Integration of Cardiac Output and Venous Return 5.12

Learning Objectives

- Explain why cardiac output generally equals venous return
- Define total peripheral resistance, TPR
- Define mean systemic pressure
- Define stressed and unstressed volume
- Draw the curve relating mean systemic pressure to blood volume
- Draw the vascular function curve as cardiac output versus right atrial pressure
- Explain the plateau, knee, slope, and intersection on the horizontal axis of the vascular function curve
- Explain the effects of vasoconstriction and vasodilation on the vascular function curve
- Determine the operating point of the cardiovascular system by the intersection of the cardiac function curve and vascular function curve
- Explain the effects of hemorrhage and transfusion on the vascular function curve
- Explain the effects of cardiac disease and sympathetic stimulation on the cardiac function curve and the operating point of the cardiovascular system
- List the components of the sympathetic tetralogy
- Describe the effects of exercise on the cardiac and vascular function curves

THE CARDIOVASCULAR SYSTEM IS CLOSED

The overall flow for the cardiovascular system is recapitulated in Figure 5.12.1. In the long term, the cardiovascular system is open because it receives input of materials and fluids from the intestine and it discards materials and fluids through the skin, lungs, intestines, and kidneys. However, the rates of fluid transfer from these inputs and outputs are slow compared to the flow through the system. Fluid exchanges vary greatly; Figure 5.12.1 shows typical values for a comfortable environment. The flow of blood around the circulation is about 5 L min^{-1} or 7200 L day^{-1}. On average, loss and gain from the environment are about equal and the blood volume does not change. Imbalances in the inputs and outputs are extremely important because they determine the circulatory volume, but they occur on a different timescale than circulation. Thus, for the minute-to-minute regulation of the circulation, the circulatory volume is very nearly constant and the circulatory system approximates a **closed system**. Inflow to any part of the system must be the same as outflow through that part, or volume would build up or be depleted wherever the imbalance occurs. The consequence is that the input to the right heart from the veins, the **venous return**, is equal to the output of the left heart, the **cardiac output**.

THE CARDIOVASCULAR SYSTEM CAN BE SIMPLIFIED FOR ANALYSIS

In Chapter 5.8, we learned about the Frank–Starling Law of the Heart: increased filling pressure stretches the heart and increases its force of contraction. Increasing the force of contraction expels more blood from the left ventricle, so that cardiac output increases when the **preload** increases. This preload is generally expressed as the **right atrial pressure**, the pressure which drives filling of the heart. The **afterload** also affects cardiac output. Typically the cardiac function curve is obtained at constant afterload. The normal cardiac function curve is reproduced in Figure 5.12.2.

The cardiac function curve was determined in isolated heart–lung preparations, which contains both sides of the heart and the intervening pulmonary circulation. In these experiments, the outflow pressure was held constant while the input pressure was varied. Thus, the cardiac function curve describes the heart without the attached systemic circulation. In this isolated heart–lung preparation, flow out of the right heart must match flow into the left heart, or else fluid would accumulate or be drawn out of the lungs. The Frank–Starling law of the heart indicates that the increased filling pressure of the right heart results in increased cardiac output. Any increase in output of the right heart is quickly communicated to the left heart as an increased filling pressure. Thus, increased output of the ***right*** heart is matched to increased output of the ***left*** heart. Because of this tight coupling, we can collapse the heart and lungs to a single equivalent pumping mechanism. Similarly, we can

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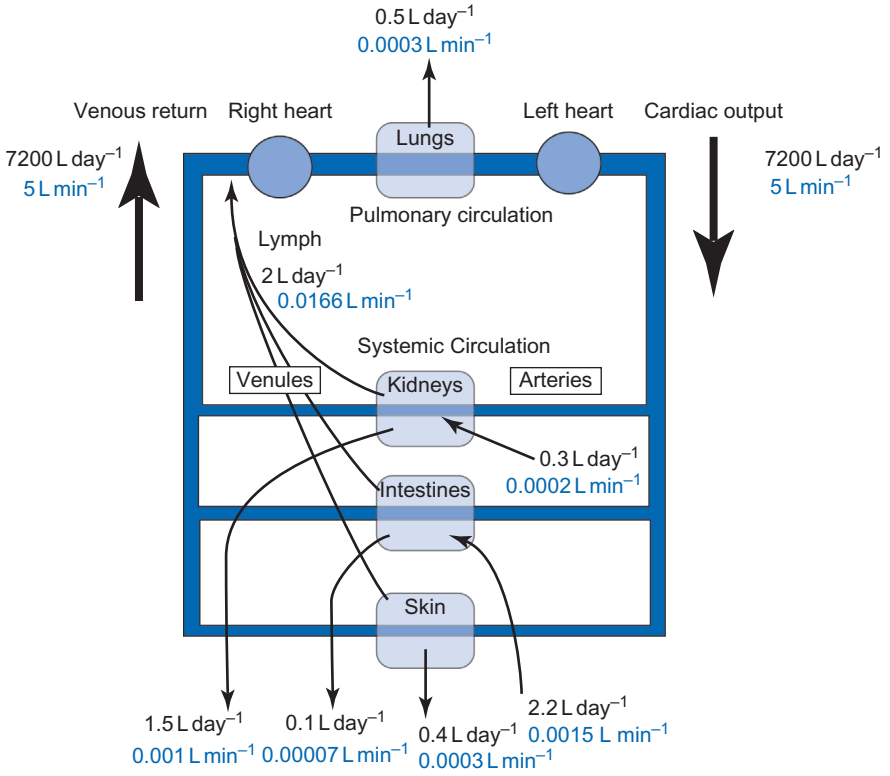

FIGURE 5.12.1 Balance of fluids that traverse the cardiovascular system. The bulk of the flow is retained inside the vessels of the cardiovascular system. Although there are exchanges of material into the blood from intestine and other tissues, and from the blood into many tissues, the flow of fluid that leaves the cardiovascular system is much smaller than the flow around the circulation. Thus, on short timescales, the circulatory system approximates a closed system.

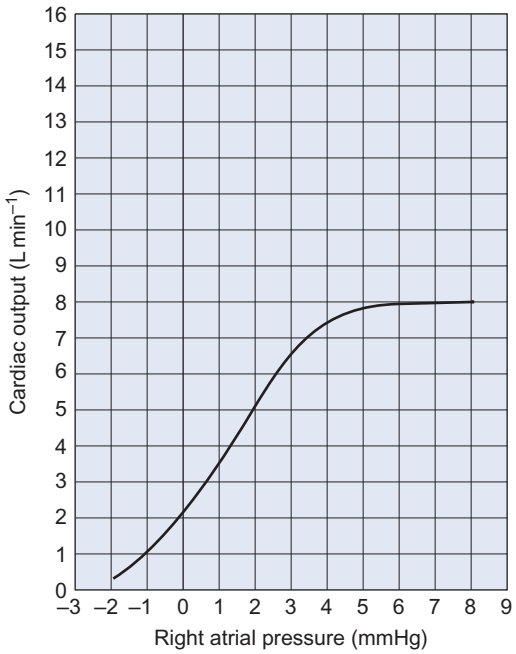

FIGURE 5.12.2 The cardiac function curve. The graph shows the output of the left ventricle when it is pumping against a constant arterial pressure and when right atrial pressure is varied.

lump the systemic circulation into a single equivalent set of vessels in series. This lumping follows the rules of combination of parallel or series resistances. Figure 5.12.3 shows this situation.

THE OPERATING POINT OF THE CARDIOVASCULAR SYSTEM MATCHES CARDIAC FUNCTION TO VASCULAR FUNCTION

Figure 5.12.3 clarifies the role of the heart and the vasculature in determining the cardiac output. The heart pumps an increment of blood, the stroke volume, from the venous side of the circulation to the arterial side. The arteries, arterioles, capillaries, venules, and veins return this blood to the heart. The analysis which follows breaks the cardiovascular system into two components: the heart and the vasculature. The heart is characterized by its output as a function of its input and output pressures: P_{RA} and P_A. P_{RA} is the pressure at the right atria, the **central venous pressure**, or the **right atrial pressure** (the preload); P_A is the arterial pressure against which the heart pumps (the afterload). For every P_A, there is a cardiac function curve.

The venous return also has a relationship between P_A and P_{RA}. It is

$$[5.12.1] \qquad Q_{veins} = \frac{P_A - P_{RA}}{R_{A \rightarrow RA}}$$

where Q_{veins} is the flow through the systemic circulation (in the intact circulatory system this is equal to the cardiac output) and $R_{A \rightarrow RA}$ is the resistance to flow from the left heart side, or arterial side, of the systemic circulation to the right heart side, or venous side. This resistance lumps together all of the resistances of arteries, arterioles, capillaries, venules, and veins that supply the peripheral

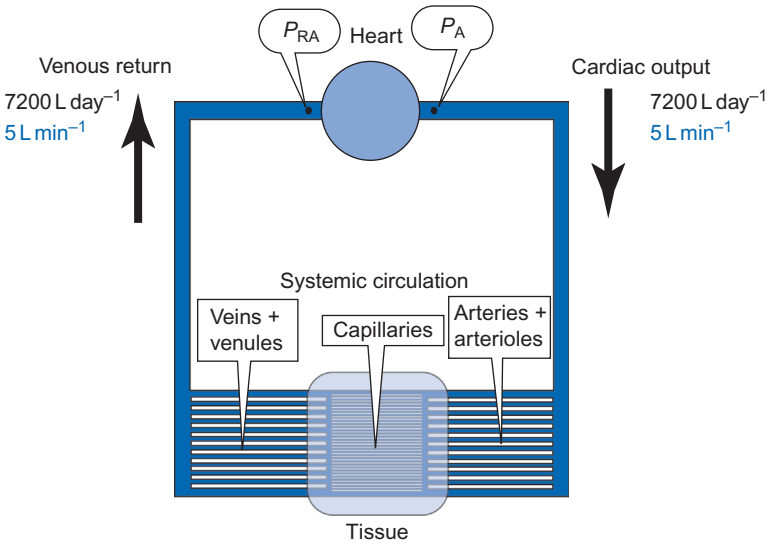

FIGURE 5.12.3 Simplified cardiovascular system. Because right and left heart outputs are tightly coupled, we collapse these two sides of the heart and its intervening pulmonary circulation into a single pump. Also, the arteries and arterioles, consisting of both series and parallel arrangements, can be combined to a single aggregate. Similarly, capillaries and veins can be combined to form their own equivalent aggregates.

tissues of the body. Hence, it is called the **total peripheral resistance**, or **TPR**. The equation is rewritten as

$$[5.12.2] \qquad Q_{veins} = \frac{P_A - P_{RA}}{TPR}$$

Although Eqn [5.12.2] is true and can be used to estimate TPR, it does not help us understand what determines the flow through the system, because TPR, P_A, and P_{RA} are not independent. What we desire is a relationship between Q and P_{RA} for the vasculature, at the same P_A used for the cardiac function curve, because the cardiac function curve is such a relation. The operating point of the combined system can then be found by the simultaneous solution of both functions. The simultaneous solutions match the cardiac output to venous return and the boundary pressures (both curves are obtained at the same P_A and P_{RA}). To derive the **vascular function curve**, we introduce the idea of mean systemic pressure.

THE MEAN SYSTEMIC PRESSURE NORMALLY EQUALS THE MEAN CIRCULATORY PRESSURE

The **mean circulatory pressure** is the pressure that would be measured at all points in the *circulatory system* when the heart is stopped and blood is instantaneously redistributed (meaning before any reflexive changes in the vasculature) so that pressure is the same everywhere. The **mean systemic pressure** is the pressure that would be measured at all points in the *systemic circulation* if all inputs and outputs to the systemic circulation were stopped and blood were distributed so that pressure is the same everywhere. The mean systemic pressure and pulmonary pressure are measured by clamping both the pulmonary artery and aorta while measuring the pressure within the two circulations. The results of the measurement show that the mean pulmonary pressure is normally about the same as the mean systemic pressure, about 7 mmHg. The mean circulatory pressure is the average of both systemic and pulmonary circulations but is heavily weighted to the systemic circulation because its compliance is some seven times greater than that of the pulmonary circulation. In normal individuals, the mean circulatory pressure is equal to the mean systemic pressure. **In man, the mean systemic pressure is normally 7 mmHg.**

FILLING THE EMPTY CIRCULATORY SYSTEM REVEALS STRESSED AND UNSTRESSED VOLUMES

Suppose that we perform a "thought experiment" in which we *completely* drain the blood from the cardiovascular system. In this experiment we stop the heart and we imagine that the vessels retain all of their characteristics that they had in the intact system before we drained the blood, with no change in caliber or compliance. Next we begin filling the system back up with blood, noting the volume of the blood and the pressure in the system. Because there is no flow, except transiently when we inject volume, the pressure is the same everywhere in the system. We find that it takes some volume to fill up the circulatory system at no pressure because many of the vessels do not collapse when blood is removed. After the circulatory system is filled to zero pressure, additional volume causes significant pressure rise, and this rise is linear with volume. Figure 5.12.4 illustrates the results of such an experiment. The graph is extrapolated from experiments in dogs in which only relatively small volumes of blood were added or removed from the circulation.

The slope of the plot is related to the compliance of the entire system, defined as

$$[5.12.3] \qquad C_S = \frac{\Delta V_S}{\Delta P_S}$$

where C_S is the **compliance** of the system, ΔV_S is the total volume of blood in the system, and ΔP_S is the pressure in the system. The entire system is comprised of

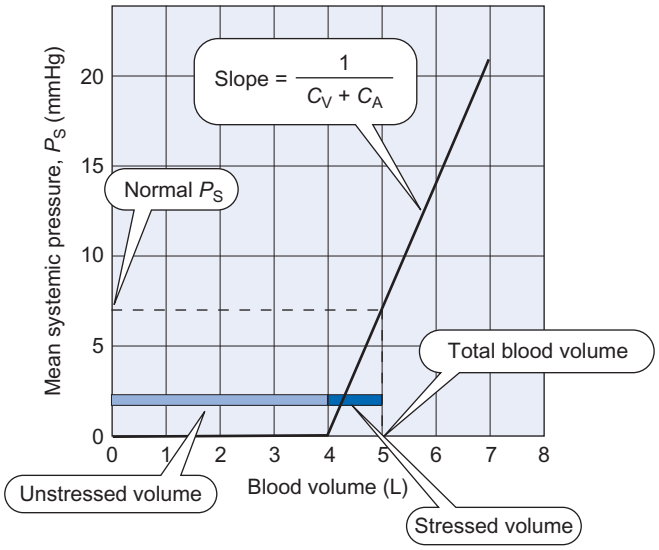

FIGURE 5.12.4 Relation between blood volume and mean systemic pressure. The graph is an extrapolation from experiments performed in dogs in which mean circulatory pressure (which approximates mean systemic pressure) was measured after withdrawal or addition of blood.

two major parts, as shown in Fig. [5.12.3]: the arteries and arterioles and the venules and veins. Each can be described by its own compliances:

$$C_V = \frac{\Delta V_V}{\Delta P_V} \qquad C_A = \frac{\Delta V_A}{\Delta P_A} \tag{5.12.4}$$

where C_V is the compliance of the venous side and C_A is the compliance of the arterial side of the vasculature. In this case, the two are connected with no flow so that $\Delta P_V = \Delta P_A = \Delta P_S$ and the total additional volume is the sum of the additional volumes on both sides of the vasculature: $\Delta V_S = \Delta V_A + \Delta V_V$

Thus, we can write

$$\begin{aligned} C_S &= \frac{\Delta V_S}{\Delta P_S} \\ &= \frac{\Delta V_A + \Delta V_V}{\Delta P_S} \\ &= \frac{\Delta V_A}{\Delta P_S} + \frac{\Delta V_V}{\Delta P_S} \\ &= \frac{\Delta V_A}{\Delta P_A} + \frac{\Delta V_V}{\Delta P_V} \\ &= C_V + C_A \end{aligned} \tag{5.12.5}$$

Thus, the compliance of the entire system is just the sum of the compliance of its components. The slope of the line in Figure 5.12.4 is thus $1/C_S = 1/(C_V + C_A)$.

The volume of blood that just fills the circulatory system with no pressure is called the **unstressed volume**. The added amount of blood necessary to bring the pressure from zero to the mean systemic pressure is the **stressed volume**. Thus, some physiologists refer to the mean systemic pressure as the **mean systemic filling pressure**. The values for the unstressed volume and stressed volume are not constant: constriction of the veins (venoconstriction) lowers the unstressed volume and increases the stressed volume. Thus, **venoconstriction increases the mean systemic pressure**. Similarly, changes in blood volume alone will change the stressed volume without changing the unstressed volume. We will return to these effects later.

THE VASCULAR FUNCTION CURVE CAN BE DERIVED FROM ARTERIAL AND VENOUS COMPLIANCES AND TPR

We now proceed to derive a relationship between flow through the veins, Q_{veins}, and the right atrial pressure, P_{RA}. This derivation is a modification of one provided by Levy (M.N. Levy, The cardiac and vascular factors that determine systemic blood flow, *Circulation Research* 44:739–747, 1979).

When the heart is stopped and no autonomic reflexes are activated, the blood redistributes itself so that pressure is equal everywhere in the circulation and there is no flow. At this point, the pressure is the mean systemic pressure, P_{MS}. If we start up the heart again, it begins pumping blood from the venous side of the circulation to the arterial side. As it does so, the added volume in the arteries expands the arteries and increases its pressure. Similarly, removal of volume from the venous side decreases its pressure. The increments or decrements in pressure are described by their respective compliances, as dictated by Eqn [5.12.4]:

$$\Delta P_A = \frac{\Delta V}{\Delta C_A} \qquad \Delta P_{RA} = \frac{-\Delta V}{C_V} \tag{5.12.6}$$

where ΔP_A is the *increment* in pressure caused by adding the volume ΔV, ΔP_{RA} is the *increment* in pressure on the venous side caused by removing the volume ΔV, C_A and C_V are the compliances for the arterial and venous part of the circulation, respectively. Note that the increment of pressure for the venous side is negative (it is really a *decrement*) because volume is being withdrawn. ΔV itself is always taken as positive. We use P_{RA}, the pressure at the level of the right atrium, as a measure of the venous compartment pressure.

The volume being added to the arterial side is equal to the volume being withdrawn from the venous side. Thus, the two equations in Eqn [5.12.6] can be combined. The increment in arterial pressure is then given as

$$\Delta P_A = -\Delta P_{RA} \frac{C_V}{C_A} \tag{5.12.7}$$

This is the *increment* in pressure that occurs on top of the pressure initially in the arteries, which was P_{MS}. The pressures are thus given as

$$P_A = P_{MS} + \Delta P_A \qquad P_{RA} = P_{MS} + \Delta P_{RA} \tag{5.12.8}$$

Note that ΔP_{RA} is negative in Eqn [5.12.6] so that the pressure in the veins is lowered by virtue of the heart pumping a volume out of it. We can rewrite the lower equation in Eqn [5.12.8] as

$$\Delta P_{RA} = P_{RA} - P_{MS} \quad [5.12.9]$$

This result can in turn be substituted into Eqn [5.12.7] to obtain

$$\Delta P_A = -[P_{RA} - P_{MS}]\frac{C_V}{C_A} \quad [5.12.10]$$

We can now substitute this result into the top equation of Eqn [5.12.8] to find

$$\begin{aligned} P_A &= P_{MS} - [P_{RA} - P_{MS}]\frac{C_V}{C_A} \\ &= P_{MS}\left[1 + \frac{C_V}{C_A}\right] - P_{RA}\frac{C_V}{C_A} \end{aligned} \quad [5.12.11]$$

The total flow through the veins is given in Eqn [5.12.2]. We can substitute in from Eqn [5.12.11] to obtain

$$\begin{aligned} Q_{veins} &= \frac{P_A - P_{RA}}{TPR} \\ &= \frac{P_{MS}[1 + (C_V/C_A)] - P_{RA}(C_V/C_A) - P_{RA}}{TPR} \\ &= \frac{P_{MS}[1 + (C_V/C_A)] - P_{RA}[1 + (C_V/C_A)]}{TPR} \\ &= -\frac{[1 + (C_V/C_A)]}{TPR}[P_{RA} - P_{MS}] \end{aligned} \quad [5.12.12]$$

The last equation is what we need, and is rewritten below:

$$Q_{veins} = -\frac{[1 + (C_V/C_A)]}{TPR}[P_{RA} - P_{MS}] \quad [5.12.13]$$

Equation [5.12.13] describes the **vascular function curve**. Q_{veins} is the flow through the veins, P_{RA} is the pressure at the right atrium, and P_{MS} is the mean systemic pressure. This equation only approximates the actual relationship between Q_{veins} and P_{RA} because we have calculated the pressures using the compliances, and this assumes no flow. We then inserted these static pressures into a formula for flow!

THE EXPERIMENTALLY DETERMINED VASCULAR FUNCTION CURVE FOLLOWS THE THEORETICAL RESULT ONLY FOR POSITIVE RIGHT ATRIAL PRESSURES

The vascular function curve was determined experimentally in dogs by replacing the heart with a pump so that the flow could be set and right atrial pressure measured. The design of this experiment should make it clear that the right atrial pressure is not an independent variable but depends on the pumping action of the heart. Indeed, according to our definition, mean systemic pressure is the pressure measured when the heart is stopped. The right atrial pressure differs from the mean systemic pressure only when the heart is pumping. We can rewrite Eqn [5.12.13] as

$$P_{RA} = -\frac{TPR}{\left[1 + \frac{C_V}{C_A}\right]}Q_{veins} + P_{MS} \quad [5.12.14]$$

The dependence of P_{RA} on Q_{veins} determined experimentally is shown in Figure 5.12.5. Here we plot P_{RA} against Q_{veins} specifically to indicate how this was accomplished: the pump rate was controlled (it is the independent variable) and the resulting right atrial pressure (P_{RA}) was measured. Here Q_{veins} is labeled "cardiac output" to indicate that in the intact system the heart beat draws down the right atrial pressure. When it pumps faster, right atrial pressure drops further.

The curve shown in Figure 5.12.5 generally agrees with the theoretical analysis that results in Eqn [5.12.14]. At zero flow, the right atrial pressure equals the mean systemic pressure. This fits the definition of the mean systemic pressure as the pressure throughout the systemic circulation at zero flow. As flow increases, the right atrial pressure becomes smaller until it reaches 0 mmHg. The negative slope agrees with the equation. At about 0 mmHg right atrial pressure, the curve bends, and this bend is *not* predicted by Eqn [5.12.14]. Here a new phenomenon occurs that we have not considered—the partial collapse of veins exposed to small or negative transmural pressures. The negative luminal pressure flattens the veins, changing their cross-sectional profile.

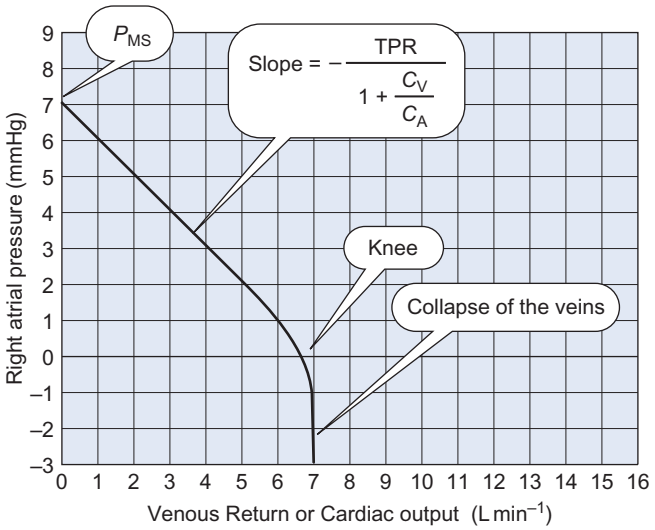

FIGURE 5.12.5 Dependence of right atrial pressure, P_{RA}, on the flow through the vasculature, which is equal to the cardiac output. The slope is related to the compliances of the venous and arterial sides of the circulation and to the TPR. At zero flow, the right atrial pressure is the mean systemic pressure. At low P_{RA}, near zero and lower, the flow levels off because the veins collapse partly due to their lower luminal pressure transmitted to the veins from the atrium. Flow remains high, but its increase is limited by reduced aggregate cross-sectional area of the veins.

Flow still continues at a high rate but cannot increase further due to the flutter of the veins.

SIMULTANEOUS SOLUTION OF THE CARDIAC FUNCTION CURVE AND VASCULAR FUNCTION CURVE DEFINES THE STEADY-STATE OPERATING POINT OF THE CARDIOVASCULAR SYSTEM

The right atrial pressure determines the stretch of the right ventricle, which in turn determines the output of the right heart, which in turn determines the output of the left heart. The output of the left heart is the cardiac output. The plot of cardiac output as a function of right atrial pressure is the cardiac function curve. The vascular function curve describes how the flow through the veins sets the right atrial pressure. In the intact cardiovascular system operating at steady state, the cardiac output is the same as the flow through the veins. Thus, the right atrial pressure sets the cardiac output, which then sets the right atrial pressure through its interaction with the vasculature. This forms a compact negative feedback system that naturally finds its steady state. The steady-state operating point of the combined cardiovascular system can be found by simultaneously solving the cardiac function curve and the vascular function curve. This can be done graphically by plotting the two curves on the same graph. To do this, we need to exchange the axes of Figure 5.12.5. This curve with right atrial pressure plotted on the abscissa (the horizontal axis) is called the **vascular function curve**. The cardiac function curve and vascular function curve are shown overlaid in Figure 5.12.6. The steady-state operating point is the intersection of the two curves: in normal resting conditions this is **5 L min^{-1} at a right atrial pressure of 2 mmHg**.

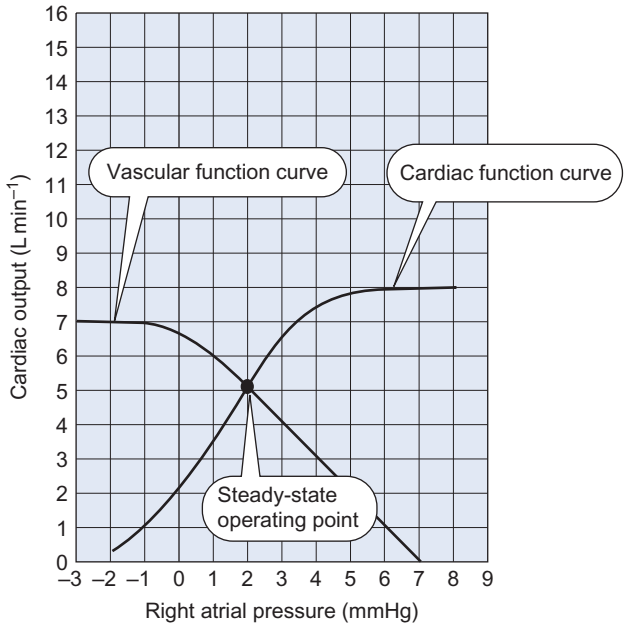

FIGURE 5.12.6 Graphical solution of the steady-state operation of the cardiovascular system. The cardiac function curve describes the dependence of cardiac output on the right atrial pressure. The vascular function curve describes the dependence of right atrial pressure on cardiac output. At steady state, both functions must be true because there is only one steady-state flow (the cardiac output) and one right atrial pressure. The steady-state operating point corresponds to the intersection of the two curves.

CHANGING ARTERIOLAR RESISTANCE ROTATES THE VASCULAR FUNCTION AROUND P_{MS}

The TPR is approximated as the sum of the aggregate arterial and venous resistances. Most of that resistance is in the arterial side of the circulation and specifically in the arterioles. **Vasodilation** refers to dilation of these resistance vessels and reduction in their resistance; **vasoconstriction** refers to a reduction in their caliber and an increase in their resistance. Equation [5.12.13] describes the vascular function curve. TPR is in the denominator of the slope of flow (cardiac output) against right atrial pressure. Increasing TPR thus decreases the slope, while leaving the intercept at P_{MS}, the mean systemic pressure. P_{MS} is unaffected by changes in TPR. Changes in TPR also do not affect the compliances. Thus, increasing TPR rotates the vascular function curve downward, and decreasing TPR rotates the curve upward, as shown in Figure 5.12.7.

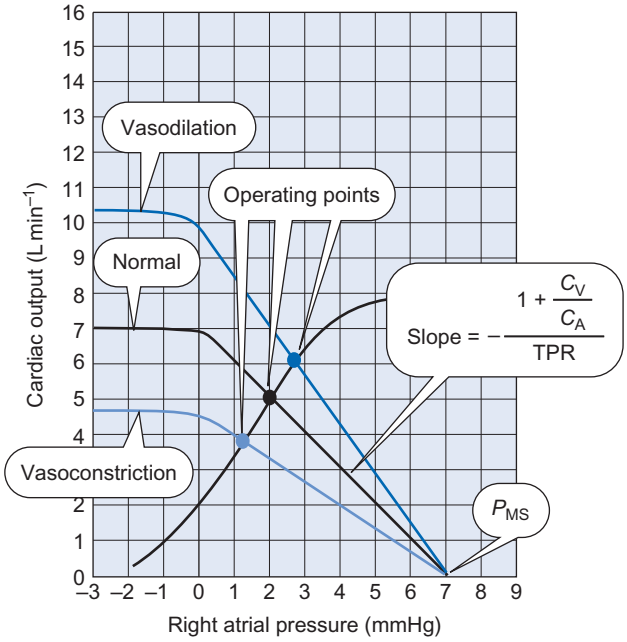

FIGURE 5.12.7 Changing arteriolar resistance rotates the vascular function curve and establishes new steady-state operating points. The normal vascular function curve and cardiac function curves are shown in black. Vasoconstriction increases the TPR which decreases the slope of the vascular function curve but does not alter its intercept at P_{MS} (the light blue curve). Thus, it rotates the curve downward around P_{MS}. The result is a decrease in the cardiac output at the steady-state operating point. Vasodilation decreases the TPR and rotates the vascular function curve upward around P_{MS} (the dark blue curve) Vasodilation increases the steady-state cardiac output.

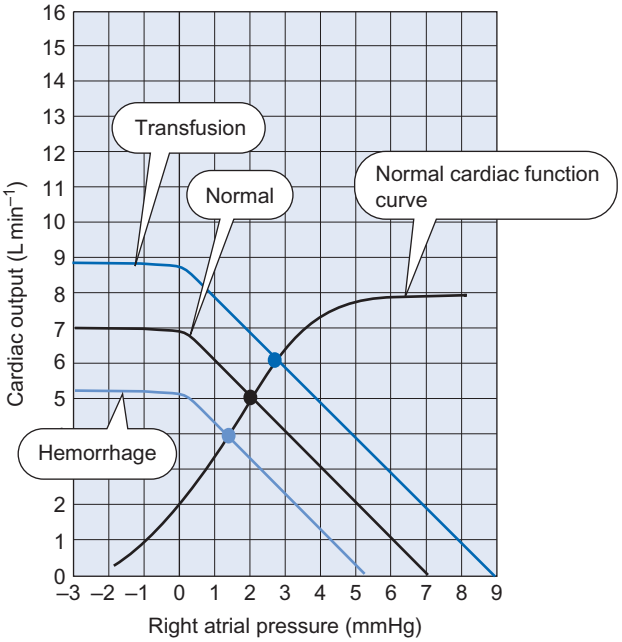

FIGURE 5.12.8 Changes in blood volume shift the vascular function curve vertically. The normal vascular function curve is shown in black. Hemorrhage causes loss of blood from the circulation, which reduces the stressed volume and lowers the mean systemic pressure. This shifts the vascular function curve downward (the light blue curve). Transfusion of extra blood increases the stressed volume and raises the mean systemic pressure, shifting the vascular function curve upward (the dark blue curve). The steady-state operating points shift accordingly to the new intersection of the vascular function curve with the normal cardiac function curve.

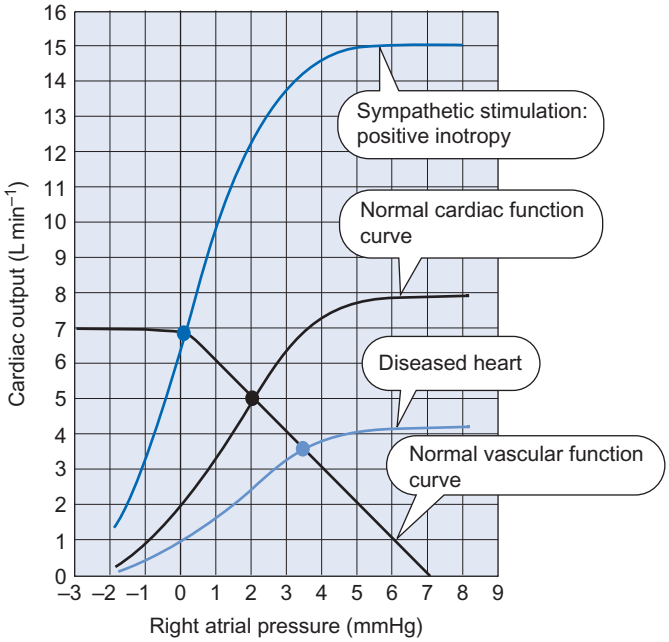

FIGURE 5.12.9 Inotropic agents shift the cardiac function curve. Positive inotropic agents such as sympathetic stimulation rotate the cardiac function curve counterclockwise, increasing the cardiac output at its steady-state operating point (dark blue curve). The normal cardiac function curve and the vascular function curve are shown in black. Depressed contractility such as in disease states reduces the cardiac output at the steady-state operating point (light blue curve).

CHANGES IN BLOOD VOLUME SHIFT THE VASCULAR FUNCTION CURVE VERTICALLY

Hemorrhage refers to the loss of blood from the cardiovascular system. Inspection of Figure 5.12.4 shows that reduction in blood volume will reduce the stressed volume, causing a decrease in the mean systemic pressure. This has the effect of shifting the vascular function curve downward. Increase in the blood volume by transfusion has the opposite effect: it increases the stressed volume and raises the mean systemic pressure. It shifts the vascular function curve upward. These shifts and their effects on the steady-state operating point are shown in Figure 5.12.8.

CHANGES IN THE CARDIAC FUNCTION CURVE CHANGE THE STEADY-STATE OPERATING POINT

As described in Chapter 5.8, the cardiac function curve can be rotated counterclockwise by positive inotropic agents such as cardiac glycosides or by sympathetic stimulation. Conversely, the cardiac function curve can rotate clockwise in pathological conditions or by negative inotropic agents. These effects are due to changes in the heart's contractility. Figure 5.12.9 illustrates the effect of these changes on the steady-state operating point of the cardiovascular system.

STRENUOUS EXERCISE ALTERS MULTIPLE PARTS OF THE CARDIOVASCULAR SYSTEM

Strenuous exercise has four major effects on the cardiovascular system. These are:

1. Increased heart rate
2. Increased cardiac contractility
3. Vasoconstriction and vasodilation
4. Venoconstriction.

Vasoconstriction occurs in some beds that are inessential to the immediate problem posed by an emergency. Vasodilation occurs in the muscle beds that are being used. The net result is a pronounced reduction in the TPR, which increases the slope of the vascular function curve. Venoconstriction has the effect of shifting the point at which the circulatory system fills with blood. By reducing the caliber of the veins, it effectively increases the stressed volume and thereby increases the mean systemic pressure. This shifts the vascular function curve upward. The increased heart rate and increased cardiac contractility combine to markedly shift the cardiac function curve upward and to the left. The net result is that the steady-state operating point shifts to much higher cardiac output. These effects are displayed in Figure 5.12.10.

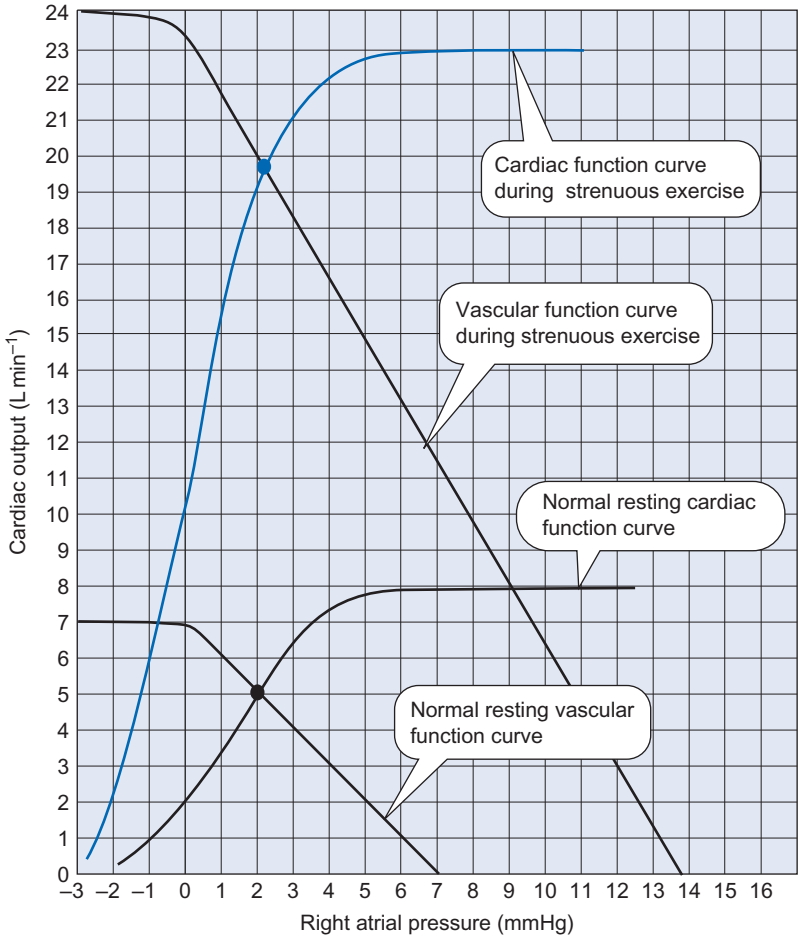

FIGURE 5.12.10 Operating point of the cardiovascular system during strenuous exercise. The cardiac function curve is greatly enhanced by increased heart rate and increased contractility. The vascular function curve is affected by venoconstriction, which raises mean systemic pressure; by vasodilation, which increases the slope of the linear portion of the curve; and by the muscle pumps, which also increase the slope and shift the vascular curve upward.

Muscular activity markedly shifts both the mean systemic pressure and the slope of the vascular function curve. It does this by providing "muscle pumps" in the venous circulation that have the effect of negative resistances. Contraction of limb muscles squeezes the vessels inside the muscle. Because veins have valves that assure unidirectional flow, this squeeze propels blood toward the heart. When the muscle relaxes during rhythmic exercise, such as running, the veins fill up again from blood that drains the muscle. In this way, blood flow into and out of the muscle is pulsatile, deriving its frequency from the frequency of activation of the muscle. Thus, each active muscle acts as a miniature auxiliary pump that assists the heart in circulating the blood. During strenuous exercise, fully one-half of the total energy of circulation can be provided by skeletal muscles.

SUMMARY

During the short term, the cardiovascular system can be regarded as being closed. Because of this, at steady state, the cardiac output must match the venous return. Mismatches between cardiac output and venous return are quickly resolved by the transfer of blood either from the venous side of the circulation to the arteries or the other way around. This transfer of volume alters the pressure in each side so that flows become equal.

The mean systemic pressure is the pressure throughout the systemic circulation when all of its inputs and outputs are simultaneously blocked. This is similar to the mean circulatory pressure, which is the pressure throughout all of the circulatory system (systemic and pulmonary systems) when the heart is stopped and fluid redistributed before any cardiovascular reflexes occur. The mean systemic pressure depends on the volume of the vessels, the compliance of the venous and arterial side of the circulation, and the volume of blood. The volume of blood required to fill the vessels to 0 mmHg pressure is the unstressed volume. The remainder of the blood volume is the stressed volume. Mean systemic pressure increases linearly with the stressed volume according to the compliance of the whole system. Transfusion of extra blood and venoconstriction raises the mean systemic pressure.

The cardiac function curve plots the cardiac output, in units of $L\,min^{-1}$, against the right atrial pressure. The right atrial pressure is the preload of the heart that determines its degree of stretch and hence its force of contraction. The cumulative volumes ejected by the heart into the arterial side of the circulation produce a pressure gradient leading back to the heart and establish the right atrial pressure. Thus there is a relation between flow through the veins and the right atrial pressure. This relationship forms the vascular function curve, which is plotted as flow against right atrial pressure. The

steady-state operating point of the system is the simultaneous solution of the cardiac function curve and the vascular function curve. It is solved graphically by the intersection of the two curves.

The vascular function curve intercepts the abscissa (right atrial pressure axis) at the mean systemic pressure. The slope of the linear portion of the vascular function curve is inversely related to the TPR. Increasing arteriolar resistance (vasoconstriction) therefore decreases the slope of the vascular function curve and lowers the cardiac output. Vasodilation has the opposite effect: the slope increases and cardiac output increases.

Hemorrhage displaces the vascular function curve downward, decreasing mean systemic pressure but it does not significantly change the slope of the vascular function curve. Transfusion of extra blood has the opposite effects: mean systemic pressure is increased and the vascular function curve is displaced upward.

Changing the contractility of the heart alters the operating point of the system by shifting the cardiac function curve. This allows for large increases in cardiac output. During strenuous exercise, the activity of the muscles helps propel blood around the circulatory system, greatly reducing the work of the heart and allowing for large cardiac output.

REVIEW QUESTIONS

1. What is the mean systemic pressure? Is this the same as mean circulatory pressure?
2. How does right atrial pressure determine cardiac output from the *left* heart?
3. What is the unstressed volume? What is the stressed volume? What is the slope of the curve of volume against pressure with the heart stopped?
4. Draw the vascular function curve (flow versus right atrial pressure). Why does flow go down when pressure rises?
5. What is the slope of the vascular function curve (flow versus right atrial pressure)? What is the relative capacitance of the venous and arterial systems? What effect does vasodilation have on the vascular function curve? What effects does vasoconstriction have?
6. What effect does hypovolemia have on the vascular function curve? What is the effect of transfusion on the vascular function curve?
7. Why is the operating point of the cardiovascular system defined by the intersection of the vascular function curve and cardiac function curve?
8. What effect does exercise have on the operating point of the cardiovascular system?