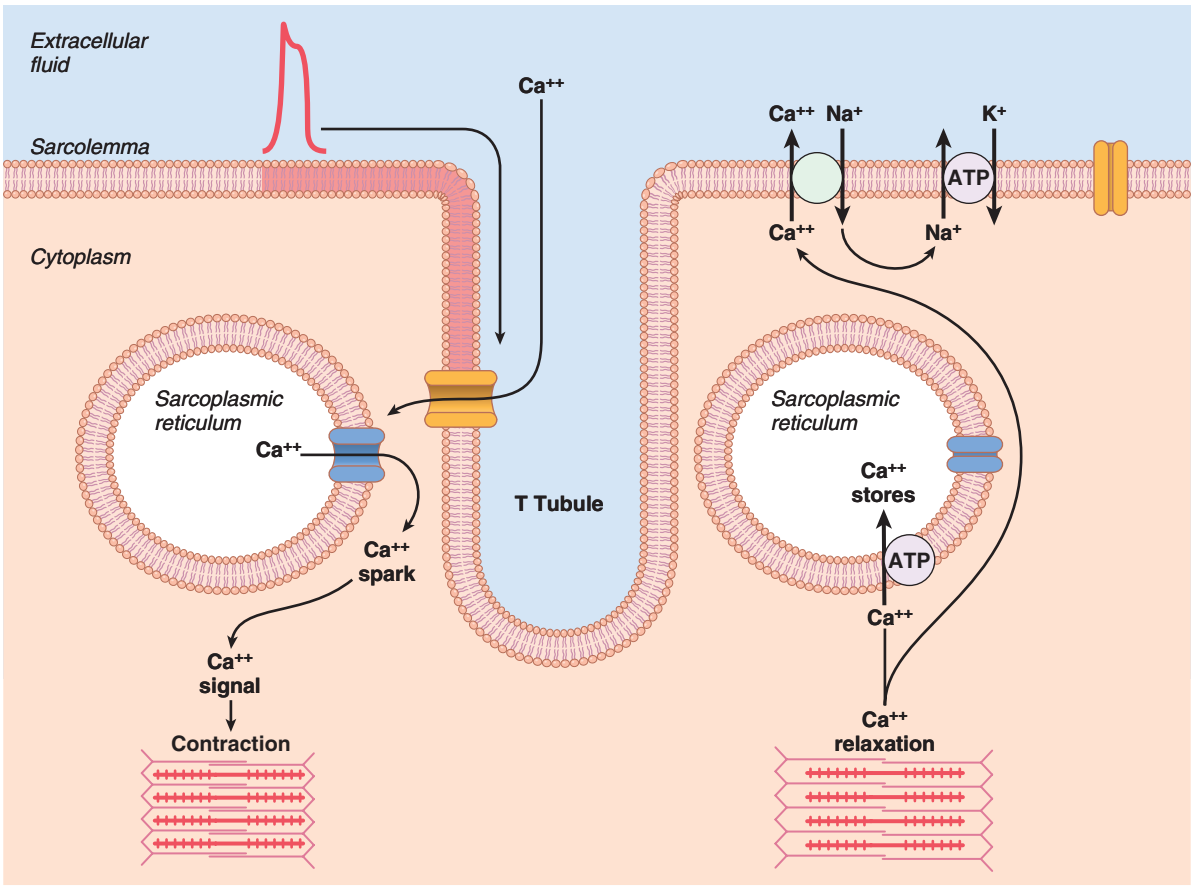

Figure 9-6. Mechanisms of excitation-contraction coupling and relaxation in cardiac muscle. ATP, adenosine triphosphate.

CARDIAC CYCLE

The cardiac events that occur from the beginning of one heartbeat to the beginning of the next are called the *cardiac cycle.* Each cycle is initiated by spontaneous generation of an action potential in the *sinus node,* as explained in Chapter 10. This node is located in the superior lateral wall of the right atrium near the opening of the superior vena cava, and the action potential travels from here rapidly through both atria and then through the A-V bundle into the ventricles. Because of this special arrangement of the conducting system from the atria into the ventricles, there is a delay of more than 0.1 second during passage of the cardiac impulse from the atria into the ventricles. This delay allows the atria to contract ahead of ventricular contraction, thereby pumping blood into the ventricles before the strong ventricular contraction begins. Thus, the atria act as *primer pumps* for the ventricles, and the ventricles in turn provide the major source of power for moving blood through the body's vascular system.

Diastole and Systole

The cardiac cycle consists of a period of relaxation called *diastole,* during which the heart fills with blood, followed by a period of contraction called *systole.*

The total *duration of the cardiac cycle,* including systole and diastole, is the reciprocal of the heart rate. For example, if heart rate is 72 beats/min, the duration of the cardiac cycle is 1/72 min/beat—about 0.0139 minutes per beat, or 0.833 second per beat.

Figure 9-7 shows the different events during the cardiac cycle for the left side of the heart. The top three curves show the pressure changes in the aorta, left ventricle, and left atrium, respectively. The fourth curve depicts the changes in left ventricular volume, the fifth depicts the electrocardiogram, and the sixth depicts a phonocardiogram, which is a recording of the sounds produced by the heart—mainly by the heart valves—as it pumps. It is especially important that the reader study in detail this figure and understand the causes of all the events shown.

Increasing Heart Rate Decreases Duration of Cardiac Cycle. When heart rate increases, the duration of each cardiac cycle decreases, including the contraction and relaxation phases. The duration of the action potential and the period of contraction (systole) also decrease, but not by as great a percentage as does the relaxation phase (diastole). At a normal heart rate of 72 beats/min, systole comprises about 0.4 of the entire cardiac cycle. At three times the normal heart rate, systole is about 0.65 of the

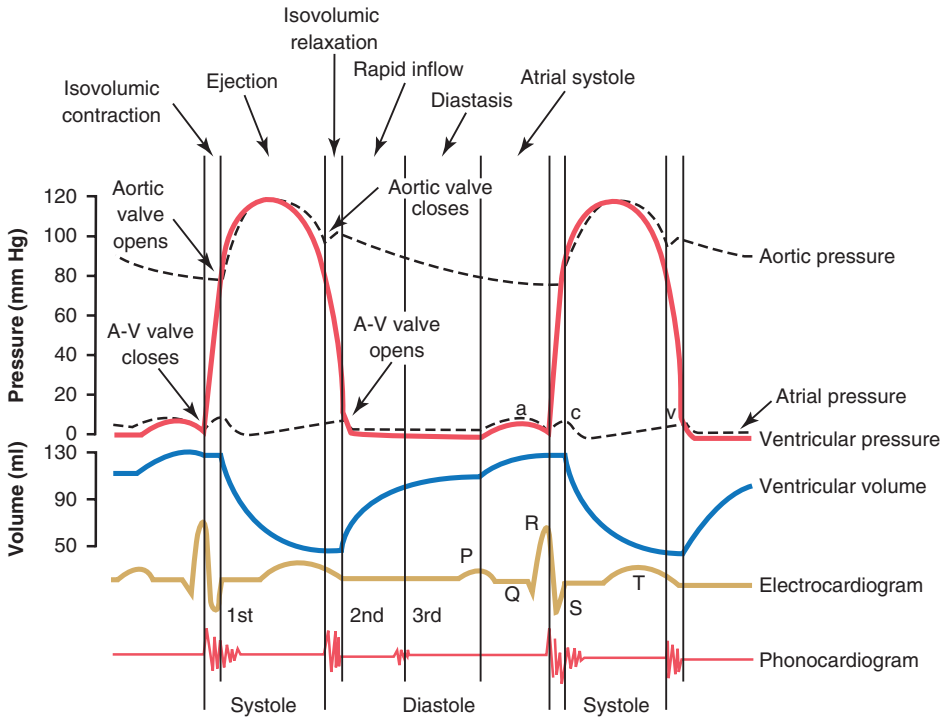

Figure 9-7. Events of the cardiac cycle for left ventricular function, showing changes in left atrial pressure, left ventricular pressure, aortic pressure, ventricular volume, the electrocardiogram, and the phonocardiogram. A-V, atrioventricular.

entire cardiac cycle. This means that the heart beating at a very fast rate does not remain relaxed long enough to allow complete filling of the cardiac chambers before the next contraction.

Relationship of the Electrocardiogram to the Cardiac Cycle

The electrocardiogram in **Figure 9-7** shows the *P, Q, R, S,* and *T waves,* which are discussed in Chapters 11, 12, and 13. They are electrical voltages generated by the heart and recorded by the electrocardiograph from the surface of the body.

The *P wave* is caused by *spread of depolarization* through the atria and is followed by atrial contraction, which causes a slight rise in the atrial pressure curve immediately after the electrocardiographic P wave.

About 0.16 second after the onset of the P wave, the *QRS waves* appear as a result of electrical depolarization of the ventricles, which initiates contraction of the ventricles and causes the ventricular pressure to begin rising. Therefore, the QRS complex begins slightly before the onset of ventricular systole.

Finally, the *ventricular T wave* represents the stage of repolarization of the ventricles when the ventricular muscle fibers begin to relax. Therefore, the T wave occurs slightly before the end of ventricular contraction.

The Atria Function as Primer Pumps for the Ventricles

Blood normally flows continually from the great veins into the atria; about 80 percent of the blood flows directly through the atria into the ventricles even before the atria contract. Then, atrial contraction usually causes an additional 20 percent filling of the ventricles. Therefore, the atria function as primer pumps that increase the ventricular pumping effectiveness as much as 20 percent. However, the heart can continue to operate under most conditions even without this extra 20 percent effectiveness because it normally has the capability of pumping 300 to 400 percent more blood than is required by the resting body. Therefore, when the atria fail to function, the difference is unlikely to be noticed unless a person exercises; then acute signs of heart failure occasionally develop, especially shortness of breath.

Pressure Changes in the Atria—a, c, and v Waves. In the atrial pressure curve of **Figure 9-7**, three minor pressure elevations, called the *a, c,* and *v atrial pressure waves,* are shown.

The *a wave* is caused by atrial contraction. Ordinarily, the *right* atrial pressure increases 4 to 6 mm Hg during atrial contraction, and the *left* atrial pressure increases about 7 to 8 mm Hg.

The *c wave* occurs when the ventricles begin to contract; it is caused partly by slight backflow of blood into the atria at the onset of ventricular contraction but mainly by bulging of the A-V valves backward toward the atria because of increasing pressure in the ventricles.

The *v wave* occurs toward the end of ventricular contraction; it results from slow flow of blood into the atria from the veins while the A-V valves are closed during ventricular contraction. Then, when ventricular contraction is

over, the A-V valves open, allowing this stored atrial blood to flow rapidly into the ventricles and causing the v wave to disappear.

FUNCTION OF THE VENTRICLES AS PUMPS

The Ventricles Fill With Blood During Diastole. During ventricular systole, large amounts of blood accumulate in the right and left atria because of the closed A-V valves. Therefore, as soon as systole is over and the ventricular pressures fall again to their low diastolic values, the moderately increased pressures that have developed in the atria during ventricular systole immediately push the A-V valves open and allow blood to flow rapidly into the ventricles, as shown by the rise of the left *ventricular volume curve* in **Figure 9-7**. This period is called the *period of rapid filling of the ventricles.*

The period of rapid filling lasts for about the first third of diastole. During the middle third of diastole, only a small amount of blood normally flows into the ventricles; this is blood that continues to empty into the atria from the veins and passes through the atria directly into the ventricles.

During the last third of diastole, the atria contract and give an additional thrust to the inflow of blood into the ventricles. This mechanism accounts for about 20 percent of the filling of the ventricles during each heart cycle.

Outflow of Blood From the Ventricles During Systole

Period of Isovolumic (Isometric) Contraction. Immediately after ventricular contraction begins, the ventricular pressure rises abruptly, as shown in **Figure 9-7**, causing the A-V valves to close. Then an additional 0.02 to 0.03 second is required for the ventricle to build up sufficient pressure to push the semilunar (aortic and pulmonary) valves open against the pressures in the aorta and pulmonary artery. Therefore, during this period, contraction is occurring in the ventricles, but no emptying occurs. This period is called the period of *isovolumic* or *isometric contraction,* meaning that cardiac muscle tension is increasing but little or no shortening of the muscle fibers is occurring.

Period of Ejection. When the left ventricular pressure rises slightly above 80 mm Hg (and the right ventricular pressure rises slightly above 8 mm Hg), the ventricular pressures push the semilunar valves open. Immediately, blood begins to pour out of the ventricles. Approximately 60 percent of the blood in the ventricle at the end of diastole is ejected during systole; about 70 percent of this portion flows out during the first third of the ejection period, with the remaining 30 percent emptying during the next two thirds. Therefore, the first third is called the *period of rapid ejection,* and the last two thirds are called the *period of slow ejection.*

Period of Isovolumic (Isometric) Relaxation. At the end of systole, ventricular relaxation begins suddenly, allowing both the right and left *intraventricular pressures* to decrease rapidly. The elevated pressures in the distended large arteries that have just been filled with blood from the contracted ventricles immediately push blood back toward the ventricles, which snaps the aortic and pulmonary valves closed. For another 0.03 to 0.06 second, the ventricular muscle continues to relax, even though the ventricular volume does not change, giving rise to the period of *isovolumic* or *isometric relaxation.* During this period, the intraventricular pressures rapidly decrease back to their low diastolic levels. Then the A-V valves open to begin a new cycle of ventricular pumping.

End-Diastolic Volume, End-Systolic Volume, and Stroke Volume Output. During diastole, normal filling of the ventricles increases the volume of each ventricle to about 110 to 120 milliliters. This volume is called the *end-diastolic volume.* Then, as the ventricles empty during systole, the volume decreases about 70 milliliters, which is called the *stroke volume output.* The remaining volume in each ventricle, about 40 to 50 milliliters, is called the *end-systolic volume.* The fraction of the end-diastolic volume that is ejected is called the *ejection fraction*—usually equal to about 0.6 (or 60 percent).

When the heart contracts strongly, the end-systolic volume may decrease to as little as 10 to 20 milliliters. Conversely, when large amounts of blood flow into the ventricles during diastole, the ventricular end-diastolic volumes can become as great as 150 to 180 milliliters in the healthy heart. By both increasing the end-diastolic volume and decreasing the end-systolic volume, the stroke volume output can be increased to more than double that which is normal.

THE HEART VALVES PREVENT BACKFLOW OF BLOOD DURING SYSTOLE

Atrioventricular Valves. The *A-V valves* (i.e., the *tricuspid* and *mitral* valves) prevent backflow of blood from the ventricles to the atria during systole, and the *semilunar valves* (i.e., the *aortic* and *pulmonary artery* valves) prevent backflow from the aorta and pulmonary arteries into the ventricles during diastole. These valves, shown in **Figure 9-8** for the left ventricle, close and open *passively.* That is, they close when a backward pressure gradient pushes blood backward, and they open when a forward pressure gradient forces blood in the forward direction. For anatomical reasons, the thin, filmy A-V valves require almost no backflow to cause closure, whereas the much heavier semilunar valves require rather rapid backflow for a few milliseconds.

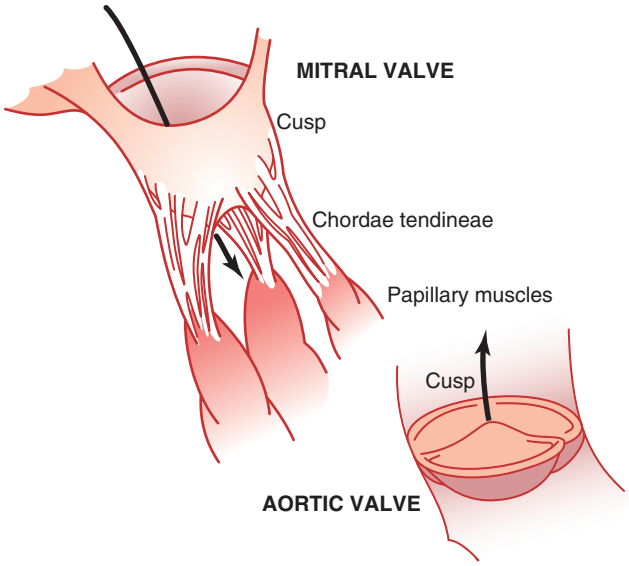

Figure 9-8. Mitral and aortic valves (the left ventricular valves).

Function of the Papillary Muscles. Figure 9-8 also shows papillary muscles that attach to the vanes of the A-V valves by the *chordae tendineae.* The papillary muscles contract when the ventricular walls contract, but contrary to what might be expected, they *do not* help the valves to close. Instead, they pull the vanes of the valves inward toward the ventricles to prevent their bulging too far backward toward the atria during ventricular contraction. If a chorda tendinea becomes ruptured or if one of the papillary muscles becomes paralyzed, the valve bulges far backward during ventricular contraction, sometimes so far that it leaks severely and results in severe or even lethal cardiac incapacity.

Aortic and Pulmonary Artery Valves. The aortic and pulmonary artery semilunar valves function quite differently from the A-V valves. First, the high pressures in the arteries at the end of systole cause the semilunar valves to snap closed, in contrast to the much softer closure of the A-V valves. Second, because of smaller openings, the velocity of blood ejection through the aortic and pulmonary valves is far greater than that through the much larger A-V valves. Also, because of the rapid closure and rapid ejection, the edges of the aortic and pulmonary valves are subjected to much greater mechanical abrasion than are the A-V valves. Finally, the A-V valves are supported by the chordae tendineae, which is not true for the semilunar valves. It is obvious from the anatomy of the aortic and pulmonary valves (as shown for the aortic valve at the bottom of Figure 9-8) that they must be constructed with an especially strong yet very pliable fibrous tissue to withstand the extra physical stresses.

AORTIC PRESSURE CURVE

When the left ventricle contracts, the ventricular pressure increases rapidly until the aortic valve opens. Then, after the valve opens, the pressure in the ventricle rises much less rapidly, as shown in Figure 9-6, because blood immediately flows out of the ventricle into the aorta and then into the systemic distribution arteries.

The entry of blood into the arteries during systole causes the walls of these arteries to stretch and the pressure to increase to about 120 mm Hg.

Next, at the end of systole, after the left ventricle stops ejecting blood and the aortic valve closes, the elastic walls of the arteries maintain a high pressure in the arteries, even during diastole.

An *incisura* occurs in the aortic pressure curve when the aortic valve closes. This is caused by a short period of backward flow of blood immediately before closure of the valve, followed by sudden cessation of the backflow.

After the aortic valve has closed, the pressure in the aorta decreases slowly throughout diastole because the blood stored in the distended elastic arteries flows continually through the peripheral vessels back to the veins. Before the ventricle contracts again, the aortic pressure usually has fallen to about 80 mm Hg (diastolic pressure), which is two thirds the maximal pressure of 120 mm Hg (systolic pressure) that occurs in the aorta during ventricular contraction.

The pressure curves in the *right ventricle* and *pulmonary artery* are similar to those in the aorta, except that the pressures are only about one sixth as great, as discussed in Chapter 14.

Relationship of the Heart Sounds to Heart Pumping

When listening to the heart with a stethoscope, one does not hear the opening of the valves because this is a relatively slow process that normally makes no noise. However, when the valves close, the vanes of the valves and the surrounding fluids vibrate under the influence of sudden pressure changes, giving off sound that travels in all directions through the chest.

When the ventricles contract, one first hears a sound caused by closure of the A-V valves. The vibration pitch is low and relatively long-lasting and is known as the *first heart sound.* When the aortic and pulmonary valves close at the end of systole, one hears a rapid snap because these valves close rapidly, and the surroundings vibrate for a short period. This sound is called the *second heart sound.* The precise causes of the heart sounds are discussed more fully in Chapter 23, in relation to listening to the sounds with the stethoscope.

Work Output of the Heart

The *stroke work output* of the heart is the amount of energy that the heart converts to work during each heartbeat while pumping blood into the arteries. *Minute work output* is the total amount of energy converted to work in 1 minute; this is equal to the stroke work output times the heart rate per minute.

Work output of the heart is in two forms. First, by far the major proportion is used to move the blood from the

low-pressure veins to the high-pressure arteries. This is called *volume-pressure work* or *external work.* Second, a minor proportion of the energy is used to accelerate the blood to its velocity of ejection through the aortic and pulmonary valves, which is the *kinetic energy of blood flow* component of the work output.

Right ventricular external work output is normally about one sixth the work output of the left ventricle because of the sixfold difference in systolic pressures that the two ventricles pump. The additional work output of each ventricle required to create kinetic energy of blood flow is proportional to the mass of blood ejected times the square of velocity of ejection.

Ordinarily, the work output of the left ventricle required to create kinetic energy of blood flow is only about 1 percent of the total work output of the ventricle and therefore is ignored in the calculation of the total stroke work output. In certain abnormal conditions, however, such as aortic stenosis, in which blood flows with great velocity through the stenosed valve, more than 50 percent of the total work output may be required to create kinetic energy of blood flow.

GRAPHICAL ANALYSIS OF VENTRICULAR PUMPING

Figure 9-9 shows a diagram that is especially useful in explaining the pumping mechanics of the *left* ventricle. The most important components of the diagram are the two curves labeled "diastolic pressure" and "systolic pressure." These curves are volume-pressure curves.

The diastolic pressure curve is determined by filling the heart with progressively greater volumes of blood and then measuring the diastolic pressure immediately before ventricular contraction occurs, which is the *end-diastolic pressure* of the ventricle.

The systolic pressure curve is determined by recording the systolic pressure achieved during ventricular contraction at each volume of filling.

Until the volume of the noncontracting ventricle rises above about 150 milliliters, the "diastolic" pressure does not increase greatly. Therefore, up to this volume, blood can flow easily into the ventricle from the atrium. Above 150 milliliters, the ventricular diastolic pressure increases rapidly, partly because of fibrous tissue in the heart that will stretch no more and partly because the pericardium that surrounds the heart becomes filled nearly to its limit.

During ventricular contraction, the systolic pressure increases even at low ventricular volumes and reaches a maximum at a ventricular volume of 150 to 170 milliliters. Then, as the volume increases still further, the systolic pressure actually decreases under some conditions, as demonstrated by the falling systolic pressure curve in **Figure 9-9**, because at these great volumes, the actin and myosin filaments of the cardiac muscle fibers are pulled apart far enough that the strength of each cardiac fiber contraction becomes less than optimal.

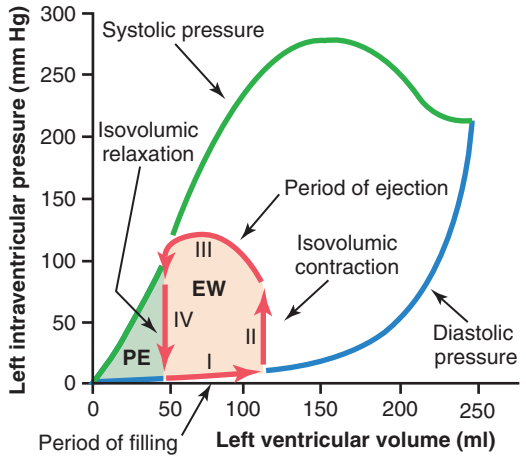

Figure 9-9. Relationship between left ventricular volume and intraventricular pressure during diastole and systole. Also shown by the red lines is the "volume-pressure diagram," demonstrating changes in intraventricular volume and pressure during the normal cardiac cycle. EW, net external work; PE, potential energy.

Note especially in the figure that the maximum systolic pressure for the normal *left* ventricle is between 250 and 300 mm Hg, but this varies widely with each person's heart strength and degree of heart stimulation by cardiac nerves. For the normal *right* ventricle, the maximum systolic pressure is between 60 and 80 mm Hg.

"Volume-Pressure Diagram" During the Cardiac Cycle; Cardiac Work Output. The red lines in **Figure 9-9** form a loop called the *volume-pressure diagram* of the cardiac cycle for normal function of the *left* ventricle. A more detailed version of this loop is shown in **Figure 9-10**. It is divided into four phases.

Phase I: Period of filling. Phase I in the volume-pressure diagram begins at a ventricular volume of about 50 milliliters and a diastolic pressure of 2 to 3 mm Hg. The amount of blood that remains in the ventricle after the previous heartbeat, 50 milliliters, is called the *end-systolic volume.* As venous blood flows into the ventricle from the left atrium, the ventricular volume normally increases to about 120 milliliters, called the *end-diastolic volume,* an increase of 70 milliliters. Therefore, the volume-pressure diagram during phase I extends along the line in **Figure 9-9** labeled "I," and from point A to point B in **Figure 9-10**, with the volume increasing to 120 milliliters and the diastolic pressure rising to about 5 to 7 mm Hg.

Phase II: Period of isovolumic contraction. During isovolumic contraction, the volume of the ventricle does not change because all valves are closed. However, the pressure inside the ventricle increases to equal the pressure in the aorta, at a pressure value of about 80 mm Hg, as depicted by point C (**Figure 9-10**).

Phase III: Period of ejection. During ejection, the systolic pressure rises even higher because of still more contraction of the ventricle. At the same time, the volume of the ventricle decreases because the aortic valve has now opened and blood flows out of the ventricle into the aorta.

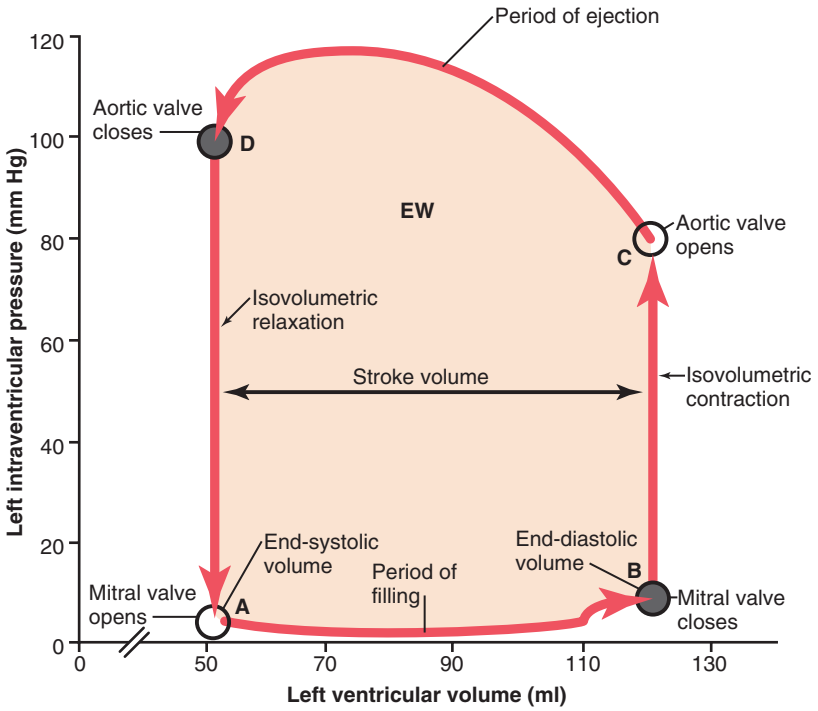

Figure 9-10. The volume-pressure diagram demonstrating changes in intraventricular volume and pressure during a single cardiac cycle *(red line)*. The shaded area represents the net external work (*EW*) output by the left ventricle during the cardiac cycle.

Therefore, in **Figure 9-9** the curve labeled "III," or "period of ejection," traces the changes in volume and systolic pressure during this period of ejection.

Phase IV: Period of isovolumic relaxation. At the end of the period of ejection (point D; **Figure 9-10**), the aortic valve closes and the ventricular pressure falls back to the diastolic pressure level. The line labeled "IV" (**Figure 9-9**) traces this decrease in intraventricular pressure without any change in volume. Thus, the ventricle returns to its starting point, with about 50 milliliters of blood left in the ventricle and at an atrial pressure of 2 to 3 mm Hg.

The area subtended by this functional volume-pressure diagram (the shaded area, labeled "EW") represents the *net external work output* of the ventricle during its contraction cycle. In experimental studies of cardiac contraction, this diagram is used for calculating cardiac work output.

When the heart pumps large quantities of blood, the area of the work diagram becomes much larger. That is, it extends far to the right because the ventricle fills with more blood during diastole, it rises much higher because the ventricle contracts with greater pressure, and it usually extends farther to the left because the ventricle contracts to a smaller volume—especially if the ventricle is stimulated to increased activity by the sympathetic nervous system.

Concepts of Preload and Afterload. In assessing the contractile properties of muscle, it is important to specify the degree of tension on the muscle when it begins to contract, which is called the *preload,* and to specify the load against which the muscle exerts its contractile force, which is called the *afterload.*

For cardiac contraction, the *preload* is usually considered to be the end-diastolic pressure when the ventricle has become filled.

The *afterload* of the ventricle is the pressure in the aorta leading from the ventricle. In **Figure 9-9**, this corresponds to the systolic pressure described by the phase III curve of the volume-pressure diagram. (Sometimes the afterload is loosely considered to be the resistance in the circulation rather than the pressure.)

The importance of the concepts of preload and afterload is that in many abnormal functional states of the heart or circulation, the pressure during filling of the ventricle (the preload), the arterial pressure against which the ventricle must contract (the afterload), or both are altered from normal to a severe degree.

Chemical Energy Required for Cardiac Contraction: Oxygen Utilization by the Heart

Heart muscle, like skeletal muscle, uses chemical energy to provide the work of contraction. Approximately 70 to 90 percent of this energy is normally derived from oxidative metabolism of fatty acids, with about 10 to 30 percent coming from other nutrients, especially lactate and glucose. Therefore, the rate of oxygen consumption by the heart is an excellent measure of the chemical energy liberated while the heart performs its work. The different chemical reactions that liberate this energy are discussed in Chapters 68 and 69.

Experimental studies have shown that oxygen consumption of the heart and the chemical energy expended during contraction are directly related to the total shaded area in **Figure 9-9**. This shaded portion consists of the *external work* (EW) as explained earlier and an additional

portion called the *potential energy,* labeled "PE". The potential energy represents additional work that could be accomplished by contraction of the ventricle if the ventricle should completely empty all the blood in its chamber with each contraction.

Oxygen consumption has also been shown to be nearly proportional to the *tension* that occurs in the heart muscle during contraction multiplied by the *duration of time* that the contraction persists, called the *tension-time index*. Because tension is high when systolic pressure is high, correspondingly more oxygen is used. Also, much more chemical energy is expended even at normal systolic pressures when the ventricle is abnormally dilated because the heart muscle tension during contraction is proportional to pressure times the diameter of the ventricle. This becomes especially important in heart failure when the heart ventricle is dilated and, paradoxically, the amount of chemical energy required for a given amount of work output is greater than normal even though the heart is already failing.

Efficiency of Cardiac Contraction. During heart muscle contraction, most of the expended chemical energy is converted into *heat,* and a much smaller portion is converted into *work output*. The ratio of work output to total chemical energy expenditure is called the *efficiency of cardiac contraction,* or simply *efficiency of the heart.* Maximum efficiency of the normal heart is between 20 and 25 percent. In persons with heart failure, this efficiency can decrease to as low as 5 to 10 percent.

REGULATION OF HEART PUMPING

When a person is at rest, the heart pumps only 4 to 6 liters of blood each minute. During strenuous exercise, the heart may be required to pump four to seven times this amount. The basic means by which the volume pumped by the heart is regulated are (1) intrinsic cardiac regulation of pumping in response to changes in volume of blood flowing into the heart and (2) control of heart rate and strength of heart pumping by the autonomic nervous system.

INTRINSIC REGULATION OF HEART PUMPING—THE FRANK-STARLING MECHANISM

In Chapter 20, we will learn that under most conditions, the amount of blood pumped by the heart each minute is normally determined almost entirely by the rate of blood flow into the heart from the veins, which is called *venous return.* That is, each peripheral tissue of the body controls its own local blood flow, and all the local tissue flows combine and return by way of the veins to the right atrium. The heart, in turn, automatically pumps this incoming blood into the arteries so that it can flow around the circuit again.

This intrinsic ability of the heart to adapt to increasing volumes of inflowing blood is called the *Frank-Starling mechanism of the heart,* in honor of Otto Frank and Ernest Starling, two great physiologists of a century ago. Basically, the Frank-Starling mechanism means that the greater the heart muscle is stretched during filling, the greater is the force of contraction and the greater the quantity of blood pumped into the aorta. Or, stated another way: *Within physiological limits, the heart pumps all the blood that returns to it by way of the veins.*

What Is the Explanation of the Frank-Starling Mechanism? When an extra amount of blood flows into the ventricles, the cardiac muscle is stretched to a greater length. This stretching in turn causes the muscle to contract with increased force because the actin and myosin filaments are brought to a more nearly optimal degree of overlap for force generation. Therefore, the ventricle, because of its increased pumping, automatically pumps the extra blood into the arteries.

This ability of stretched muscle, up to an optimal length, to contract with increased work output is characteristic of all striated muscle, as explained in Chapter 6, and is not simply a characteristic of cardiac muscle.

In addition to the important effect of lengthening the heart muscle, still another factor increases heart pumping when its volume is increased. Stretch of the right atrial wall directly increases the heart rate by 10 to 20 percent, which also helps increase the amount of blood pumped each minute, although its contribution is much less than that of the Frank-Starling mechanism.

Ventricular Function Curves

One of the best ways to express the functional ability of the ventricles to pump blood is by *ventricular function curves.* **Figure 9-11** shows a type of ventricular function curve called the *stroke work output curve.* Note that as the atrial pressure for each side of the heart increases, the stroke work output for that side increases until it reaches the limit of the ventricle's pumping ability.

Figure 9-12 shows another type of ventricular function curve called the *ventricular volume output curve.*

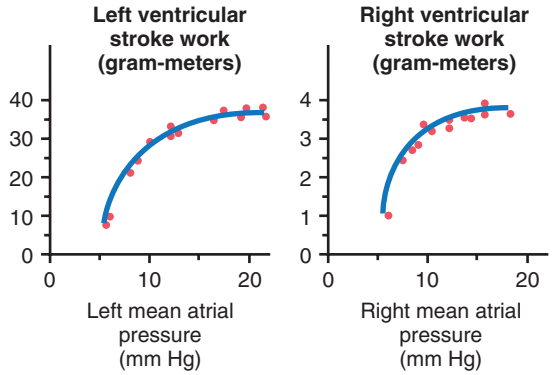

Figure 9-11. Left and right ventricular function curves recorded from dogs, depicting *ventricular stroke work output* as a function of left and right mean atrial pressures. *(Data from Sarnoff SJ: Myocardial contractility as described by ventricular function curves. Physiol Rev 35:107, 1955.)*

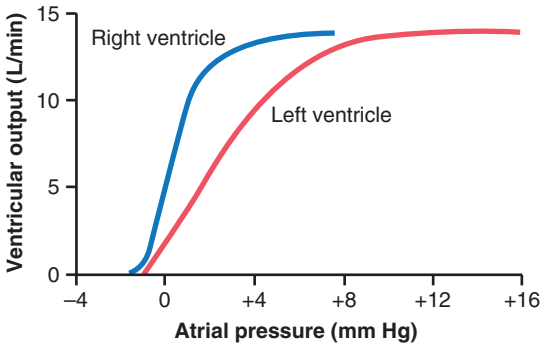

Figure 9-12. Approximate normal right and left *ventricular volume output curves* for the normal resting human heart as extrapolated from data obtained in dogs and data from human beings.

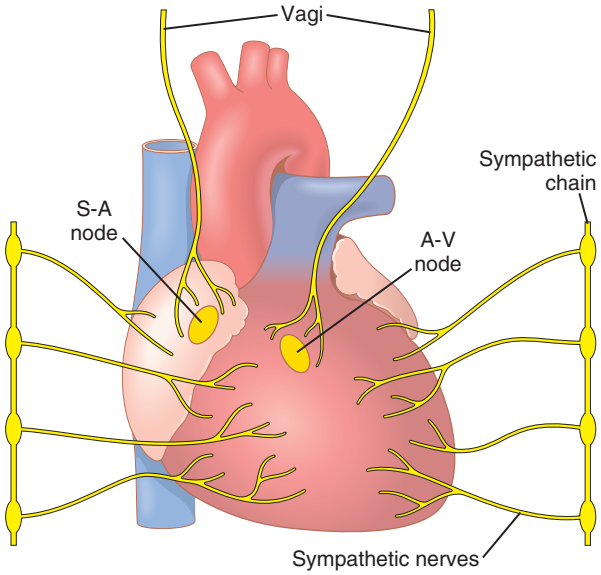

Figure 9-13. Cardiac *sympathetic* and *parasympathetic* nerves. (The vagus nerves to the heart are parasympathetic nerves.) A-V, atrioventricular; S-A, sinoatrial.

The two curves of this figure represent function of the two ventricles of the human heart based on data extrapolated from experimental animal studies. As the right and left atrial pressures increase, the respective ventricular volume outputs per minute also increase.

Thus, *ventricular function curves* are another way of expressing the Frank-Starling mechanism of the heart. That is, as the ventricles fill in response to higher atrial pressures, each ventricular volume and strength of cardiac muscle contraction increase, causing the heart to pump increased quantities of blood into the arteries.

Control of the Heart by the Sympathetic and Parasympathetic Nerves

The pumping effectiveness of the heart also is controlled by the *sympathetic* and *parasympathetic (vagus)* nerves, which abundantly supply the heart, as shown in **Figure 9-13**. For given levels of atrial pressure, the amount of blood pumped each minute *(cardiac output)* often can be increased more than 100 percent by sympathetic stimulation. By contrast, the output can be decreased to almost zero by vagal (parasympathetic) stimulation.

Mechanisms of Excitation of the Heart by the Sympathetic Nerves. Strong sympathetic stimulation can increase the heart rate in young adult humans from the normal rate of 70 beats/min up to 180 to 200 and, rarely, even 250 beats/min. Also, sympathetic stimulation increases the force of heart contraction to as much as double the normal rate, thereby increasing the volume of blood pumped and increasing the ejection pressure. Thus, sympathetic stimulation often can increase the maximum cardiac output as much as twofold to threefold, in addition to the increased output caused by the Frank-Starling mechanism already discussed.

Conversely, *inhibition* of the sympathetic nerves to the heart can decrease cardiac pumping to a moderate extent. Under normal conditions, the sympathetic nerve fibers to the heart discharge continuously at a slow rate that maintains pumping at about 30 percent above that with no sympathetic stimulation. Therefore, when the activity of the sympathetic nervous system is depressed below normal, both the heart rate and strength of ventricular muscle contraction decrease, thereby decreasing the level of cardiac pumping as much as 30 percent below normal.

Parasympathetic (Vagal) Stimulation Reduces Heart Rate and Strength of Contraction. Strong stimulation of the parasympathetic nerve fibers in the vagus nerves to the heart can stop the heartbeat for a few seconds, but then the heart usually "escapes" and beats at a rate of 20 to 40 beats/min as long as the parasympathetic stimulation continues. In addition, strong vagal stimulation can decrease the strength of heart muscle contraction by 20 to 30 percent.

The vagal fibers are distributed mainly to the atria and not much to the ventricles, where the power contraction of the heart occurs. This distribution explains why the effect of vagal stimulation is mainly to decrease the heart rate rather than to decrease greatly the strength of heart contraction. Nevertheless, the great decrease in heart rate combined with a slight decrease in heart contraction strength can decrease ventricular pumping 50 percent or more.

Effect of Sympathetic or Parasympathetic Stimulation on the Cardiac Function Curve. **Figure 9-14** shows four cardiac function curves. These curves are similar to the ventricular function curves of **Figure 9-12**. However, they represent function of the entire heart rather than of a single ventricle. They show the relation between right atrial pressure at the input of the right heart and cardiac output from the left ventricle into the aorta.

The curves of **Figure 9-14** demonstrate that at any given right atrial pressure, the cardiac output increases during increased sympathetic stimulation and decreases during increased parasympathetic stimulation. These

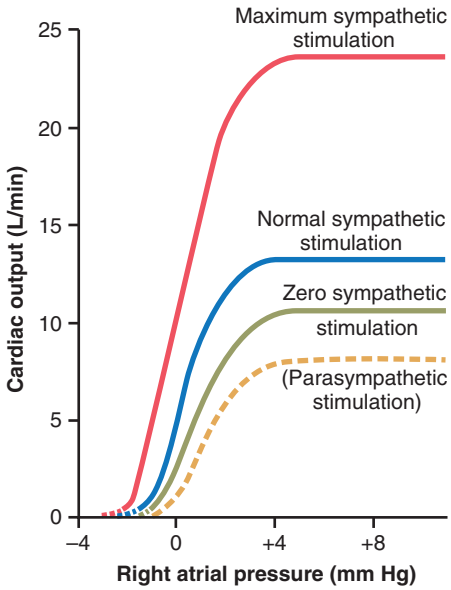

Figure 9-14. Effect on the cardiac output curve of different degrees of sympathetic or parasympathetic stimulation.

changes in output caused by autonomic nervous system stimulation result both from *changes in heart rate* and from *changes in contractile strength of the heart.*

EFFECT OF POTASSIUM AND CALCIUM IONS ON HEART FUNCTION

In the discussion of membrane potentials in Chapter 5, it was pointed out that potassium ions have a marked effect on membrane potentials, and in Chapter 6 it was noted that calcium ions play an especially important role in activating the muscle contractile process. Therefore, it is to be expected that the concentrations of each of these two ions in the extracellular fluids also have important effects on cardiac pumping.

Effect of Potassium Ions. Excess potassium in the extracellular fluids causes the heart to become dilated and flaccid and also slows the heart rate. Large quantities of potassium also can block conduction of the cardiac impulse from the atria to the ventricles through the A-V bundle. Elevation of potassium concentration to only 8 to 12 mEq/L—two to three times the normal value—can cause severe weakness of the heart, abnormal rhythm, and death.

These effects result partially from the fact that a high potassium concentration in the extracellular fluids decreases the resting membrane potential in the cardiac muscle fibers, as explained in Chapter 5. That is, high extracellular fluid potassium concentration partially depolarizes the cell membrane, causing the membrane potential to be less negative. As the membrane potential decreases, the intensity of the action potential also decreases, which makes contraction of the heart progressively weaker.

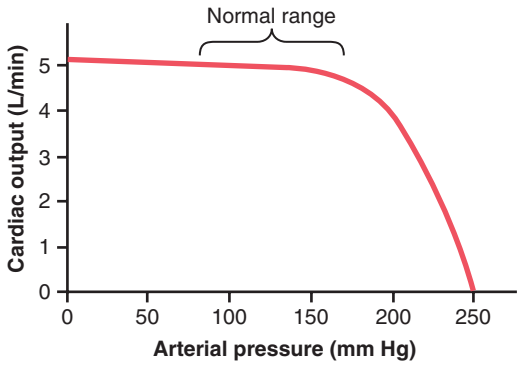

Figure 9-15. Constancy of cardiac output up to a pressure level of 160 mm Hg. Only when the arterial pressure rises above this normal limit does the increasing pressure load cause the cardiac output to fall significantly.

Effect of Calcium Ions. Excess calcium ions cause effects almost exactly opposite to those of potassium ions, causing the heart to move toward spastic contraction. This effect is caused by a direct effect of calcium ions to initiate the cardiac contractile process, as explained earlier in this chapter.

Conversely, deficiency of calcium ions causes cardiac weakness, similar to the effect of high potassium. Fortunately, calcium ion levels in the blood normally are regulated within a very narrow range. Therefore, cardiac effects of abnormal calcium concentrations are seldom of clinical concern.

EFFECT OF TEMPERATURE ON HEART FUNCTION

Increased body temperature, such as that which occurs when one has fever, greatly increases the heart rate, sometimes to double the normal rate. Decreased temperature greatly decreases heart rate, which may fall to as low as a few beats per minute when a person is near death from hypothermia in the body temperature range of 60° to 70°F. These effects presumably result from the fact that heat increases the permeability of the cardiac muscle membrane to ions that control heart rate, resulting in acceleration of the self-excitation process.

Contractile strength of the heart often is enhanced temporarily by a moderate increase in temperature, such as that which occurs during body exercise, but prolonged elevation of temperature exhausts the metabolic systems of the heart and eventually causes weakness. Therefore, optimal function of the heart depends greatly on proper control of body temperature by the temperature control mechanisms explained in Chapter 74.

INCREASING THE ARTERIAL PRESSURE LOAD (UP TO A LIMIT) DOES NOT DECREASE THE CARDIAC OUTPUT

Note in **Figure 9-15** that increasing the arterial pressure in the aorta does not decrease the cardiac output until the

mean arterial pressure rises above about 160 mm Hg. In other words, during normal function of the heart at normal systolic arterial pressures (80 to 140 mm Hg), the cardiac output is determined almost entirely by the ease of blood flow through the body's tissues, which in turn controls *venous return* of blood to the heart. This mechanism is the principal subject of Chapter 20.

Bibliography

Bers DM, Shannon TR: Calcium movements inside the sarcoplasmic reticulum of cardiac myocytes. J Mol Cell Cardiol 58:59, 2013.

Chantler PD, Lakatta EG, Najjar SS: Arterial-ventricular coupling: mechanistic insights into cardiovascular performance at rest and during exercise. J Appl Physiol 105:1342, 2008.

Cingolani HE, Pérez NG, Cingolani OH, Ennis IL: The Anrep effect: 100 years later. Am J Physiol Heart Circ Physiol 304:H175, 2013.

Couchonnal LF, Anderson ME: The role of calmodulin kinase II in myocardial physiology and disease. Physiology (Bethesda) 23:151, 2008.

Doenst T, Nguyen TD, Abel ED: Cardiac metabolism in heart failure: implications beyond ATP production. Circ Res 113:709, 2013.

Eisner D, Caldwell J, Trafford A: Sarcoplasmic reticulum Ca-ATPase and heart failure 20 years later. Circ Res 113:958, 2013.

Guyton AC, Jones CE, Coleman TG: Circulatory Physiology: Cardiac Output and Its Regulation, 2nd ed. Philadelphia: WB Saunders, 1973.

Ibrahim M, Gorelik J, Yacoub MH, Terracciano CM: The structure and function of cardiac t-tubules in health and disease. Proc Biol Sci 278:2714, 2011.

Kho C, Lee A, Hajjar RJ: Altered sarcoplasmic reticulum calcium cycling—targets for heart failure therapy. Nat Rev Cardiol 9:717, 2012.

Korzick DH: From syncytium to regulated pump: a cardiac muscle cellular update. Adv Physiol Educ 35:22, 2011.

Luo M, Anderson ME: Mechanisms of altered Ca^{2+} handling in heart failure. Circ Res 113:690, 2013.

Mangoni ME, Nargeot J: Genesis and regulation of the heart automaticity. Physiol Rev 88:919, 2008.

Marks AR: Calcium cycling proteins and heart failure: mechanisms and therapeutics. J Clin Invest 123:46, 2013.

Puglisi JL, Negroni JA, Chen-Izu Y, Bers DM: The force-frequency relationship: insights from mathematical modeling. Adv Physiol Educ 37:28, 2013.

Sarnoff SJ: Myocardial contractility as described by ventricular function curves. Physiol Rev 35:107, 1955.

Solaro RJ, Henze M, Kobayashi T: Integration of troponin I phosphorylation with cardiac regulatory networks. Circ Res 112:355, 2013.

Starling EH: The Linacre Lecture on the Law of the Heart. London: Longmans Green, 1918.

ter Keurs HE: The interaction of Ca^{2+} with sarcomeric proteins: role in function and dysfunction of the heart. Am J Physiol Heart Circ Physiol 302:H38, 2012.