue (**myocardium-derived**) or
   b. are connective in nature.
2. Functional Anatomic Elements of the heart and the tissues that make them up are as follows:
   a. **Contractile tissue**: also called **myocardium** this tissue produces the muscular tension used to pressurize blood and impel it around the circulation. The majority of the heart is myocardium.

b. **Electrical system**: this system is responsible for initiating and coordinating the heartbeat. It consists of entirely of either **myocardial tissue or tissue derived from modified myocardium**. Thus, it includes all of the myocardium and specialized areas such as:

1. **Sinoatrial (SA) Node**(the usual pacemaker), located in the right atrium near the junction with the vena cavae.
2. **Specialized atrial conduction tissues** such as Bachmann's bundle (see below)
3. **Atrial Myocardium**
4. **Atrio-ventricular (AV) Node** located between the right atrium and the muscular septum between the ventricles, this is the only place where a coordinating action potential can be transmitted between the atria and ventricles. It also delays the signal, as we will see later.
5. **Bundles His** conduction pathways that extend from the AV node half way down the septum to near the bottom ("apex" of the ventricles, it divides into a **Left and Right Bundle Branches**.
6. **Purkinje Fibers**: a series of fibers (modified myocardium) extending from the bundle branches and ending on the ventricular myocardium where the coordinating signal normally dies out here as the contraction is completed.

c. **Connective Tissue**: is used to construct

1. **Valves** between the atria and ventricles and between the ventricles and great arteries.

a) the **AV (atrio-ventricular) valves** are called the:

(i) **Bicuspid or Mitral Valve** on the left side

(ii) **Tricuspid** on the right side

Both of the AV valves are joined to a series of connective tissue "tendons" or "strings" called the **chordae tendinae**. The chordae terminate on a number of thickened pieces of the ventricular myocardium that extend into the ventricle called **papillary muscles**. These contract along with the rest of the ventricle and the force they exert on the tendinae keeps the leaves of the AV valve from being blown back into the atrium.

b) the ventricular/artery valves are called the **semilunar valves;** they are distinguished from each other based on the artery they serve:

(i) pulmonary semilunar valve

(ii) aortic semi-lunar valve

2. **Connective tissue between the atria and ventricles** (contiguous with the A-V valves) that serves to electrically **isolates certain parts of the heart from each other**.

II. The Mechanical Operation of the Heart: How the Heart Pumps Blood.

A. Cardiac Output -- What is it and how can it be measured?: the useful work the heart does is called the cardiac output. All of the regulation of the heart is centered on regulation of cardiac output so that it is adequate to meet the metabolic needs at the moment. Generally if demand related to respiratory gas is met, then demand for other functions of the circulation such as delivery of foodstuffs to cells can be easily met (this is not always the case -- one good exception would be temperature regulation).

? When would temperature regulation require a higher cardiac output than needed to meet respiratory gas needs?

1. Mathematically, cardiac output ($\dot{Q}$), given usually as liters of blood per minute, is simply the product of the average **STROKE VOLUME (**$\overline{SV}$**)** (liters) and the heart rate (***HR***), given as 1/s:

1. $$\dot{Q} = \overline{SV} * HR$$

2. For convenience sake, we usually measure *SV* as an average ($\overline{SV}$)

3 . We can measure the components of stroke volume a number of ways. **Heart rate is the most obvious; it can be determined by pulse, ekg** etc. Stroke volume determinations are more difficult. SV can be found a number of ways.

a. **Direct Measurements of stroke volume** are done using either Doppler techniques or by placement of a device that responds to changes in magnetic fields around either the pulmonary artery or the aorta. Since such fields are changed as blood pulses through the vessel it is possible to monitor the instantaneous changes in SV. However, it should be obvious that this device can only be used after surgical implantation and we will not be concerned with them in this course.

b. **Indirect Measurement of Stroke Volume**:

i. For our purposes, the stroke volume can be found indirectly as an average if the cardiac output and heart rate are known. The most common way of doing this is to use the **FICK PRINCIPLE** (not law).

ii. Fick Principle calculations **rely on the use of substances that are either added or removed from the blood somewhere**. **One example would be respiratory gases**.

iii. It should be obvious that **if we know the concentrations of a substance in the arterial and venous bloods and if we also know the rate that the body is using (or producing or removing) the substance, then we can calculate Q**.

iv. As an example, let's use oxygen.

(a) Suppose that **we know the** $\dot{V}_{O_2}$ **from measures of inspired and expired gas and minute volume**.

(b) Also assume that we can get **samples of arterial blood and mixed venous blood** (the blood that we find in the **RA**: it averages the O_2 content of blood from all over the body). Then:

2. $$\dot{V}_{O_2} = (C_{aO_2} - C_{vO_2}) * \dot{Q}$$

and rearranging this equation we find:

3. $$\dot{Q} = \frac{\dot{V}_{O_2}}{(C_{aO_2} - C_{vO_2})}$$

Once we know $\dot{Q}$, it is a simple matter to estimate average *SV* if we know the heart rate, which is easy to measure!

? Have you seen equation #2 before in this course? Where?
Can you find a similar equation based on CO_2?

What two blood oxygen factors does C_{aO2} take into account? (What do you need to know to calculate C_{ao2}? -- review O_2 transport notes)

If the heart rate is 72 b/min. and if $\dot{M}_{CO_2}$ = 0.0111 mols/min and if C_{aCO2} = 40 ml CO_2/dl blood and C_{vCO2} = 46 ml CO_2/ dl blood, what is the cardiac output in liters/min.? What is the average stroke volume in ml?
(*ANS.: 4.14 l/min., 57 ml/beat.*)

B. Cardiac Work

1. Earlier in the course we saw work diagrams for muscles. We will now consider the work diagram for the heart.

2. **Pressure-Volume (Work) Curve for the heart -- General**

a. **Diastole**: the period of time when the heart is completely relaxed, or when a particular chamber is completely relaxed.

(1) Most commonly, this refers to the time when the heart or a chamber **starts** to relax until when it begins to contract again.

(2) One way around the imprecision of this nomenclature is to speak of "entering diastole" and "full or complete" diastole, the latter referring to when the entire heart or chamber is relaxed.

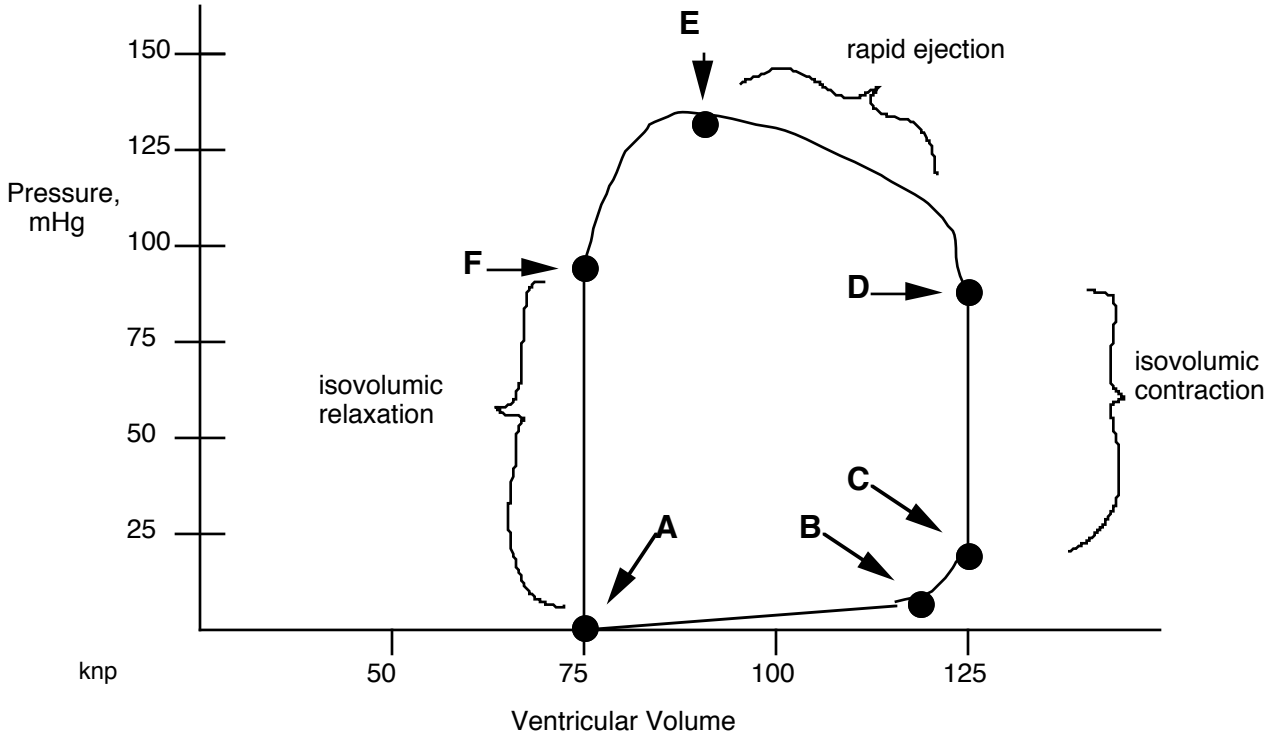
(3) The complete period to which the term "diastole" is often applied is from the first start of relaxation to the beginning of the next contraction.

b. **Systole**: the period of time when the heart or a single chamber is completely contracted (full systole), entrance into systole includes the time from the first start of contraction until the entire chamber is contracting.

(1) Once again, the entire systole period can be thought of as extending from the beginning of the contraction to the beginning of relaxation (start of diastole).

(2) Thus the systolic period is the sum of the period of time entering into systole and the maximal systole.

3. **The pressure-volume curve for the left ventricle of a human**: (please see the next page)



The lengths of the various segments of the curve do not correspond to the time spent in each part of the curve. Some of these events occur very quickly while others occur slowly.

The Following Refers to a Series of Points on the Graph Just Shown:

POINT A. **COMPLETE DIASTOLE**. The Mitral valve opens and blood flows through the LA from the pulmonary veins and the volume starts to increase.

1. The mitral valve will open when the pressure in the ventricle is less than that of the venous blood in the LA and veins.

2. The pressure at this point is near zero or is often even slightly sub-atmospheric due to **elastic rebound** of the ventricle walls as they spring back outward to their normal shape (like the chest in a maximal expiration).

3. Notice that there is a considerable amount of blood already present in the chamber -- in other words, not nearly all of the blood in the ventricle was pumped out in the previous beat.

4. **IN THE TIME BETWEEN A AND B**, during ventricular diastole, the Volume has been steadily increasing in the ventricle as blood continuously pours into the ventricle.

5. As the ventricular walls are passively stretched by the blood, they resist the blood due to the elastic properties of the myocardium. Thus, the pressure in the ventricle begins to increase.

a. Filling is most rapid early in complete diastole since the ventricular walls at first rebound (sucking in blood) and then do not resist blood that would enter until the chamber has been stretched to a considerable degree. This is called the **PERIOD OF RAPID FILLING**.

b. Thus, the first half of the line from A --> B occurs in a very short time, the second part takes much longer until:

POINT B: **BEGINNING OF ATRIAL SYSTOLE**: When the ventricle is between 60 (heavy exercise) to 90% (profound rest) full, the atrium contracts and "tops off" the ventricles. This last bit of filling occurs rapidly. Recall that this additional volume causes more stretch and more tension in the walls of the

ventricle -- this was induced by the rapid increase in volume and pressure. Very little time is required to move between B and C.

About the Role of the Atria: Notice from the graph (for the left ventricle of a human) on the last page that only about 10-20% of the blood that was added to the ventricle (so, even less if the whole volume is included) entered as a result of atrial contraction. At rest, the atria are not very important and one can survive without functional atria (although this is not good. At rest, most blood that entered the ventricles simply flows through the atria! By contrast, in exercise, when there is little time for the ventricles to fill (reduction in diastole is one of the primary means whereby the heart rate is increased), the role of the atrial contraction in filling the ventricles and providing adequate preload becomes far more important -- their contraction may account for far more than 50% of the added blood (blood that will be pumped out in the next beat)!

POINT C: **THE START OF VENTRICULAR SYSTOLE**

1. The mitral (A-V valve closes almost immediately due to the large pressures generated by the ventricular myocardium. Further increase in volume stops. Incidentally, the atrial have largely entered diastole by the time the ventricular beat starts.
2. The time between points C and D is referred to as the period of **isovolumic contraction** since no blood is ejected. Pressure increases rapidly and the amount of time for this to happen is small.
3. During this entire period of time the **AORTIC SEMILUNAR VALVE** that sits between the LV and the aorta is closed since the pressure in the aorta is greater than in the LV (see the figure at the end of the previous set of notes).

POINT D:. The **START OF EJECTION OF BLOOD**. At this point the semilunar valve opens since the LV pressure exceeds that of the aorta.

POINTS D TO E: the **PERIOD OF RAPID EJECTION**. This period is very brief, but roughly half of the stroke volume is ejected. The pressure continues to increase during this phase the force of contraction by the ventricle is continuing to increase for most of this segment

POINT E: **BEGINNING OF VENTRICULAR DIASTOLE**: Maximum pressure has been reached and now pressure will start to fall as some of ventricular myocardium starts to relax.

1. Between E and F, chamber pressure decreases as more of the ventricle enters diastole.
2. Meanwhile, the difference in pressure between the chamber and the aorta decreases since:
    a. LV pressure is dropping.
    b. the aortic pressure remains high due to blood still being added to it at a greater rate than it can leave and thus the elasticity induced pressure of the aorta remains high.
3. This is a rather long period.

POINT F: **SEMILUNAR VALUE CLOSE AND NO MORE BLOOD IS EJECTED**.

1. From here to point A no more blood enters or leaves the chamber. Thus, volume does not change.
2. The pressure drops rapidly as more and more of the ventricular myocardium enters diastole.
3. The **period from F to A** is called the **PERIOD OF ISOVOLUMETRIC RELAXATION**.
4. F to A takes only a short period of time.

? Would the relative time relationships between the different events mentioned in the descriptions above be independent of heart rate? Explain.

Be able to explain when different valves are opened.
Relate the lower portion (A to C) to the Frank-Starling Law of the Heart. How would the upper portion (C to A) change with different amounts of venous return?
How would this graph vary as a function of: (i) HR?
(ii) Chamber?
(iii) Parasympathetic Stimulation?
iv) Sympathetic Stimulation?
Be careful when considering autonomic stimulation. Consider chronotropic in addition to ionotropic effects.
Relate the entire graph to the pressure in the great artery connected to the chamber.
This graph was for a ventricle. What is the atrium doing between C and A?

C. Calculations of work in a cardiac cycle:

1. The pressure/volume curve we just considered is often referred to as a work diagram.
2. This should be of no surprise since we calculated the work of inflating the lung using a similar diagram.
3. In any pressure/volume relationship, the work done over a full cycle (Θ) is:
4. $$W = \int_{\Theta} PdV$$

where Θ denotes one complete cycle.

4. Notice that in this case (unlike the lung) the work is being done both by the heart and on the heart.

? In what sense was work done on the heart? What portions of the P-V plot showed work done on the heart and what portions showed work done by the heart?

Separate from this packet is a graph that summarizes much of what we have gone over concerning the heart. Be sure you understand it; you should know it well enough to be able to interpret or critique other similar curves.

<u>Cardiac Glycosides and the heart</u>

Recall that at the start of the course we learned about a class of compounds called cardiac glycosides that reversibly inhibit the Na^+/K^+ pump. We learned about the use of ouabain in electrophysiological research. A more famous example of a cardiac glycoside is the compound **digitalis** or **<u>digoxin</u>** that comes from the foxglove plant (genus *Digitalis* , a common biennial in flower gardens). Digitalis has a long history in the treatment of congestive heart failure. In medieval times, this condition was called dropsy. Regardless of the name, it occurs when the heart muscle is weakened by gross damage or myopathy. The heart becomes a less and less effective pump. Herbalists noticed (in the middle ages, if not earlier) that preparations made from *Digitalis* often helped people with dropsy -- physicians ever since then have used the drug. The question is how does it work?

By the middle of the 1900s it was known to be an inhibitor of the Na^+ pump. So how does that help people with congestive heart failure? In the 1960s and 1970s it was discovered that one of the ways the concentration of free Ca^{++} in myocardial cells is determined is via a Ca^{++} / Na^+ exchanger or " Ca^{++}/Na^+

cotransport protein". In this case it is an "antiporter" -- Na^+ is transported in one direction and Ca^{++} in the opposite. Normally the Na^+/K^+ pump keeps Na^+ levels in cardiac cells at a very low value. As Na^+ enters the cell, for instance during an AP, it can leave either via the Na^+/K^+ pump or via this cotransporter. The energy for the movement of Na^+ out of the cell and up its electro-chemical gradient comes from the Ca^{++} moving down its electro-chemical gradient. Looked at another way, if something causes Na^+ concentration inside of the cell to increase, Ca^{++} can more easily enter the cell in exchange for Na^+.

Using what you have learned in this course, explain the chain of events starting with partial inhibition of the Na^+ / K^+ pump to increase contractile force? Explain why not every pump molecule needs to be inhibited. List at least two ways that Ca^{++} concentration can increase in a myocardial cell and two ways that Na^+ can leave the cell.

Note this entire example is a classic result of physicians using something that worked but for the longest time they had no idea why!