CHAPTER 13

The Electrical Activity of the Heart

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CHAPTER OUTLINE

KEY CONCEPTS

1. The electrical activity of cardiac cells is caused by the selective opening and closing of plasma membrane channels for sodium, potassium, and calcium ions.
2. Depolarization is achieved by the opening of sodium and calcium channels and the closing of potassium channels.
3. Repolarization is achieved by the opening of potassium channels and the closing of sodium and calcium channels.
4. Pacemaker potentials are achieved by the opening of channels for sodium and calcium ions and the closing of channels for potassium ions.
5. Electrical activity is normally initiated in the sinoatrial (SA) node where pacemaker cells reach threshold first.
6. Electrical activity spreads across the atria, through the atrioventricular (AV) node, through the Purkinje system, and to ventricular muscle.
7. Norepinephrine increases pacemaker activity and the speed of action potential conduction.
8. Acetylcholine decreases pacemaker activity and the speed of action potential conduction.
9. Voltage differences between repolarized and depolarized regions of the heart are recorded by an electrocardiogram (ECG).
10. The ECG provides clinically useful information about rate, rhythm, pattern of depolarization, and mass of electrically active cardiac muscle.

The heart beats in the absence of any nervous connections because the electrical (pacemaker) activity that generates the heartbeat resides within the cardiac muscle. After initiation, the electrical activity spreads throughout the heart, reaching every cardiac cell rapidly with the correct timing. This enables coordinated contraction of individual cells.

The electrical activity of cardiac cells depends on the ionic gradients across their plasma membranes and changes in permeability to selected ions brought about by the opening and closing of cation channels. This chapter describes how these ionic gradients and changes in membrane permeability result in the electrical activity of individual cells and how this electrical activity is propagated throughout the heart.

THE IONIC BASIS OF CARDIAC ELECTRICAL ACTIVITY: THE CARDIAC MEMBRANE POTENTIAL

The cardiac membrane potential is divided into 5 phases, phases 0 to 4 (Fig. 13.1). Phase 0 is the rapid upswing of the action potential; phase 1 is the small repolarization just after rapid depolarization; phase 2 is the plateau of the action potential; phase 3 is the repolarization to the resting membrane potential; and phase 4 is the resting membrane potential in atrial, ventricular, and Purkinje cells and the pacemaker potential in nodal cells. In resting ventricular muscle cells, the potential inside the membrane is stable at approximately −90 mV relative to the outside of the cell (see phase 4, Fig. 13.1A). When the cell is brought to threshold, an action potential occurs (see Chapter 3). First, there is a rapid depolarization from −90 mV to +20 mV (phase 0). This is followed by a slight decline in membrane potential (phase 1) to a plateau (phase 2), at which time the membrane potential is close to 0 mV. Next, rapid repolarization (phase 3) returns the membrane potential to its resting value (phase 4).

In contrast to ventricular cells, cells of the **sinoatrial (SA) node** and **atrioventricular (AV) node** exhibit a progressive depolarization during phase 4 called the **pacemaker potential** (see Fig. 13.1B). When the membrane po-

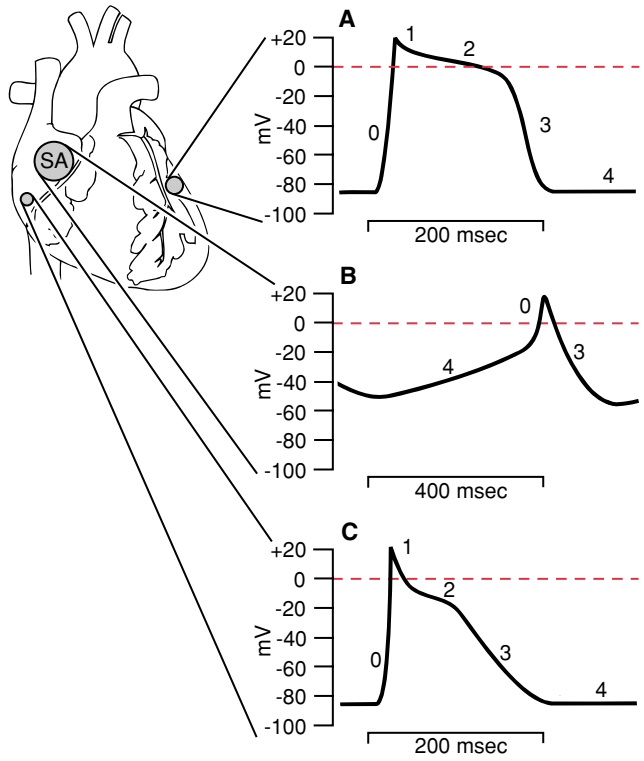

FIGURE 13.1 **Cardiac action potentials (mV) recorded from A, ventricular,** B, sinoatrial, and **C,** atrial cells. Note the difference in the time scale of the sinoatrial cell. Numbers 0 to 4 refer to the phases of the action potential (see text).

tential reaches threshold potential, there is a rapid depolarization (phase 0) to approximately +20 mV. The membrane subsequently repolarizes (phase 3) without going through a plateau phase, and the pacemaker potential resumes. Other myocardial cells combine various characteristics of the electrical activity of these two cell types. Atrial cells, for example (see Fig. 13.1C), have a steady diastolic resting membrane potential (phase 4) but lack a definite plateau (phase 2).

The Cardiac Membrane Potential Depends on Transmembrane Movements of Sodium, Potassium, and Calcium

The membrane potential of a cardiac cell depends on concentration differences in Na^+, K^+, and Ca^{2+} across the cell membrane and the opening and closing of channels that transport these cations. Some Na^+, K^+, and Ca^{2+} channels (voltage-gated channels) are opened and closed by changes in membrane voltage, and others (ligand-gated channels) are opened by a neurotransmitter, hormone, metabolite, and/or drug. Tables 13.1 and 13.2 list the major membrane channels responsible for conducting the ionic currents in cardiac cells.

The ion concentration gradients that determine transmembrane potentials are created and maintained by active transport. The transport of Na^+ and K^+ is accomplished by the plasma membrane Na^+/K^+-ATPase (see Chapter 2). Calcium is partially transported by means of a Ca^{2+}-ATPase and partially by an antiporter that uses energy derived from the Na^+ electrochemical gradient to remove Ca^{2+} from the cell. If the energy supply of myocardial cells is restricted by inadequate coronary blood flow, ATP synthesis (and, in turn, active transport) may be impaired. This situation leads to a reduction in ionic concentration gradients that eventually disrupts the electrical activity of the heart.

The magnitude of the intracellular potential depends on the relative permeability of the membrane to Na^+, Ca^{2+}, and K^+. The relative permeability to these cations at a particular time depends on which of the various cation channels listed in Table 13.1 are open. For example, during rest, mostly K^+ channels are open and the measured potential is close to that which would exist if the membrane were per-

TABLE 13.1 **Major Channels Involved in Purkinje and Ventricular Myocyte Membrane Potentials**

Name	Voltage (V)- or Ligand(L)-Gated	Functional Role
Voltage-gated Na^+ channel (fast, I_{Na})	V	Phase 0 of action potential (permits influx of Na^+)
Voltage-gated Ca^{2+} channel (long-lasting, I_{CaL})	V	Contributes to phase 2 of action potential (permits influx of Ca^{2+}) when membrane is depolarized). β-adrenergic agents increase the probability of channel opening and raise Ca^{2+} influx. ACh lowers the probability of channel opening.
Inward rectifying K^+ channel (i_{K1})	V	Maintains resting membrane potential (phase 4) by permitting outflux of K^+ at highly negative membrane potentials.
Outward (transient) rectifying K^+ channel (i_{to1})	V	Contributes briefly to phase 1 by transiently permitting outflux of K^+ at positive membrane potentials.
Outward (delayed) rectifying K^+ channels (i_{Kr}, i_{Ks})	V	Cause phase 3 of action potential by permitting outflux of K^+ after a delay when membrane depolarizes. I_{Kr} channel is also called HERG channel.
G protein-activated K^+ channel ($i_{K.G}$, $i_{K.ACh}$, $i_{K.ado}$)	L	G protein operated channel, opened by ACh and adenosine. This channel hyperpolarizes membrane during phase 4 and shortens phase 2.

TABLE 13.2 Major Channels Involved in Nodal Membrane Potentials

Name	Voltage (V)- or Ligand(L)-Gated	Functional Role
Voltage-gated Ca^{2+} channel (long-lasting, i_{CaL})	V	Phase 0 of action potential of SA and AV nodal cells (carries influx of Ca^{2+} when membrane is depolarized); contributes to early pacemaker potential of nodal cells. β-adrenergic agents increase the probability of channel opening and raise Ca^{2+} influx. ACh lowers the probability of channel opening.
Voltage-gated Ca^{2+} channel (transient, i_{CaT})	V	Contributes to the pacemaker potential.
Mixed cation channel (funny, I_f)	V	Carries Na^+ (mostly) and K^+ inward when activated by hyperpolarization. Contributes to pacemaker potential.
K^+ channel (delayed outward rectifier, i_K)	V	Contributes to phase 3 of action potential. Closing early in phase 4 contributes to pacemaker potential.
G protein-activated K^+ channel ($i_{K.G}$, $i_{K.ACh}$, $i_{K.ado}$)	L	G protein operated channel, opened by ACh and adenosine. This channel hyperpolarizes membrane during phase 4, slowing pacemaker potential.

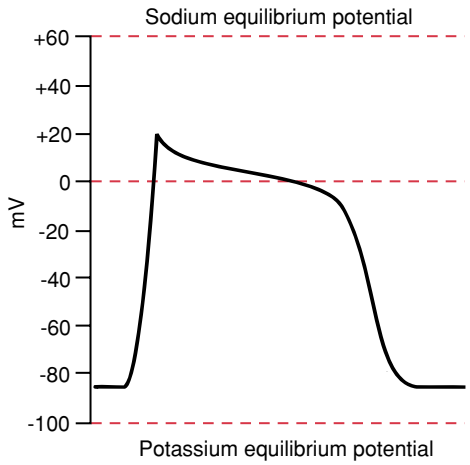

FIGURE 13.2 Effect of ionic permeability on membrane potential, primarily determined by the relative permeability of the membrane to Na^+, K^+, and Ca^{2+}. Relatively high permeability to K^+ places the membrane potential close to the K^+ equilibrium potential, and relatively high permeability to Na^+ places it close to the Na^+ equilibrium potential. The same is true for Ca^{2+}. An equilibrium potential is not shown for Ca^{2+} because, unlike Na^+ and K^+, it changes during the action potential. This is because cytosolic Ca^{2+} concentration changes approximately 5-fold during excitation. During the plateau of the action potential, the equilibrium potential for Ca^{2+} is approximately +90 mV. Membrane permeability to Na^+, K^+, and Ca^{2+} depends on ion channel proteins (see Table 13.1).

meable only to K^+ (potassium equilibrium potential). In contrast, when open Na^+ channels predominate (as occurs at the peak of phase 0 of the action potential), the measured potential is closer to the potential that would exist if the membrane were permeable only to Na^+ (sodium equilibrium potential) (see Fig. 13.2). The opening of Ca^{2+} channels causes the membrane potential to be closer to the calcium equilibrium potential, which is also positive; this occurs in phase 2. Specific changes in the number of open channels for these three cations are responsible for changes in membrane permeability and the different phases of the action potential.

The Opening and Closing of Cation Channels Causes the Ventricular Action Potential

In the normal heart, the sodium-potassium pump and calcium ion pump keep the ionic gradients constant. With constant ion gradients, the opening and closing of cation channels and the resulting changes in membrane permeability determine the membrane potential. Figures 13.3 and 13.4 depict the membrane changes that occur during an action potential in ventricular cells.

Depolarization Early in the Action Potential: Selective Opening of Sodium Channels. Depolarization occurs when the membrane potential moves away from the K^+ equilibrium potential and toward the Na^+ equilibrium potential. In ventricular cell membranes, this occurs passively at first, in response to the depolarization of adjacent membranes (discussed later). Once the ventricular cell membrane is brought to threshold, voltage-gated Na^+ channels open, causing the initial rapid upswing of the action potential (phase 0). The opening of Na^+ channels causes Na^+ permeability to increase. As permeability to Na^+ exceeds permeability to K^+, the membrane potential approaches the Na^+ equilibrium potential, and the inside of the cell becomes positively charged relative to the outside.

Phase 1 of the ventricular action potential is caused by a decrease in the number of open Na^+ channels and the opening of a particular type of K^+ channel (see Fig. 13.3 and Table 13.1). These changes tend to repolarize the membrane slightly.

Late Depolarization (Plateau): Selective Opening of Calcium Channels and Closing of Potassium Channels. The plateau of phase 2 results from a combination of the closing of K^+ channels (see Fig. 13.3 and Table 13.1) and the opening of voltage-gated Ca^{2+} channels. These chan-

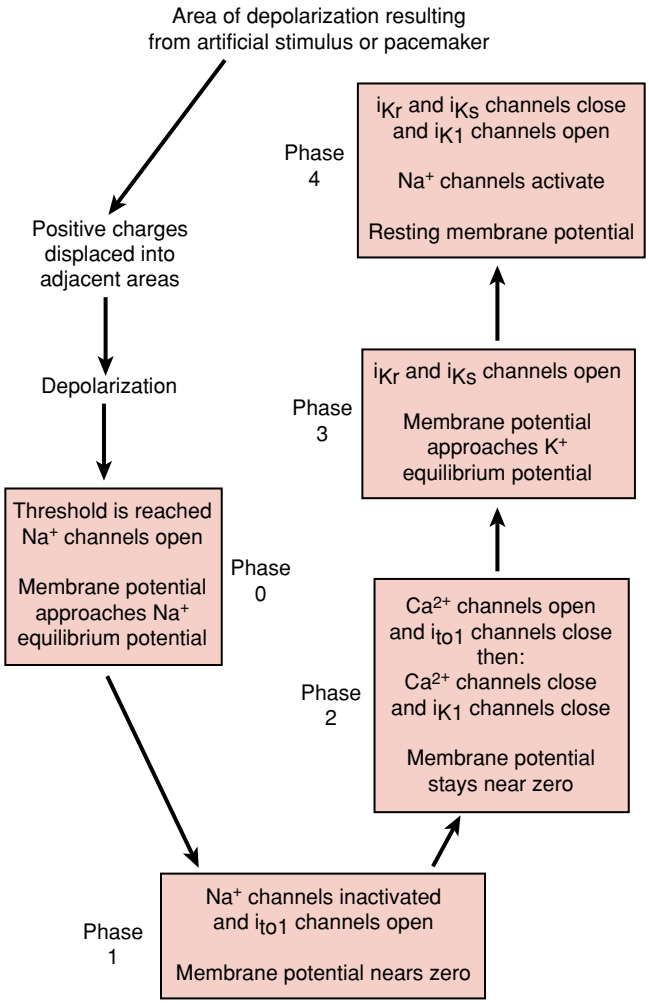

FIGURE 13.3 **Events associated with the ventricular action potential.** (See Table 13.1 for channel details.)

nels open more slowly than voltage-gated Na^+ channels and do not contribute to the rapid upswing of the ventricular action potential.

Repolarization: Selective Opening of Potassium Channels. The return of the membrane potential (phase 3, or repolarization) to the resting state is caused by the closing of Ca^{2+} channels and the opening of particular classes of K^+ channels (see Fig. 13.3 and Table 13.1). This relative increase in permeability to K^+ drives the membrane potential toward the K^+ equilibrium potential.

Resting Membrane Potential: Open Potassium Channels. The resting (diastolic) membrane potential (phase 4) of ventricular cells is maintained primarily by K^+ channels that are open at highly negative membrane potentials. They are called inward rectifying K^+ channels because, when the membrane is depolarized (e.g., by the opening of voltage-gated Na^+ channels), they do not permit outward movement of K^+. Other specialized K^+ channels help stabilize the resting membrane potential (see Table 13.1) and, in their absence, serious disorders of cardiac electrical activity can develop.

The Opening of Na^+ and Ca^{2+} and the Closing of K^+ Channels Causes the Pacemaker Potential of the SA and AV Nodes

When the electrical activity of a cell from the SA or AV node is compared with that of a ventricular muscle cell, three important differences are observed (see Fig. 13.1, Fig. 13.5): (1) the presence of a pacemaker potential, (2) the slow rise of the action potential, and (3) the lack of a well-defined plateau. The pacemaker potential results from changes in the permeability of the nodal cell membrane to all three of the major cations (see Table 13.2). First, K^+ channels, primarily responsible for repolarization, begin to close. Second, there is a steady increase in the membrane

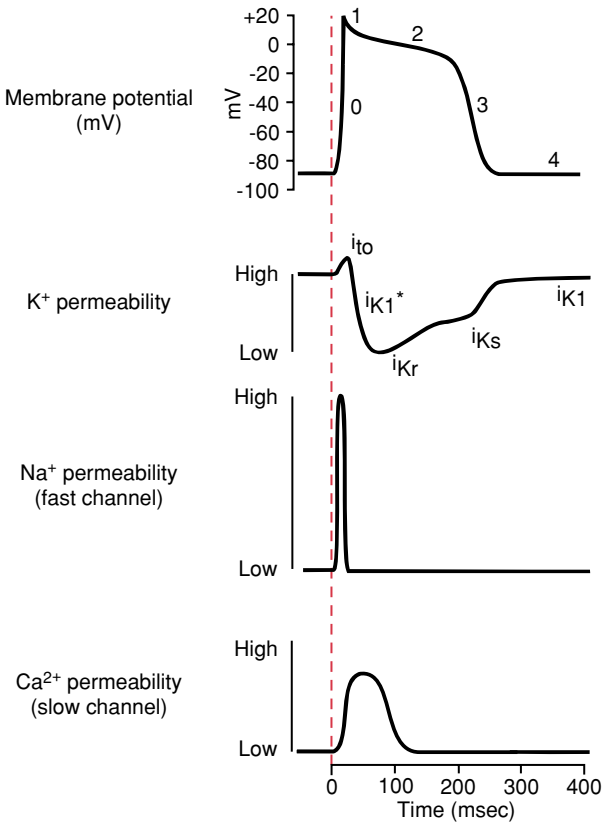

FIGURE 13.4 **Changes in cation permeabilities during a Purkinje fiber action potential (compare with Fig. 13.3).** The rise in action potential (phase 0) is caused by rapidly increasing Na^+ current carried by voltage-gated Na^+ channels. Na^+ current falls rapidly because voltage-gated Na^+ channels are inactivated. K^+ current rises briefly because of opening of i_{to1} channels and then falls precipitously because i_{K1} channels are closed by depolarization (*closing of i_{K1} channels). Ca^{2+} channels are opened by depolarization and are responsible, along with closed i_{K1} channels, for phase 2. K^+ current begins to increase because i_{Kr} and i_{Ks} channels are opened by depolarization, after a delay. Once repolarization occurs, Na^+ channels are activated. Reopened i_{K1} channels maintain phase 4.

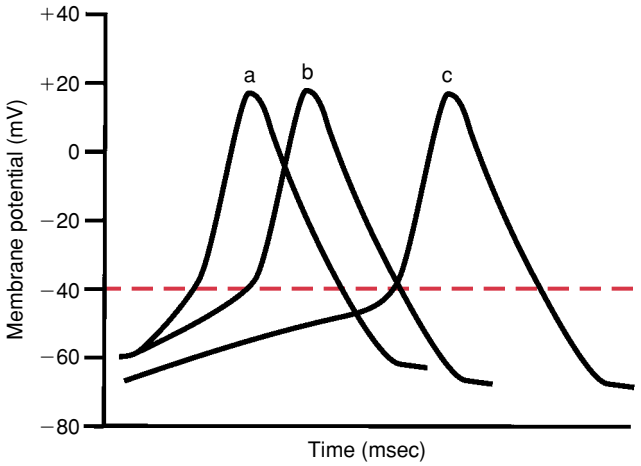

FIGURE 13.5 **Sinoatrial plasma membrane potential as a function of time.** Normal pacemaker potential (b) is affected by norepinephrine (a) and acetylcholine (c). The dashed line indicates threshold potential. The more rapidly rising pacemaker potential in the presence of norepinephrine (a) results from increased Na^+ permeability. The hyperpolarization and slower rising pacemaker potential in the presence of ACh results from decreased Na^+ permeability and increased K^+ permeability, due to the opening of ACh-activated K^+ channels.

permeability to Na^+ caused by the opening of a cation channel. Third, calcium moves in through the voltage-gated Ca^{2+} channel early in diastole. All three of these changes move the membrane potential in a positive direction toward the Na^+ and Ca^{2+} equilibrium potentials. An action potential is triggered when threshold is reached. This action potential rises more slowly than the ventricular action potential because the fast voltage-gated Na^+ channels play an insignificant role. Instead, the opening of slow voltage-gated Ca^{2+} channels is primarily responsible for the upstroke of the action potential in nodal cells. The absence of a well-defined plateau occurs because K^+ channels open and pull the membrane potential toward the K^+ equilibrium potential.

Purkinje fibers are also capable of pacemaker activity, but the rate of depolarization during phase 4 is much slower than that of the nodal cells. In the normal heart, phase 4 of Purkinje fibers is usually thought to be a stable resting membrane potential.

The Refractory Period Is Caused by a Delay in the Reactivation of Na^+ Channels

As discussed in Chapter 10, cardiac muscle cells display long refractory periods and, as a result, cannot be tetanized by fast, repeated stimulation. A prolonged refractory period eliminates the possibility that a sustained contraction might occur and prevent the cyclic contractions required to pump blood. The refractory period begins with depolarization and continues until nearly the end of phase 3 (see Fig. 10.2). This occurs because the Na^+ channels that open to cause phase 0 close and are inactive until the membrane repolarizes.

Neurotransmitters and Other Ligands Can Influence Membrane Ion Conductance

The normal pacemaker cells are under the influence of **parasympathetic nerves** (vagus) and **sympathetic nerves** (cardioaccelerator). The vagus nerves release acetylcholine (ACh) and the cardioaccelerator nerves release norepinephrine at their terminals in the heart. ACh slows the heart rate by reducing the rate of spontaneous depolarization of pacemaker cells (see Fig. 13.5), increasing the time required to reach threshold. Slowed heart rate is called **bradycardia,** or when the heart rate is below 60 beats/min. ACh exerts this effect by increasing the number of open K^+ channels and decreasing the number of open channels carrying Na^+ and Ca^{2+}; both actions hold the pacemaker potential closer to the K^+ equilibrium potential.

In contrast, norepinephrine causes an increase in the slope of the pacemaker potential so that the threshold is reached more rapidly and the heart rate increases. Increased heart rate is called **tachycardia,** or when the heart rate is above 100 beats/min. Norepinephrine increases the slope of the pacemaker potential by opening channels carrying Na^+ and Ca^{2+} and closing K^+ channels. Both effects result in faster movement of the pacemaker potential toward the Na^+ and Ca^{2+} equilibrium potentials. Norepinephrine and ACh exert these effects via G_s and G_i protein-mediated events.

Many other ligands, including metabolites (e.g., adenosine) and drugs (e.g., those which act on the autonomic nervous system), alter the heart rate by mechanisms similar to the ones outlined above.

THE INITIATION AND PROPAGATION OF CARDIAC ELECTRICAL ACTIVITY

Cardiac electrical activity is normally initiated and spread in an orderly fashion. The heart is said to be a **functional syncytium** because the excitation of one cardiac cell eventually leads to the excitation of all cells. The cellular basis for the functional syncytium is low-resistance areas of the intercalated disks (the end-to-end junctions of myocardial cells) called **gap junctions** (see Chapter 10). Gap junctions between adjacent cells allow small ions to move freely from one cell to the next, meaning that action potentials can be propagated from cell to cell, similar to the way an action potential is propagated along an axon (see Chapter 3).

Excitation Starts in the SA Node Because SA Cells Reach Threshold First

Excitation of the heart normally begins in the SA node because the pacemaker potential of this tissue (see Fig. 13.1) reaches threshold before the pacemaker potential of the AV node. The pacemaker rate of the SA node is normally 60 to 100 beats/min versus 40 to 55 beats/min for the AV node. Pacemaker activity in the bundle of His and the Purkinje system is even slower, at 25 to 40 beats/min. Normal atrial and ventricular cells do not exhibit pacemaker activity.

Many cells of the SA node reach threshold and depolarize almost simultaneously, creating a migration of ions be-

tween these depolarized SA nodal cells and nearby resting atrial cells. This leads to depolarization of the neighboring right atrial cells and a wave of depolarization begins to spread over the right and left atria.

The Action Potential Is Propagated by Local Currents Created During Depolarization

As Na^+ ions enter a cell during phase 0, their positive charge repels intracellular K^+ ions into nearby areas where depolarization has not yet occurred. Potassium is even driven into adjacent resting cells through gap junctions. The local buildup of K^+ depolarizes adjacent areas until threshold is reached. The cycle of depolarization to threshold, Na^+ entry, and subsequent displacement of positive charges into nearby areas explains the spread of electrical activity. Excitation proceeds as succeeding cycles of local ion current and action potential move out of the SA node and across the atria. This process is called the **propagation of the action potential.**

Excitation Usually Spreads From the SA Node to Atrial Muscle to the AV Node to the Purkinje System to Ventricular Muscle

A fibrous, nonconducting connective tissue ring separates the atria from the ventricles everywhere except at the AV node. For this reason, the transmission of electrical activity from the atria to the ventricles occurs only through the AV node. Action potentials in atrial muscle adjacent to the AV node produce local ion currents that invade the node and trigger intranodal action potentials.

Slow Conduction Through the AV Node. Excitation proceeds throughout the atria at a speed of approximately 1 m/sec. It requires 60 to 90 msec to excite all regions of the atria (Fig. 13.6). Propagation of the action potential continues within the AV node, but at a much slower velocity (0.05 to 0.1 m/sec). The slower conduction velocity is partially explained by the small size of the nodal cells. Less current is produced by the depolarization of a small nodal cell (compared with a large atrial or ventricular cell), and the relatively smaller current brings neighboring cells to threshold more slowly, decreasing the rate at which electrical activation spreads. Other significant factors are the slow upstroke of the action potential because it depends on slow voltage-gated Ca^{2+} channels and, possibly, weak electrical coupling as a result of relatively few gap junctions. Propagation of the action potential through the AV node takes approximately 120 msec. Excitation then proceeds through the AV bundle (bundle of His), the left and right bundle branches, and the Purkinje system.

The AV node is the weak link in the excitation of the heart. Inflammation, hypoxia, vagus nerve activity, and certain drugs (e.g., digitalis, beta blockers, and calcium entry blockers) can cause failure of the AV node to conduct some or all atrial depolarizations to the ventricles. On the other hand, its tendency to conduct slowly is sometimes of benefit in pathological situations in which atrial depolarizations are too frequent and/or uncoordinated, as in atrial flutter or fibrillation. In these conditions, not all of the electrical impulses that reach the AV node are conducted to the ventricles, and the ventricular rate tends to stay below the level at which diastolic filling is impaired (see Chapter 14). The benefit of slow AV nodal conduction in a normal heart is that it allows the ventricular filling associated with atrial systole to occur before the ventricles are excited.

Rapid Conduction Through the Ventricles. The **Purkinje system** is composed of specialized cardiac muscle cells with large diameters. These cells rapidly conduct (conduction velocity up to 2 m/sec) action potentials throughout the subendocardium of both ventricles. Depolarization then proceeds from endocardium to epicardium (see Fig. 13.6). The conduction velocity through ventricular muscle is 0.3 m/sec; complete excitation of both ventricles takes approximately 75 msec. The rapid completion of excitation of the ventricles assures synchronized contraction of all ventricular muscle cells and maximal effectiveness in ejecting blood.

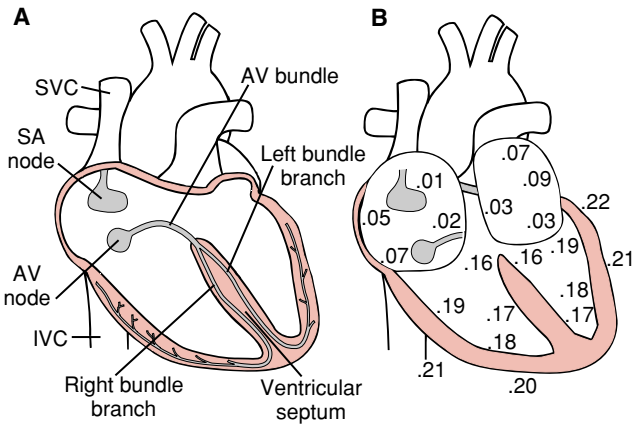

FIGURE 13.6 **The timing of excitation of various areas of the heart (in fractions of a second).**

THE ELECTROCARDIOGRAM

The **electrocardiogram** (ECG) is a continuous record of cardiac electrical activity obtained by placing sensing electrodes on the surface of the body and recording the voltage differences generated by the heart. The equipment amplifies these voltages and causes a pen to deflect proportionally on a paper moving under it. This gives a plot of voltage as a function of time.

The ECG Records the Dipoles Produced by the Electrical Activity of the Heart

To understand the ECG, it is necessary to understand the behavior of electrical potentials in a three-dimensional conductor of electricity. Consider what happens when wires are run from the positive and negative terminals of a battery into a dish containing salt solution. Positively charged ions flow toward the negative wire (negative pole) and negatively charged ions simultaneously flow in the opposite direction toward the positive wire (positive pole).

The combination of two poles that are equal in magnitude and opposite in charge and located close to one another, is called a **dipole**. The flow of ions (current) is greatest in the region between the two poles, but some current flows at every point surrounding the dipole, reflecting the fact that voltage differences exist everywhere in the solution.

Measurement of the Voltage Associated With a Dipole. What points encircling the dipole in Figure 13.7 have the greatest voltage difference between them? Points A and B do because A is closest to the positive pole and B is closest to the negative pole. Positive charges are drawn from the area around point B by the negative end of the dipole, which is relatively near. The positive end of the dipole is relatively distant and, therefore, has little ability to attract negative charges from point B (although it can draw negative charges from point A). As positive charges are drawn away, point B is left with a negative charge (or negative voltage). The opposite happens between the positive end of the dipole and point A, leaving A with a net positive charge (or voltage). Points C and D have no voltage difference between them because they are equally distant from both poles and are, therefore, equally influenced by positive and negative charges. Any other two points on the circle, E and F, for example, have a voltage difference between them that is less than that between A and B and greater than that between C and D. This is also true of other combinations of points, such as A and C, B and D, and D and F. Voltage differences exist in all cases and are determined by the relative influences of the positive and negative ends of the dipole.

Changes in Dipole Magnitude and Direction. What would happen if the dipole were to change its orientation relative to points C and D? Figure 13.8 diagrams an apparatus in which electrodes from a voltmeter are placed at the edges of a dish of salt solution in which the dipole can be rotated. This solution is analogous to that depicted in Figure 13.7, except the dipole position is changed relative to the electrodes instead of the electrode being changed relative to the dipole. Figure 13.8 shows the changes in measured voltage that occur if the dipole is rotated 90 degrees. The measured voltage increases slowly as the dipole is turned and is maximal when the positive end of the dipole points to C and the negative end points to D. In each position, the dipole sets up current fields similar to those shown in Figure 13.7. The voltage measured depends on how the electrodes are positioned relative to those currents. Figure 13.8 also shows that the voltage between C and D will decrease to a new steady-state level as the voltage applied to the wires by the battery is decreased. These imaginary experiments illustrate two characteristics of a dipole that determine the voltage measured at distant points in a volume conductor: **direction** of the dipole relative to the measuring points and **magnitude** (voltage) of the dipole; this is another way of saying that a dipole is a **vector**.

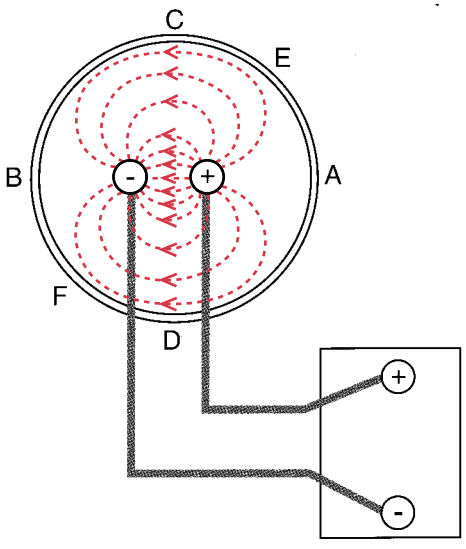

FIGURE 13.7 **Creating a dipole in a tub of salt solution.** The dashed lines indicate current flow; the current flows from the positive to the negative poles (See text for details.).

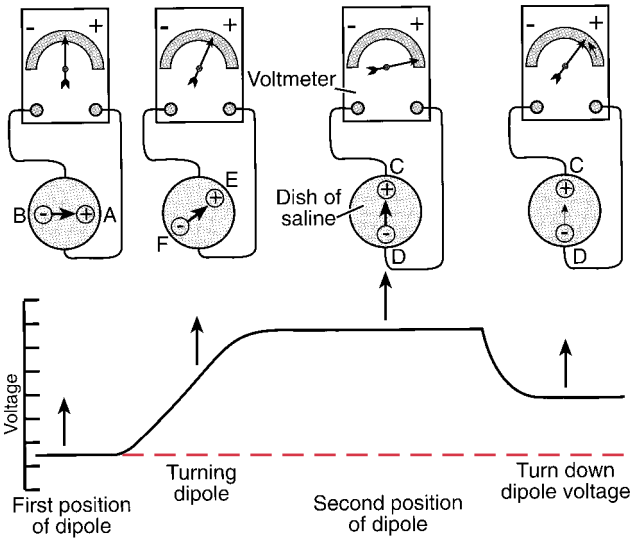

FIGURE 13.8 **Effect of dipole position and magnitude on recorded voltage.** In a salt solution, the dipole can be represented as a vector having a length and direction determined by the dipole magnitude and position, respectively. In this example, electrodes for the voltmeter are at points C and D. When a vector is directed parallel to a line between C and D, the voltage is maximum. If the magnitude of the vector is decreased, the voltage decreases.

Portions of the ECG Are Associated With Electrical Activity in Specific Cardiac Regions

We can use this analysis of a dipole in a volume conductor to rationalize the waveforms of the ECG. Of course, the actual case of the heart located in the chest is not as simple as the dipole in the tub of salt solution for two main reasons. First, excitation of the heart does not create one dipole; instead, there are many simultaneous dipoles. We will focus with the net dipole emerging as an average of all the individual dipoles. Second, the body is not a homogeneous vol-

ume conductor. The most significant problem is that the lungs are full of air, not salt solution. Despite these problems, the model is useful in an initial understanding of the generation of the ECG.

At rest, myocardial cells have a negative charge inside and a positive charge outside the cell membrane. As cells depolarize, the depolarized cells become negative on the outside, whereas the cells in the region ahead of the depolarized cells remain positive on the outside (Fig. 13.9). When the entire myocardium is depolarized, no voltage differences exist between any regions of myocardium because all cells are negative on the outside. When the cells in a given region depolarize during normal excitation, that portion of the heart generates a dipole. The depolarized portion constitutes the negative side, and the yet-to-be-depolarized portion constitutes the positive side of the dipole. The tub of salt solution is analogous to the rest of the body in that the heart is a dipole in a volume conductor. With electrodes located at various points around the volume conductor (i.e., the body), the voltage resulting from the dipole generated by the electrical activity of the heart can be measured.

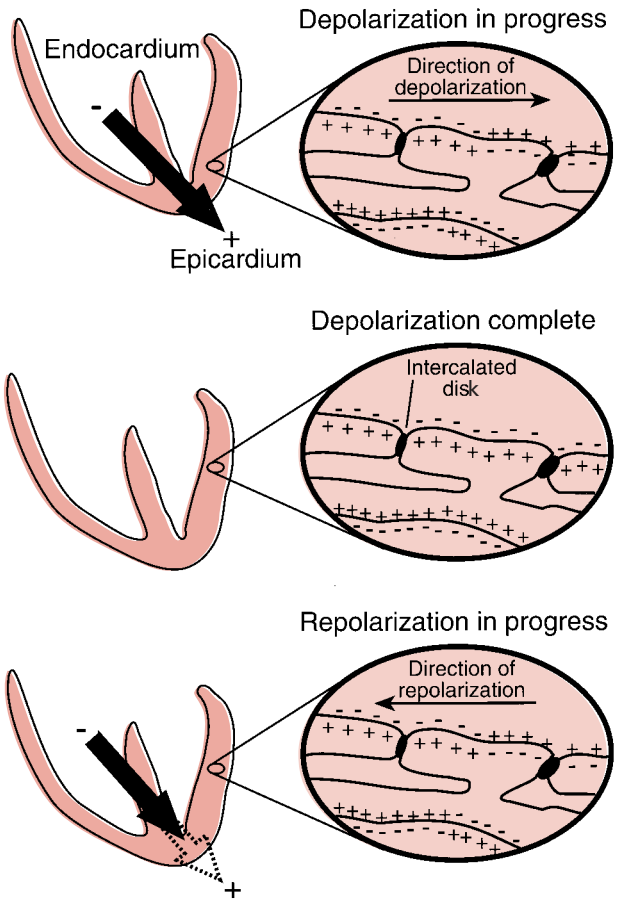

FIGURE 13.9 **Cardiac dipoles.** Partially depolarized or repolarized myocardium creates a dipole. Arrows show the direction of depolarization (or repolarization). Dipoles are present only when myocardium is undergoing depolarization or repolarization.

Consider the voltage changes produced by a two-dimensional model in which the body serves as a volume conductor and the heart generates a collection of changing dipoles (Fig. 13.10). An electrocardiographic recorder (a voltmeter) is connected between points A and B (lead I, see below). By convention, when point A is positive relative to point B, the ECG is deflected upward, and when B is positive relative to A, downward deflection results. The black arrows show (in two dimensions) the direction of the net dipole resulting from the many individual dipoles present at any one time. The lengths of the arrows are proportional to the magnitude (voltage) of the net dipole, which is related to the mass of myocardium generating the net dipole. The colored arrows show the magnitude of the dipole component that is parallel to the line between points A and B (the recorder electrodes); this component determines the voltage that will be recorded.

The P Wave and Atrial Depolarization. Atrial excitation results from a wave of depolarization that originates in the SA node and spreads over the atria, as indicated in panel 1 of Figure 13.10. The net dipole generated by this excitation has a magnitude proportional to the mass of the atrial muscle involved and a direction indicated by the solid arrow. The head of the arrow points toward the positive end of the dipole, where the atrial muscle is not yet depolarized. The negative end of the dipole is located at the tail of the arrow, where depolarization has already occurred. Point A is, therefore, positive relative to point B, and there will be an upward deflection of the ECG as determined by the magnitude and direction of the dipole. Once the atria are completely depolarized, no voltage difference exists between A and B, and the voltage recording returns to 0. The voltage change associated with atrial excitation appears on the ECG as the **P wave.**

The PR Segment and Atrioventricular Conduction. After the P wave, the ECG returns to the baseline present before the P wave. The ECG is said to be **isoelectric** when there is no deflection from the baseline established before the P wave. During this time, the wave of depolarization moves slowly through the AV node, the AV bundle, the bundle branches, and the Purkinje system. The dipoles created by depolarization of these structures are too small to produce a deflection on the ECG. The isoelectric period between the end of the P wave and the beginning of the QRS complex, which signals ventricular depolarization is called the **PR segment.** The P wave plus the PR segment is the **PR interval**. The duration of the PR interval is usually taken as an index of AV conduction time.

The QRS Complex and Ventricular Depolarization. The depolarization wave emerges from the AV node and travels along the AV bundle (bundle of His), bundle branches, and Purkinje system; these tracts extend down the interventricular septum. The net dipole that results from the initial depolarization of the septum is shown in panel 2 of Figure 13.10. Point B is positive relative to point A because the left side of the septum depolarizes before the right side. The small downward deflection produced on the ECG is the **Q wave.** The normal Q wave is often so small that it is not apparent.

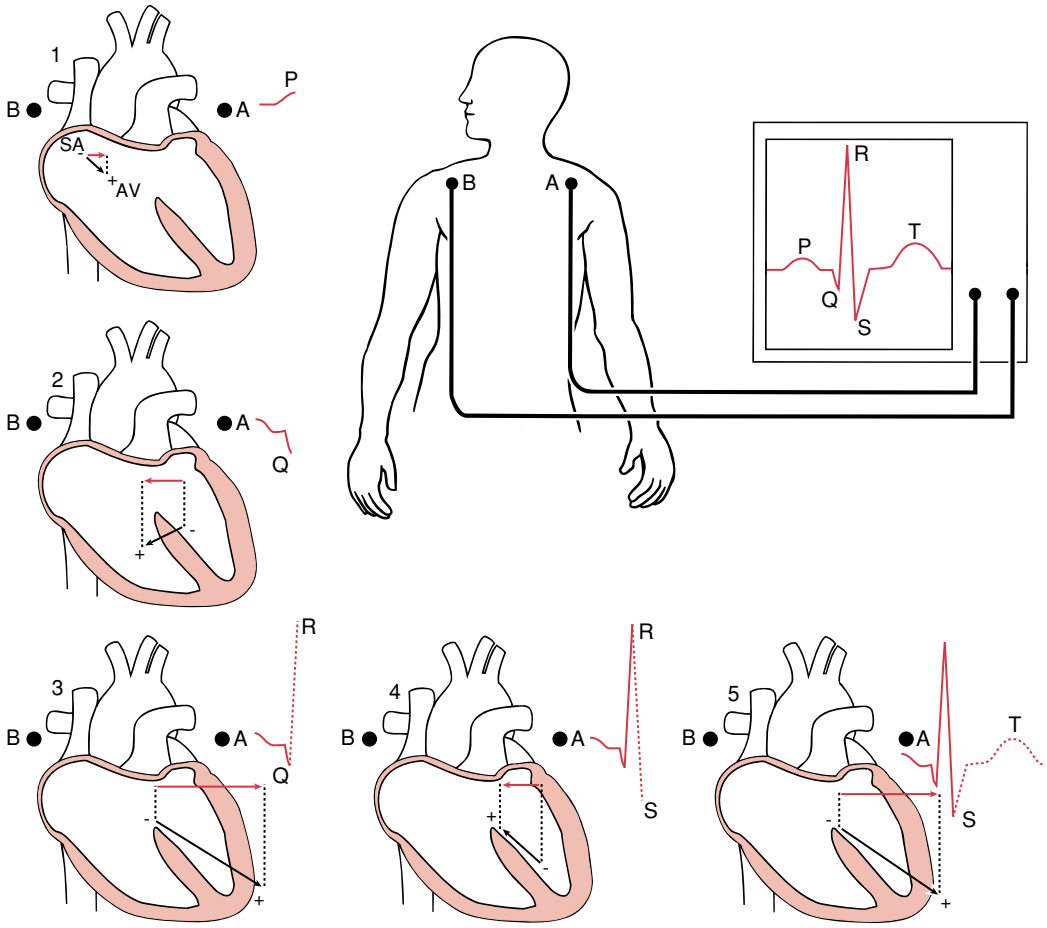

FIGURE 13.10 The sequence of major dipoles giving rise to ECG waveforms. The black arrows are vectors that represent the magnitude and direction of a major dipole. The magnitude is proportional to the mass of myocardium involved. The direction is determined by the orientation of depolarized and polarized regions of the myocardium. The vertical dashed lines project the vector onto the A-B coordinate (lead I); it is this component of the vector that is sensed and recorded (colored arrow). In panel 5, the tail of the vector (black arrow) shows the yet-to-be-repolarized region of the myocardium (negative) and the head points to the repolarized region (positive). The last areas of the ventricles to depolarize are the first to repolarize, i.e., repolarization appears to proceed in a direction opposite to that of depolarization. The projection of the vector (colored arrow) for repolarization points to the more positive electrode (A) as opposed to the less positive electrode (B), and so an upward deflection is recorded on this lead.

The wave of depolarization spreads via the Purkinje system across the inside surface of the free walls of the ventricles. Depolarization of free wall ventricular muscle proceeds from the innermost layers of muscle (subendocardium) to the outermost layers (subepicardium). Because the muscle mass of the left ventricle is much greater than that of the right ventricle, the net dipole during this phase has the direction indicated in panel 3. The deflection of the ECG is upward because point A is positive relative to point B, and it is large because of the great mass of tissue involved. This upward deflection is the **R wave.**

The last portions of the ventricle to depolarize generate a net dipole with the direction shown in panel 4. Point B is positive compared with point A, and the deflection on the ECG is downward. This final deflection is the **S wave.** The ECG tracing returns to baseline as all of the ventricular muscle becomes depolarized and all dipoles associated with ventricular depolarization disappear. The Q, R, and S waves together are known as the **QRS complex** and show the progression of ventricular muscle depolarization. The duration of the QRS complex is roughly equivalent to the duration of the P wave, despite the much greater mass of muscle of the ventricles. The relatively brief duration of the QRS complex is the result of the rapid, synchronous excitation of the ventricles.

The ST Segment and Phase 2 of the Ventricular Action Potential. The ST segment is the period between the end of the S wave and the beginning of the T wave. The ST segment is normally isoelectric, or nearly so. This indicates that no dipoles large enough to influence the ECG exist because all ventricular muscle is depolarized; that is, the action potentials of all ventricular cells are in phase 2 (Fig. 13.11).

The T Wave and Ventricular Repolarization. Repolarization, like depolarization, generates a dipole because the voltage of the depolarized area is different from that of the repolarized areas. The dipole associated with atrial repolarization does not appear as a separate deflection on the ECG because it generates a very low voltage and because it is

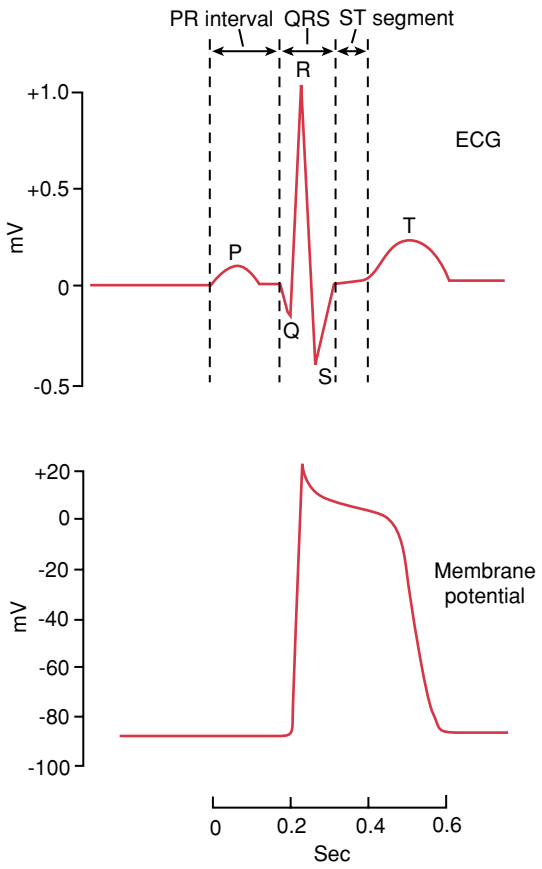

FIGURE 13.11 **The timing of the ventricular membrane potential and the ECG.** Note that the ST segment occurs during the plateau of the action potential.

masked by the much larger QRS complex that is present at the same time.

Ventricular repolarization is not as orderly as ventricular depolarization. The duration of ventricular action potentials is longer in subendocardial myocardium than in subepicardial myocardium. The longer duration of subendocardial action potentials means that even though subendocardial cells were the first to depolarize, they are the last to repolarize. Because subepicardial cells repolarize first, the subepicardium is positive relative to the subendocardium (see Fig. 13.9). That is, the polarity of the net dipole of repolarization is the same as the polarity of the dipole of depolarization. This results in an upward deflection because, as in depolarization, point A is positive with respect to point B. This deflection is the **T wave** (see panel 5, Fig. 13.10). The T wave has a longer duration than the QRS complex because repolarization does not proceed as a synchronized, propagated wave. Instead, the timing of repolarization is a function of properties of individual cells, such as numbers of particular K^+ channels.

The QT Interval. The **QT interval** is the time from the beginning of the QRS complex to the end of the T wave. If ventricular action potential and QT interval are compared, the QRS complex corresponds to depolarization, the ST segment to the plateau, and the T wave to repolarization (see Fig. 13.11). The relationship between a single ventricular action potential and the events of the QT interval are approximate because the events of the QT interval represent the combined influence of all of the ventricular action potentials.

The QT interval measures the total duration of ventricular activation. If ventricular repolarization is delayed, the QT interval is prolonged. Because delayed repolarization is associated with genesis of ventricular arrhythmias, this is clinically significant (see Clinical Focus Box 13.1).

ECG Leads Give the Voltages Measured Between Different Sites on the Body

An **electrocardiographic lead** is the pair of *electrical conductors* used to detect cardiac potential differences. An ECG lead is also used to refer to the *record* of potential differences made by the ECG machine. **Bipolar leads** give the potential difference between two electrodes placed at different sites. Elec-

CLINICAL FOCUS BOX 13.1

Long QT Syndrome

Some families have a rare inherited abnormality called **congenital long QT syndrome** (LQTS). Individuals with LQTS are often discovered because the individual or a family member presents to a physician with episodes of syncope (fainting) or because an otherwise healthy person dies suddenly and an alert physician suggests that their close relatives get an ECG. The ECG of affected individuals reveals either a long, irregular T wave, a prolonged ST segment, or both. Their hearts have delayed repolarization, which prolongs the ventricular action potential. In addition, when repolarization does occur, the freshly repolarized myocardium is subject to sudden, early depolarizations, called **afterdepolarizations**. These occur because the membrane potential in a small region of myocardium begins to depolarize before it has stabilized at the resting value. Afterdepolarizations may disrupt the normal, synchronized pattern of depolarization, and the ventricles may begin to depolarize in a chaotic pattern called **ventricular fibrillation**. With ventricular fibrillation, there is no synchronized contraction of ventricular muscle and the heart cannot pump the blood. Arterial pressure drops, blood flow to the brain and other parts of the body ceases, and sudden death occurs.

A single mutation of one of at least four genes, each of which codes for a particular cardiac muscle ion channel, causes LQTS. Mutations of three potassium channels have been discovered. The mutations decrease their function, decreasing potassium current and, thereby, increasing the tendency of the membrane to depolarize. A mutation of the sodium channel has also been found in some patients with LQTS. This mutation increases the sodium channel function, increasing sodium current and the tendency of the membrane to depolarize.

Individuals with congenital LQTS may be children or adults when the abnormality is identified. It is now apparent that at least one cause of sudden infant death syndrome (SIDS) involves a form of LQTS.

trodes of the traditional **bipolar limb leads** are placed on the left arm, right arm, and left leg (Fig. 13.12). The potential differences between each combination of two of these electrodes give leads I, II, and III. By convention, the left arm in lead I is the positive pole, and the left leg is the positive pole in leads II and III. A **unipolar lead** is the pair of electrical conductors giving the potential difference between an **exploring electrode** and a reference input, sometimes called the indifferent electrode. The reference input comes from a combination of electrodes at different sites, which is supposed to give roughly zero potential throughout excitation of the heart. Assuming this to be the case, the recorded electrical activity is the result of the influence of cardiac electrical activity on the exploring electrode. By convention, when the exploring electrode is positive relative to the reference input, an upward deflection is recorded.

The exploring electrode for the **precordial** or **chest leads** is the single electrode placed on the anterior and left lateral chest wall. For the chest leads, the reference input is obtained by connecting the three limb electrodes (Fig. 13.13). The observed ECGs recorded from the chest leads are each the result of voltage changes at a specified point on the surface of the chest. Unipolar chest leads are designated V_1 to V_6 and are placed over the areas of the chest

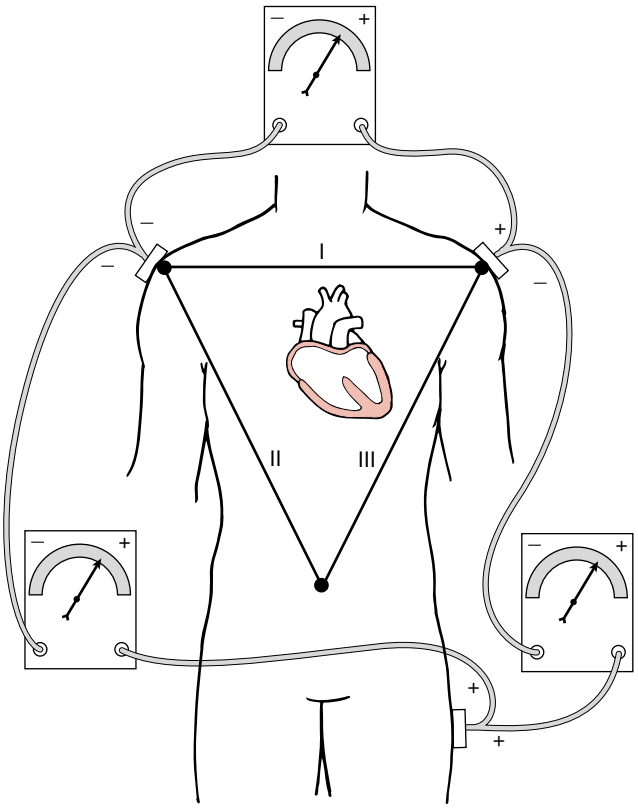

FIGURE 13.12 **Einthoven triangle.** Einthoven codified the analysis of electrical activity of the heart by proposing that certain conventions be followed. The heart is considered to be at the center of a triangle, each corner of which serves as the location for an electrode for two leads to the ECG recorder. The three resulting leads are I, II, and III. By convention, one electrode causes an upward deflection on the recorder when it is under the influence of a positive dipole relative to the other electrode.

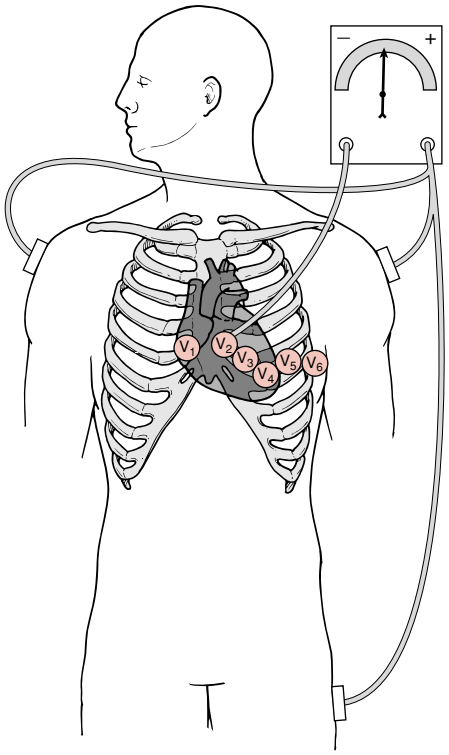

FIGURE 13.13 **Unipolar chest leads.** V_1 is just to the right of the sternum in the fourth intercostal space. V_2 is just to the left of the sternum in the fourth interspace. V_4 is in the fifth interspace in the midclavicular line. V_3 is midway between V_2 and V_4. V_5 is in the fifth interspace in the anterior axillary line. V_6 is in the fifth interspace in the midaxillary line. The three limb leads are combined to give the reference voltage (zero) for the unipolar chest lead (V).

shown in Figure 13.13. The generation of the QRS complex in the chest leads can be explained in a way similar to that for lead I.

The exploratory electrode for an **augmented limb lead** is an electrode on a single limb. The reference input is the two other limb electrodes connected together. Lead aVR gives the potential difference between the right arm (exploring electrode) and the combination of the left arm and the left leg (reference). Lead aVL gives the potential difference between the left arm and the combination of the right arm and left leg. Lead aVF gives the potential difference between the left leg and the combination of the left arm and right arm.

A standard 12-lead ECG, including six limb leads and six chest leads, is shown in Figure 13.14. The ECG is calibrated so that two dark horizontal lines (1 cm) represent 1 mV, and five dark vertical lines represent 1 second. This means that one light vertical line represents 0.04 sec.

The ECG Provides Information About Cardiac Dipoles as Vectors

Cardiac dipoles are vectors with both magnitude and direction. The net vector produced by all cardiac dipoles at a given time can be determined from the ECG. The direction of the vectors can be determined in the frontal and horizontal planes of the body.

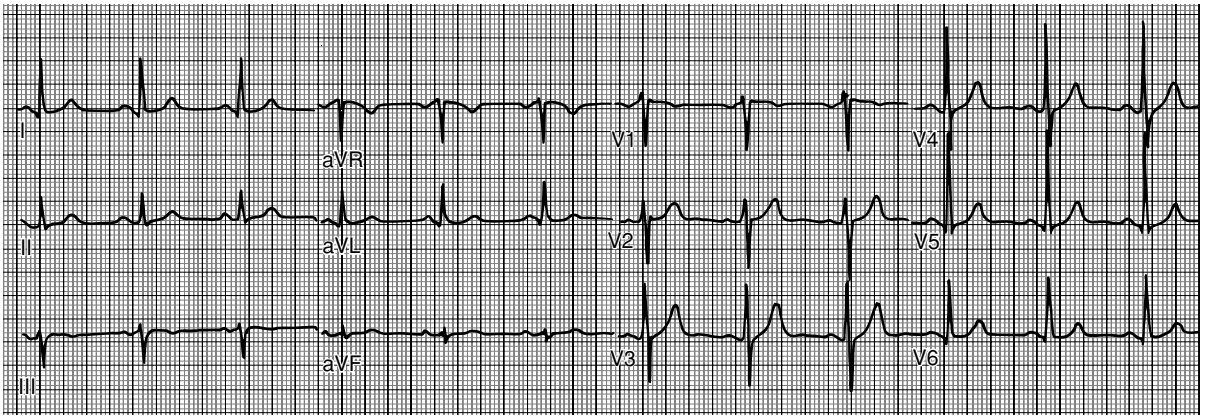

FIGURE 13.14 **Standard 12-lead ECG.** Six limb leads and six chest leads are shown. Two dark horizontal lines (10 mm) are calibrated to be 1 mV. Dark vertical lines represent 0.2 sec.

The bipolar limb leads (leads I, II, and III) and the augmented limb leads (aVR, aVL, and aVF) provide information about the electrical activity of the heart as observed in the frontal plane. As we have seen, lead I is the record of potential differences between the left and right arms. It records only the component of the electrical vector that is parallel to its **axis**. Lead I can be symbolized by a horizontal line (axis) going through the center of the chest (Fig. 13.15A) in the direction of right arm to left arm. Likewise, lead II can be symbolized by a 60° line drawn through the middle of the chest in the direction of right arm to left leg. The same type of representation can be done for lead III and for the augmented limb leads. The positive ends of the leads are shown by the arrowheads (see Fig. 13.15A). The diagram that results (see Fig. 13.15A) is called the **hexaxial reference system**.

A net cardiac dipole with its positive charge directed toward the positive end of the axis of a lead results in the recording of an upward deflection. A net cardiac dipole with its positive charge directed toward the negative end of the axis of a lead results in a downward deflection. A net cardiac dipole with its positive charge directed at a right angle to the axis of a lead results in no deflection. The hexaxial reference system can be used to predict the influence of a cardiac dipole on any of the six leads in the frontal plane. As we will see, this system is useful in understanding changes in the leads of the ECG associated with different diseases.

The unipolar chest leads provide information about cardiac dipoles generated in the horizontal plane (Figure 13.15B). Each chest lead can be represented as having an axis coming from the center of the chest to the site of the exploring electrode in the horizontal plane. The deflections recorded in each chest lead can be understood in terms of this axial system.

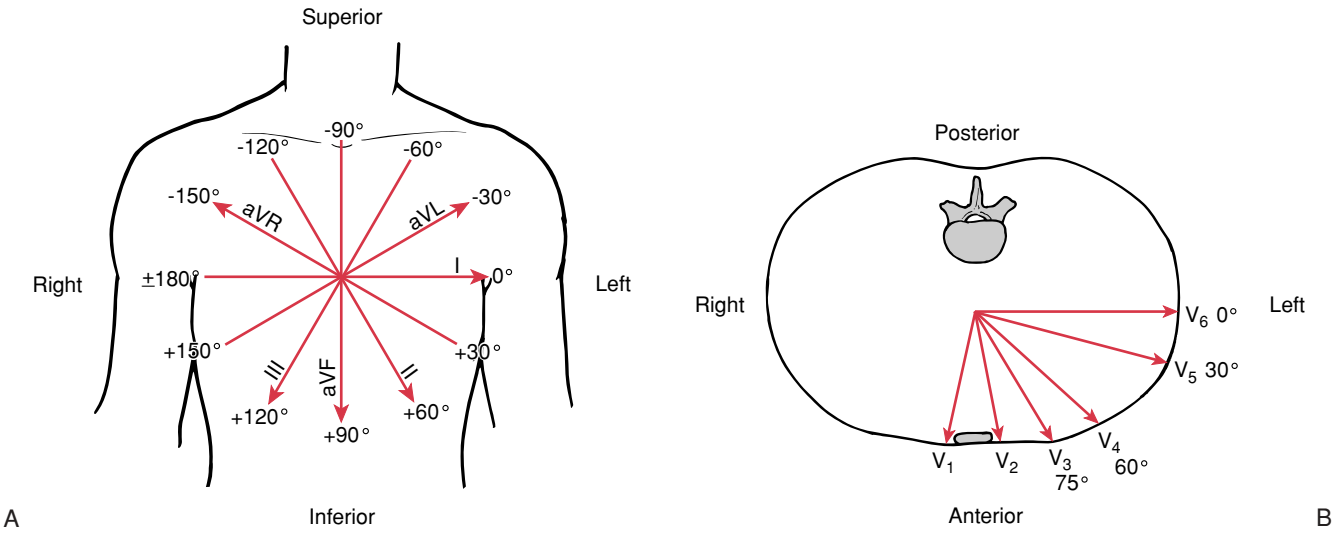

FIGURE 13.15 **Hexaxial reference system.** A, The limb leads give information on cardiac dipole vectors in the frontal plane. B, Chest leads are influenced by dipole vectors in the horizontal plane.

The Mean QRS Electrical Axis Is Determined From the Limb Leads

As explained above, changes in the magnitude and direction of the cardiac dipole will cause changes in a given ECG lead, as predicted by the axial reference system. By examining the limb leads, the observer can determine the **mean electrical axis** during ventricular depolarization. One approach involves the use of **Einthoven's triangle.** Einthoven's triangle is an equilateral triangle with each side representing the axis of one of the bipolar limb leads (Fig. 13.16). The net magnitude of the QRS complex of any two of the three leads is measured and plotted on the appropriate axis. A perpendicular is dropped from each of the plotted points. A vector drawn between the center of the triangle and the intersection of the two perpendiculars gives the mean electrical axis. In this example, the data taken from the ECG in Figure 13.14 give a mean electrical axis of 3 degrees.

A second approach employs the hexaxial reference system (see Fig. 13.15A). First, the six limb leads are inspected to find the one in which the net QRS complex deflection is closest to zero. As discussed earlier, when the cardiac dipole is perpendicular to a particular lead, the net deflection is zero. Once the net QRS deflection closest to zero is identified, it follows that the mean electrical axis is perpendicular to that lead. The hexaxial reference system can be consulted to determine the angle of that axis. In Figure 13.14, the lead in which the net QRS deflection is closest to zero is lead aVF (the bipolar limb leads and lead aVF are enlarged in Figure 13.16). Lead I is perpendicular to the axis of lead aVF (see Fig. 13.15A). Because the QRS complex is upward in lead I, the mean electrical axis points to the left arm and is estimated to be about 0 degrees.

The mean QRS electrical axis is influenced by (a) the position of the heart in the chest, (b) the properties of the cardiac conduction system, and (c) the excitation and repolarization properties of the ventricular myocardium. Because the last two of these influences are most significant, the mean QRS electrical axis can provide valuable information about a variety of cardiac diseases.

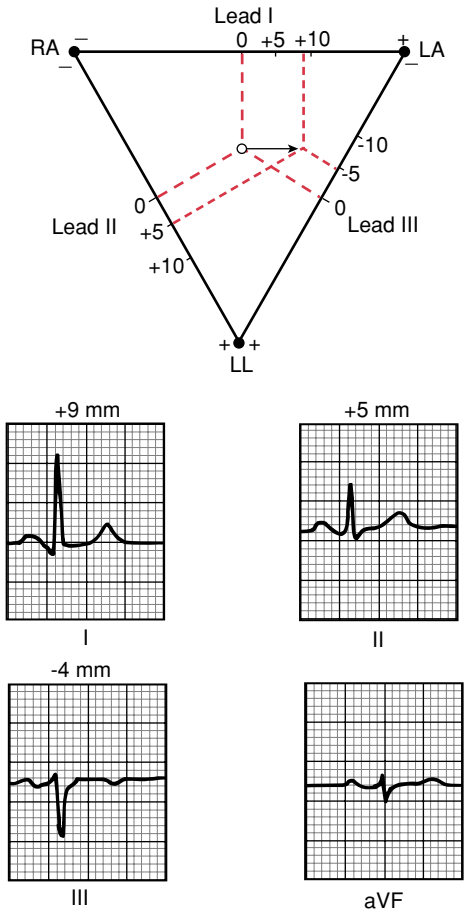

FIGURE 13.16 **Mean QRS electrical axis.** This axis can be estimated by using Einthoven's triangle and the net voltage of the QRS complex in any two of the bipolar limb leads. It can also be estimated by inspection of the six limb leads (see text for details). ECG tracings are from Figure 13.14.

The ECG Permits the Detection and Diagnosis of Irregularities in Heart Rate and Rhythm

The ECG provides information about the rate and rhythm of excitation, as well as the pattern of conduction of excitation throughout the heart. The following illustrations of cardiac rate and rhythm irregularities are not comprehensive; they were chosen to describe basic physiological principles. Disorders of cardiac rate and rhythm are referred to as **arrhythmias.**

Figure 13.14 shows the standard 12-lead ECG from an individual with normal sinus rhythm. We see that the P wave is always followed by a QRS complex of uniform shape and size. The PR interval (beginning of the P wave to the beginning of the QRS complex) is 0.16 sec (normal, 0.10 to 0.20 sec). This measurement indicates that the conduction velocity of the action potential from the SA node to the ventricular muscle is normal. The average time between R waves (successive heart beats) is about 0.84 sec, making the heart rate approximately 71 beats/min.

Figure 13.17A shows **respiratory sinus arrhythmia,** an increase in the heart rate with inspiration and a decrease with expiration. The presence of a P wave before each QRS complex indicates that these beats originate in the SA node. Intervals between successive R waves of 1.08, 0.88, 0.88, 0.80, 0.66, and 0.66 seconds correspond to heart rates of 56, 68, 68, 75, 91, and 91 beats/min. The interval between the beginning of the P wave and the end of the T wave is uniform, and the change in the interval between beats is primarily accounted for by the variation in time between the end of the T wave and the beginning of the P wave. Although the heart rate changes, the interval during which electrical activation of the atria and ventricles occurs does not change nearly as much as the interval between beats. Respiratory sinus arrhythmia is caused by cyclic changes in sympathetic and parasympathetic neural activity to the SA node that accompany respiration. It is observed in individuals with healthy hearts.

Figure 13.17B shows an ECG during excessive stimulation of the parasympathetic nerves. The stimulation releases ACh from nerve endings in the SA and AV nodes; ACh suppresses the pacemaker activity, slows the heart

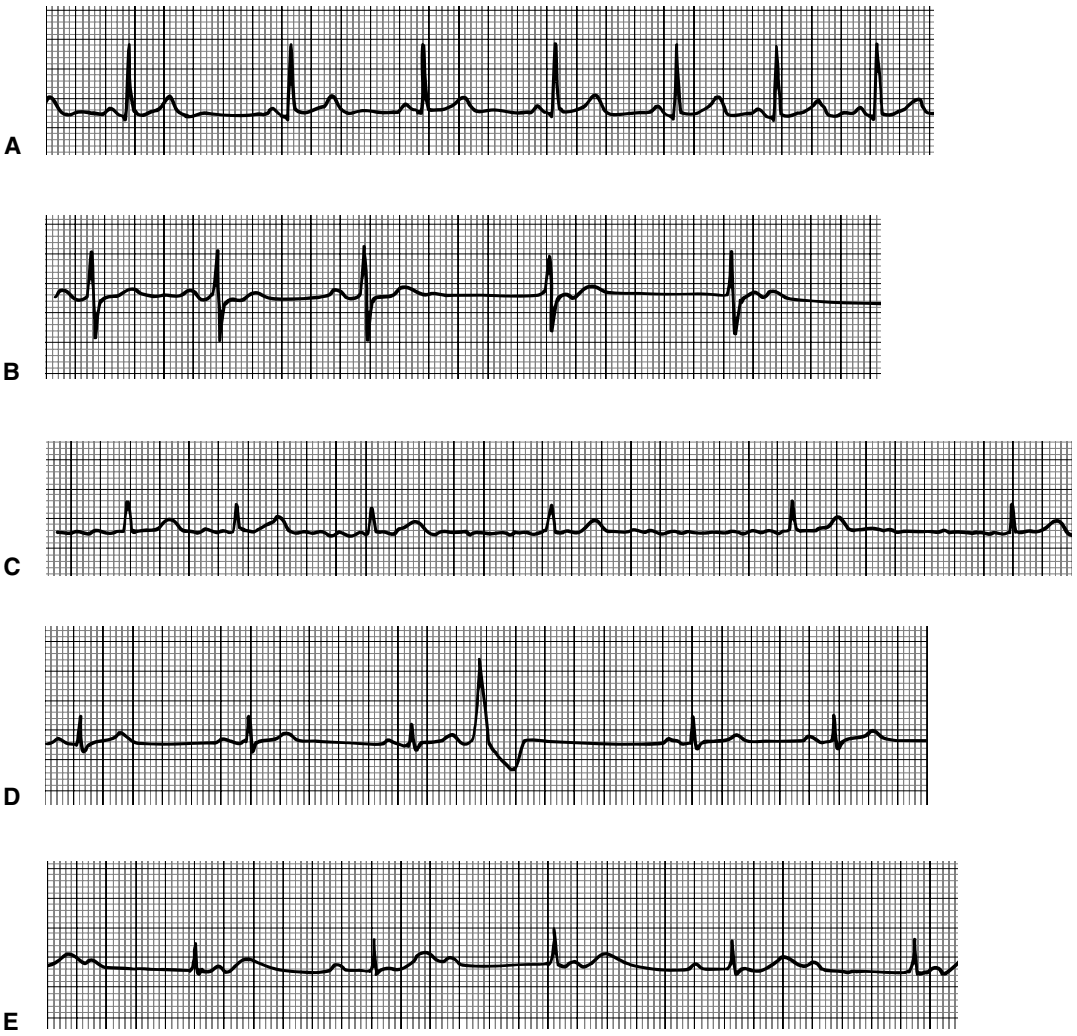

FIGURE 13.17 **ECGs (lead II) showing abnormal rhythms.** **A,** Respiratory sinus arrhythmia. **B,** Sinus arrest with vagal escape. **C,** Atrial fibrillation. **D,** Premature ventricular complex. **E,** Complete atrioventricular block.

rate, and increases the distance between P waves. The fourth and fifth QRS complexes are not preceded by P waves. When a QRS complex is recorded without a preceding P wave, it reflects the fact that ventricular excitation has occurred without a preceding atrial contraction, which means that the ventricles were excited by an impulse that originated below the atria. The normal configuration of the QRS complex suggests that the new pacemaker was in the AV node or bundle of His and that ventricular excitation proceeded normally from that point. This is called **junctional escape.**

The ECG in Figure 13.17C is from a patient with **atrial fibrillation.** In this condition, atrial systole does not occur because the atria are excited by many chaotic waves of depolarization. The AV node conducts excitation whenever it is not refractory and a wave of atrial excitation reaches it. Unless there are other abnormalities, conduction through the AV node and ventricles is normal and the resulting QRS complex is normal. The ECG shows QRS complexes that are not preceded by P waves. The ventricular rate is usually rapid and irregular. Atrial fibrillation is associated with numerous disease states, such as cardiomyopathy, pericarditis, hypertension, and hyperthyroidism, but it sometimes occurs in otherwise normal individuals.

The ECG in Figure 13.17D shows a **premature ventricular complex** (PVC). The first three QRS complexes are preceded by P waves; then after the T wave of the third QRS complex, a QRS complex of increased voltage and longer duration occurs. This premature complex is not preceded by a P wave and is followed by a pause before the next normal P wave and QRS complex. The premature ventricular excitation is initiated by an **ectopic focus,** an area of pacemaker activity in other than the SA node. In panel D, the focus is probably in the Purkinje system or ventricular muscle, where an aberrant pacemaker reaches threshold before being depolarized by the normal wave of excitation. Once the ectopic focus triggers an action potential, the excitation is propagated over the ventricles. The abnormal pattern of excitation accounts for the greater voltage, change of mean electrical axis, and longer duration (inefficient conduction) of the QRS complex. Although the abnormal wave of excitation reached the AV node, retrograde

conduction usually dies out in the AV node. The next normal atrial excitation (P wave) occurs but is hidden by the inverted T wave associated with the abnormal QRS complex. This normal wave of atrial excitation does not result in ventricular excitation. Ventricular excitation does not occur because, when the impulse arrives, a portion of the AV node is still refractory following excitation by the premature complex. As a consequence, the next "scheduled" ventricular beat is missed. A prolonged interval following a premature ventricular beat is the **compensatory pause.**

Premature beats can also arise in the atria. In this case, the P wave is abnormal but the QRS complex is normal. Premature beats are often called extrasystoles, frequently a misnomer because there is no "extra" beat. However, in some cases, the premature beat is interpolated between two normal beats, and the premature beat is indeed "extra."

In Figure 13.17E, both P waves and QRS complexes are present, but their timing is independent of each other. This is **complete atrioventricular block** in which the AV node fails to conduct impulses from the atria to the ventricles. Because the AV node is the only electrical connection between these areas, the pacemaker activities of the two become entirely independent. In this example, the distance between P waves is about 0.8 sec, giving an atrial rate of 75 beats/min. The distance between R waves averages 1.2 sec, giving a ventricular rate of 50 beats/min. The atrial pacemaker is probably in the SA node, and the ventricular pacemaker is probably in a lower portion of the AV node or bundle of His.

AV block is not always complete. Sometimes the PR interval is lengthened, but all atrial excitations are eventually conducted to the ventricles. This is **first-degree atrioventricular block.** When some, but not all, of the atrial excitations are conducted by the AV node, it is **second-degree atrioventricular block.** If atrial excitation never reaches the ventricles, as in the example in Figure 13.17E, it is **third-degree (complete) atrioventricular block.**

The ECG Provides Three Types of Information About the Ventricular Myocardium

The ECG provides information about the pattern of excitation of the ventricles, changes in the mass of electrically active ventricular myocardium, and abnormal dipoles resulting from injury to the ventricular myocardium. It provides no direct information about the mechanical effectiveness of the heart; other tests are used to study the efficiency of the heart as a pump (see Chapter 14).

The Pattern of Ventricular Excitation. Disease or injury can affect the pattern of ventricular depolarization and produce an abnormality in the QRS complex. Figure 13.18 shows a normal QRS complex (Fig. 13.18A) and two examples of complexes that have been altered by impaired conduction. In Figure 13.18B, the AV bundle branch to the right side of the heart is not conducting (i.e., there is right bundle-branch block), and depolarization of right-sided myocardium, therefore, depends on delayed electrical activity coming from the normally depolarized left side of the heart. The resulting QRS complex has an abnormal shape because of aberrant electrical conduction and is prolonged because of the increased time necessary to fully depolarize the heart. In Figure 13.18C, the AV bundle branch to the left side of the heart is not conducting (i.e., there is left bundle-branch block), also resulting in a wide, deformed QRS complex.

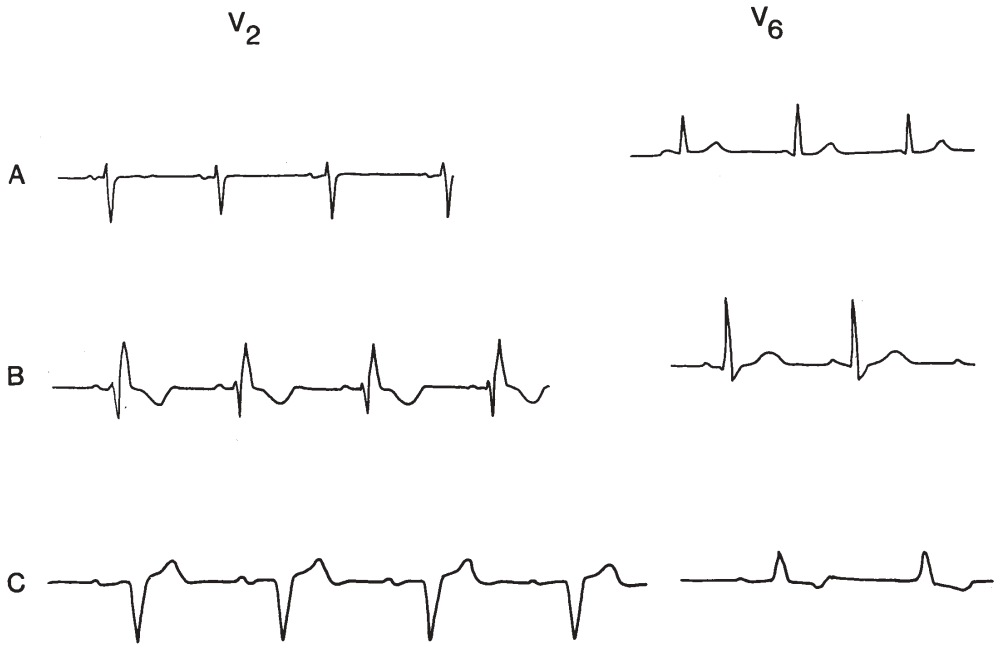

FIGURE 13.18 ECGs (leads V_2 and V_6) of patients with various conditions. A, patient with normal QRS complex. B, patient with right bundle-branch block. C, patient with left bundle-branch block.

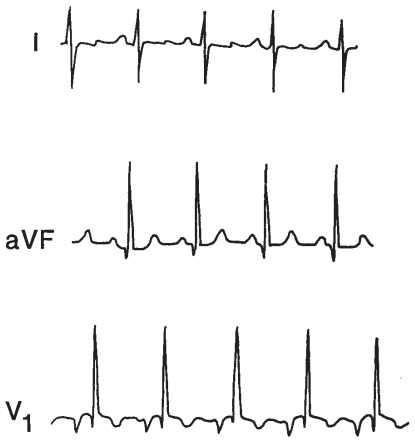

FIGURE 13.19 **Right ventricular hypertrophy.** Leads I, aVF, and V_1 of a patient are shown.

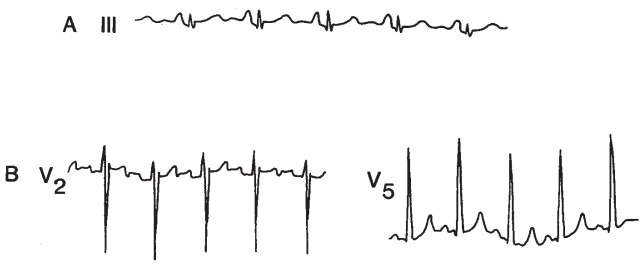

FIGURE 13.20 **Effects of** A, Large P waves (lead III) caused by atrial hypertrophy. **B,** Altered QRS complex (leads V_1 and V_5) produced by left ventricular hypertrophy.

Changes in the Mass of Electrically Active Ventricular Myocardium. The recording in Figure 13.19 shows the effect of right ventricular enlargement on the ECG. The increased mass of right ventricular muscle changes the direction of the major dipole during ventricular depolarization, resulting in large R waves in lead V_1. The large S waves in lead I and the large R waves in lead aVF are also characteristic of a shift in the dipole of ventricular depolarization to the right. This illustrates how a change in the mass of excited tissue can affect the amplitude and direction of the QRS complex.

Figure 13.20 shows the effects of atrial hypertrophy on the P waves of lead III (see Fig. 13.20A) and the altered QRS complexes in leads V_1 and V_5 associated with left ventricular hypertrophy (see Fig. 13.20B). Left ventricular hypertrophy rotates the direction of the major dipole associated with ventricular depolarization to the left, causing large S waves in V_1 and large R waves in V_5.

Abnormal Dipoles Resulting From Ventricular Myocardial Injury. **Myocardial ischemia** is present when a portion of the ventricular myocardium fails to receive sufficient blood flow to meet its metabolic needs. In this case, the supply of ATP may decrease below the level required to maintain the active transport of ions across the cell membrane. The resulting alterations in the membrane potential in the ischemic region can affect the ECG. Normally, the ECG is at baseline (zero voltage) during

- The interval between the completion of the T wave and the onset of the P wave (the TP interval), during which all cardiac cells are at their resting membrane potential
- The ST segment, during which depolarization is complete and all ventricular cells are at the plateau (phase 2) of the action potential

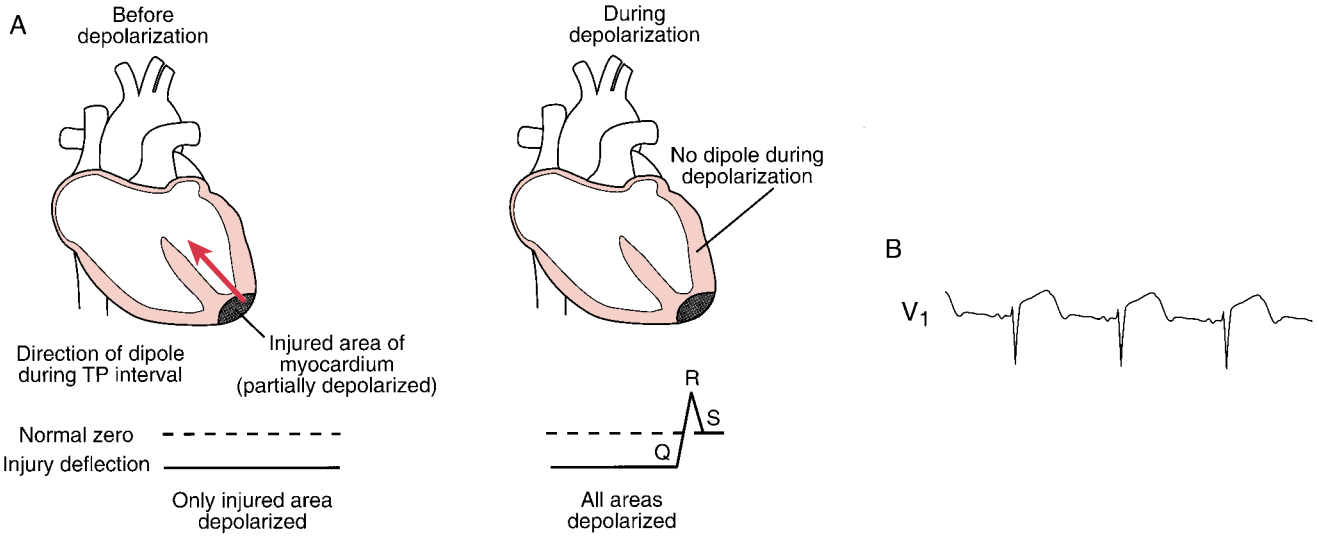

FIGURE 13.21 **Electrocardiogram changes in myocardial injury.** **A,** Dark shading depicts depolarized ventricular tissue. ST segment elevation can occur with myocardial injury. The apparent zero baseline of the ECG before depolarization is below zero because of partial depolarization of the injured area (shading). After depolarization (during the action potential plateau), all areas are depolarized and true zero is recorded. Because zero baseline is set arbitrarily (on the ECG recorder), a depressed diastolic baseline (TP segment) and an elevated ST segment cannot be distinguished. Regardless of the mechanism, this is referred to as an elevated ST segment. **B,** The ECG (lead V_1) of a patient with acute myocardial infarction.

With myocardial ischemia, the cells in the ischemic region partially depolarize to a lower resting membrane potential because of a lowering of the potassium ion concentration gradient, although they are still capable of action potentials. As a consequence, a dipole is present during the TP interval in injured hearts because of the voltage difference between normal (polarized) and abnormal (partially polarized) tissue. However, no dipole is present during the ST interval because depolarization is uniform and complete in both injured and normal tissue (this is the plateau period of ventricular action potentials). Because the ECG is designed so that the TP interval is recorded as zero voltage, the true zero during the ST interval is recorded as a positive or negative deflection (Fig. 13.21). These deflections during the ST interval are of major clinical utility in the diagnosis of cardiac injury.

REVIEW QUESTIONS

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

1. Rapid depolarization (phase 0) of the action potential of ventricular muscle results from opening of
   (A) Voltage-gated Ca^{2+} channels
   (B) Voltage-gated Na^{+} channels
   (C) Acetylcholine-activated K^{+} channels
   (D) Inward rectifying K^{+} channels
   (E) ATP-sensitive K^{+} channels
2. A 72-year-old man with an atrial rate of 80 beats/min develops third-degree (complete) AV block. A pacemaker site located in the AV node below the region of the block triggers ventricular activity, but at a rate of only 40 beats/min. What would be observed?
   (A) One P wave for each QRS complex
   (B) An inverted T wave
   (C) A shortened PR interval
   (D) A normal QRS complex
3. To ensure an adequate heart rate, a temporary electronic pacemaker lead is attached to the apex of the right ventricle, and the heart is paced by electrically stimulating this site at a rate of 70 beats/min. When the ECG during pacing is compared with the ECG before pacing, there would be a
   (A) Shortened PR interval
   (B) QRS complex similar to that seen with left bundle-branch block
   (C) QRS complex of shortened duration
   (D) P wave following each QRS complex
   (E) QRS complex similar to that seen with right bundle-branch block
4. What is most responsible for phase 0 of a cardiac nodal cell?
   (A) Voltage-gated Na^{+} channels
   (B) Acetylcholine-activated K^{+} channels
   (C) Inward rectifying K^{+} channels
   (D) Voltage-gated Ca^{2+} channels
   (E) Pacemaker channels
5. Atrial repolarization normally occurs during the
   (A) P wave
   (B) QRS complex
   (C) ST segment
   (D) T wave
   (E) Isoelectric period
6. The P wave is normally positive in lead I of the ECG because
   (A) Depolarization of the ventricles proceeds from subendocardium to subepicardium
   (B) When the ECG electrode attached to the right arm is positive relative to the electrode attached to the left arm, an upward deflection is recorded
   (C) AV nodal conduction is slower than atrial conduction
   (D) Depolarization of the atria proceeds from right to left
   (E) When cardiac cells are depolarized, the inside of the cells is negative relative to the outside of the cells
7. Stimulation of the sympathetic nerves to the normal heart
   (A) Increases duration of the TP interval
   (B) Increases the duration of the PR interval
   (C) Decreases the duration of the QT interval
   (D) Leads to fewer P waves than QRS complexes
   (E) Decreases the frequency of QRS complexes
8. A drug that raises the heart rate from 70 to 100 beats per minute could
   (A) Be an adrenergic receptor antagonist
   (B) Cause the opening of acetylcholine-activated K^{+} channels
   (C) Be a cholinergic receptor agonist
   (D) Be an adrenergic receptor agonist
   (E) Cause the closing of voltage-gated Ca^{2+} channels
9. Excitation of the ventricles
   (A) Always leads to excitation of the atria
   (B) Results from the action of norepinephrine on ventricular myocytes
   (C) Proceeds from the subendocardium to subepicardium
   (D) Is initiated during the plateau (phase 2) of the ventricular action potential
   (E) Results from pacemaker potentials of ventricular cells
10. AV nodal cells
    (A) Exhibit action potentials characterized by rapid depolarization (phase 0)
    (B) Exhibit increased conduction velocity when exposed to acetylcholine
    (C) Conduct impulses more slowly than either atrial or ventricular cells
    (D) Are capable of pacemaker activity at an intrinsic rate of 100 beats/min
    (E) Exhibit slowed conduction velocity when exposed to norepinephrine
11. Stimulation of the parasympathetic nerves to the normal heart can lead to complete inhibition of the SA node for several seconds. During that period
    (A) P waves would become larger
    (B) There would be fewer T waves than QRS complexes
    (C) There would be fewer P waves than T waves
    (D) There would be fewer QRS complexes than P waves
    (E) The shape of QRS complexes would change
12. The R wave in lead I of the ECG
    (A) Is larger than normal with right ventricular hypertrophy
    (B) Reflects a net dipole associated with ventricular depolarization
    (C) Reflects a net dipole associated with ventricular repolarization
    (D) Is largest when the mean electrical axis is directed perpendicular to a line drawn between the two shoulders
    (E) Is associated with atrial depolarization
13. The ST segment of the normal ECG
    (A) Occurs during a period when both ventricles are completely repolarized
    (B) Occurs when the major dipole is directed from subendocardium to subepicardium

(continued)

(C) Occurs during a period when both ventricles are completely depolarized
(D) Is absent in lead I of the ECG
(E) Occurs during depolarization of the Purkinje system

SUGGESTED READING

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