CIRCULATORY PHYSIOLOGY SECTION 6:
REGULATION OF THE SYSTEMIC CIRCULATION*

Summary: This set of notes integrates what we have learned about vascular and cardiac function into a whole so that we can see how the entire circulation is regulated. These are very important concepts and their mastery will move you a long way towards a real understanding of the operation of the circulatory system.

I. The Systemic Vascular System -- The influence of cardiac output on the partition of blood between the venous and arterial sides of the systemic circulation.

A. Earlier we have indicated that at rest most of the blood in the systemic circulation is located in the venous side. This is in part due to the relatively high capacitance of the venous system when compared to the arterial system. This gives a reserve of blood that can be used when demands for respiratory gas circulation increase as in exercise.

B. When there is no circulation (death or experimental interruption of the cardiac output), there is still a blood pressure in both the arterial and venous systems.

1. As we indicated earlier, this is due to the elastic forces stored in the walls of the vessels -- since in the absence of a hemorrhage the vessels contain enough fluid to increase their volume beyond resting volume, there must be a pressure even if the blood is not moving.

2. This low pressure is referred to as the **mean circulatory pressure** (Guyton) and for normal blood volumes is about 7mmHg (know this value).

3. Due to the greater compliance of the venous system, the greatest relative proportion of the total blood volume will reside in the venous system when operating at the mean circulatory pressure (i.e., when the heart is stopped).

C. In any situation where the heart is pumping blood, there will be a redistribution of blood from the venous to the arterial side; the greater the CO, the more blood will be moved to the arterial side.

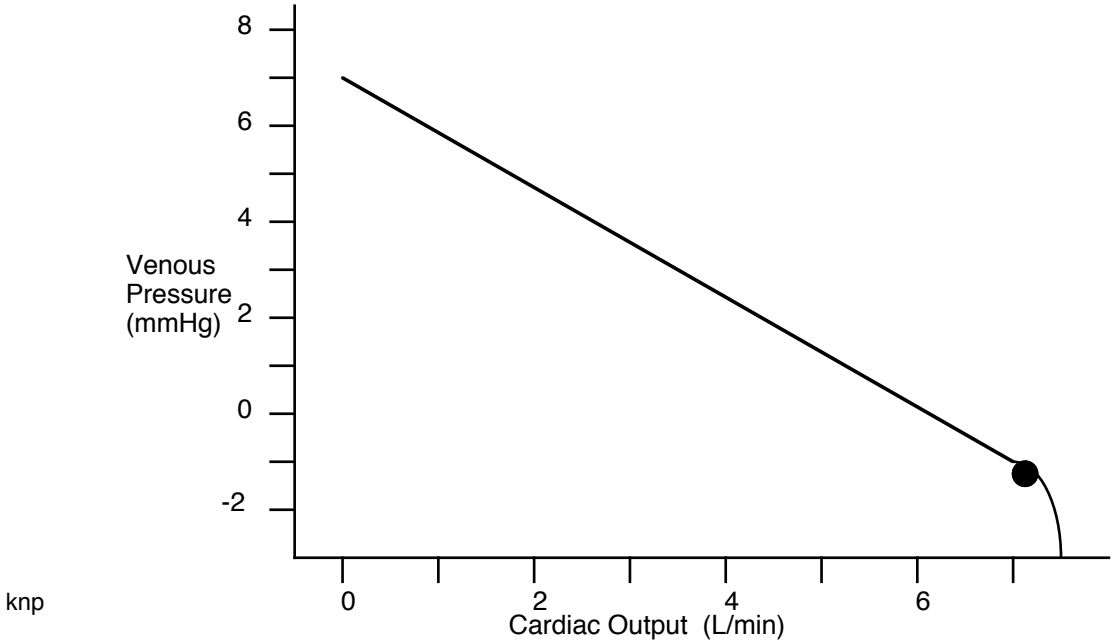
1. This is because the heart will pump blood from the venous side to the arterial side and the boundary between the arterial and venous sides is a high resistance (arterioles and capillaries).

2. Since circulation represents a non-steady (dynamic) state, due to the frequent intermittent addition of blood in greater volumes than it can flow out followed by a greater outflow, but always maintaining a situation where the pressure in the arterial side is greater than in the venous side (and thus flow is maintained), the result is that blood has been shifted to the arterial side to fill the arteries to an extent that insures a high pressure; this blood came from the veins.

3. Thus, arterial volume and pressure increase as CO increases and venous volume and pressure decrease as that blood is moved to the arterial system.

kprestwich@holycross.edu

Figure C-4.1



As the cardiac output increases the venous pressure decreases. This paradoxical result is due to the fact that there is only so much blood in the circulation and an increase in cardiac output is accompanied by an increase in the proportion of blood in the arterial system. The decreased volume of the venous system results in less stretch and therefore lower pressures.

Note that at high C.O., the venous pressure actually becomes negative as blood is literally sucked through the system. **This is shown at the point marked by the large black dot.**

Note the correspondance between this figure and the plot of venous and arterial pressures vs. C.O. (see below -- next plot) -- as C.O. increased, arterial pressure goes up while venous pressure goes down as more of the blood is placed in the arterial side of the circulation.

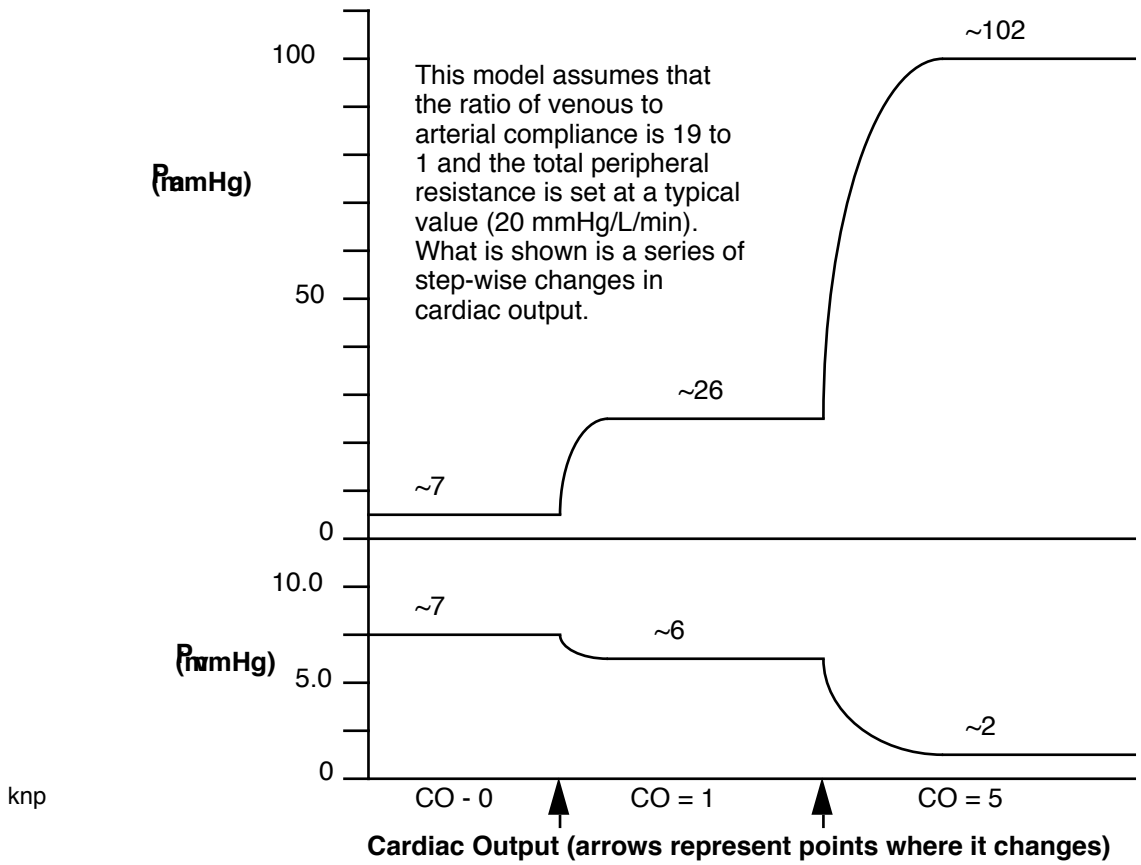
4. Since the compliances of the two sides of the circulation are not the same, a decrease of a certain volume in the venous system accompanied by an identical increase in arterial volume will not result in identical changes in mean venous and mean arterial pressures.

! To make the discussion below simple, from now on when we talk about venous pressures, these pressures will refer to the vena cava (and relaxed right atrium).

? If the relative differences in compliance are known in the venous vs. arterial sides of the circulation, and if we know that say an increase of C.O. of some amount causes arterial pressure to increase by some amount, can we calculate the change in venous pressure? If not, what additional variables would be of importance?

5. Below is an experiment that shows the result of going from a cardiac output of 0 (say due to extreme parasympathetic stimulation) to outputs of 1 and 5 liters per minute. Note this is a model system but real systems operate in a very similar manner:

Figure C-4.2

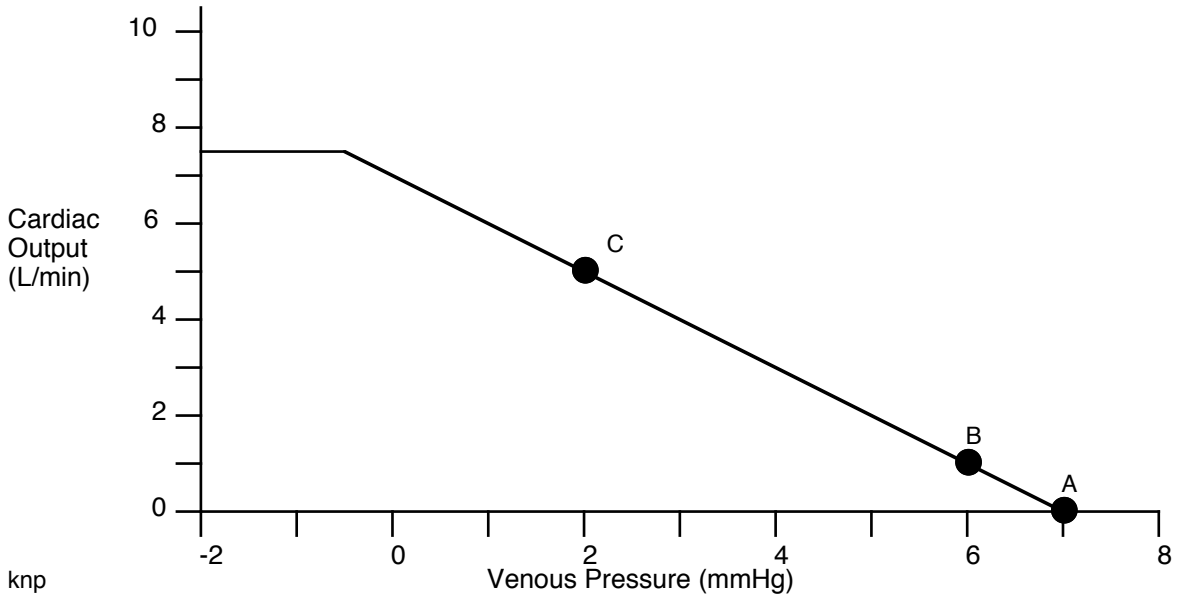


knp

after Berne and Levy, fig 34-5, *Physiology*Mosby 1983

C. A useful plot of venous pressure can be made (we will use it for the rest of our discussions of the regulation of the systemic circulation) by reversing the axes of the plot shown as figure C-4.1 (previous page). This new plot is shown on the next page:

Fig. C-4.3:



The same as the first plot except the axes have been reversed. This will be useful with a different type of plot shown later.

Pt A is for the mean circulatory pressure; defined as the pressure found in the circulation when there is no cardiac output. It is due to the filling of the circulation and compliance of the system (both arterial and venous, but measured in the venous system).

Pts B and C: venous pressures with cardiac outputs of 1 and 5 liters/nin. See previous example for an explanation for this inverse relationship.

Figure based on Berne and Levy, 34-7, *Physiology*, Mosby 1983

1. Notice that this plot shows the decrease in cardiac output as a function of venous pressure -- of course this is not the best way to view these variables in terms of dependence but we will see the reason for doing this shortly when we consider the interaction of the heart and the venous system.

2. Fig. C-4.3 also shows that eventually cardiac outputs get high enough (at around 7.5 liters/min.) so that venous pressure goes negative (subatmospheric).

a. Obviously when this is the case the veins will collapse and it will be difficult for blood to return to the heart

b. Thus, further increases in CO are not possible unless some other changes occur in the circulation -- these will be discussed below.

c. Finally, note that the plot has three points labeled on it:

1. **Pt. A** represents the mean circulatory pressure (when CO = 0), it was discussed in detail above.

2. **Pts. B and C** represent COs of 1 and 5 l/min and correspond to the plateaus shown for figure C4-2.

D. The effects of changes in blood volume and venous tone (capacitance) on CO vs. venous pressure curve.

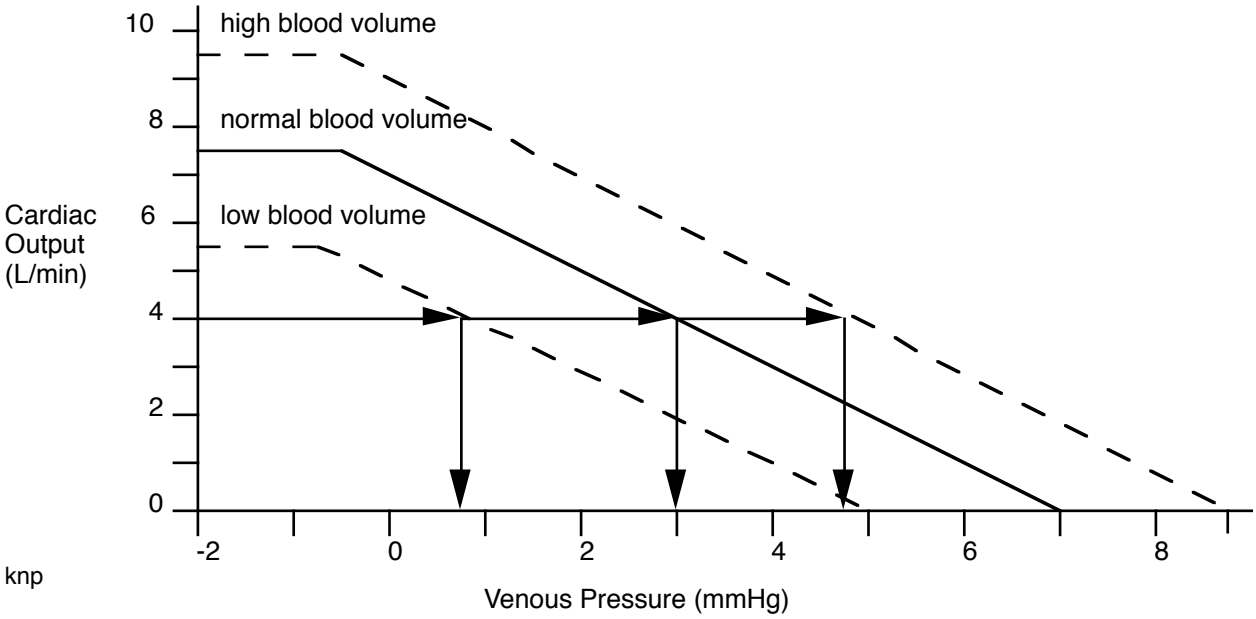
1. One important additional effect that we should consider is the effect of change in blood volume. As we already know, increase in blood volume should result in an increase in blood pressure. However, how should the curves actually look?

a. If resistance remains constant, then one would expect that for any change in cardiac output venous pressures should mirror each other in terms of rate but the overall pressures should increase with greater blood volumes.

b. The critical C.O.s where the blood pressure goes subatmospheric should also increase since the amount of blood that would need to be repartitioned to the arterial side in order to cause the great veins to collapse would be greater the greater the vascular filling

c. Likewise, the mean circulatory pressures should also increase with increased filling:

Figure C-4.4:



The effects of changes in blood volume on the C.O. vs. Pv curve. For any C.O. notice that the greater the blood volume, the greater the venous pressure (since the vessels are more filled)

2. The other variable of importance is change in venous tone. As we have seen earlier, tone can be changed by disease or by autonomic effects (for our example we will consider normal autonomic adjustments):

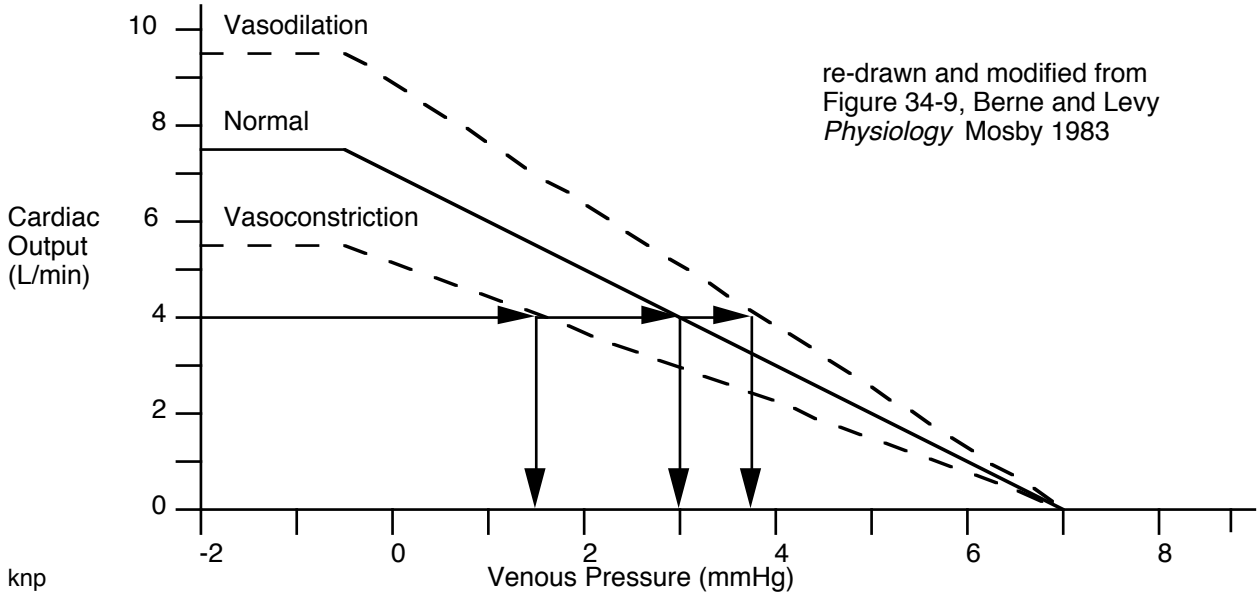
a. **If the capacitance is lowered by an increase in venous tone (vasoconstriction), then *for a given volume of blood and given cardiac output the venous pressure will decrease*. This is because the volume is effectively lowered and blood is shifted by such a constriction relative to a less constricted state.**

b. It will also mean that **the cardiac output at which venous pressure will go subatmospheric will be lower in constricted states, again, due to the low volume of blood in constricted veins** (so less change in volume is needed before they collapse).

c. However, the mean circulatory pressure will be the same since the blood can simply go to the arterial side from the constricted venous side when C.O. is 0. (Note that in fact the mean circulatory pressure will increase very slightly due to the greater elastance and filling of the arterial side, but the extent of the increase for realistic changes in vasomotor tone is slight.

d. ***Thus, one should not think of the situation of an increase in venomotor tone as being the equivalent of an increase in blood volume -- there are some similarities but there are also many differences.***

Figure C-4.5:



re-drawn and modified from Figure 34-9, Berne and Levy *Physiology* Mosby 1983

In this figure, dufferent **venomotor** tone (alterable by either structural changes such as in disease or by changes in muscle contraction) alter the compliance of the venous system
Clearly, the greater the tone (more constriction) the lower the venous pressure for a given C.O. -- the reason being that to maintain a given C.O. less compliant (lower volume vessels) will be less filled (essentially more of the blood is shifted to the arterial side if venomotor tone increases independently of arterial tone -- and in any case, a general change in vascular tone will affect the venous system's volume more since the volume change wll be relatively large in this essentially compliant systemwhencompared to the arterial system.

! Be sure that you thoroughly understand the differences in the two graphs above and the reasons for these differences.
? What would be the effect of a change in peripheral resistance (in the arterioles) on the shape of the venous curve?

II. Cardiac Function and its Relationship to Venous Conditions

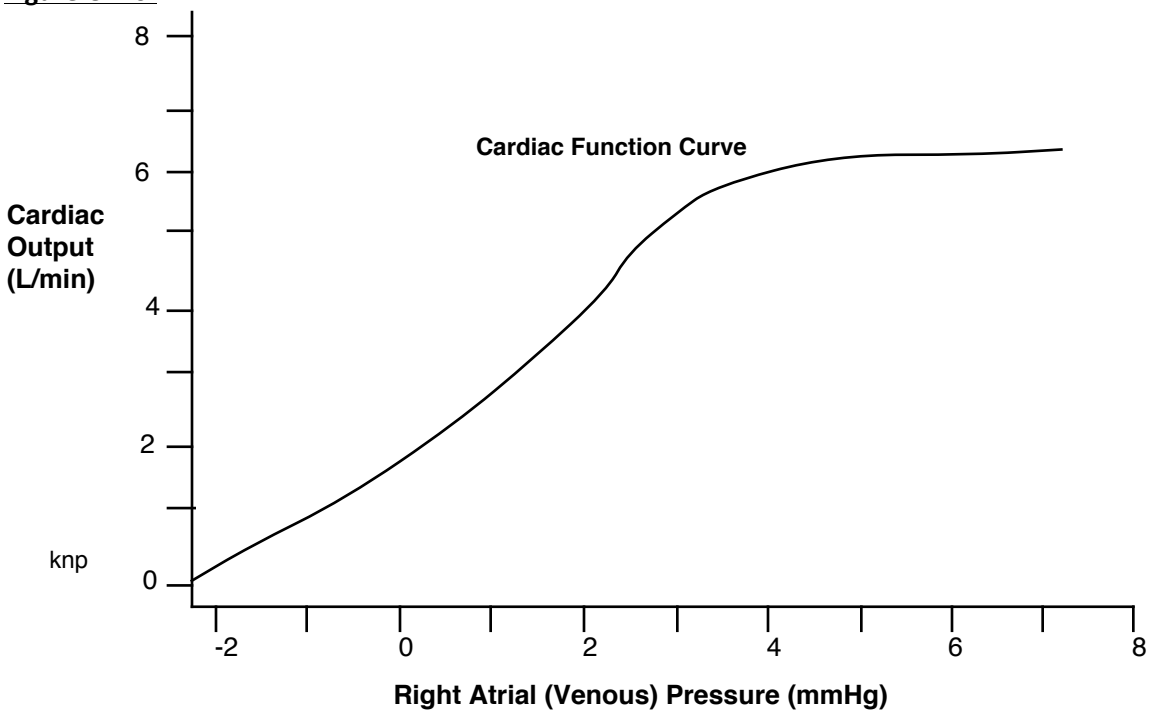
A. The **Cardiac Function Curve**:

1. Recall from packet #C-3 that within limits the heart will pump all of the blood that comes to it -- this is referred to as the Frank-Starling law of the Heart. Recall also that we learned at that time that one measure of the amount of blood that returns to the heart is diastolic pressure of the heart. A stand-in for diastolic pressure in the heart is the venous pressure -- which we have just considered in great detail.

? Why is venous pressure a good predictor of cardiac output?

2. Plotted below (figure C-4.6) is a version of the Frank-Starling curve that considers all cases up to actual decompensation (less pumped than arrives). Notice that fig. C-4.6 only goes as far as a leveling of CO even with a further increase in venous pressure. Finally, note that only one curve for one degree of sympathetic stimulation (one range of contractility) is shown, although later we will consider the effect of sympathetic stimulation:

Figure C-4.6:

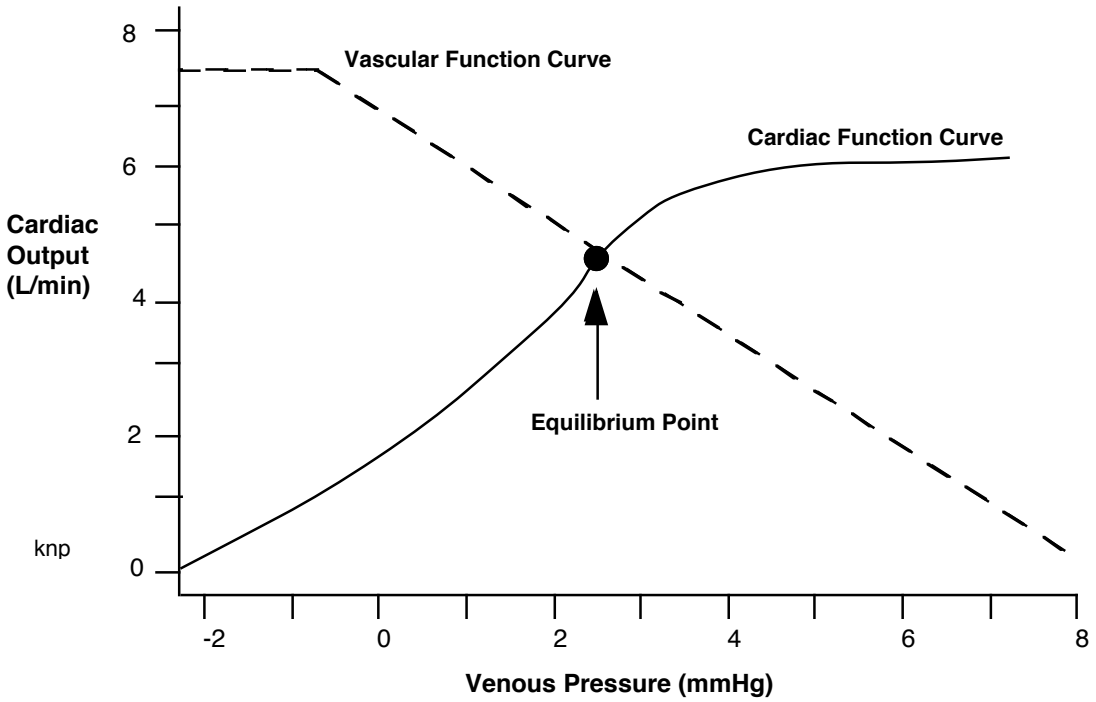


B. Combination of the Venous and Cardiac Function Curves:

1. We can now see the utility of making the earlier venous function plots a bit different than might have been expected (with the axes reversed from convention). This allows us to plot the cardiac and venous function curves on the same graph. The utility is that we can now use these curves to integrate the action of the vasculature and heart in terms of how they influence each other and produce the overall pattern of regulation.

2. The most important point to note on this plot is the intersection of the two graphs -- this point is the stable equilibrium point of cardiac output and venous pressure for a given set of conditions of circulatory volume, tone, resistance, and cardiac contractility. This is shown on the next page:

Figure C-4.7:



Combined cardiac and vascular function curves. Notice that the cardiac function curve is essentially a Frank-Starling curve except that volumes that will result in decompensation are not shown.
For a given venous volume and compliance and given contractility, there will exist one stable equilibrium point defined by the fact that cardiac output and venous return are equal.

Figure based on Berne and Levy, 34-10, *Physiology*, Mosby 1983

C. The interaction between the heart and vascular systems. The concept of the equilibrium point

1. This first example assumes constants in terms of: resistance, volume, tone, and autonomic stimulation to the heart. Thus, it is not very realistic but it will give us a general idea of how the entire system functions.

2. **We will now examine how the system acts under non-steady state conditions and how it returns to a steady-state (misnamed but nevertheless still called an "equilibrium")**.
Suppose that venous pressure is instantaneously increased. This could be done by increasing venous return to the heart, either by a change in posture (for example, you could stand on your head!), by increased contraction of the muscles surrounding the leg veins, or perhaps increased thoracic abdominal pumping.

3. The series of events can now be viewed as a series of straight line segments (but in fact you should be sophisticated enough at this point to realize that in most if not all cases curved lines will result).

a. At first, the venous pressure increases due to greater venous return and therefore greater filling of the venous system (including the chambers of the heart).

b. The increased stretch results in an increase in contractile force via the Frank-Starling mechanism and therefore an increased stroke volume.

c. This means that the volume of blood in the veins connecting to the heart will soon be reduced.

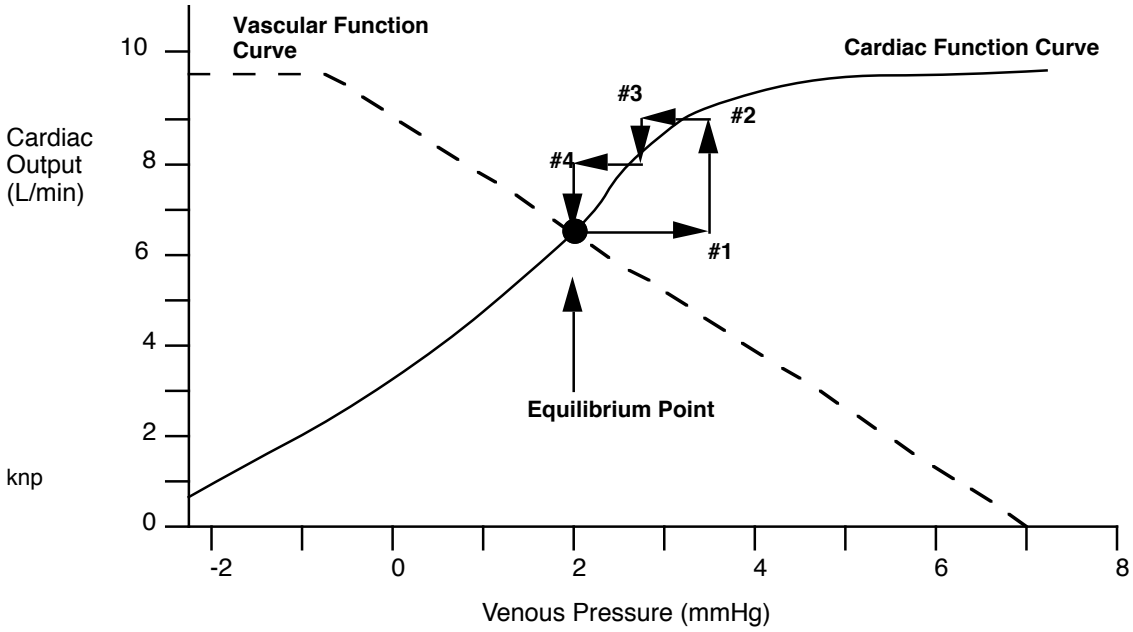
d. The result of this reduction is a lowered venous pressure

e. This lowered pressure results in a less stretch of the chamber walls and therefore a lowered stroke volume.

f. The eventual result is a return to the same venous conditions and CO that existed prior to the enhanced venous return.

g. This is the only stable point for these contractility and vascular conditions -- notice that as long as no other perturbation occurs the system will have to return to this point since the venous pressure is determining the CO and the venous pressure is the current equilibrium for a given CO, venomotor tone, blood volume and peripheral resistance:

Figure C-4.8:



This figure shows why the euqilibrium point illustrated in the previous plot is stable. If anything upsets the equilibrium, for instance, suppose that venous pressure is momentarily increased to point #1 (for instance by addition of venous blood and simultaneous removal of an equal volume of arterial blood in order to keep volume constant (see previous figure).

This will cause increased stretch on the heart and increae the force of contraction (point #2). The resulting increase in stroke volume and cardiac output will decrease the venous volume and therefore decrease venous pressure (pt #3). Further iterations will eventuslly result in return to the equilibrium point (pts #4 and beyond).

Figure based on Berne and Levy, 34-10, *Physiology*, Mosby 1983

? Make a cogent explanation for how an increase in venous return to the right atrium will eventually result in an increased left ventricular stroke volume. In other words, think about what the effects are on the pulmonary circulation and on the LA and LV.

Notice that one of the plots is a Frank-Starling plot and therefore deals with stroke volume, not CO. Why is it nevertheless still appropriate to talk about CO? Does increased venous pressure affect both SV and HR? Explain.

Which parts of the non-steady state portions (lines 1-4) would most likely be curved under the experimental conditions outlined above? Explain.

D. Changes in Contractility:

1. As we saw in packet #C-3, contractility is also affected by sympathetic stimulation. We saw that we could generate a whole series of different Frank-Starling curves for different degrees of sympathetic stimulation.

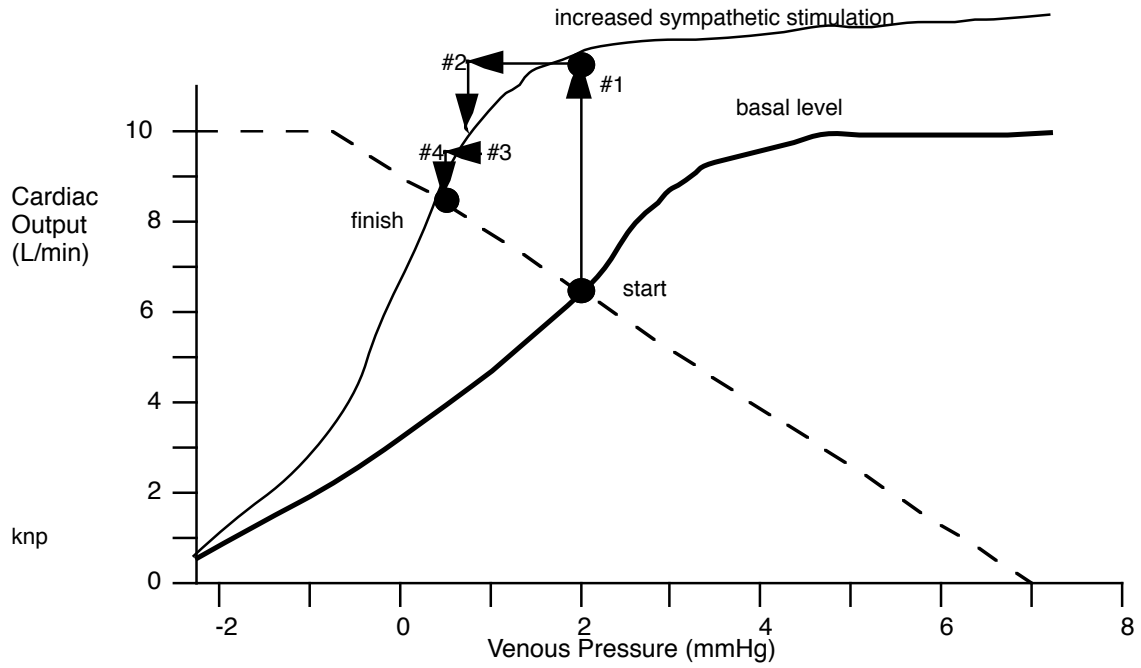
2. In our second rather unrealistic example (although probably a bit more common than the last one), let's see what happens when there is no change in the venous system (including venous return) but when we add an agent with a positive inotropic effect. To make this simple, let's assume the effect is instantaneous and only affects contractility.

a. the immediate result is for a given venous pressure (distention) the heart pumps much more forcibly -- thus, since the after-load has not changed (there has been no change in arteriole resistance and great artery pressure), the SV increases immediately.

b. The result is movement of blood from the veins to the arteries and a concomitant decrease in venous pressure and therefore stroke volume (C.O.).

c. Eventually a new steady-state is reached where the venous volume is constant (but less than before) and the C.O. is greater:

Fig. C-4.9



In this experiment, sympathetic stimulation (ideally ionotropically only) is administered to the heart and vasucalture sitting at "start". The contractility increases for a given degree of stretch as is shown by the arrow going to pt#1. The result is a transient increase in C.O. This reduces the blood on the venous side and by the Frank-Starling effect reduces the C.O. over what it was a moment ago (but it is still large). After several iterantions of this, a new equilibrium point consistent with the increased contractility result s in a greater C.O. than before at a lower P_V (since blood has been shifted from the venous system). Figure based on Berne and Levy, 34-11, *Physiology*, Mosby 1983

? When the new steady-state is reached, what will be the arterial volume as compared to before the sympathetic stimulation? How about the venous volume?
How about the size of the afterload?

E. <u>Changes in Blood Volume, Constant Contractility</u>:

1. Another simplistic experiment, but like the two above, it will also help us see how the more complicated real type interactions occur.

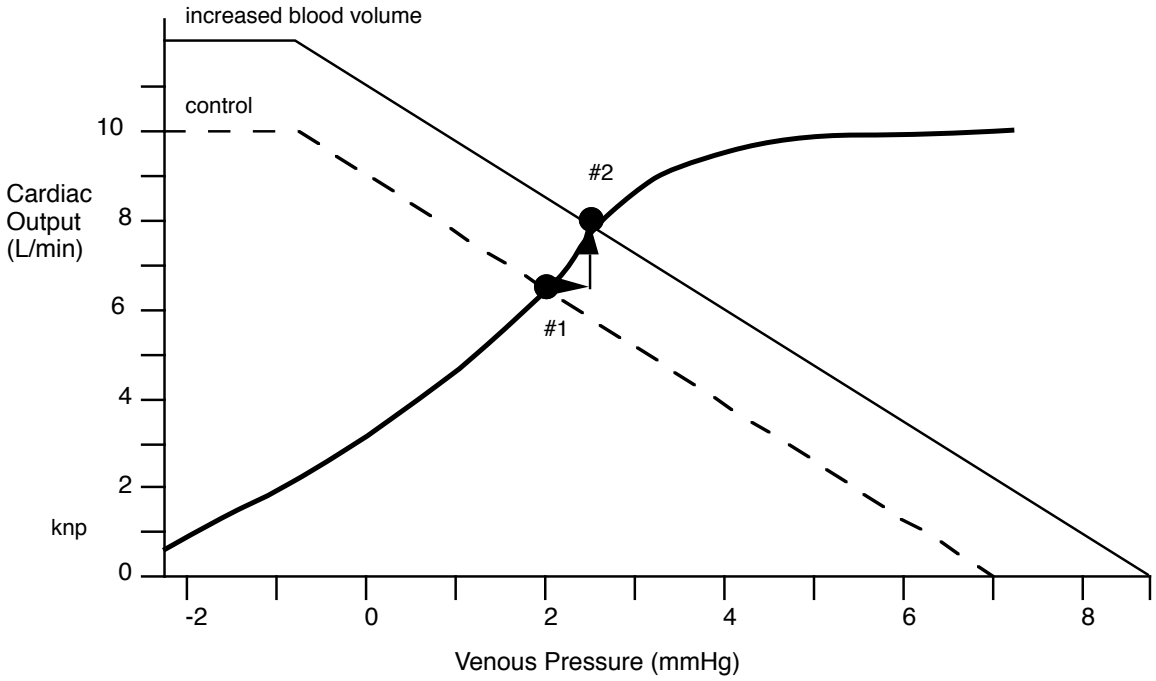
2. Suppose that this time we keep contractility, venomotor tone, and resistance constant but we instantaneously increase blood volume:

a. this time, we instantaneously generate a new venous curve.

b. the increased volume instantly increases the venous pressure before the CO is affected (since we added the extra fluid to the venous system).

c. The result is that the pressure increases and therefore the stroke volume; the eventual result is a new steady state with a higher stroke volume:

Fig. C-4.10



Addition or removal of blood simply shifts the equilbrium point between the intersections, exactly as would be predicted by the Frank-Starling Law. For instance in this case if we assume the venous volume is instantaneously increased, the pressure increases which results in an increased stretch and an increased C.O. that is shown by pt#2.

Figure based on Berne and Levy, 34-13, *Physiology*, Mosby 1983

? Why would the venous pressure remain greater and the SV (CO) remains higher even after the adjustment to the addition of additional blood?

How would this sort of experiment be done?

To achieve the effects shown above, would only the difference CO (~2.0 L in this case, see graph) need to be added? Explain. (Hint -- think about arterial and venous capacitances).

F. <u>A Real Example -- Heart Failure:</u>

1. The example below is more realistic view of the way adjustments would occur.

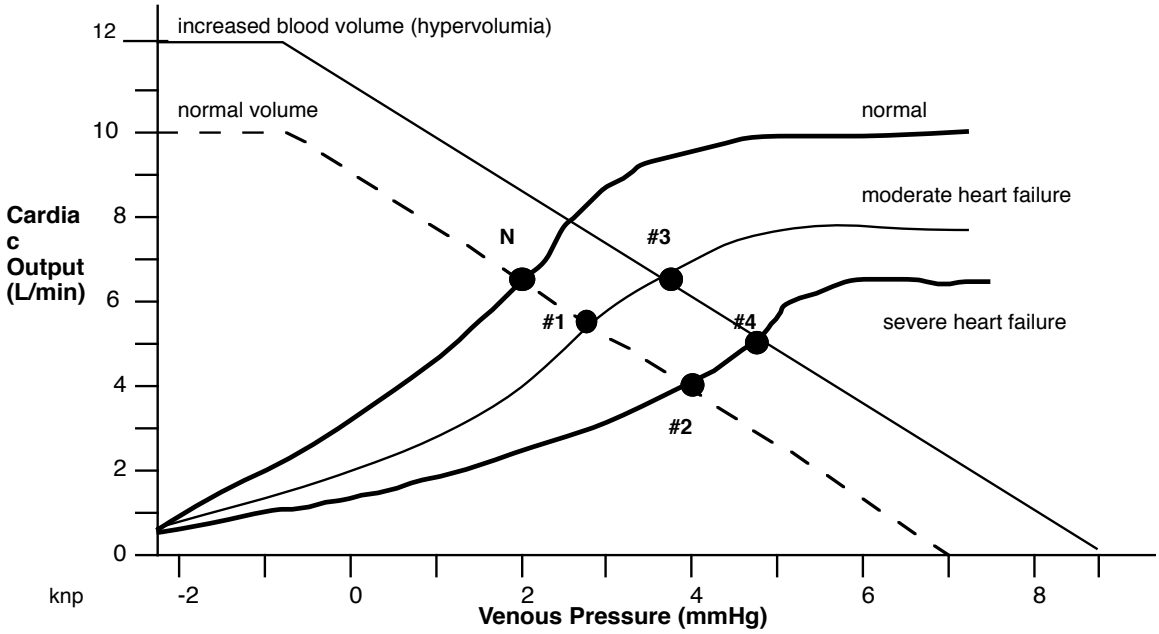
2. In heart failure there is progressive weakening of the heart as a muscle. The result is that even with sympathetic stimulation the cardiac function curve shifts down and to the right.

3. As is shown, if this was all that happened things would be very serious because C.O. output would tend to drop.

4. However, the lowered cardiac function tends to result in fluid retention (edema) and lowered ability of the kidneys to remove water (due in large part to lowered **arterial** pressures (see next section)).

5. This results in an increase in venous pressure (due to both the increased venous volume and the increased intracellular volume (edema). The higher pressures actually tend to maintain C.O. although they have many other deleterious effects and in no way should be viewed as a compensatory mechanism:

Fig. C-4.11:



Minimally heart failure involves a decrease in strength as is indicated by the progressive shift of hte cardiac function curve to the right. If this were all that happened, cardiac output would decrease (in the absense of increased sympathetic sitmulation). This is shown by moving along the normal blood volume plot from point N to #s 1 and 2.

However, the usual situation is that accompanying heart failure there is an increase in blood volume. Independent of sympathetic stimulation, C.O. will be nearly normal (moderate failure, pt #3 -- compare with C.O. at N or slightly instead of severely reduced (pt. #4). This is _not a compensation mechanism however and the increase in volume has a number of problems all its own independent of this apparent beneficial effect.

Figure based on Berne and Levy, 34-14, *Physiology*, Mosby 1983

? What are two bad effects of the edema that relate to respiratory gas exchange?

Design an experiment to investigate the effects of increased resistance only on cardiac function? Would it be possible to graph this experiment in the manner of the others above of would there be additional effects that would make comparisons difficult?

How about for increased venomotor tone?

How would you control or quickly change the following physiological variables? (Be specific) (i) contractility, (ii) heart rate, (iii) peripheral resistance, (iv) blood volume.

Make a plot and show steady state points and paths for a long term dehydrating exercise. Show the following steady-states: (i) pre-exercise, (ii) initial exercise, (iii) exercise after severe water loss. Assume that the exercise is performed at a constant power output regardless of hydration state.