The Cardiac Pump

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CHAPTER OUTLINE

- **THE CARDIAC CYCLE**
- **CARDIAC OUTPUT**
- **THE MEASUREMENT OF CARDIAC OUTPUT**
- **THE ENERGETICS OF CARDIAC FUNCTION**

KEY CONCEPTS

1. Learning to correlate the ECG, pressures, volumes, flows, and heart sounds in time is fundamental to a working knowledge of the heart.
2. Cardiac output is the product of stroke volume times heart rate.
3. Stroke volume is determined by end-diastolic fiber length, contractility, afterload, and hypertrophy.
4. Heart rate influences ventricular filling time and stroke volume.
5. The influence of heart rate on cardiac output depends on simultaneous effects on ventricular contractility.

6. Cardiac output can be measured by methods that rely on mass balance or cardiac imaging.
7. Cardiac energy production depends primarily on the supply of oxygen to the heart.
8. Cardiac energy consumption depends on the work of the heart.
9. The external work of the heart depends on the volume of blood pumped and the pressure against which it is pumped.

The heart consists of a series of four separate chambers (two atria and two ventricles) that use one-way valves to direct blood flow. Its ability to pump blood depends on the integrity of the valves and the proper cyclic contraction and relaxation of the muscular walls of the four chambers. An understanding of the cardiac cycle is a prerequisite for understanding the performance of the heart as a pump.

THE CARDIAC CYCLE

The **cardiac cycle** refers to the sequence of electrical and mechanical events occurring in the heart during a single beat and the resulting changes in pressure, flow, and volume in the various cardiac chambers. The functional interrelationships of the cardiac cycle described below are represented in Figure 14.1.

Sequential Contractions of the Atria and Ventricles Pump Blood Through the Heart

The cycle of events described here occurs almost simultaneously in the right and left heart; the main difference is

that the pressures are higher on the left side. The focus is on the left side of the heart, beginning with electrical activation of the atria.

Atrial Systole and Diastole. The P wave of the electrocardiogram (ECG) reflects atrial depolarization, which initiates **atrial systole**. Contraction of the atria "tops off" ventricular filling with a final, small volume of blood from the atria, producing the **a wave**. Under resting conditions, atrial systole is not essential for ventricular filling and, in its absence, ventricular filling is only slightly reduced. However, when increased cardiac output is required, as during exercise, the absence of atrial systole can limit ventricular filling and stroke volume. This happens in patients with atrial fibrillation, whose atria do not contract synchronously.

The P wave is followed by an electrically quiet period, during which atrioventricular (AV) node transmission occurs (the PR segment). During this electrical pause, the mechanical events of atrial systole and ventricular filling are concluded before excitation and contraction of the ventricles begin.

Atrial diastole follows atrial systole and occurs during ventricular systole. As the left atrium relaxes, blood enters the atrium from the pulmonary veins. Simultane-
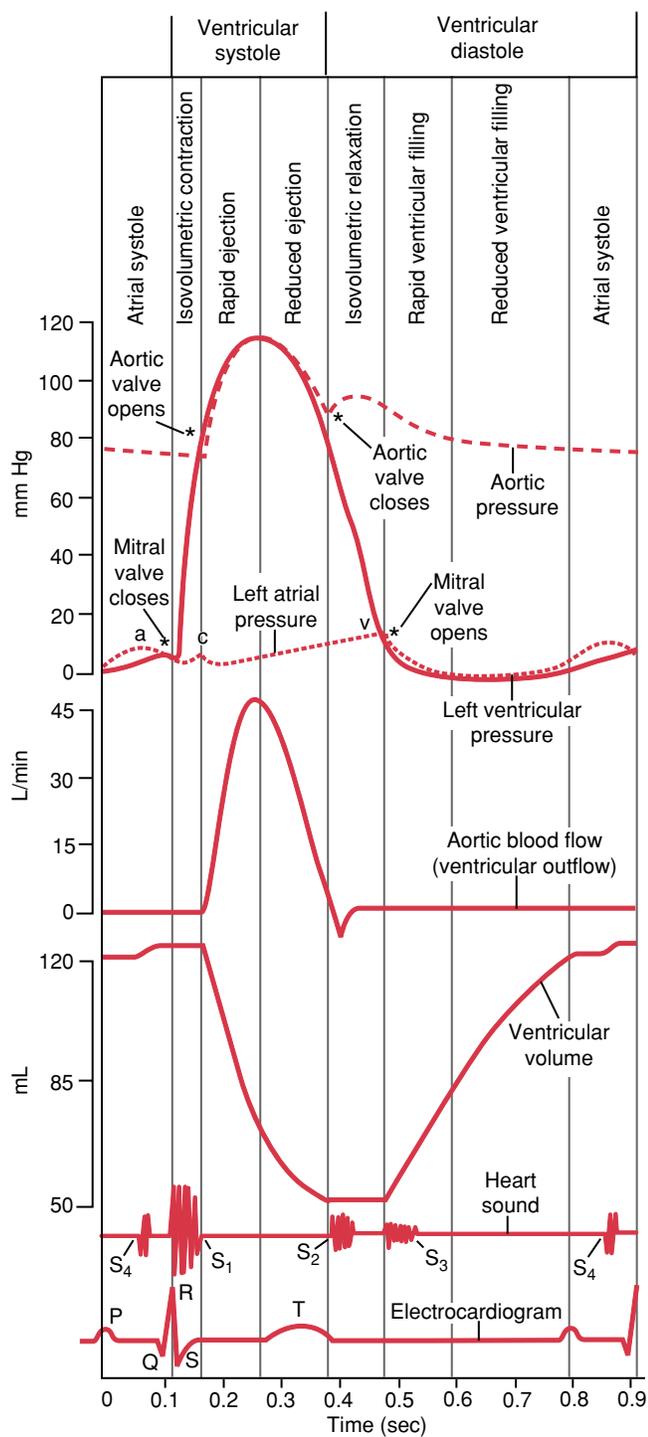
FIGURE 14.1 The timing of various events in the cardiac cycle.

Ventricular Systole. The QRS complex reflects excitation of ventricular muscle and the beginning of **ventricular systole** (see Fig. 14.1). As ventricular pressure rises above atrial pressure, the left **atrioventricular (mitral) valve** closes. Contraction of the papillary muscles prevents the mitral valve from everting into the left atrium and enables the valve to prevent the regurgitation of blood into the atrium as ventricular pressure rises. The aortic valve does not open until left ventricular pressure exceeds aortic pressure. During the interval when both mitral and aortic valves are closed, the ventricle contracts **isovolumetrically** (i.e., the ventricular volume does not change). The contraction causes ventricular pressure to rise, and when ventricular pressure exceeds aortic pressure (at approximately 80 mm Hg), the aortic valve opens and allows blood to flow from the ventricle into the aorta. At this point, ventricular muscle begins to shorten, reducing the volume of the ventricle.

When the rate of ejection begins to fall (see the aortic blood flow record in Fig. 14.1), the aortic and ventricular pressures decline. Ventricular pressure actually decreases slightly below aortic pressure prior to closure of the aortic valve, but flow continues through the aortic valve because of the inertia imparted to the blood by ventricular contraction. (Think of a rubber ball connected to a paddle by a rubber band. The ball continues to travel away from the paddle after you pull back because the inertial force on the ball exceeds the force generated by the rubber band.)

Ventricular Diastole. Ventricular repolarization (producing the T wave) initiates ventricular relaxation or **ventricular diastole.** When the ventricular pressure drops below the atrial pressure, the mitral valve opens, allowing the blood accumulated in the atrium during systole to flow rapidly into the ventricle; this is the rapid phase of ventricular filling. Both pressures continue to decrease—the atrial pressure because of emptying into the ventricle and the ventricular pressure because of continued ventricular relaxation (which, in turn, draws more blood from the atrium). About midway through ventricular diastole, filling slows as ventricular and atrial pressures converge. Finally, atrial systole tops off ventricular volume.

Pressures, Flows, and Volumes in the Cardiac Chambers, Aorta, and Great Veins Can Be Matched With the ECG and Heart Sounds

The pressures, flows, and volumes in the cardiac chambers, aorta, and great veins can be studied in conjunction with the ECG and heart sounds to yield an understanding of the coordinated activity of the heart. Ventricular diastole and systole can be defined in terms of both electrical and mechanical events. In electrical terms, ventricular systole is defined as the period between the QRS complex and the end of the T wave. In mechanical terms, it is the period between the closure of the mitral valve and the subsequent closure of the aortic valve. In either case, ventricular diastole comprises the remainder of the cycle.

The **first (S₁)** and **second (S₂) heart sounds** signal the beginning and end of mechanical systole. The first heart sound (usually described as a "lub") occurs as the ventricle contracts and ventricular pressure rises above atrial pressure, causing

ously, blood enters the right atrium from the superior and inferior vena cavae. The gradual rise in left atrial pressure during atrial diastole produces the **v wave** and reflects its filling. The small pressure oscillation early in atrial diastole, called the **c wave**, is caused by bulging of the mitral valve and movements of the heart associated with ventricular contraction.

the atrioventricular valves to close. The relatively low-pitched sound associated with their closure is caused by vibrations of the valves and walls of the heart that occur as a result of their elastic properties when the flow of blood through the valves is suddenly stopped. In contrast, the aortic and pulmonic valves close at the end of ventricular systole, when the ventricles relax and pressures in the ventricles fall below those in the arteries. The elastic properties of the aortic and pulmonic valves produce the second heart sound, which is relatively high-pitched (typically described as a "dup"). Mechanical events other than vibrations of the valves and nearby structures contribute to these two sounds, especially S_1; these factors include movement of the great vessels and turbulence of the rapidly moving blood. The second heart sound often has two components—the first corresponds to aortic valve closure and the second to pulmonic valve closure. In normal individuals, **splitting** widens with inspiration and narrows or disappears with expiration.

A **third heart sound (S_3)** results from vibrations during the rapid phase of ventricular filling and is associated with ventricular filling that is too rapid. Although it may be heard in normal children and adolescents, its appearance in a patient older than age 35 usually signals the presence of a cardiac abnormality. A **fourth heart sound (S_4)** may be heard during atrial systole. It is caused by blood movement resulting from atrial contraction and, like S_3, is more common in patients with abnormal hearts.

CARDIAC OUTPUT

Cardiac output (CO) is defined as the volume of blood ejected from the heart per unit time. The usual resting values for adults are 5 to 6 L/min, or approximately 8% of body weight per minute. Cardiac output divided by body surface area is called the **cardiac index.** When it is necessary to normalize the value to compare the cardiac output among individuals of different sizes, either cardiac index or cardiac output divided by body weight can be used. Cardiac output is the product of heart rate (HR) and **stroke volume** (SV), the volume of blood ejected with each beat:

$$CO = SV \times HR \qquad (1)$$

Stroke volume is the difference in the volume of blood in the ventricle at the end of diastole—**end-diastolic volume**—and the volume of blood in the ventricle at the end of systole—**end-systolic volume**. This is shown in Figure 14.1.

If heart rate remains constant, cardiac output increases in proportion to stroke volume, and stroke volume increases in proportion to cardiac output. Table 14.1 outlines the factors that influence cardiac output.

Ejection fraction (EF) is a commonly used measure of cardiac performance. It is the ratio of stroke volume to end-diastolic volume (EDV), expressed as a percentage:

$$EF = (SV/EDV) \times 100 \qquad (2)$$

Ejection fraction is normally more than 55%. It is dependent on heart rate, preload, afterload, and contractility (all to be discussed below) and provides a nonspecific index of ventricular function. Still, it has proved to be valuable in predicting the severity of heart disease in individual patients.

TABLE 14.1   **Factors Influencing Cardiac Output**

I. Stroke volume
  A. Force of contraction
    1. End-diastolic fiber length (Starling's law, preload)
      a. End-diastolic pressure
      b. Ventricular diastolic compliance
    2. Contractility
      a. Sympathetic stimulation via norepinephrine acting on β_1 receptors
      b. Circulating epinephrine acting on β_1 receptors (minor)
      c. Intrinsic changes in contractility in response to changes in heart rate and afterload
      d. Drugs (positive inotropic drugs, e.g., digitalis; negative inotropic drugs, e.g., general anesthetics; toxins)
      e. Disease (coronary artery disease, myocarditis, cardiomyopathy, etc.)
    3. Hypertrophy
  B. Afterload
    1. Ventricular radius
    2. Ventricular systolic pressure
II. Heart rate (and pattern of electrical excitation)

Stroke Volume Is a Determinant of Cardiac Output

Stroke volume increases with increases in the force of contraction of ventricular muscle and decreases with increases in the afterload. The force of contraction is affected by end-diastolic fiber length, contractility, and hypertrophy. **Afterload**, the force against which the ventricle must contract to eject blood, is affected by the ventricular radius and ventricular systolic pressure. Because the pressure drop across the aortic valve is normally small, aortic pressure is often used as a substitute for ventricular pressure in such considerations.

Effect of End-Diastolic Fiber Length.   The relationship between ventricular end-diastolic fiber length and stroke volume is known as **Starling's law of the heart.** Within limits, increases in the left ventricular end-diastolic fiber length augment the ventricular force of contraction, which increases the stroke volume. This reflects the relationship between the length of a muscle and the force of contraction (see Chapter 10). After reaching an optimal diastolic fiber length, stroke volume no longer increases with further stretching of the ventricle.

End-diastolic fiber length is determined by end-diastolic volume, which is dependent on end-diastolic pressure. End-diastolic pressure is the force that expands the ventricle to a particular volume. In Chapter 10, **preload** was defined as the passive force that establishes the muscle fiber length before contraction. For the intact heart, preload can be defined as end-diastolic pressure. For a given ventricular compliance (change in volume caused by a given change in pressure), a higher end-diastolic pressure (preload) increases both diastolic volume and fiber length. The end-diastolic pressure depends on the degree of ventricular filling during ventricular diastole, which is influenced largely by atrial pressure.

In heart disease, ventricular compliance can decrease because of impaired ventricular muscle relaxation or a build up of connective tissue within the walls of the heart. In either case, the relationship between ventricular filling, end-diastolic pressure, and end-diastolic volume is altered. The effect is a decrease in end-diastolic fiber length and a resulting decrease in stroke volume.

The curve expressing the relationship between ventricular filling and ventricular contractile performance is called a **Starling curve** or a **ventricular function curve** (Fig. 14.2). This curve can be plotted with end-diastolic volume, end-diastolic pressure, or atrial pressure as the abscissa, as proxies for end-diastolic fiber length.

The ordinate on the plot of Starling's law (Fig. 14.2) can also be a variable other than stroke volume. For example, if heart rate remains constant, cardiac output can be substituted for stroke volume. The effect of arterial pressure on stroke volume can also be taken into account by plotting stroke work on the ordinate. **Stroke work** is stroke volume times mean arterial pressure. An increase in arterial pressure (afterload) decreases stroke volume by increasing the force that opposes the ejection of blood during systole. If stroke work is on the ordinate, any increase in the force of contraction that results in either increased arterial pressure or stroke volume shifts the stroke work curve upward and to the left. If stroke volume alone were the dependent variable, a change in the performance of the heart causing increased pressure would not be expressed by a change in the curve.

Starling's law explains the remarkable balancing of the output between the two ventricles. If the right heart were to pump 1% more blood than the left heart each minute without a compensatory mechanism, the entire blood volume of the body would be displaced into the pulmonary circulation in less than 2 hours. A similar error in the opposite direction would likewise displace all the blood volume into the systemic circuit. Fortunately, Starling's law prevents such an occurrence. If the right ventricle pumps slightly more blood than the left ventricle, left atrial filling (and pressure) will increase. As left atrial pressure increases,
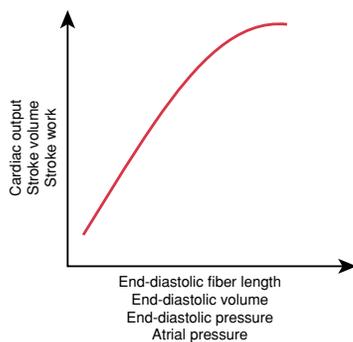
left ventricular pressure and left ventricular end-diastolic fiber length increase both the force of contraction and the stroke volume of the left ventricle. If the stroke volume rises too much, the left heart begins to pump more blood than the right heart and left atrial pressure drops; this decreases left ventricular filling and reduces stroke volume. The process continues until left heart output is exactly equal to right heart output.

The descending limb of the ventricular function curve, analogous to the descending limb of the length-tension curve (see Chapter 10), is probably never reached in a living heart because the resistance to stretch increases as the end-diastolic volume reaches the limit for optimum stroke volume. Further enlargement of the ventricle would require end-diastolic pressures that do not occur. As a result of increased resistance to stretch or decreased compliance, the atrial pressures necessary to produce further filling of the ventricles are probably never reached. The limited compliance, therefore, prevents optimal sarcomere length from being exceeded. In heart failure, the ventricles can dilate beyond the normal limit because they exhibit increased compliance. Even under these conditions, optimal sarcomere length is not exceeded. Instead, the sarcomeres appear to realign so that there are more of them in series, allowing the ventricle to dilate without stretching sarcomeres beyond their optimal length.

Effect of Changes in Contractility.   Factors other than end-diastolic fiber length can influence the force of ventricular contraction. Different conditions produce different relationships between stroke volume (or work) to end-diastolic fiber length. For example, increased sympathetic nerve activity causes release of norepinephrine (see Chapter 3). Norepinephrine increases the force of contraction for a given end-diastolic fiber length (Fig. 14.3). The increase in force of contraction causes more blood to be ejected against a given aortic pressure and, thus, raises stroke volume. A change in
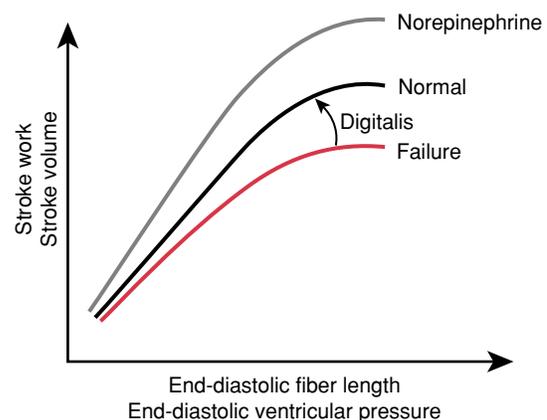

FIGURE 14.2 **A Starling (ventricular function) curve.** Stroke work increases with increased end-diastolic fiber length. Several other combinations of variables can be used to plot a Starling curve, depending on the assumptions made. For example, cardiac output can be substituted for stroke volume if heart rate is constant, and stroke volume can be substituted for stroke work if arterial pressure is constant. End-diastolic fiber length and volume are related by laws of geometry, and end-diastolic volume is related to end-diastolic pressure by ventricular compliance.

FIGURE 14.3 **Effect of norepinephrine and heart failure on the ventricular function curve.** Norepinephrine raises ventricular contractility (i.e., stroke volume and/or stroke work are elevated at a given end-diastolic fiber length). In heart failure, contractility is decreased, so that stroke volume and/or stroke work are decreased at a given end-diastolic fiber length. Digitalis raises the intracellular calcium ion concentration and restores the contractility of the failing ventricle.

the force of contraction at a constant end-diastolic fiber length reflects a change in the **contractility** of the heart. (The cellular mechanisms governing contractility are discussed in Chapter 10.) A shift in the ventricular function curve to the left indicates increased contractility (i.e., more force and/or shortening occurring at the same initial fiber length), and shifts to the right indicate decreased contractility. When an increase in contractility is accompanied by an increase in arterial pressure, the stroke volume may remain constant, and the increased contractility will not be evident by plotting the stroke volume against the end-diastolic fiber length. However, if stroke work is plotted, a leftward shift of the ventricular function curve is observed (see Fig. 14.3). A ventricular function curve with stroke volume on the ordinate can be used to indicate changes in contractility only when arterial pressure does not change.

During heart failure, the ventricular function curve is shifted to the right, causing a particular end-diastolic fiber length to be associated with less force of contraction and/or shortening and a smaller stroke volume. As described in Chapter 10, cardiac glycosides, such as digitalis, tend to normalize contractility; that is, they shift the ventricular curve of the failing heart back to the left (see Fig. 14.3).

The collection of ventricular function curves reflecting changes in contractility in a particular heart is known as a family of ventricular function curves.

Effect of Hypertrophy. In the normal heart, the force of contraction is also increased by **myocardial hypertrophy.** Regular, intense exercise results in increased synthesis of contractile proteins and enlargement of cardiac myocytes. The latter is the result of increased numbers of parallel myofilaments, increasing the number of actomyosin cross-bridges that can be formed. As each cell enlarges, the ventricular wall thickens and is capable of greater force development. The ventricular lumen may also increase in size, and this is accompanied by an increase in stroke volume. The hearts of appropriately trained athletes are capable of producing much greater stroke volumes and cardiac outputs than those of sedentary individuals. These changes are reversed if the athlete stops training. Myocardial hypertrophy also occurs in heart disease. In heart disease, although myocardial hypertrophy initially has positive effects, it ultimately has negative effects on myocardial force development. A thorough discussion of pathological hypertrophy is beyond the scope of this book.

Effect of Afterload. The second determinant of stroke volume is afterload (see Table 14.1), the force against which the ventricular muscle fibers must shorten. In normal circumstances, afterload can be equated to the aortic pressure during systole. If arterial pressure is suddenly increased, a ventricular contraction (at a given level of contractility and end-diastolic fiber length) produces a lower stroke volume. This decrease can be predicted from the force-velocity relationship of cardiac muscle (see Chapter 10). The shortening velocity of ventricular muscle decreases with increasing load, which means that for a given duration of contraction (reflecting the duration of the action potential), the lower velocity results in less shortening and a decrease in stroke volume (Fig. 14.4).
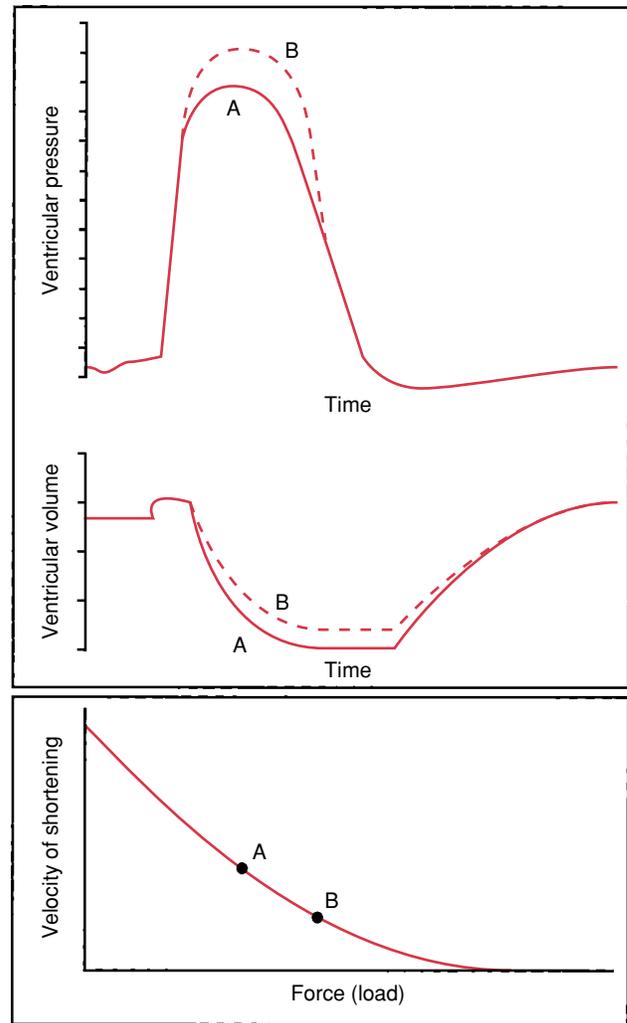

FIGURE 14.4 **Effect of aortic pressure on ventricular function.** Ventricular pressure, ventricular volume, and the force-velocity relationship are shown for (A) normal and (B) elevated aortic pressure. Increased afterload slows the velocity of shortening, decreasing ventricular emptying, and stroke volume.

Fortunately, the heart can compensate for the decrease in left ventricular stroke volume produced by increased afterload. Although a sudden rise in systemic arterial pressure causes the left ventricle to eject less blood per beat, the output from the right heart remains constant. Left ventricular filling subsequently exceeds its output. As the end-diastolic volume and fiber length of the left ventricle increase, the ventricular force of contraction is enhanced. A new steady state is quickly reached in which the end-diastolic fiber length is increased and the previous stroke volume is maintained. Within limits, an additional compensation also occurs. During the next 30 seconds, the end-diastolic fiber length returns toward the control level, and the stroke volume is maintained despite the increase in aortic pressure. If arterial pressure times stroke volume (stroke work) is plotted against end-diastolic fiber length, it is

apparent that stroke work has increased for a given end-diastolic fiber length. This leftward shift of the ventricular function curve indicates an increase in contractility.

Effect of the Ventricular Radius.   The ventricular radius influences stroke volume because of the relationship between ventricular pressures (P_v) and ventricular wall tension (T). For a hollow structure, such as a ventricle, Laplace's law states that

$$P_v = T \times (1/r_1 + 1/r_2) \tag{3}$$

where r_1 and r_2 are the radii of curvature for the ventricular wall. Figure 14.5 shows this relationship for a simpler structure, in which curvature occurs in only one dimension (i.e., a cylinder). In this case, r_2 approaches infinity. Therefore:

$$P_v = T \times (1/r_1) \text{ or } T = P_v \times r_1 \tag{4}$$

The internal pressure expands the cylinder until it is exactly balanced by the wall tension. The larger the radius, the larger the tension needed to balance a particular pressure. For example, in a long balloon that has an inflated part with a large radius and an uninflated parted with a much smaller radius, the pressure inside the balloon is the same everywhere, yet the tension in the wall is much higher in the inflated part because the radius is much greater (Fig. 14.6). This general principle also applies to noncylindrical objects, such as the heart and tapering blood vessels.

When the ventricular chamber enlarges, the wall tension required to balance a given intraventricular pressure increases. As a result, the force resisting ventricular wall shortening (afterload) likewise increases with ventricular size. Despite the effect of increased radius on afterload, an increase in ventricular size (within physiological limits) raises both wall tension and stroke volume. This occurs because the positive effects of adjustment in sarcomere length overcompensate for the negative effects of increasing ventricular radius. However, if a ventricle becomes pathologically dilated, the myocardial fibers may be unable to generate enough tension to raise pressure to the normal systolic level, and the stroke volume may fall.

Effect of Diastolic Compliance.   Several diseases—including hypertension, myocardial ischemia, and cardiomyopathy—cause the left ventricle to be less compliant during diastole. In the presence of decreased diastolic compliance, a normal end-diastolic pressure stretches the ventricle less. Reduced stretch of the ventricle results in lowered stroke vol-
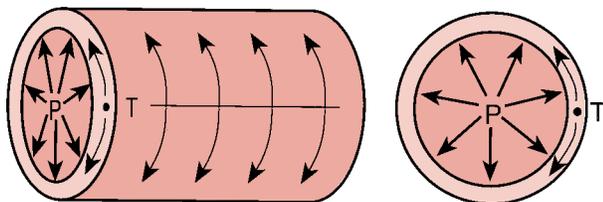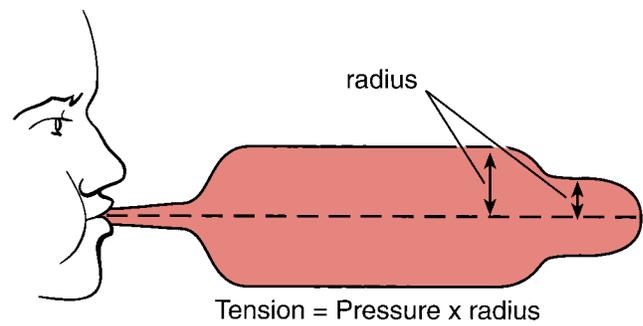

Effect of the radius of a cylinder on tension. The pressure inside an inflated balloon is the same everywhere. With the same inside pressure, the tension in the wall is proportional to the radius. The tension is lower in the portion of the balloon with the smaller radius.

ume. In this situation, compensatory events increase central blood volume and end-diastolic pressure (see Chapter 18). A higher end-diastolic pressure stretches the stiffer ventricle and helps restore the stroke volume to normal. The physiological price for this compensation is higher left atrial and pulmonary pressures. Several pathological consequences, including pulmonary congestion and edema, can result.

Pressure-Volume Loops Provide Information Regarding Ventricular Performance

Figure 14.7A shows a plot of left ventricular pressure as a function of left ventricular volume. One cardiac cycle is represented by one counterclockwise circuit of the loop. At point 1, the mitral valve opens and the volume of the ventricle begins to increase. As it does, diastolic ventricular pressure rises a little, depending on given ventricular diastolic compliance. (Remember that compliance is $\Delta V/\Delta P$.) The less the pressure rises with the filling of the ventricle, the greater the compliance. The volume increase between point 1 and point 2 occurs during rapid and reduced ventricular filling and atrial systole (see Fig. 14.1). At point 2, the ventricle begins to contract and pressure rises rapidly. Because the mitral valve closes at this point and the aortic valve has not yet opened, the volume of the ventricle cannot change (isovolumetric contraction). At point 3, the aortic valve opens. As blood is ejected from the ventricle, ventricular volume falls. At first, ventricular pressure continues to rise because the ventricle continues to contract and build up pressure—this is the period of rapid ejection in Figure 14.1. Later, pressure begins to fall—this is the period of reduced ejection in Figure 14.1. The reduction in ventricular volume between points 3 and 4 is the difference between end-diastolic volume (3) and end-systolic volume (4) and equals stroke volume.

At point 4, ventricular pressure drops enough below aortic pressure to cause the aortic valve to close. The ventricle continues to relax after closure of the aortic valve, and this is reflected by the drop in ventricular pressure. Because the mitral valve has not yet opened, ventricular volume cannot change (isovolumetric relaxation). The loop returns to point 1 when the mitral valve opens and, once more, the ventricle begins to fill.

Pressure and tension in a cylindrical blood vessel. The tension tends to open an imaginary slit along the length of the blood vessel. The Laplace law relates pressure (P), radius, and tension (T), as described in the text.
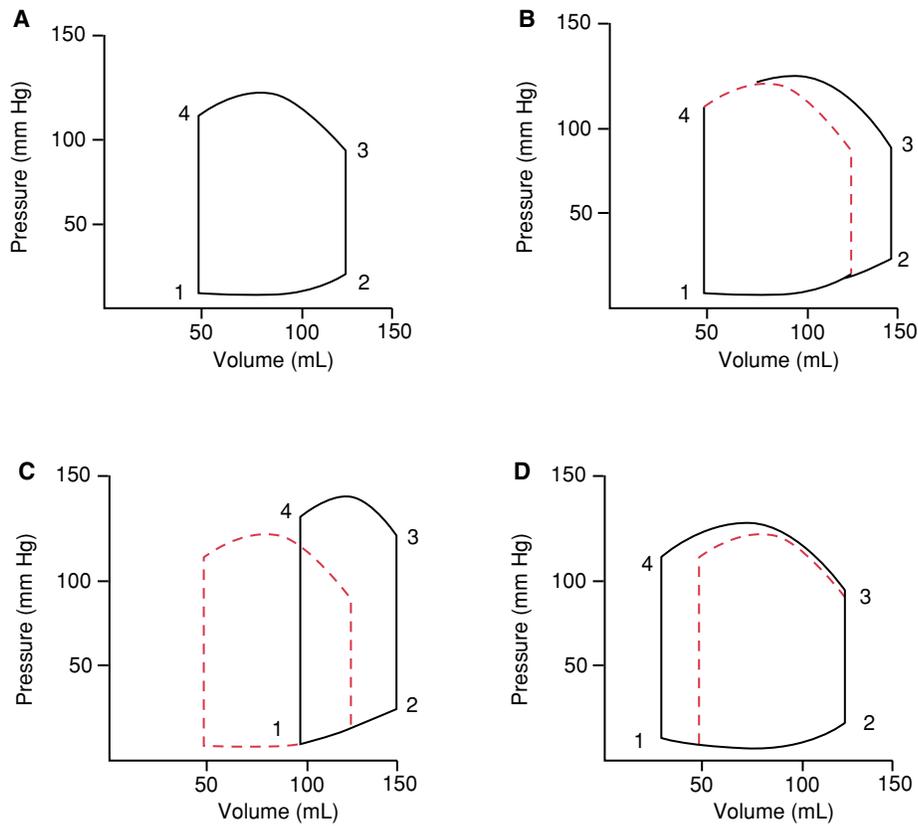
CHAPTER 14   The Cardiac Pump   **243**

FIGURE 14.7 **Pressure-volume loops for the left ventricle.** 1: Mitral valve opens. 2. Mitral valve closes. 3. Aortic valve opens. 4: Aortic valve closes. **A,** The loop with normal values for ventricular volumes and pressures. **B,** The addition of a loop with increased preload. **C,** The addition of a loop with increased afterload. **D,** The addition of a loop with increased contractility.

Increased Preload.   Figure 14.7B shows a pressure-volume loop from the same heart in the presence of increased preload. After opening of the mitral valve at point 1 in Figure 14.7B, diastolic pressure and volume increase to a higher value than in Figure14.7A. When isovolumetric contraction begins at point 2, end-diastolic volume is higher. Because afterload is unchanged, the aortic valve opens at the same pressure (point 3). In the idealized graph in Figure 14.7B, the greater force of contraction associated with higher preload causes the ventricle to eject all of the extra volume that entered during diastole. This means that, when the aortic valve closes at point 4, the volume and pressure of the ventricle are identical to the values in Figure 14.7A. The difference in volume between points 3 and 4 is larger, representing the larger stroke volume associated with increased preload.

Increased Afterload.   Figure 14.7C shows the effect of increased afterload on the pressure-volume loop. In this situation, the aortic valve opens (point 3) at a higher pressure because aortic pressure is increased, as compared with Figure 14.7A. The higher aortic pressure decreases stroke volume, and the aortic valve closes (point 4) at a higher pressure and volume. Mitral valve opening and ventricular filling (point 1) begin at a higher pressure and volume because more blood is left in the ventricle at the end of systole. Filling of the ventricle proceeds along the same diastolic pressure-volume curve from point 1 to point 2.

Because the ventricle did not empty as much during systole and the atrium delivers as much blood during diastole, end-diastolic volume and pressure (preload) are increased.

Increased Contractility.   Figure 14.7D shows the effect of increased contractility on the pressure-volume loop. In this idealized situation, there is no change in end-diastolic volume, and mitral valve closure occurs at the same pressure and volume (point 2). Afterload is also the same; therefore, the aortic valve opens at the same arterial pressure (point 3). The increased force of contraction causes the ventricle to eject more blood and the aortic valve closes at a lower end-systolic volume (point 4). This means that the mitral valve opens at a lower end-diastolic volume (point 1). Because diastolic compliance is unchanged, filling proceeds along the same pressure-volume curve from point 1 to point 2.

When there are changes in diastolic compliance, the pressure-volume curve between (1) and (2) is changed. This and other changes, such as heart failure, are beyond the scope of this text.

Heart Rate Interacts With Stroke Volume to Influence Cardiac Output

Heart rate can vary from less than 50 beats/min in a resting, physically fit individual to greater than 200 beats/min during maximal exercise. If stroke volume is held constant, in-

creases in heart rate cause proportional increases in cardiac output. However, heart rate affects stroke volume; changes in heart rate do not necessarily cause proportional changes in cardiac output. In considering the influence of heart rate on cardiac output, it is important to recognize that as the heart rate increases and the duration of the cardiac cycle decreases, the duration of diastole decreases. As the duration of diastole decreases, the time for filling of the ventricles is diminished. Less filling of the ventricles leads to a reduced end-diastolic volume and decreased stroke volume.

Effect of Decreased Heart Rate on Cardiac Output.   A consequence of the reciprocal relationship between heart rate and the duration of diastole is that, within limits, decreasing the rate of a normal resting heart does not decrease cardiac output. The lack of a decrease in cardiac output is because stroke volume increases as heart rate decreases. Stroke volume increases because as the heart rate falls, the duration of ventricular diastole increases, and the longer duration of diastole results in greater ventricular filling. The resulting elevated end-diastolic fiber length increases stroke volume, which compensates for the decreased heart rate. This balance works until the heart rate is below 20 beats/min. At this point, additional increases in end-diastolic fiber length cannot augment stroke volume further because the maximum of the ventricular function curve has been reached. At heart rates below 20 beats/min, cardiac output falls in proportion to decreases in heart rate.

Effect of Increased Heart Rate as a Result of Electronic Pacing.   If an electronic pacemaker is attached to the right atrium and the heart rate is increased by electrical stimulation, surprisingly little increase in cardiac output results. This is because as the heart rate increases, the interval between beats shortens and the duration of diastole decreases. The decrease in diastole leaves less time for ventricular filling, producing a shortened end-diastolic fiber length, which subsequently reduces both the force of contraction and the stroke volume. The increased heart rate is, therefore, offset by the decrease in stroke volume. When the rate increases above 180 beats/min secondary to an abnormal pacemaker, stroke volume begins to fall as a result of poor diastolic filling. A person with abnormal tachycardia (e.g., caused by an ectopic ventricular pacemaker) may have a reduction in cardiac output despite an increased heart rate.

Events in the myocardium compensate to some degree for the decreased time available for filling. First, increases in heart rate reduce the duration of the action potential and, thus, the duration of systole, so the time available for diastolic filling decreases less than it would otherwise. Second, faster heart rates are accompanied by an increase in the force of contraction, which tends to maintain stroke volume. The increased contractility is sometimes called **treppe** or the **staircase phenomenon**. These internal adjustments are not very effective and, by themselves, would be insufficient to permit increases in heart rate to raise cardiac output.

Effects of Increased Heart Rate as a Result of Changes in Autonomic Nerve Activity.   Increased heart rate usually occurs because of decreased parasympathetic and increased sympathetic neural activity. The release of norep-

inephrine by sympathetic nerves not only increases the heart rate (see Chapter 13) but also dramatically increases the force of contraction (see Fig. 14.3). Furthermore, norepinephrine increases conduction velocity in the heart, resulting in a more efficient and rapid ejection of blood from the ventricles. These effects, summarized in Figure 14.8, maintain the stroke volume as the heart rate increases. When the heart rate increases physiologically as a result of an increase in sympathetic nervous system activity (as during exercise), cardiac output increases proportionately over a broad range.

Influences on Stroke Volume and Heart Rate Regulate Cardiac Output

In summary, cardiac output is regulated by changing stroke volume and heart rate. Stroke volume is influenced by the contractile force of the ventricular myocardium and by the force opposing ejection (the aortic pressure or afterload). Myocardial contractile force depends on ventricular end-diastolic fiber length (Starling's law) and myocardial contractility. Contractility is influenced by four major factors:

1) Norepinephrine released from cardiac sympathetic nerves and, to a much lesser extent, circulating norepinephrine and epinephrine released from the adrenal medulla

2) Certain hormones and drugs, including glucagon, isoproterenol, and digitalis (which increase contractility) and anesthetics (which decrease contractility)
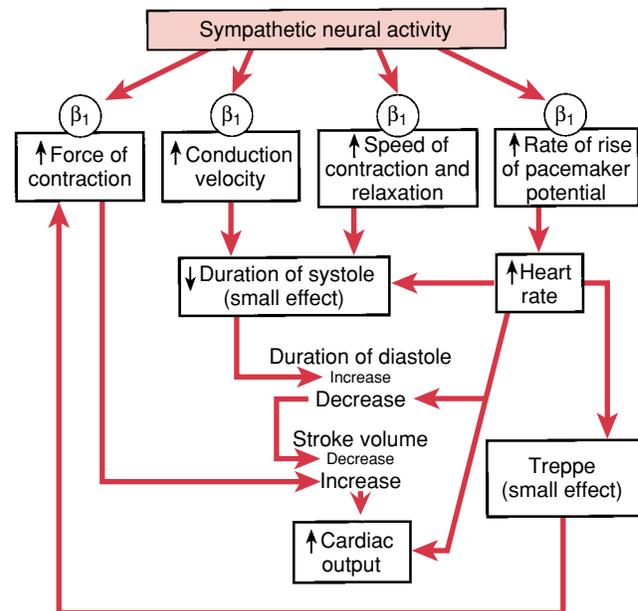

FIGURE 14.8 **Effects of increased sympathetic neural activity on heart rate, stroke volume, and cardiac output.** Various effects of norepinephrine on the heart compensate for the decreased duration of diastole and hold stroke volume relatively constant, so that cardiac output increases with increasing heart rate. The words "Increase" and "Decrease" in small type denote quantitatively less important effects than the same words in large type.

3) Disease states, such as coronary artery disease, myocarditis (see Chapter 10), bacterial toxemia, and alterations in plasma electrolytes and acid-base balance

4) Intrinsic changes in contractility with changes in heart rate and/or afterload

Heart rate is influenced primarily by sympathetic and parasympathetic nerves to the heart and, by a lesser extent, by circulating norepinephrine and epinephrine. The effect of heart rate on cardiac output depends on the extent of concomitant changes ventricular filling and contractility.

Heart failure is a major problem in clinical medicine (see Clinical Focus Box 14.1).

THE MEASUREMENT OF CARDIAC OUTPUT

The ability to measure output accurately is essential for performing physiological studies involving the heart and managing clinical problems in patients with heart disease or heart failure. Cardiac output is measured either by one of several applications of the Fick principle or by observing changes in the volume of the heart during the cardiac cycle.

Cardiac Output Can Be Measured Using Variations of the Principle of Mass Balance

The use of mass balance to measure cardiac output is best understood by considering the measurement of an unknown volume of liquid in a beaker (Fig. 14.9). The volume can be determined by dispersing a known quantity of dye throughout the liquid and then measuring the concentration of dye in a sample of liquid. Because mass is conserved, the quantity of dye (A) in the liquid is equal to the concentration of dye in the liquid (C) times the volume of liquid (V):
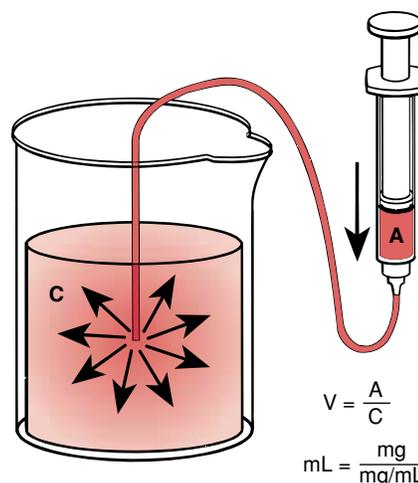

$$V = \frac{A}{C}$$

$$mL = \frac{mg}{mg/mL}$$

FIGURE 14.9 **The measurement of volume using the indicator dilution method.** The indicator is a dye. The volume (V) of liquid in the beaker equals the amount (A) of dye divided by the concentration (C) of the dye after it has dispersed uniformly in the liquid.

$$A = C \times V \qquad (5)$$

Because A is known and C can be measured, V can be calculated:

$$V = A/C \qquad (6)$$

When the principle of mass balance is applied to cardiac output, the goal is to measure the volume of blood flowing through the heart per unit of time. A known amount of dye or other indicator is injected and concentration of the dye or indicator is measured over time.

CLINICAL FOCUS BOX 14.1

Congestive Heart Failure

Heart failure occurs when the heart is unable to pump blood at a rate sufficient to meet the body's metabolic needs. One possible consequence of heart failure is that blood may "back up" on the atrial/venous side of the failing ventricle, leading to the engorgement and distention of veins (and the organs they drain) as the venous pressure rises. The signs and symptoms typically associated with this occurrence constitute **congestive heart failure** (CHF). This syndrome can be limited to the left ventricle (producing pulmonary venous distention, pulmonary edema, and symptoms such as dyspnea or cough) or the right ventricle (producing symptoms such as pedal edema, abdominal edema or ascites, and hepatic venous congestion), or it may affect both ventricles. Left heart failure (which increases pulmonary venous pressure) can eventually cause pulmonary artery pressure to rise and right heart failure to occur. Indeed, left heart failure is the most common reason for right heart failure.

The causes of CHF are numerous and include acquired and congenital conditions, such as valvular disease, myocardial infarction, assorted infiltrative processes (e.g., amy-

loid or hemochromatosis), inflammatory conditions (e.g., myocarditis), and various types of **cardiomyopathies** (a diverse assortment of conditions in which the heart becomes pathologically dilated, hypertrophied, or stiff).

The treatment of heart failure hinges on treating the underlying problem, when possible, and the judicious use of medical therapy. Medical treatment may include **diuretics** to reduce the venous fluid overload, **cardiac glycosides** (e.g., digitalis) to improve myocardial contractility, and **afterload reducing agents** (e.g., arterial vasodilators) to reduce the load against which the ventricle must contract. **Angiotensin converting enzyme inhibitors, aldosterone antagonists**, and **beta blockers** have all been shown to be effective in the treatment of CHF.

Heart transplantation is becoming an increasingly viable option for severe, intractable, unresponsive CHF. Although tens of thousands of patients worldwide have received new hearts for end-stage heart failure, the supply of donor hearts falls far below demand. For this reason, cardiac-assist devices, artificial hearts, and genetically modified animal hearts are undergoing intensive development and evaluation.

The Indicator Dilution Method.   In the **indicator dilution method**, a known amount of indicator (A) is injected into the circulation, and the blood downstream is serially sampled after the indicator has had a chance to mix (Fig. 14.10). The indicator is usually injected on the venous side of the circulation (often into the right ventricle or pulmonary artery but, occasionally, directly into the left ventricle), and sampling is performed from a distal artery. The resulting concentration of indicator in the distal arterial blood (C) changes with time. First, the concentration rises as the portion of the indicator carried by the fastest-moving blood reaches the arterial sampling point. Concentration rises to a peak as the majority of indicator arrives and falls off as the indicator carried by the slower moving blood arrives. Before the last of the indicator arrives, the indicator carried by the blood flowing through the shortest pathways comes around again (recirculation). To correct for this recirculation, the downslope of the curve is assumed to be semilogarithmic and the arterial value is extrapolated to zero indicator concentration. The average concentration of indicator can be determined by measuring the indicator concentration continuously from its first appearance (t_1) until its disappearance (t_2). The average concentration during that period ($\overline{C}$) is determined and cardiac output is calculated as:

$$CO = \frac{A}{\overline{C}}(t_2 - t_1) \qquad (7)$$

Note the similarity between this equation and the one for calculating volume in a beaker. On the left is volume per minute (rather than volume, as in equation 6). In the numerator on the right is amount of indicator and in the denominator is the mean concentration over time (rather than concentration, as in equation 6). Concentration, volume, and amount appear in both equations 6 and 7, but time is present in the denominator on both sides in equation 7.

The Thermodilution Method.   In most clinical situations, cardiac output is measured using a variation of the indicator dilution method called **thermodilution.** A Swan-Ganz catheter (a soft, flow-directed catheter with a balloon at the tip) is placed into a large vein and threaded through the right atrium and ventricle so that its tip lies in the pulmonary artery. The catheter is designed to allow a known amount of ice-cold saline solution to be injected into the right side of the heart via a side port in the catheter. This solution decreases the temperature of the surrounding blood. The magnitude of the decrease in temperature depends on the volume of blood that mixes with the solution, which depends on cardiac output. A thermistor on the catheter tip (located downstream in the pulmonary artery) measures the fall in blood temperature. The cardiac output can be determined using calculations similar to those described for the indicator dilution method.

The Fick Procedure.   Another way the principle of mass balance is used to calculate cardiac output takes advantage of the continuous entry of oxygen into the blood via the
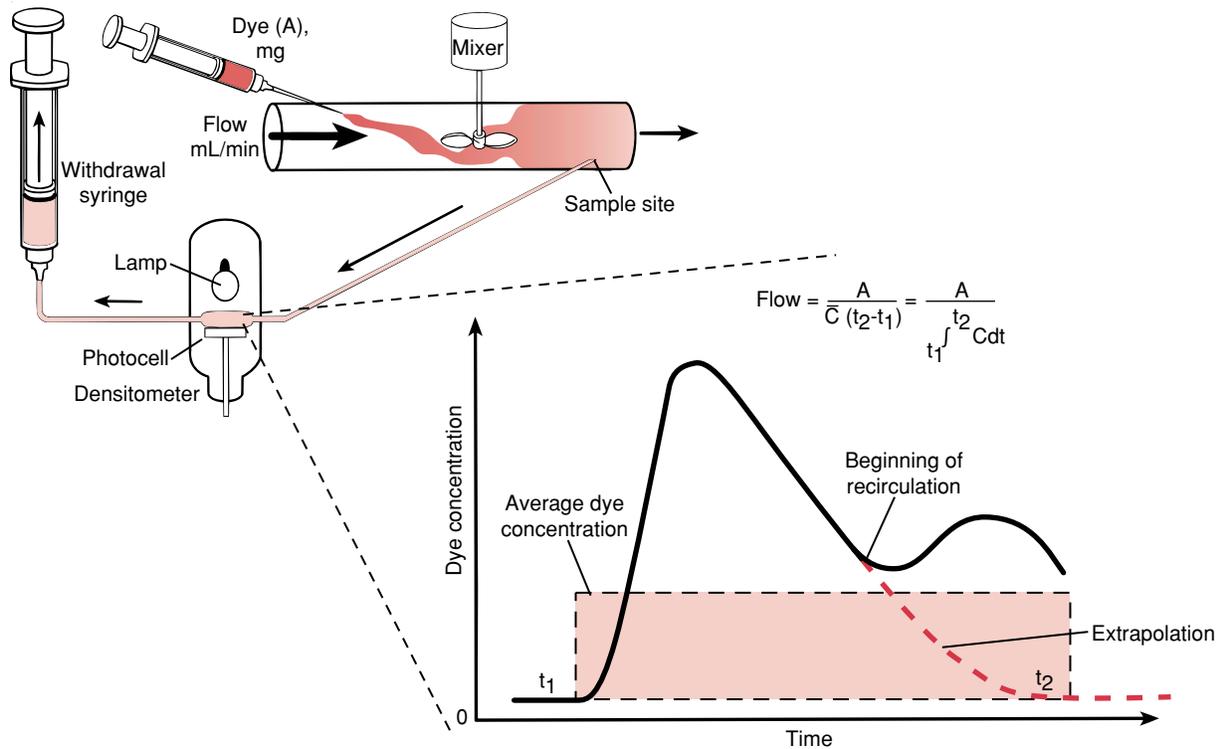

$$Flow = \frac{A}{\overline{C}(t_2 - t_1)} = \frac{A}{\int_{t_1}^{t_2} C\,dt}$$

FIGURE 14.10 **The indicator dilution method for determining flow through a tube.** The volume per minute flowing in the tube equals the quantity of indicator (in this example, a dye) injected divided by the average dye concentration ($\overline{C}$) at the sample site, multiplied by the time between the appearance (t_1) and disappearance (t_2) of the dye. Note the analogy between this time-dependent measurement (volume/time) and the simple volume measurement in Figure 14.9. The downslope of the dye concentration curve shows the effects of recirculation of the dye (solid line) and the semilogarithmic extrapolation of the downslope (dashed line) used to correct for recirculation.

lungs (Fig. 14.11). In a steady state, the oxygen leaving the lungs (per unit time) via the pulmonary veins must equal the oxygen entering the lungs via the (mixed) venous blood and respiration (in a steady state, the amount of oxygen entering the blood through respiration is equal to the amount consumed by body metabolism):

O_2 in blood leaving the lungs =
O_2 in blood and air entering the lungs   (8)

or

O_2 output via pulmonary veins = O_2 input via pulmonary artery + O_2 added by respiration   (9)

The O_2 output via the pulmonary veins is equal to the pulmonary vein O_2 content multiplied by the cardiac output (CO). Because O_2 is neither added nor subtracted from the blood as it passes from the pulmonary veins through the left heart to the systemic arteries, the O_2 output via pulmonary veins is also equal to the arterial O_2 content (aO_2) multiplied by the cardiac output (CO). Similarly, O_2 input via the pulmonary artery is equal to mixed venous blood oxygen input to the right heart and is mixed venous blood O_2 content ($\overline{v}O_2$) multiplied by the cardiac output (CO). As indicated above, in the steady state, O_2 added by respiration is equal to oxygen consumption ($\dot{V}O_2$). By substitution in equation 9,

$$(CO)\,(aO_2) = [(CO)\,(\overline{v}O_2)] + \dot{V}O_2 \qquad (10)$$

which rearranges to

$$CO = \dot{V}O_2/(aO_2 - \overline{v}O_2) \qquad (11)$$

Systemic arterial blood oxygen content, pulmonary arterial (mixed venous) blood oxygen content, and oxygen consumption can all be measured and, therefore, cardiac output can be calculated. The theory behind this method is sounder than the theory behind the indicator dilution method because it avoids the need for extrapolation. However, because the cardiac catheterization required to measure pulmonary artery oxygen content is avoided, the indicator dilution method is more popular. The two methods agree well in a wide variety of circumstances.

Imaging Techniques Are Also Used for Measuring Cardiac Output

A variety of other techniques, many of which employ imaging modalities, can be used to measure or estimate cardiac output. All of them use time dependent images of the heart to estimate the difference between end-diastolic and end-systolic volumes. This difference gives stroke volume and, with heart rate, allows calculation of cardiac output.

Radionuclide Techniques. In **radionuclide techniques**, a radioactive substance (usually technetium-99) can be made to circulate throughout the vascular system by attaching (tagging) it to red blood cells or albumin. The radiation (gamma rays) emitted by the large pool(s) of blood in the cardiac chambers is measured using a specially designed **gamma camera**. The emitted radiation is proportional to the amount of technetium bound to the blood (easily determined by sampling the tagged blood) and the volume of blood in the heart. Using computerized analysis, the amount of radiation emitted by the left (or right) ventricle during various portions of the cardiac cycle can be determined (Fig. 14.12A and B). The amount
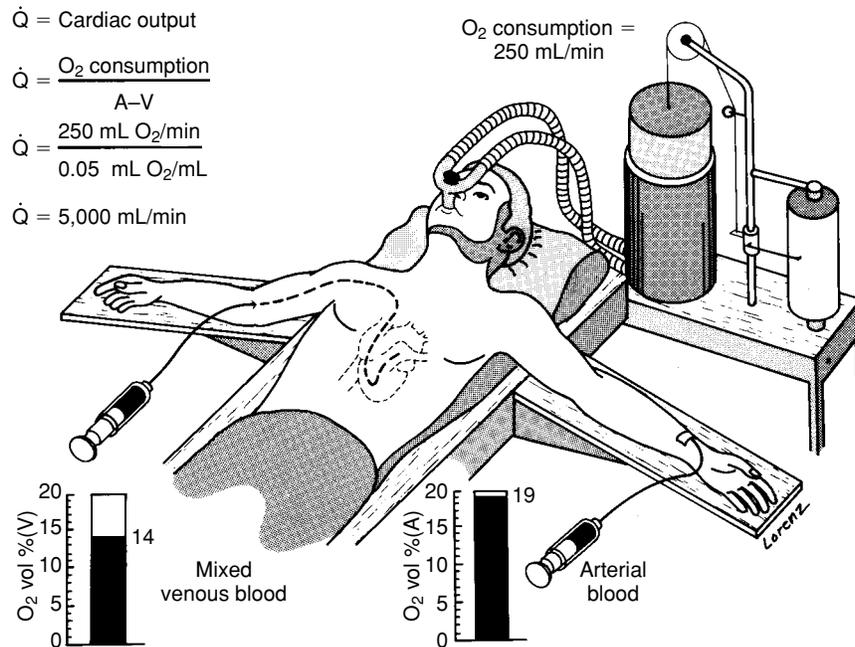

$\dot{Q}$ = Cardiac output

$\dot{Q} = \dfrac{O_2\text{ consumption}}{A\text{–}V}$

$\dot{Q} = \dfrac{250\text{ mL }O_2/\text{min}}{0.05\ \text{ mL }O_2/\text{mL}}$

$\dot{Q}$ = 5,000 mL/min

O_2 consumption = 250 mL/min

O_2 vol %(V) — 14 — Mixed venous blood

O_2 vol %(A) — 19 — Arterial blood

FIGURE 14.11 **Calculating cardiac output using the oxygen uptake/consumption method.** Oxygen is the "indicator" that is "added" to the mixed venous blood. For oxygen, 1 vol % = 1 mL oxygen/100 mL blood.
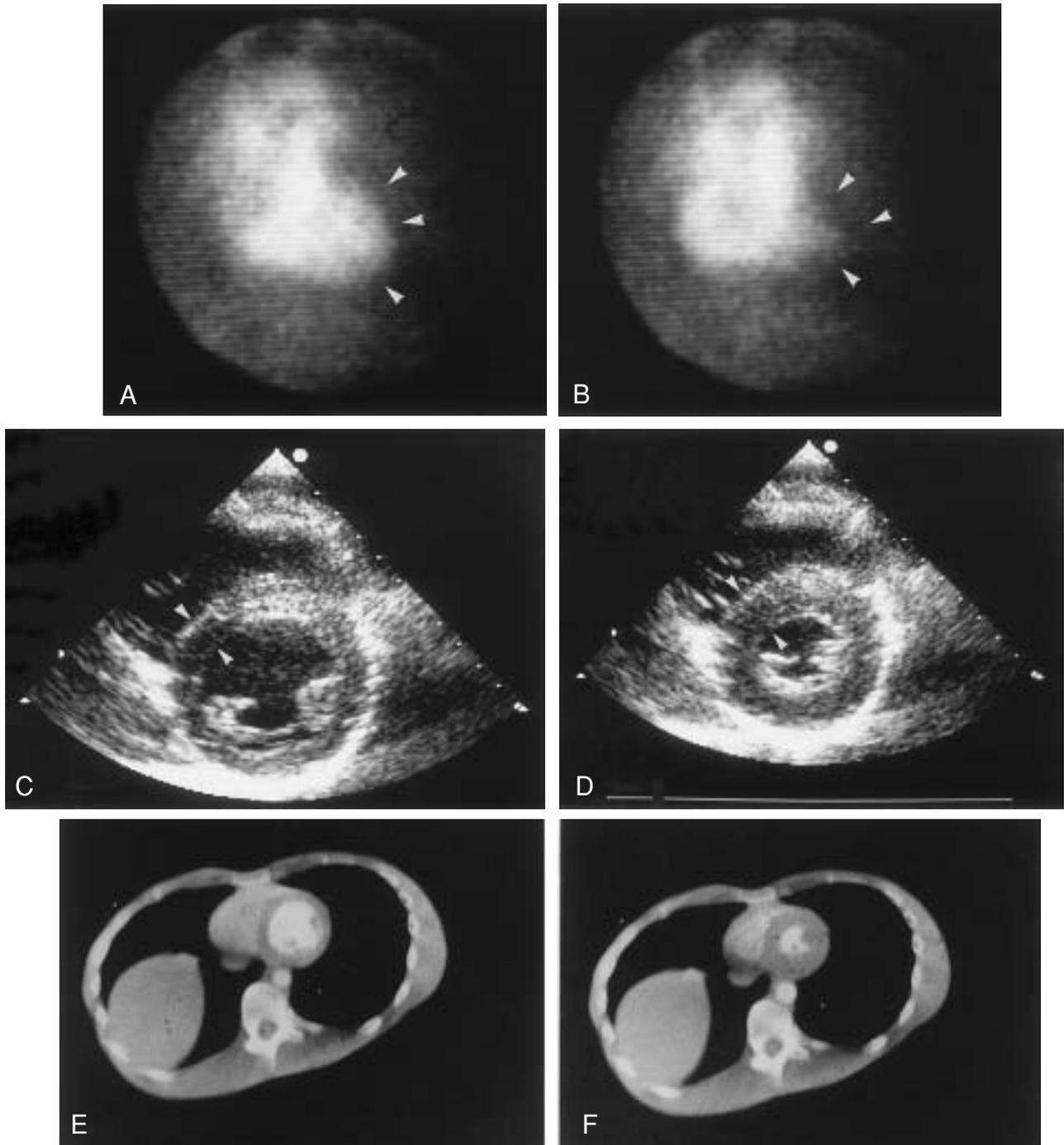
FIGURE 14.12 **Imaging techniques for measuring cardiac output.** A and B, Radionuclide angiograms. The white arrows in A show the boot-shaped left ventricle during cardiac diastole when it is maximally filled with radionuclide-labeled blood. In B, much of the apex appears to be missing (white arrows) because cardiac systole has caused the blood to be ejected as the intraventricular volume decreases. C and D, Two-dimensional echocardiograms. In this cross-sectional view, the left ventricle appears as a ring. White arrows indicate wall thickness. In diastole (C), the ventricle is large and the wall is thinned; during systole (D), the wall thickens and the ventricular size decreases. E and F, Ultrafast (cine) computed tomography. The ventricular size and wall thickness can be assessed during diastole and systole, and the change in ventricular size can be used to calculate cardiac output.

of blood ejected with each heartbeat (stroke volume) is determined by comparing the amount of radiation measured at the end of systole with that at the end of diastole; multiplying this number by the heart rate yields cardiac output.

Echocardiography.   **Echocardiography** (ultrasound cardiography) provides two-dimensional, real-time images of the heart. In addition, the velocity of blood flow can be determined by measuring the Doppler shift (change in sound frequency) that occurs when the ultrasound wave is re-

flected off moving blood. Echocardiography can, therefore, be used to measure changes in ventricular chamber size (Fig. 14.12C and D), aortic diameter, and aortic blood flow velocity occurring throughout the cardiac cycle. With this information, cardiac output may be estimated in one of two ways. First, the change in ventricular volume occurring with each beat (stroke volume) can be determined and multiplied by the heart rate. Second, the average aortic blood flow velocity can be measured (just above or below the aortic valve) and multiplied by the measured aortic cross-sectional area to give aortic blood flow (which is nearly identical to cardiac output).

Computed Tomography.   **Ultrafast (cine) computed tomography** and **magnetic resonance imaging** (MRI) provide cross-sectional views of the heart during different phases of the cardiac cycle (Fig. 14.12E and F). Stroke volume (and cardiac output) can be calculated using the same principles described for radionuclide techniques or echocardiography. When ventricular volume changes are estimated from cross-sectional data, assumptions are made about ventricular geometry. Although these assumptions can lead to errors in calculating cardiac output, these methods have proven to be highly useful.

THE ENERGETICS OF CARDIAC FUNCTION

The heart converts chemical energy in the form of ATP into mechanical work and heat. The relationship between the supply of oxygen and nutrients needed to synthesize ATP and the output of mechanical work by the heart is at the center of many clinical problems.

Cardiac Energy Production Depends Primarily on Oxidative Phosphorylation

The sources of energy for cardiac muscle function were described in Chapter 10. Although the major source of energy for the formation of ATP is oxidative phosphorylation, glycolysis can briefly compensate for a transient lack of aerobic production of ATP when a portion of the heart receives too little oxygen, as during brief coronary artery occlusion.

Oxidative phosphorylation in the heart can use either carbohydrates or fatty acids as metabolic substrates. The formation of ATP depends on a steady supply of oxygen via coronary blood flow. Oxygen delivery by coronary blood flow is, therefore, the most important determinant of an adequate supply of ATP for the mechanical, electrical, and metabolic energy needs of cardiac cells. Furthermore, cardiac oxygen consumption is an accurate measure of the use of energy by the heart. (Coronary blood flow is discussed in Chapter 17.)

As in skeletal muscle, ATP in cardiac muscle is in near equilibrium with phosphocreatine. The presence of phosphocreatine adds to the storage capacity of high-energy phosphate and speeds its transport from mitochondria to actomyosin crossbridges.

Cardiac Energy Consumption Is Required to Support External and Internal Cardiac Work

Cardiac energy consumption (which is equivalent to cardiac oxygen consumption) provides the energy for both **external work** and **internal work**.

Most of the external work of the heart involves the ejection of blood from the ventricles into the aorta and pulmonary artery. The work of ejecting blood from the ventricles is the stroke work. Stroke work, strictly speaking, is equal to the product of the volume of blood ejected (stroke volume, SV) and the pressure against which the blood is ejected (aortic and pulmonary artery pressure during systole). Because the systolic pressure in the pulmonary artery is about one sixth of the pressure in the aorta, more than 80% of external work is done by the left ventricle. Left ventricular stroke work (SW) is usually calculated as:

$$SW = SV \times P_a \qquad (12)$$

Mean arterial pressure (P_a) is used instead of mean arterial pressure during systole because it is more readily available and is a reasonable index of mean systolic pressure.

A small additional component of external work (usually <10%) is kinetic work. Kinetic energy is the energy imparted to blood in the form of flow velocity as it is ejected with each heartbeat. We do not elaborate on this component of external work because it is of little importance in most situations.

Cardiac contractions involve many events that do not result in external work. These include internal mechanical events such as developing force by stretching series elasticity (see Chapter 10), overcoming internal viscosity, and rearranging the muscular architecture of the heart as it contracts. These activities, known as internal work, use far more energy (perhaps 5 times as much) than external work.

Cardiac Efficiency.   The efficiency of the heart in performing external work can be estimated by dividing the external work of the heart by the energy equivalent of the oxygen consumed by the heart. Only 5 to 20% of the energy liberated by cardiac oxygen consumption is used for external work under most conditions. Therefore, changes in external work do not reveal much about changes in energy consumption in the heart. This is because internal work, the major determinant of oxygen consumption and, thereby, cardiac efficiency, varies independently of external work. As we shall see, large increases in internal work can occur in the absence of changes in external work. When this happens, oxygen consumption increases and efficiency decreases. The difference between pressure work and volume work illustrates this point.

"Pressure Work" Versus "Volume Work".   Most of the cardiac energy devoted to internal work is used to maintain the force of contraction (and, thus, ventricular pressure) rather than to eject the blood. The importance of this is seen by comparing two tasks: lifting a 20-pound weight from the floor to a table and lifting the weight to the table height and continuing to hold it. The second task is clearly more difficult, even though the external work done (i.e., the force multiplied by the distance the object was moved)

in each case is the same. The ventricles not only develop the pressure required to move the blood, but must maintain the pressure during systole. This takes far more energy than the external work alone as calculated from arterial pressure and stroke volume. In fact, if the external work of the heart is raised by increasing stroke volume but not mean arterial pressure, the oxygen consumption of the heart increases very little. Alternatively, if arterial pressure is increased, the oxygen consumption per beat goes up much more. In other words, pressure work by the heart is far more expensive in terms of oxygen consumption than volume work. This makes sense because internal work consumes far more energy than external work.

Afterload.   The discussion of pressure work versus volume work emphasizes the importance of afterload as a determinant of energy use and oxygen consumption by the heart. Because of Laplace's law, an increase in ventricular radius is equivalent to an increase in arterial pressure. Thus, an increase in ventricular radius, as can occur with heart failure, also causes a proportional increase in internal work and energy use, independent of any change in external work.

Heart Rate.   Thus far, we have considered only the energetic events associated with a single cardiac contraction. The energy consumed per unit time is equal to the energy consumed in a single heartbeat multiplied by the heart rate. It follows that the production of energy from oxidative phosphorylation per unit time must be sufficient to match the energy consumed in a single heartbeat multiplied by the heart rate.

There is another important consideration related to heart rate. Much of the internal work of the heart occurs during isovolumetric contraction, when force is being developed but no external work is being done. If cardiac output is increased by increasing heart rate, the energy expended in the internal work of isovolumetric contraction increases proportionately. By contrast, if cardiac output is increased by increasing stroke volume, there is a much smaller increase in internal work. This means that increasing cardiac output by increasing heart rate is more energetically costly than the same increase by means of stroke volume.

Contractility.   Altered myocardial contractility has significant energetic consequences because of differential effects on external and internal work. Inotropic agents (e.g., norepinephrine) may increase pressure work by raising arterial pressure and, thereby, increase internal work. However, inotropic agents can also cause the heart to do the same stroke work at a smaller end-diastolic volume, reducing both afterload and internal work. During exercise, increased contractility causes end-diastolic volume to decrease despite the increase in venous return. This lowers the contribution of ventricular radius to afterload and avoids the inefficiency of an increase in end-diastolic volume.

The Double Product Is Used Clinically to Estimate the Energy Requirements of Cardiac Work

A useful index of the cardiac oxygen consumption is the product of aortic pressure and heart rate—the **double product**. This index includes one of the determinants of external work (pressure) and the determinant of energy use as a function of time, heart rate. The double product does not include the effect of changes in stroke volume on energy consumption, but these are less significant than changes in pressure. In addition, the double product does not take into account effect of changes in radius of the ventricle on energy consumption. The extra energy required by pathologically dilated hearts is not reflected in the double product.

REVIEW QUESTIONS

DIRECTIONS: Each of the numbered items or incomplete statements in this section is followed by answers or by completions of the statement. Select the ONE lettered answer or completion that is BEST in each case.

1. The figure below shows pressure-volume loops for two situations. When compared with loop A, loop B demonstrates
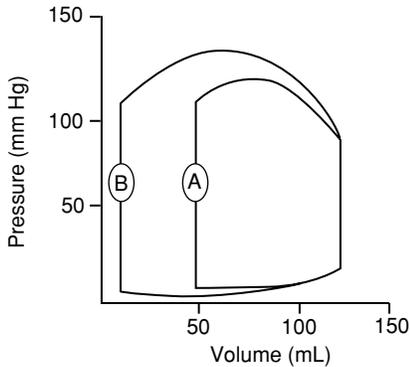
(A) Increased preload
(B) Decreased preload
(C) Increased contractility
(D) Increased afterload
(E) Decreased afterload

2. During the cardiac cycle,
(A) The aortic and mitral valves are never open at the same time
(B) The first heart sound is caused by the rapid ejection of blood from the ventricles
(C) The mitral valve is open throughout diastole
(D) Left ventricular pressure is always less than aortic pressure
(E) Ventricular filling occurs primarily during systole

3. During the cardiac cycle,
(A) The second heart sound is associated with opening of the aortic valve
(B) Left atrial pressure is always less than left ventricular pressure
(C) Aortic pressure reaches its lowest value during ventricular systole
(D) The ventricles eject blood during all of systole
(E) Ventricular end-systolic volume is greater than end-diastolic volume

4. Point Y in the figure below is the control point. Which point corresponds to a combination of increased contractility and increased ventricular filling?
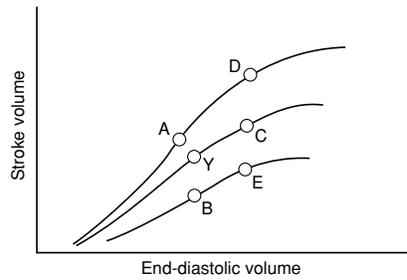
(A) Point A
(B) Point B
(C) Point C
(D) Point D
(E) Point E

5. Drug A causes a 33% increase in stroke volume and no change in systolic aortic blood pressure. Starting with the same baseline, drug B causes a 33% increase in systolic and mean aortic blood pressure and no change in stroke volume. Neither drug changes heart rate.
(A) Drug A increases the external work of the left ventricle more than drug B
(B) Drug B increases the internal work of the left ventricle more than drug A
(C) Drug A increases the oxygen consumption of the heart more than drug B
(D) The "double product" is greater for drug A than for drug B
(E) Cardiac efficiency is higher with drug B than with drug A

6. Using the data below, which is correct?
Volume in ventricle at end of diastole: 130 mL
Volume in ventricle at end of systole: 60 mL
Heart rate: 70 beats/min
Mean arterial blood pressure: 90 mm Hg
(A) Cardiac output is 9,100 mL/min
(B) Cardiac output is 4,200 mL/min
(C) Stroke work is 11,700 mL × mm Hg
(D) Stroke work is 6,300 mL × mm Hg
(E) Stroke work is 4,900 mL/min

7. The data below are from an athletic 70-kg man during heavy exercise. Which statement is correct?
Oxygen consumption: 4 L/min
Arterial oxygen content: 19 mL/100 mL blood
Mixed venous oxygen content: 3 mL/100 mL blood
Heart rate: 180 beats/min
(A) Cardiac output is 12 L/min
(B) Cardiac output is 25 L/min
(C) Stroke volume is 67 mL
(D) Stroke volume is 100 mL
(E) Stroke volume cannot be calculated without data on end-diastolic and end-systolic volume

8. Which of the following would cause a decrease in stroke volume, compared with the normal resting value?
(A) Reduction in afterload
(B) An increase in end-diastolic pressure
(C) Stimulation of the vagus nerves
(D) Electrical pacing to a heart rate of 200 beats/min
(E) Stimulation of sympathetic nerves to the heart

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