Heart Muscle; The Heart as a Pump

CHAPTER 9

With this chapter we begin discussion of the heart and circulatory system. The heart, shown in Figure 9–1, is actually two separate pumps: a *right heart* that pumps the blood through the lungs and a *left heart* that pumps the blood through the peripheral organs. In turn, each of these hearts is a pulsatile two-chamber pump composed of an *atrium* and a *ventricle.* The atrium functions principally as a weak primer pump for the ventricle, helping to move the blood into the ventricle. The ventricle in turn supplies the main force that propels the blood through either the pulmonary or the peripheral circulation.

Special mechanisms in the heart provide cardiac rhythmicity and transmit action potentials throughout the heart muscle to cause the heart's rhythmical beat. This rhythmical control system is explained in Chapter 10. In this chapter, we explain how the heart operates as a pump, beginning with the special features of heart muscle itself.

PHYSIOLOGY OF CARDIAC MUSCLE

The heart is composed of three major types of cardiac muscle: atrial muscle, ventricular muscle, and specialized excitatory and conductive muscle fibers. The atrial and ventricular types of muscle contract in much the same way as skeletal muscle except that the duration of contraction is much longer. On the other hand, the specialized excitatory and conductive fibers contract only feebly because they contain few contractile fibrils; instead, they exhibit rhythmicity and varying rates of conduction, providing an excitatory system for the heart.

Physiologic Anatomy of Cardiac Muscle

Figure 9–2 shows a typical histological picture of cardiac muscle, demonstrating the cardiac muscle fibers arranged in a latticework, the fibers dividing, then recombining, and then spreading again. One notes immediately from this figure that cardiac muscle is *striated* in the same manner as typical skeletal muscle. Furthermore, cardiac muscle has typical myofibrils that contain *actin* and *myosin filaments* almost identical to those found in skeletal muscle, and these filaments interdigitate and slide along one another during contraction in the same manner as occurs in skeletal muscle. (See Chapter 6.) In other ways, cardiac muscle is quite different from skeletal muscle, as we shall see.

Cardiac Muscle as a Syncytium. The dark areas crossing the cardiac muscle fibers in Figure 9–2 are called *intercalated discs;* they are actually cell membranes that separate individual cardiac muscle cells from one another. That is, cardiac muscle fibers are made up of many individual cells connected in series with one another. Yet electrical resistance through the intercalated disc is only ¼00 the resistance through the outside membrane of the cardiac muscle fiber because the cell membranes fuse with one another in such a way that they form permeable "communicating" junctions (gap junctions) that allow relatively free diffusion of ions. Therefore, from a functional point of view, ions move with ease along the longitudinal axes of the cardiac muscle fibers, so that action potentials travel from one cardiac muscle cell to another, past the intercalated discs, with only slight hindrance. Thus, cardiac muscle is a *syncytium* of many heart muscle cells, in which the cardiac cells are so interconnected that

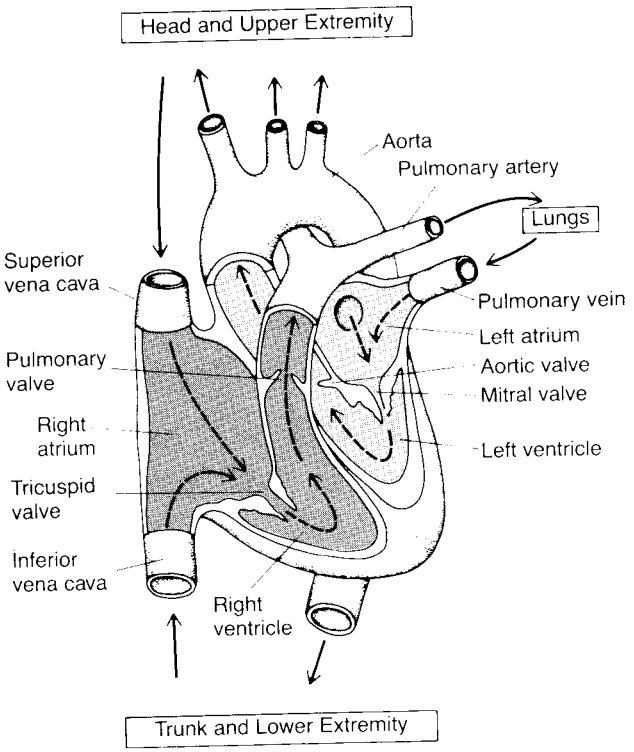

Figure 9–1. Structure of the heart and course of blood flow through the heart chambers.

when one of these cells becomes excited, the action potential spreads to all of them, spreading from cell to cell as well as throughout the latticework interconnections.

The heart is actually composed of two syncytiums: the *atrial syncytium* that constitutes the walls of the two atria and the *ventricular syncytium* that constitutes the walls of the two ventricles. The atria are separated from the ventricles by fibrous tissue that surrounds the valvular openings between the atria and ventricles. Normally, action potentials can be conducted from the atrial syncytium into the ventricular syncytium only by way of a specialized conductive system, the *atrioventricular (A-V) bundle*, a bundle of conductive fibers several millimeters in diameter that is discussed in detail in Chapter 10. This division of the muscle mass of the heart into two functional syncytiums allows the atria to contract a short time ahead of ventricular contraction, which is important for the effectiveness of heart pumping.

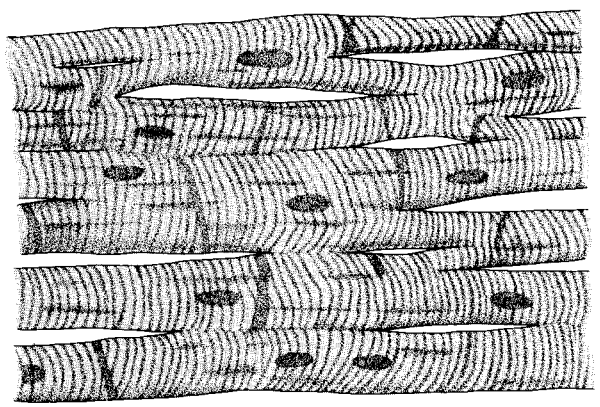

Figure 9–2. "Syncytial," interconnecting nature of cardiac muscle.

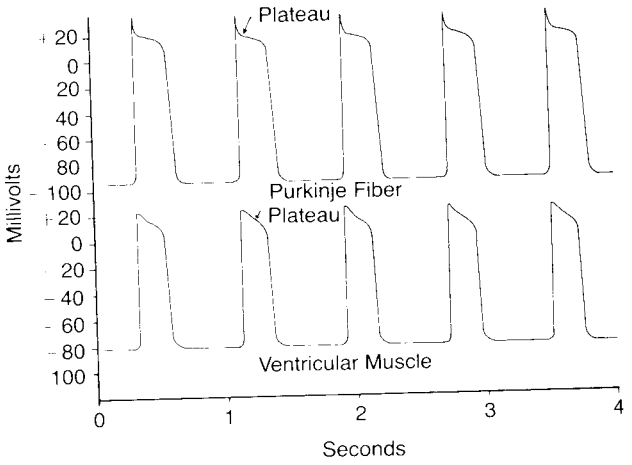

Figure 9–3. Rhythmical action potentials from a Purkinje fiber and from a ventricular muscle fiber recorded by means of microelectrodes.

Action Potentials in Cardiac Muscle

The *resting membrane potential* of normal cardiac muscle is about −85 to −95 millivolts and about −90 to −100 millivolts in the specialized conductive fibers, the Purkinje fibers, which are discussed in Chapter 10.

The *action potential* recorded in ventricular muscle, shown by the bottom record of Figure 9–3, is 105 millivolts, which means that the membrane potential rises from its normally very negative value to a slightly positive value of about +20 millivolts. The positive portion is called the *overshoot potential*. After the initial *spike*, the membrane remains depolarized for about 0.2 second in atrial muscle and about 0.3 second in ventricular muscle, exhibiting a *plateau* as shown in Figure 9–3, followed at the end of the plateau by abrupt repolarization. The presence of this plateau in the action potential causes muscle contraction to last 3 to 15 times as long in cardiac muscle as in skeletal muscle.

Why the Long Action Potential and the Plateau? At this point, we must ask the question: Why is the action potential of cardiac muscle so long, and why does it have a plateau, whereas that of skeletal muscle does not? The basic biophysical answers to these questions are presented in Chapter 5, but they merit summarizing again.

At least two major differences between the membrane properties of cardiac and skeletal muscle account for the prolonged action potential and the plateau in cardiac muscle.

First, the action potential of skeletal muscle is

caused almost entirely by sudden opening of large numbers of so-called *fast sodium channels* that allow tremendous numbers of sodium ions to enter the skeletal muscle fiber. These channels are called "fast" channels because they remain open for only a few 10,000ths of a second and then abruptly close. At the end of this closure, repolarization occurs, and the action potential is over within another 10,000th of a second or so. In cardiac muscle, on the other hand, the action potential is caused by the opening of two types of channels: (1) the same *fast sodium channels* as those in skeletal muscle and (2) another entire population of so-called *slow calcium channels*, also called *calcium-sodium channels*. This second population of channels differs from the fast sodium channels in being slower to open; but more important, they remain open for several tenths of a second. During this time, a large quantity of both calcium and sodium ions flows through these channels to the interior of the cardiac muscle fiber, and this maintains a prolonged period of depolarization, causing the plateau in the action potential. Furthermore, the calcium ions that enter the muscle during this action potential play an important role in helping excite the muscle contractile process, which is another difference between cardiac muscle and skeletal muscle, as we discuss later in this chapter.

The second major functional difference between cardiac muscle and skeletal muscle that helps account for both the prolonged action potential and its plateau is this: Immediately after the onset of the action potential, the permeability of the cardiac muscle membrane for potassium *decreases* about fivefold, an effect that does not occur in skeletal muscle. This decreased potassium permeability may be caused by the excess calcium influx through the calcium channels just noted. Regardless of the cause, the decreased potassium permeability greatly decreases the outflux of potassium ions during the action potential plateau and thereby prevents early return of the potential to its resting level. When the slow calcium-sodium channels do close at the end of 0.2 to 0.3 second and the influx of calcium and sodium ions ceases, the membrane permeability for potassium increases rapidly; this rapid loss of potassium from the fiber returns the membrane potential to its resting level, thus ending the action potential.

Velocity of Conduction in Cardiac Muscle. The velocity of conduction of the action potential in both atrial and ventricular muscle fibers is about 0.3 to 0.5 m/sec, or about ½₅₀ the velocity in very large nerve fibers and about ¹⁄₁₀ the velocity in skeletal muscle fibers. The velocity of conduction in the specialized conductive system—the Purkinje fibers—varies from 0.02 to 4 m/sec in different parts of the system, which allows rapid conduction of the excitatory signal in the heart, as explained in Chapter 10.

Refractory Period of Cardiac Muscle. Cardiac muscle, like all excitable tissue, is refractory to restimulation during the action potential. Therefore, the refractory period of the heart is the interval of time, as shown to the left in Figure 9–4, during which a normal cardiac impulse cannot re-excite an already excited area of cardiac muscle. The normal refractory period of the ventricle is 0.25 to 0.3 second, which is about the duration of the action potential. There is an additional *relative refractory period* of about 0.05 second during which the muscle is more difficult than normal to excite but nevertheless can be excited, as demonstrated by the early premature contraction in the second example of Figure 9–4.

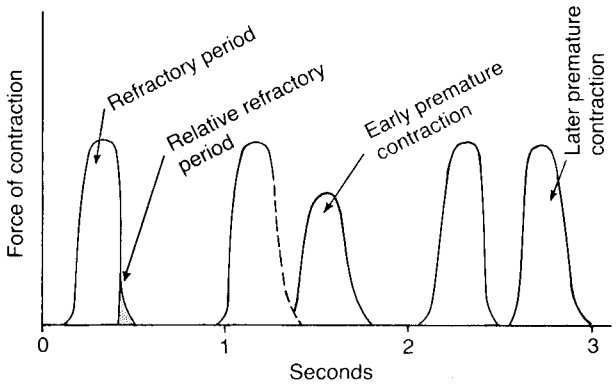

Figure 9–4. Contraction of the heart showing the durations of the refractory period and the relative refractory period, the effect of an early premature contraction, and the effect of a later premature contraction. Note that the premature contractions do not cause wave summation, as occurs in skeletal muscle.

The refractory period of atrial muscle is much shorter than that for the ventricles (about 0.15 second), and the relative refractory period is another 0.03 second. Therefore, the rhythmical rate of contraction of the atria can be faster than that of the ventricles.

Excitation-Contraction Coupling—Function of Calcium Ions and the Transverse Tubules

The term "excitation-contraction coupling" means the mechanism by which the action potential causes the myofibrils of muscle to contract. This is discussed for skeletal muscle in Chapter 7. Once again, there are differences in this mechanism in cardiac muscle that have important effects on the characteristics of cardiac muscle contraction.

As is true for skeletal muscle, when an action potential passes over the cardiac muscle membrane, the action potential also spreads to the interior of the cardiac muscle fiber along the membranes of the transverse (T) tubules. The T tubule action potentials in turn act on the membranes of the longitudinal sarcoplasmic tubules to cause instantaneous release of calcium ions into the muscle sarcoplasm from the sarcoplasmic reticulum. In another few thousandths of a second, these calcium ions diffuse into the myofibrils and catalyze the chemical reactions that promote sliding of the actin and myosin filaments along one another; this in turn produces the muscle contraction.

Thus far, this mechanism of excitation-contraction coupling is the same as that for skeletal muscle, but

there is a second effect that is quite different. In addition to the calcium ions released into the sarcoplasm from the cisternae of the sarcoplasmic reticulum, a large quantity of extra calcium ions diffuses into the sarcoplasm from the T tubules themselves at the time of the action potential. Indeed, without this extra calcium from the T tubules, the strength of cardiac muscle contraction would be considerably reduced because the sarcoplasmic reticulum of cardiac muscle is less well developed than that of skeletal muscle and does not store enough calcium to provide full contraction. On the other hand, the T tubules of cardiac muscle have a diameter 5 times as great as that of the skeletal muscle tubules, which means a volume 25 times as great. Also, inside the T tubules is a large quantity of mucopolysaccharides that are electronegatively charged and bind an abundant store of even more calcium ions, keeping them always available for diffusion to the interior of the cardiac muscle fiber when the T tubule action potential occurs.

The strength of contraction of cardiac muscle depends to a great extent on the concentration of calcium ions in the extracellular fluids. The reason for this is that the ends of the T tubules open directly to the outside of the cardiac muscle fibers, allowing the same extracellular fluid that is in the cardiac muscle interstitium to percolate through the T tubules as well. Consequently, the quantity of calcium ions in the T tubule system—that is, the availability of calcium ions to cause cardiac muscle contraction—depends to a great extent on the extracellular fluid calcium ion concentration.

By way of contrast, the strength of skeletal muscle contraction is hardly affected by the extracellular fluid calcium concentration because its contraction is caused almost entirely by calcium ions released from the sarcoplasmic reticulum inside the skeletal muscle fiber itself.

At the end of the plateau of the cardiac action potential, the influx of calcium ions to the interior of the muscle fiber is suddenly cut off, and the calcium ions in the sarcoplasm are rapidly pumped back into both the sarcoplasmic reticulum and the T tubules. As a result, the contraction ceases until a new action potential occurs.

Duration of Contraction. Cardiac muscle begins to contract a few milliseconds after the action potential begins and continues to contract until a few milliseconds after the action potential ends. Therefore, the duration of contraction of cardiac muscle is mainly a function of the duration of the action potential—about 0.2 second in atrial muscle and 0.3 second in ventricular muscle.

Effect of Heart Rate on Duration of Contraction. When the heart rate increases, the duration of each total cycle of the heart, including both the contraction phase and the relaxation phase, decreases. 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 per minute, the period of contraction is about 0.40 of the entire cycle. At three times normal heart rate, this period is about 0.65 of the entire cycle, which means that the heart beating at a very fast rate sometimes does not remain relaxed long enough to allow complete filling of the cardiac chambers before the next contraction.

THE 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 rapidly through both atria and thence through the A-V bundle into the ventricles. Because of a special arrangement of the conducting system from the atria into the ventricles, there is a delay of more than 1/10 second between passage of the cardiac impulse from the atria into the ventricles. This allows the atria to contract ahead of the ventricles, thereby pumping blood into the ventricles before the strong ventricular contraction. Thus, the atria act as *primer pumps* for the ventricles, and the ventricles then provide the major source of power for moving blood through the vascular system.

Systole and Diastole

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.*

Figure 9–5 shows the different events during the cardiac cycle. The top three curves show the pressure changes in the aorta, left ventricle, and left atrium, respectively. The fourth curve depicts the changes in ventricular volume, the fifth the electrocardiogram, and the sixth 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 the diagram of this figure and understand the causes of all the events shown.

Relationship of the Electrocardiogram to the Cardiac Cycle

The electrocardiogram in Figure 9–5 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 the *spread of depolarization* through the atria, and this is followed by atrial contraction, which causes a slight rise in the atrial pressure curve immediately after the P wave. About 0.16 second after the onset of the P wave, the *QRS waves* appear as a result of depolarization of the ventricles, which initiates contraction of the ventricles and causes the ventricular pressure to begin

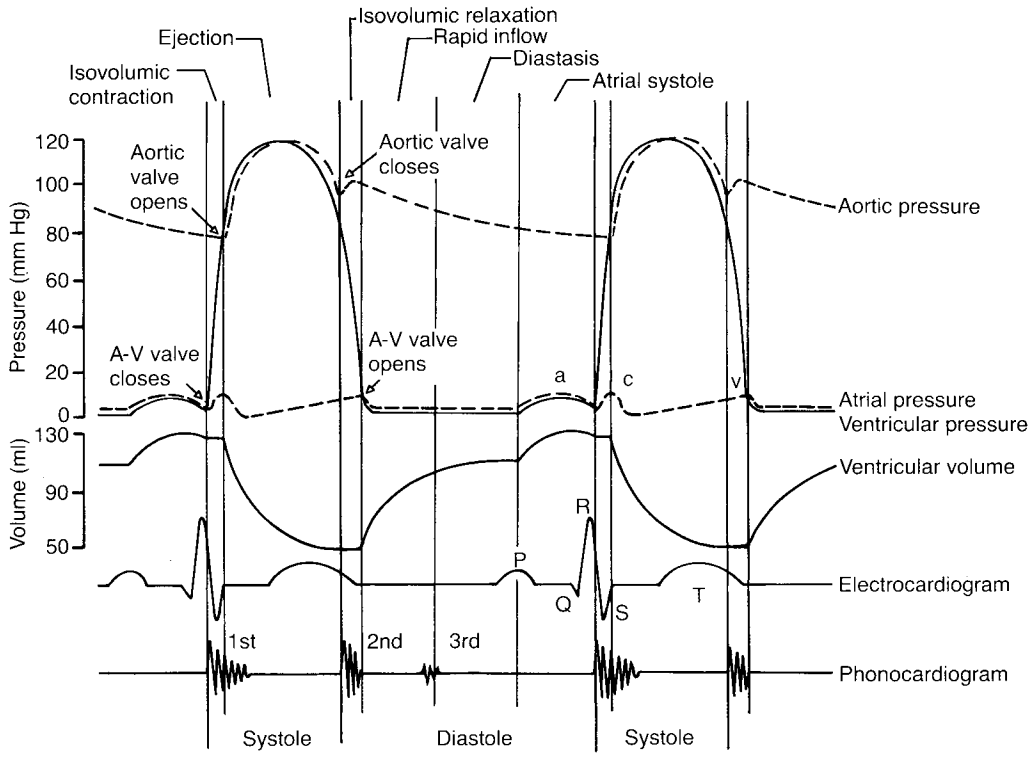

Figure 9–5. Events of the cardiac cycle for left ventricular function showing changes in left atrial pressure, left ventricular pressure, aortic pressure, ventricular volume, the electrocardiogram, and the phonocardiogram.

rising, as also shown in the figure. Therefore, the QRS complex begins slightly before the onset of ventricular systole.

Finally, one observes the *ventricular T wave* in the electrocardiogram. This represents the stage of repolarization of the ventricles at which time the ventricular muscle fibers begin to relax. Therefore, the T wave occurs slightly before the end of ventricular contraction.

Function of the Atria as Primer Pumps

Blood normally flows continually from the great veins into the atria; about 75 per cent of the blood flows directly through the atria into the ventricles even before the atria contract. Then, atrial contraction usually causes an additional 25 per cent filling of the ventricles. Therefore, the atria simply function as primer pumps that increase the ventricular pumping effectiveness as much as 25 per cent. Yet the heart can continue to operate satisfactorily under most conditions even without this extra 25 per cent effectiveness because it normally has the capability of pumping 300 to 400 per cent more blood than is required by the 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—The a, c, and v Waves. In the atrial pressure curve of Figure 9–5, three major pressure elevations, called the *a*, *c*, and *v atrial pressure waves*, can be noted.

The *a wave* is caused by atrial contraction. Ordinarily, the *right* atrial pressure rises 4 to 6 mm Hg during atrial contraction, whereas the *left* atrial pressure rises 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 probably 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 blood to flow rapidly into the ventricles and causing the v wave to disappear.

Function of the Ventricles as Pumps

Filling of the Ventricles. During ventricular systole, large amounts of blood accumulate in the atria because of the closed A-V valves. Therefore, just as soon as systole is over and the ventricular pressures fall again to their low diastolic values, the moderately increased pressures in the atria immediately push the A-V valves open and allow blood to flow rapidly into the ventricles, as shown by the rise of the *ventricular*

volume curve in Figure 9–5. This 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 on 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 accounts for about 25 per cent of the filling of the ventricles during each heart cycle.

Emptying of the Ventricles During Systole

Period of Isovolumic (Isometric) Contraction. Immediately after ventricular contraction begins, the ventricular pressure abruptly rises, as shown in Figure 9–5, 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 there is no emptying. This period is called the period of *isovolumic* or *isometric contraction,* meaning by these terms that tension is increasing in the muscle but no shortening of the muscle fibers is occurring. (This is not strictly true because there is apex-to-base shortening and circumferential elongation.)

Period of Ejection. When the left ventricular pressure rises slightly above 80 mm Hg (and the right ventricular pressure slightly above 8 mm Hg), the ventricular pressures now push the semilunar valves open. Immediately, blood begins to pour out of the ventricles, with about 70 per cent of the emptying occurring during the first third of the period of ejection and the remaining 30 per cent during the next two thirds. Therefore, the first third is called the *period of rapid ejection* and the last two thirds, the *period of slow ejection.*

For a peculiar reason, the ventricular pressure falls to a value slightly *below* that in the aorta during the period of slow ejection, despite the fact that some blood is still leaving the left ventricle. The reason is that the blood flowing out of the ventricle has built up momentum. As this momentum decreases during the latter part of systole, the kinetic energy of the momentum is converted into pressure in the aorta, which makes the arterial pressure slightly greater than the pressure inside the ventricle.

Period of Isovolumic (Isometric) Relaxation. At the end of systole, ventricular relaxation begins suddenly, allowing the intraventricular pressures to fall rapidly. The elevated pressures in the distended large arteries 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 fall rapidly 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, filling of the ventricles normally increases the volume of each ventricle to about 110 to 120 milliliters. This volume is known as 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 60 per cent.

When the heart contracts strongly, the end-systolic volume can fall to as little as 10 to 20 milliliters. On the other hand, when large amounts of blood flow into the ventricles during diastole, their end-diastolic volumes can become as great as 150 to 180 milliliters in the normal heart. And by both increasing the end-diastolic volume and decreasing the end-systolic volume, the stroke volume output can at times be increased to about double normal.

Function of the Valves

Atrioventricular Valves. The *A-V valves* (the *tricuspid* and the *mitral* valves) prevent backflow of blood from the ventricles to the atria during systole, and the *semilunar valves* (the *aortic* and *pulmonary* valves) prevent backflow from the aorta and pulmonary arteries into the ventricles during diastole. All these valves, which are shown in Figure 9–6, 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

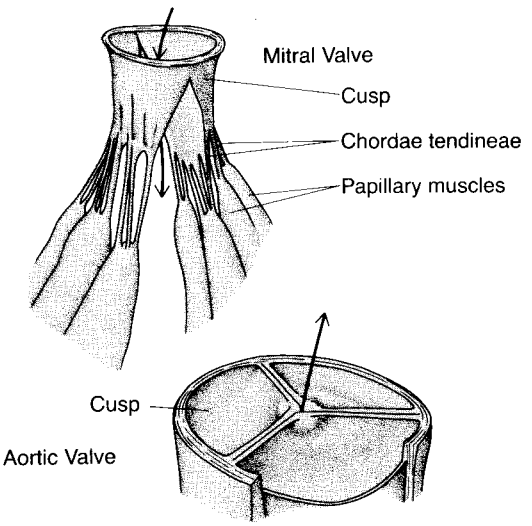

Figure 9–6. Mitral and aortic valves.

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 strong backflow for a few milliseconds.

Function of the Papillary Muscles. Figure 9–6 also shows the 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, sometimes so far that it leaks severely and results in severe or even lethal cardiac incapacity.

Aortic and Pulmonary Valves. The aortic and pulmonary 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 to the closed position in comparison with a 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 semilunar valves are subjected to much greater mechanical abrasion than are the A-V valves. And, 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 in Figure 9–6, that they are well adapted to withstand the extra physical stresses.

The Aortic Pressure Curve

When the left ventricle contracts, the ventricular pressure rises rapidly until the aortic valve opens. Then the pressure in the ventricle rises much less thereafter, as shown in Figure 9–5, because blood immediately flows out of the ventricle into the aorta.

The entry of blood into the arteries causes the walls of these arteries to stretch and the pressure to rise. Then, at the end of systole, after the left ventricle stops ejecting blood and the aortic valve closes, the elastic recoil of the arteries maintains a high pressure in the arteries even during diastole.

A so-called *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 then by sudden cessation of the backflow.

After the aortic valve has closed, pressure in the aorta falls slowly throughout diastole because 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 falls 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 curve in the pulmonary artery is similar to that 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 slowly developing process that makes no noise. However, when the valves close, the vanes of the valves and the surrounding fluids vibrate under the influence of the sudden pressure differentials that develop, giving off sound that travels in all directions through the chest.

When the ventricles contract, one first hears a sound that is caused by closure of the A-V valves. The vibration is low in pitch and relatively long continued and is known as the *first heart sound.* When the aortic and pulmonary valves close at the end of systole, one hears a relatively rapid snap because these valves close rapidly, and the surroundings vibrate for only a short period. This sound is known as the *second heart sound.*

Occasionally, one can hear an *atrial sound* when the atria beat because of vibrations associated with the flow of blood into the ventricles. Also, a *third heart sound* sometimes occurs at about the end of the first third of diastole, believed to be caused by blood flowing with a rumbling motion into the almost-filled ventricles. The precise causes of the heart sounds are discussed more fully in Chapter 23, in relation to auscultation.

Work Output of the Heart

Stroke Work Output and Minute Work Output. 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 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. This is the *kinetic energy of blood flow* component of the work output.

External Work (Volume-Pressure Work). The work performed by the left ventricle to raise the pressure of the blood during each heartbeat (the left ventricular external work output) is equal to the *stroke volume* times (*left ventricular mean ejection pressure* minus *mean left ventricular input pressure during diastolic filling*). When pressure is expressed in dynes per square centimeter and stroke volume in milliliters, the external work output is in ergs.

Right ventricular external work output is normally about one sixth the work output of the left ventricle because of the difference in systolic pressure against which the two ventricles must pump.

Kinetic Energy of Blood Flow. 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. That is,

$$\text{Kinetic energy} = \frac{mv^2}{2}$$

When the mass is expressed in *grams* of blood ejected and the velocity in *centimeters per second,* the work output is in *ergs.*

Ordinarily, the work output of the left ventricle required to create kinetic energy of blood flow is only about 1 per cent 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, such as aortic stenosis in which the blood flows with great velocity through the stenosed valve, more than 50 per cent of the total work output may be required to create kinetic energy of blood flow.

Graphical Analysis of Ventricular Pumping

Figure 9–7 shows a graphical diagram that is especially useful in explaining the pumping mechanics of the left ventricle. The most important components of the diagram are the two heavy black 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 quantities 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 preventing any outflow of blood from the heart and measuring the maximum systolic pressure that is achieved during ventricular contraction at each volume of filling.

Until the volume of the 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 diastolic pressure does increase rapidly, partly because of fibrous tissue in the heart that will stretch no more and partly because the pericardium that surrounds the heart becomes stretched nearly to its limit. During ventricular contraction, the systolic pressure increases rapidly at progressively greater ventricular volumes but 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, because at these great volumes, the actin and myosin filaments of the cardiac muscle fibers are pulled apart enough for the strength of cardiac fiber contraction to become less than optimal.

Note especially in the figure that the maximum systolic pressure for the normal unstimulated left ventricle is between 250 and 300 mm Hg, but this varies widely with strength of the heart. For the normal right ventricle, it is between 60 and 80 mm Hg.

"Volume-Pressure Diagram" During the Cardiac Cycle; Cardiac Work Output. The red curves in Figure 9–7 form a loop called the *volume-pressure diagram* of the cardiac cycle for the left ventricle. It is divided into four phases.

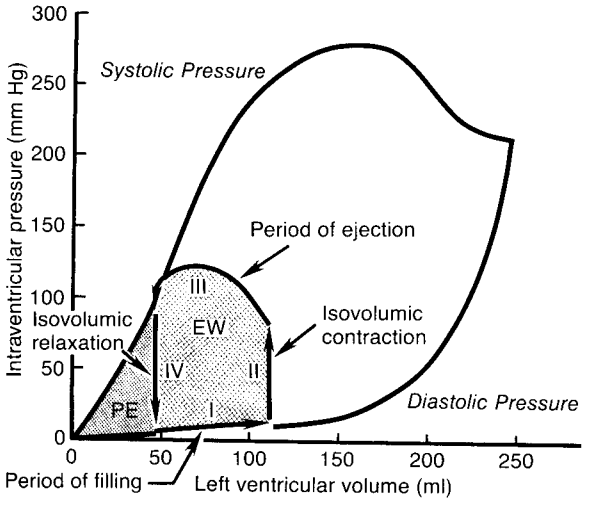

Figure 9–7. Relationship between left ventricular volume and intraventricular pressure during diastole and systole. Also shown by the heavy red lines is the "volume-pressure diagram" that demonstrates the changes in intraventricular volume and pressure during the cardiac cycle.

Phase I: *Period of filling.* This phase in the volume-pressure diagram begins at a ventricular volume of about 45 milliliters and a diastolic pressure near 0 mm Hg. Forty-five milliliters is the amount of blood that remains in the ventricle after the previous heartbeat and is called the *end-systolic volume.* As venous blood flows into the ventricle from the left atrium, the ventricular volume normally increases to about 115 milliliters, called the *end-diastolic volume,* an increase of 70 milliliters. Therefore, the volume-pressure diagram during phase I extends along the line labeled "I," with the volume increasing to 115 milliliters and the diastolic pressure rising to about 5 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 rises to equal the pressure in the aorta, a pressure value of about 80 mm Hg, as depicted by the line labeled "II."

Phase III: *Period of ejection.* During ejection, the systolic pressure rises even higher because of still more contraction of the heart. At the same time, the volume of the ventricle decreases because the aortic valve opens and blood now flows out of the ventricle into the aorta. Therefore, the curve labeled "III" 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, the aortic valve closes, and the ventricular pressure falls back to the diastolic pressure level. The line labeled "IV" traces this decrease in intraventricular pressure without any change in volume. Thus, the ventricle returns to its starting point, with about 45 milliliters of blood left in the ventricle and at an atrial pressure usually close to 0 mm Hg.

Work Output Calculated from the Volume-Pressure Diagram. Readers well trained in the basic principles of physics should recognize that the area subtended by this volume-pressure diagram (the right-hand portion of the shaded area, labeled EW) is representative of 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 work diagram becomes much larger. That is, it extends far to the right because the ventricle now fills with more blood during diastole, it rises much higher because the ventricle contracts with greater pressure, and it usually extends further 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 artery leading from the ventricle. In Figure 9–7, 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 severely altered from the normal.

Chemical Energy for Cardiac Contraction: Oxygen Utilization by the Heart

Heart muscle, like skeletal muscle, uses chemical energy to provide the work of contraction. This energy is derived mainly from oxidative metabolism of fatty acids and, to a lesser extent, 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 67 and 68.

Experimental studies on isolated hearts have shown that the oxygen consumption of the heart, and therefore the chemical energy expended during contraction, is directly related to the total shaded area of Figure 9–7. 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 output that could be accomplished by contraction of the ventricle if the ventricle should empty completely all the blood in its chamber with each contraction.

It has also been found experimentally that oxygen consumption is nearly proportional to the *tension* that occurs in the heart muscle during contraction *times* the *duration of time* that the contraction persists, called the *tension-time index*. Because tension is high when the 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 is especially important in heart failure because the ventricle is then dilated, and paradoxically, the amount of chemical energy required for a given amount of work output must be greater than ever even though the heart is already failing.

Efficiency of Cardiac Contraction. During muscle contraction, most of the chemical energy is converted into heat and a much smaller portion into work output. The ratio of work output to chemical energy expenditure is called the efficiency of cardiac contraction, or simply *efficiency of the heart*. The maximum efficiency of the normal heart is between 20 and 25 per cent. In heart failure, this may fall to as low as 5 to 10 per cent.

REGULATION OF HEART PUMPING

When a person is at rest, the heart pumps only 4 to 6 liters of blood each minute. During severe exercise, the heart may be required to pump four to seven times this amount. This section discusses the means by which the heart can adapt to such extreme increases in cardiac output.

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 the heart by the autonomic nervous system.

Intrinsic Regulation of Heart Pumping—The Frank-Starling Mechanism

In Chapter 20, we see that the amount of blood pumped by the heart each minute is determined 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 blood flow, and the total of all the local blood flow through all the peripheral tissues returns by way of the veins to the right atrium. The heart in turn automatically pumps this incoming blood into the systemic arteries, so that it can flow around the circuit again.

This intrinsic ability of the heart to adapt to changing volumes of inflowing blood is called the *Frank-Starling mechanism of the heart*, in honor of Frank and Starling, two great physiologists of nearly a century ago. Basically, the Frank-Starling mechanism means that the greater the heart muscle is stretched during filling, the greater will be the force of contraction and the greater will be the quantity of blood pumped into the aorta. Or another way to express this is: *Within physiological limits, the heart pumps all the blood that comes to it without allowing excessive damming of blood in the veins.*

What Is the Explanation of the Frank-Starling Mechanism? When an extra amount of blood flows into the ventricles, the cardiac muscle itself is stretched to a greater length. This in turn causes the muscle to contract with increased force because the actin and myosin filaments are then brought to a more nearly optimal degree of interdigitation 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 force is characteristic of all striated muscle, as explained in Chapter 6, not simply of cardiac muscle.

In addition to the important effect of stretching 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 per cent; this, too, helps increase the amount of blood pumped each minute, although its contribution is much less than that of the Frank-Starling mechanism.

Lack of Effect on Cardiac Output of Changes in Arterial Pressure Load. One of the most important consequences of the Frank-Starling mechanism of the heart is that, within reasonable limits, changes in the arterial pressure against which the heart pumps have almost no effect on the rate at which blood is pumped by the heart each minute (the cardiac output). This effect is shown in Figure 9–8, which is a curve extrapolated to the human from data in dogs in which the arterial pressure was progressively changed by constricting the aorta, while the cardiac output was measured simultaneously. The significance of this effect is the following: Regardless of the arterial pressure load up to a reasonable limit, the important factor that determines the amount of blood pumped by the heart is still the rate of entry of blood into the heart.

Ventricular Function Curves

One of the best ways to express the functional ability of the ventricles to pump blood is by ventricular function curves, as shown in Figures 9–9 and 9–10. Figure 9–9 shows a type of ventricular function curve called the *stroke work output curve.* Note that as the atrial pressures increase, the stroke work outputs also increase until they reach the limit of the heart's ability.

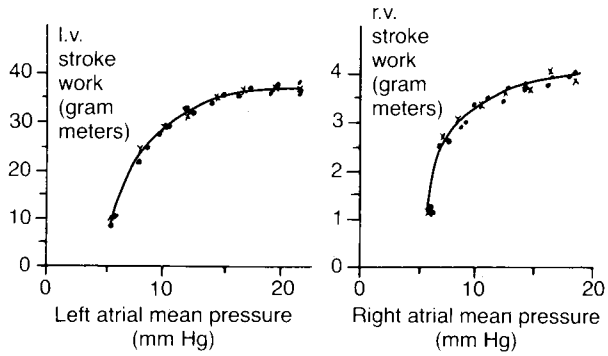

Figure 9–9. Left and right ventricular function curves in a dog depicting ventricular stroke work output as a function of left and right mean atrial pressures. (Curves reconstructed from data in Sarnoff: *Physiol. Rev. 35:*107, 1955.)

Figure 9–10 shows another type of ventricular function curve called the *minute ventricular output curve.* These two curves represent function of the two ventricles of the human heart based on data extrapolated from lower animals. As each atrial pressure rises, the respective ventricular volume output per minute also increases.

Thus, ventricular function curves are another way of expressing the Frank-Starling mechanism of the heart. That is, as the ventricles fill to higher atrial pressures, the ventricular volume and strength of cardiac 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 is highly controlled by the *sympathetic* and *parasympathetic* (vagus) nerves, which abundantly supply the heart, as

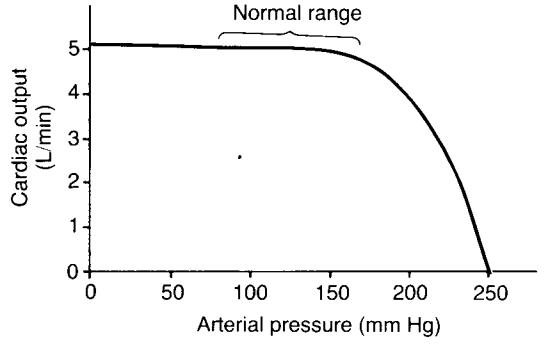

Figure 9–8. Constancy of cardiac output even in the face of wide changes in arterial pressure up to a pressure level of 160 mm Hg. Only when the arterial pressure rises above the normal operating pressure range does the pressure load cause the heart output to fall.

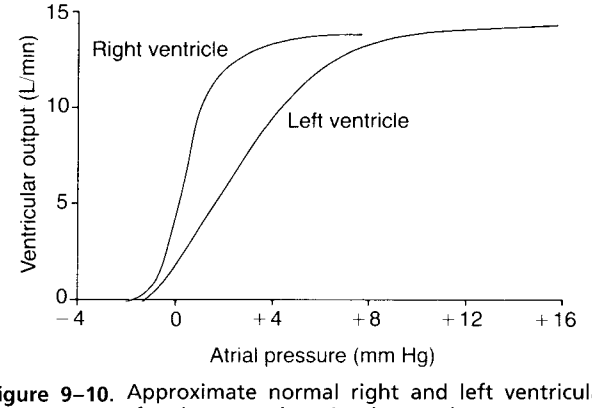

Figure 9–10. Approximate normal right and left ventricular output curves for the normal resting human heart as extrapolated from data obtained in dogs.

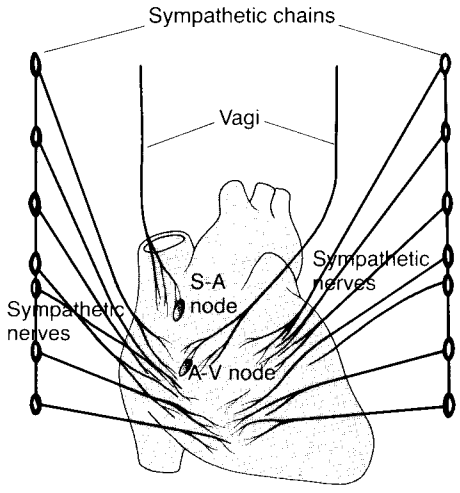

Figure 9–11. Cardiac nerves.

shown in Figure 9–11. The amount of blood pumped by the heart each minute, the *cardiac output,* can often be increased more than 100 per cent by sympathetic stimulation. By contrast, it can be decreased to as low as zero or almost zero by vagal (parasympathetic) stimulation.

Excitation of the Heart by the Sympathetic Nerves. Strong sympathetic stimulation can increase the heart rate in adult humans to 180 to 200 and, rarely, even 250 beats per minute in young people. Also, sympathetic stimulation increases the force with which the heart muscle contracts, therefore increasing the volume of blood pumped and increasing the ejection pressure. Thus, sympathetic stimulation can often increase the cardiac output as much as twofold to threefold, in addition to the increased output that might be caused by the Frank-Starling mechanism already discussed.

On the other hand, inhibition of the sympathetic nervous system can be used to decrease cardiac pumping to a moderate extent in the following way: Under normal conditions, the sympathetic nerve fibers to the heart discharge continuously at a slow rate that maintains pumping at about 30 per cent above that with no sympathetic stimulation. Therefore, when the activity of the sympathetic nervous system is depressed below normal, this decreases both the heart rate and the strength of ventricular contraction, thereby decreasing the level of cardiac pumping to as much as 30 per cent below normal.

Parasympathetic (Vagal) Stimulation of the Heart. Strong vagal stimulation of 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 per minute thereafter. In addition, strong vagal stimulation can decrease the strength of heart contraction by 20 to 30 per cent. This decrease is not greater because the vagal fibers are distributed mainly to the atria but not much to the ventricles where the power contraction of the heart occurs. Nevertheless, the great decrease in heart rate combined with a slight decrease in heart contraction can decrease ventricular pumping 50 or more per cent, especially so when the heart is working under great workload.

Effect of Sympathetic or Parasympathetic Stimulation on the Cardiac Function Curve. Figure 9–12 shows four cardiac function curves. They are much the same as the ventricular function curves of Figure 9–10. However, they represent function of the entire heart rather than of a single ventricle; they show the relation between the right atrial pressure at the input of the heart and cardiac output into the aorta.

The curves of Figure 9–12 demonstrate that at any given right atrial pressure, the cardiac output increases with increasing sympathetic stimulation and decreases with increasing parasympathetic stimulation. The changes in output caused by nerve stimulation result from *changes in heart rate* and *changes in contractile strength of the heart* because both of these affect cardiac output.

Effect of Heart Rate on Function of the Heart as a Pump

In general, the more times the heart beats per minute, the more blood it can pump, but there are important limitations to this effect. For instance, once the heart rate rises above a critical level, the heart strength itself decreases, presumably because of overuse of metabolic substrates in the cardiac muscle. In addition, the period of diastole between the contractions becomes so reduced that blood does not have time to flow adequately from the atria into the ventricles. For these reasons, when the heart rate is increased artificially by *electrical stimulation,* the normal large animal heart has its peak ability to pump large quantities of blood at a heart rate between 100 and 150 beats per minute. On the other hand, when its rate is increased by *sympathetic stimulation,* it reaches its peak ability

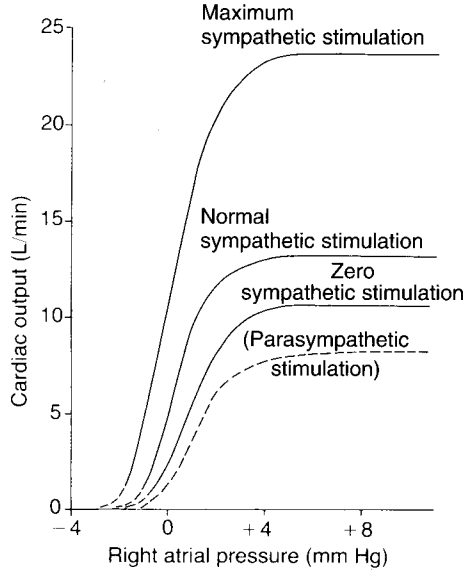

Figure 9–12. Effect on the cardiac output curve of different degrees of sympathetic and parasympathetic stimulation.

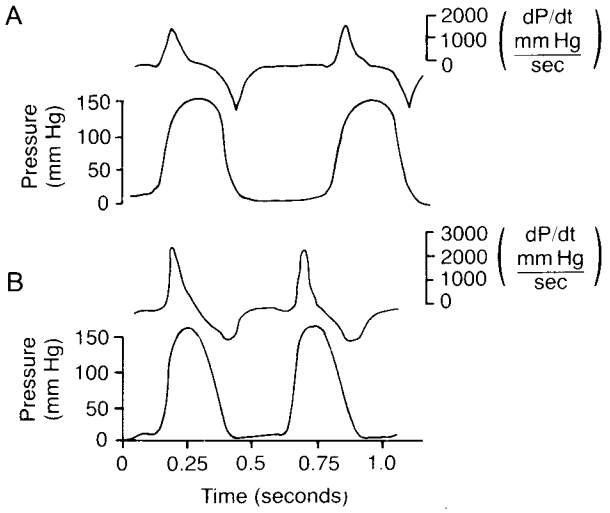

Figure 9–13. Simultaneous recordings of ventricular pressure and dP/dt. *A* shows results from a normal heart, and *B* shows results from a heart stimulated by isoproterenol. (Modified from Mason et al., in Sodeman and Sodeman (eds.): Pathologic Physiology. 6th Ed. Philadelphia, W.B. Saunders Company, 1979.)

to pump blood at a heart rate between 170 and 220 beats per minute. The reason for this difference is that sympathetic stimulation not only increases the heart rate but also increases heart strength. At the same time, it decreases the duration of systolic contraction and allows more time for filling during diastole.

Assessment of Cardiac Contractility

Although it is easy to determine the heart rate by simply timing the pulse, it has always been difficult to determine the strength of contraction of the heart, commonly called *cardiac contractility.* The change in contractility often is exactly opposite to the change in heart rate. Indeed, this effect occurs almost invariably in heart-debilitating diseases.

One of the ways in which cardiac contractility can be determined with great precision is to record one or more of the cardiac function curves. This can be done easily only in laboratory animals. Therefore, many physiologists and clinicians have searched for methods to assess the cardiac contractility in a simple way in the human being. One of these methods is to determine the so-called dP/dt.

dP/dt as a Measure of Cardiac Contractility. dP/dt means the *rate of change of the ventricular pressure* with respect to time. The dP/dt record is generated by an electronic computer that *differentiates* the measured ventricular pressure wave, thus giving a record of the *rate of change of the ventricular pressure.* Figure 9–13 shows two recordings of the ventricular pressure wave as well as simultaneous recordings (in color) of the dP/dt. In the upper part of the figure, the heart was beating normally, and in the lower part, the heart had been stimulated by isoproterenol, a drug that has essentially the same effect on the heart as sympathetic stimulation.

Note in the upper record that at the same time the ventricular pressure is increasing at its most rapid rate, the recording of the dP/dt record reaches its greatest height. On the other hand, at the time the ventricular pressure is falling most rapidly, the dP/dt record reaches its lowest level. When the ventricular pressure is neither rising nor falling, the dP/dt record is at zero value.

Experimental studies have shown that the rate of rise of ventricular pressure, the dP/dt, in general correlates well with the strength of contraction of the ventricle. This effect is demonstrated by a comparison of the dP/dt record in the upper part of Figure 9–13 with that in the lower part, showing a much higher peak dP/dt in the lower record when the heart contractility was increased by isoproterenol. Thus, the *peak* dP/dt is often used as a means for comparing the contractilities of hearts in different functional states.

The quantitative value for peak dP/dt is also affected by factors that are not related to cardiac contractility. For instance, the value is increased by both increased input pressure to the left ventricle (the end-diastolic ventricular pressure), which is the *preload* of the ventricle, and the pressure in the aorta against which the heart is pumping the blood, called the *afterload.* Therefore, it is often difficult to use dP/dt as a measure of contractility in comparing hearts from one person to another because one of these factors may differ. For this reason, other quantitative measures have been used in attempts to assess cardiac contractility. One of these has been to use dP/dt divided by the instantaneous pressure in the ventricle, or (dP/dt)/P.

Effect of Potassium and Calcium Ions on Heart Function

In the discussion of membrane potentials in Chapter 5, it is pointed out that potassium ions have a marked effect on membrane potentials and action potentials, and in Chapter 6, it is 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 these two ions in the extracellular fluids also has important effects on cardiac pumping.

Effect of Potassium Ions. Excess potassium in the extracellular fluids causes the heart to become extremely dilated and flaccid and slows the heart rate. Large quantities can also 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/liter—two to three times the normal value—can cause such weakness of the heart and abnormal rhythm that this can cause death.

These effects are caused partially by 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. As the membrane potential decreases, the intensity of the action potential also decreases, which makes the contraction of the heart progressively weaker.

Effect of Calcium Ions. An excess of calcium ions causes effects almost exactly opposite to those of potassium ions, causing the heart to go into spastic contraction. This is caused by the direct effect of calcium ions in exciting the cardiac contractile process, as

explained earlier in the chapter. Conversely, a deficiency of calcium ions causes cardiac flaccidity, similar to the effect of high potassium. Because the calcium ion levels in the blood are normally regulated within narrow ranges, these cardiac effects of abnormal calcium concentrations seldom are of clinical concern.

Effect of Temperature on the Heart

Increased temperature, as occurs when one has fever, causes greatly increased heart rate, sometimes to as great as double normal. Decreased temperature causes greatly decreased heart rate, falling to as low as a few beats per minute when a person is near death from hypothermia in the range of 60° to 70°F (15.5° to 21.1°C). These effects presumably result from the fact that heat causes increased permeability of the muscle membrane to the ions, resulting in acceleration of the self-excitation process.

Contractile strength of the heart is often enhanced temporarily by a moderate increase in temperature, but prolonged elevation of the temperature exhausts the metabolic systems of the heart and causes weakness.

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(See also Chapter 10.)