

Cardiac Pacing,
Defibrillation and
Resynchronization

Dedication

For Sharonne, Sarah, Drew, and my parents, Audrey and Henry Hayes.

DLH

To my wife, Vicki, my daughters, Lindsay, Hannah, and Maddy, and my parents, Charles and Ety Friedman, for your love, support, patience, and encouragement.

PAF

Cardiac Pacing, Defibrillation and Resynchronization: A Clinical Approach

SECOND EDITION

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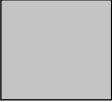
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Preface

In preparing this edition of *Cardiac Pacing, Defibrillation and Resynchronization: A Clinical Approach*, our intention remained the same as for the previous edition, that is, to be a text that is uniformly written with sensible, matter-of-fact methods for understanding and caring for patients with permanent pacemakers, implantable cardioverter-defibrillators (ICDs), and, to a much greater extent in this edition, cardiac resynchronization therapy (CRT) devices. Once again, our intent was not to create an encyclopedic text. Instead, we want to provide practical clinical information for those involved in cardiac pacing, defibrillation and CRT. Several excellent multi-authored texts provide encyclopedic information.

Cardiac pacing, cardiac defibrillation, and, more recently CRT, have become fields unto themselves as the technology has proliferated and the devices have rapidly become increasingly more sophisticated. We have witnessed unbelievably rapid advances in the technology of implantable cardiac devices. With the first pacemaker implant in 1958, the first ICD implantation in 1980, and the first biventricular pacing report in 1994, few would have imagined the progress and improvements made in such a relatively short period of time. Having witnessed the continued improvements in pacemakers, ICDs and CRT in recent years, we would not underestimate the potential for future improvements of these devices and can see many opportunities for expansion of these therapies.

This text is meant to help the reader understand the technical capabilities of pacemakers, ICDs and CRT and how to apply this knowledge clinically. Whether the reader is new to these disciplines or sees patients with implantable devices every day, we hope that the information we have included will make clinical encounters easier.

We feel strongly that there is merit in a text written by a small number of contributors. Not to detract from the

expertise of the contributors or editors of the excellent multiauthored texts available, limiting the number of authors allows a connection from chapter to chapter and a consistent writing style. Our hope is that this choice will make reading and comprehension easier.

We (DLH and PAF) are involved in all of the chapters. However, we need to thank a number of colleagues who have contributed to the preparation of this edition of the text. First, we acknowledge our colleague Dr Margaret (Peg) Lloyd, MD, an author on the first edition of this text. We have built upon her prior contributions in specific chapters and greatly appreciate the foundations she helped lay. Our special thanks to our colleague Samuel J. Asirvatham, MD, who became progressively more involved as this edition moved forward. We genuinely appreciate his expertise, tireless efforts, and counsel. Our friend Dr Charles (Chuck) D. Swerdlow, MD, is an innovator in the field who enriched the chapters on Troubleshooting and Programming with significant contributions. Others who have contributed include Apoor Gami, MD, Jared Bunch, MD, and Niloufar Tabatabaei, MD – many thanks for your energy and contributions. We have enjoyed long and fruitful collaborations with Michael Glikson, MD, and Paul J. Wang, MD,, and appreciate their contribution to this effort.

The text has also been influenced by and we have been given incredible assistance from friends and colleagues in industry. A special thanks to Paul Levine, MD, who has graciously allowed us to use a number of examples from his personal collection and who remains one of the “giants” in the field. Others who have responded to many questions, and have reviewed sections of text to ensure its technical accuracy; we are grateful for their efforts. They include: Doug Welter and Mario Bradley (Biotronik, Inc.); Jodie Alwin, Dan Heffron, Tom Ermis, and Jim Gilkerson (Boston Scientific Company); Nancy Magnotto, Gregg Deutsch, Jay Wilcox, Jim Glover, Jeff Gilberg, Nancy Magnotto,

and Dave Furland (Medtronic, Inc.); Jim Gerrity and Marcel Limousin (Sorin Group); Leslie Meyer, Daryel Davis, Dan Hecker, and Steve Heinrich (St Jude Medical).

Many others have influenced this project. All our physician and nursing colleagues in the Heart Rhythm Services group at Mayo Clinic Rochester have had either a direct or an indirect influence on portions of this text. Our intention is not to officially represent our entire practice of pacing and electrophysiology with this text. However, given a significant consistency in the way we practice and how we approach patients, we would expect general agreement with the clinical management strategies put forward in this text.

Although the content of this text is patterned after the first edition, we have reorganized some sections, expanded ICD information and added CRT discussions to almost all chapters, to reflect the evolution of device practice. Internet-based remote monitoring has become a reality, “recalls” must be addressed, and new insights have revised how device therapy can prolong life and improve its quality; these important topics are extensively addressed. We have attempted to provide a logical progression from a description of device indications to selection of hardware, implantation, complications, programming, troubleshooting, and follow-up. It is our deepest hope that this effort will enhance the care of patients with arrhythmias.

David L. Hayes, MD & Paul A. Friedman, MD

Clinically Relevant Basics of Pacing and Defibrillation

T. Jared Bunch, David L. Hayes, Paul A. Friedman

Anatomy and physiology of the cardiac conduction system

The cardiac conduction system consists of specialized tissue involved in the generation and conduction of electrical impulses throughout the heart. In this book, we review how device therapy can be optimally utilized for various forms of conduction system disturbances, tachyarrhythmias, and for heart failure. Knowledge of the normal anatomy and physiology of the cardiac conduction system is critical to understanding appropriate utilization of device therapy.

The sinoatrial (SA) node, located at the junction of the right atrium and the superior vena cava, is normally the site of impulse generation (Fig. 1.1). The SA node is composed of a dense collagen matrix containing a variety of cells. The large, centrally located P cells are thought to be the origin of electrical impulses in the SA node, which is surrounded by transitional cells and fiber tracts extending through the perinodal area into the right atrium proper. The SA node is richly innervated by the autonomic nervous system, which has a key function in heart rate regulation. Specialized fibers, such as Bachmann's bundle, conduct the impulse throughout the right and left atria. The SA node has the highest rate of spontaneous depolarization and under normal circumstances is responsible for generating most impulses.

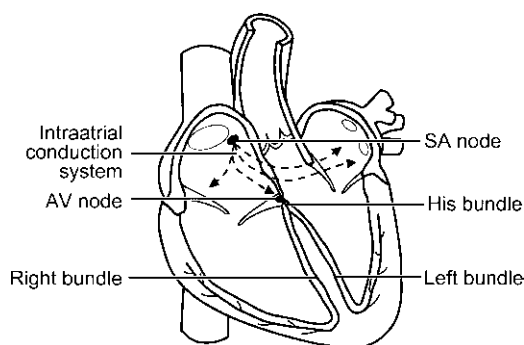


Fig. 1.1 Drawing of the cardiac conduction system. AV, atrioventricular; SA, sinoatrial. See text for details.

Atrial conduction fibers converge, forming multiple inputs into the atrioventricular (AV) node, a small subendocardial structure located within the interatrial septum (Fig. 1.1). The AV node likewise receives abundant autonomic innervation, and it is histologically similar to the SA node because it is composed of a loose collagen matrix in which P cells and transitional cells are located. Additionally, Purkinje cells and myocardial contractile fibers may be found. The AV node allows for physiological delay between atrial and ventricular contraction, resulting in optimal cardiac hemodynamic function. It can also function as a subsidiary “pacemaker” should the SA node fail. Finally, the AV node functions (albeit typically suboptimally) to regulate the number of impulses eventually reaching the ventricle in instances of atrial tachyarrhythmia.

Purkinje fibers emerge from the distal AV node to form the bundle of His, which runs through the mem-

branous septum to the crest of the muscular septum, where it divides into the various bundle branches. The bundle branch system exhibits significant individual variation and is invariably complex. The right bundle is typically a discrete structure running along the right side of the interventricular septum to the anterior papillary muscle, where it divides. The left bundle is usually a large band of fibers fanning out over the left ventricle, sometimes forming functional fascicles. Both bundles eventually terminate in individual Purkinje fibers interdigitating with myocardial contractile fibers. The His-Purkinje system has little in the way of autonomic innervation.

Because of their key function and location, the SA and AV nodes are the most common sites of conduction system failure; it is therefore understandable that the most common indications for pacemaker implantation are SA node dysfunction and high-grade AV block. It should be noted, however, that conduction system disease is frequently diffuse and may involve the specialized conduction system at multiple sites.

Although the earliest pacemakers were designed to treat life-threatening ventricular bradyarrhythmias, indications have drastically expanded to include conditions that do not specifically involve intrinsic conduction system disease. Guidelines have been developed to provide uniform criteria for device implantation, but the importance of the patient's clinical status and any extenuating circumstances should also be considered.

Electrophysiology of myocardial stimulation

Stimulation of the myocardium by a pacemaker re-

quires the initiation of a self-propagating wave of depolarization from the site of initial activation, whether from a native "pacemaker" or from an artificial stimulus. Myocardium exhibits a biological property referred to as "excitability," which is a response to a stimulus out of proportion to the strength of that stimulus.¹ Excitability is maintained by separation of chemical charge, which results in an electrical transmembrane potential. In cardiac myocytes, this electrochemical gradient is created by differing intracellular and extracellular concentrations of sodium (Na^+) and potassium (K^+) ions; Na^+ ions predominate extracellularly and K^+ ions predominate intracellularly. Although this transmembrane gradient is maintained by the high chemical resistance intrinsic to the lipid bilayer of the cellular membrane, passive leakage of these ions occurs across the cellular membrane through ion channels. Passive leakage is offset by two active transport mechanisms, each transporting three positive charges out of the myocyte in exchange for two positive charges that are moved into the myocyte, producing cellular polarization.^{2,3} These active transport mechanisms require energy and are susceptible to disruption when energy-generating processes are interrupted.

The chemical gradient has a key role in the generation of the transmembrane action potential (Fig. 1.2). The membrane potential of approximately -90 mV drifts upward to the threshold potential of approximately -70 to -60 mV . At this point, specialized membrane-bound channels modify their conformation from an inactive to an active state, which allows the abrupt influx of extracellular Na^+ ions into the myocyte^{4,5}, creating phase 0 of the action potential and rapidly raising the transmembrane potential to approximately $+20 \text{ mV}$.^{6,7}

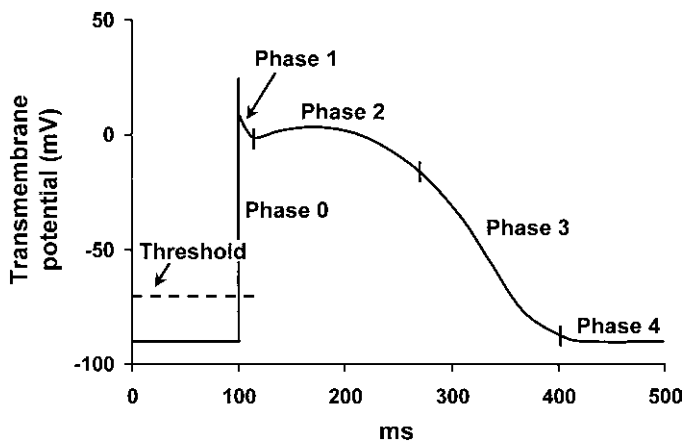


Fig. 1.2 Action potential of a typical Purkinje fiber, with the various phases of depolarization and repolarization (described in the text). (From Stokes KB, Kay GN. Artificial electric cardiac stimulation. In: Ellenbogen KA, Kay GN, Wilkoff BL, eds. *Clinical cardiac pacing*. Philadelphia: WB Saunders Co., 1995:3–37. By permission of the publisher.)

This rapid upstroke creates a short period of overshoot potential (phase 1), which is followed by a plateau period (phase 2) created by the inward calcium (Ca^{2+}) and Na^+ currents balanced against outward K^+ currents.^{8–10} During phase 3 of the action potential, the transmembrane potential returns to normal, and during phase 4 the gradual upward drift in transmembrane potential repeats. The shape of the transmembrane potential and the relative distribution of the various membrane-bound ion channels differ between the components of the specialized cardiac conduction system.

Depolarization of neighboring cells occurs as a result of passive conduction via low-resistance intercellular connections called “gap junctions,” with active regeneration along cellular membranes.^{11,12} The velocity of depolarization throughout the myocardium depends on the speed of depolarization of the various cellular components of the myocardium and on the geometrical arrangement and orientation of the myocytes. Factors such as myocardial ischemia, electrolyte imbalance, metabolic abnormalities, and drugs may affect the depolarization and depolarization velocity.

Pacing basics

Stimulation threshold

Artificial pacing involves delivery of an electrical impulse from an electrode of sufficient strength to cause depolarization of the myocardium in contact with that electrode and propagation of that depolarization to the rest of the myocardium. The minimal amount of energy required to produce this depolarization is called the

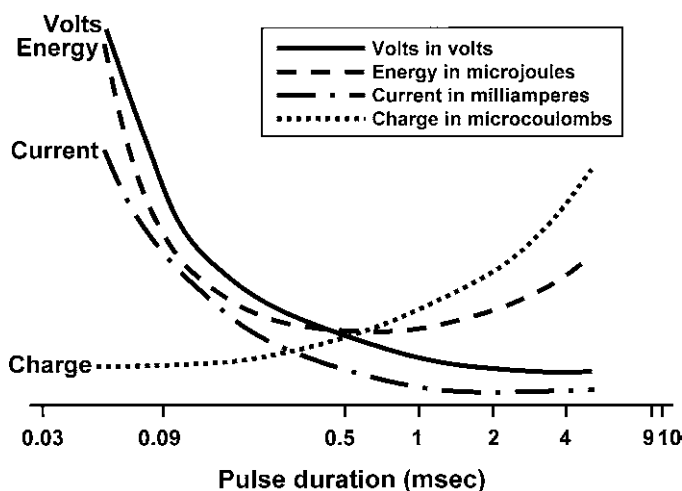
stimulation threshold. The components of the stimulus include the pulse amplitude (measured in volts) and the pulse duration (measured in milliseconds). An exponential relationship exists between the stimulus amplitude and the duration, resulting in a hyperbolic strength–duration curve. At short pulse durations, a small change in the pulse duration is associated with a significant change in the pulse amplitude required to achieve myocardial depolarization; conversely, at long pulse durations, a small change in pulse duration has relatively little effect on threshold amplitude (Fig. 1.3). Two points on the strength–duration curve should be noted (Fig. 1.4). The *rheobase* is defined as the smallest amplitude (voltage) that stimulates the myocardium at an infinitely long pulse duration (milliseconds). The *chronaxie* is the threshold pulse duration at twice the stimulus amplitude, which is twice the rheobase voltage. The chronaxie is important in the clinical practice of pacing because it approximates the point of minimum threshold energy (microjoules) required for myocardial depolarization.

The relationship of voltage, current, and pulse duration to stimulus energy is described by the formula

$$E = V^2/R \times t$$

in which E is the stimulus energy, V is the voltage, R is the total pacing impedance, and t is the pulse duration. This formula demonstrates the relative increase in energy with longer pulse durations. The energy increase due to duration is offset by a decrement in the needed voltage.

Fig. 1.3 Relationship of charge, energy, voltage, and current to pulse duration. As the pulse duration is shortened, voltage and current requirements increase. Charge decreases as pulse duration shortens. At threshold, energy is lowest at a pulse duration of 0.5–1.0 ms and increases at pulse widths of shorter and longer duration. (Modified from Furman S. Basic concepts. In: Furman S, Hayes DL, Holmes DR Jr, eds. *A practice of cardiac pacing*. Mount Kisco, NY: Futura Publishing Co. By permission of the publisher.)



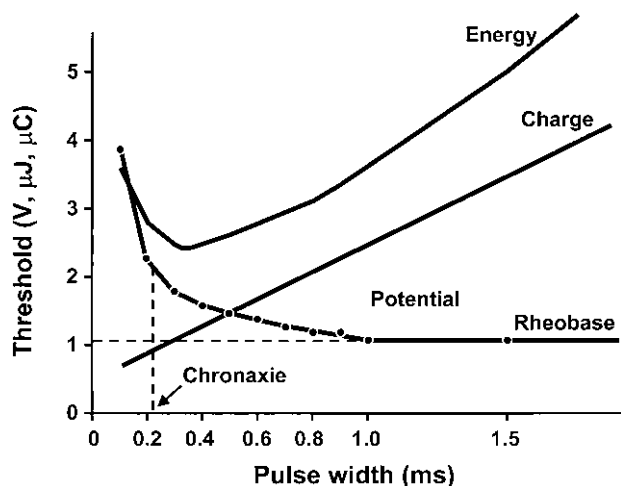


Fig. 1.4 Relationships among chronic ventricular strength-duration curves from a canine, expressed as potential (V), charge (μC), and energy (μJ). Rheobase is the threshold at infinitely long pulse duration. Chronaxie is the pulse duration at twice rheobase. (From Stokes K, Bornzin G. The electrode-biointerface stimulation. In: Barold SS, ed. *Modern cardiac pacing*. Mount Kisco, NY: Futura Publishing Co., 1985:33–77. By permission of the publisher.)

The strength-duration curve discussed thus far has been that of a constant voltage system, because contemporary permanent pacemakers are constant voltage systems. Constant current devices are no longer used (Fig. 1.5). It should be recognized, however, that constant current strength-duration curves can also be constructed.¹³ These strength-duration curves, like constant voltage curves, are hyperbolic in shape, but they have a much more gradual decline in current requirements as the pulse width lengthens. Because of this gradual de-

cline, chronaxie of a constant current system is significantly greater than that in a constant voltage system.

Impedance is the term applied to the impediment to current flow in the pacing system. Ohm's law describes the relationship among voltage, current, and resistance as

$$V = IR$$

in which V is the voltage, I is the current, and R is the resistance. Although Ohm's law is used for determining impedance, technically impedance and resistance are not interchangeable terms. Impedance implies inclusion of all factors that contribute to current flow impediment, including lead conductor resistance, electrode resistance, resistance due to electrode polarization, capacitance and inductance. Technically, the term "resistance" does not include the effects of capacitance (storage of charge) or inductance (storage of current flow) to impede current flow. Nevertheless, Ohm's law (substituting impedance for R) is commonly used for calculating impedance. In constant voltage systems, the lower the pacing impedance, the greater the current flow; conversely, the higher the pacing impedance, the lower the current flow. Ideally, the lead conductor material would have a low resistance to minimize the generation of energy-wasting heat as the current flows along the lead, and the electrode would have a high resistance to minimize current flow and negligible electrode polarization. Decreasing the electrode radius minimizes current

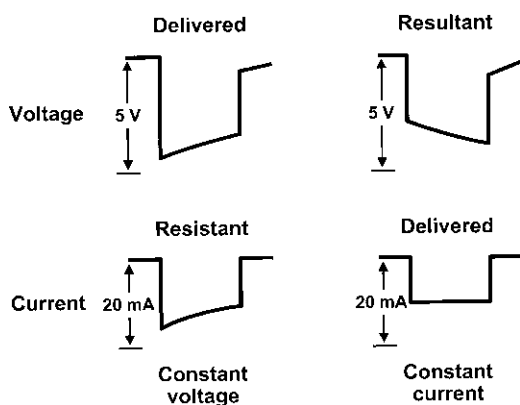


Fig. 1.5 Diagrammatic representation of the delivered voltage and resultant current in a constant-voltage system compared with the delivered current and resultant voltage in a constant-current system. (Modified from Stokes K, Bornzin G. The electrode-biointerface stimulation. In: Barold SS, ed. *Modern cardiac pacing*. Mount Kisco, NY: Futura Publishing Co., 1985:33–77. By permission of the publisher.)

flow by providing greater electrode resistance and increased current density, resulting in greater battery longevity and lower stimulation thresholds.¹⁴

“Polarization” refers to layers of oppositely charged ions that surround the electrode during the pulse stimulus. It is related to the movement of positively charged ions (Na^+ and H_3O^+) to the cathode; the layer of positively charged ions is then surrounded by a layer of negatively charged ions (Cl^- , HPO_4^{2-} , and OH^-). These layers of charge develop during the pulse stimulus, reaching peak formation at the termination of the pulse stimulus, after which they gradually dissipate. Polarization impedes the movement of charge from the electrode to the myocardium, resulting in a need for increased voltage. Since polarization develops with increasing pulse duration, one way to combat formation of polarization is to shorten the pulse duration. Electrode design has incorporated the use of materials that discourage polarization, such as platinum black, iridium oxide, titanium nitride, and activated carbon.¹⁵ Finally, polarization is inversely related to the surface area of the electrode. To maximize the surface area (to reduce polarization) but minimize the radius (to increase electrode impedance), electrode design incorporates a small radius but a porous, irregular surface construction.¹⁶ Leads designed to maximize these principles are considered “high-impedance” leads.

Variations in stimulation threshold

Myocardial thresholds typically fluctuate, occasionally dramatically, during the first weeks after implantation. After implantation of earlier generations of endocardial leads, the stimulation threshold would typically rise rapidly in the first 24 h and then gradually increase to a peak at approximately 1 week (Fig. 1.6). Over the ensuing 6–8 weeks, the stimulation threshold would usually decline to a level somewhat higher than that at implantation, but less than the peak threshold, known as the “chronic threshold”.^{17,18} The magnitude and duration of this early increase in threshold is highly dependent on lead design, the interface between the electrode and the myocardium, and individual patient variation, but chronic thresholds would typically be reached by 3 months. The single most important lead design change to alter pacing threshold evolution was incorporation of steroid elution at the lead tip. With steroid elution there is a slight increase in thresholds post implantation, with subsequent reduction to almost that of acute thresholds.^{19,20}

Transvenous pacing leads have used passive or active fixation mechanisms to provide a stable electrode–myocardium interface. Active fixation leads may have higher initial pacing thresholds at implantation, but frequently decline significantly within the first 5–30 min after placement.¹⁷ This effect has been at-

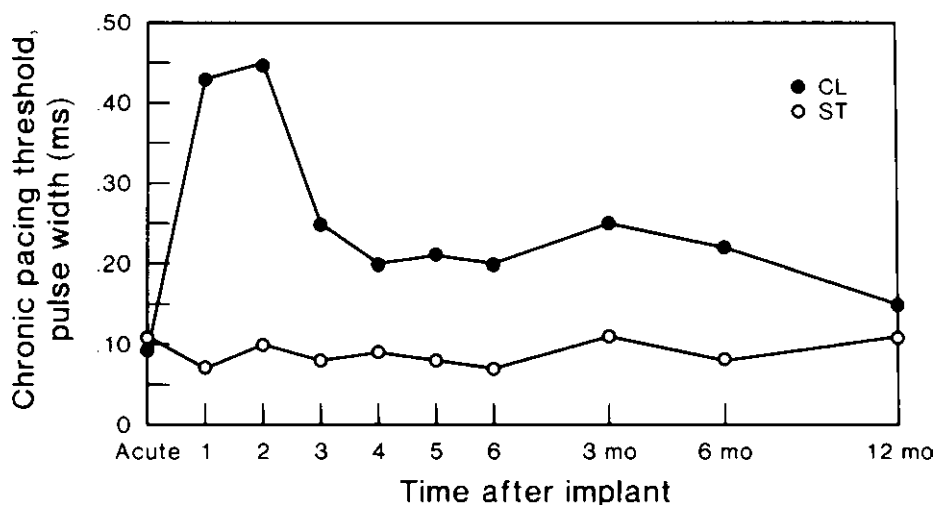


Fig. 1.6 Long-term pacing thresholds from a conventional lead (no steroid elution) (CL; closed circles) and a steroid-eluting lead (ST; open circles). With the conventional lead, an early increase in threshold decreases to a plateau at approximately 4 weeks. The threshold for the steroid-eluting lead remains relatively flat, with no significant

change from short-term threshold measurements. (From Furman S. Basic concepts. In: Furman S, Hayes DL, Holmes DR Jr, eds. *A practice of cardiac pacing*, second edn. Mount Kisco, NY: Futura Publishing Co., 1989:23–78. By permission of Mayo Foundation.)

tributed to hyperacute injury due to advancement of the screw into the myocardium. On a cellular level, implantation of a transvenous pacing lead results in acute injury to cellular membranes, which is followed by the development of myocardial edema and coating of the electrode surface with platelets and fibrin. Subsequently, various chemotactic factors are released, and an acute inflammatory reaction develops, consisting of mononuclear cells and polymorphonuclear leukocytes. After the acute response, release of proteolytic enzymes and oxygen free radicals by invading macrophages accelerates cellular injury. Finally, fibroblasts in the myocardium begin producing collagen, leading to production of the fibrotic capsule surrounding the electrode. This fibrous capsule ultimately increases the effective radius of the electrode, with a smaller increase in surface area.^{21,22} Steroid-eluting leads are believed to minimize fibrous capsule formation. In both atrial and ventricular active fixation leads, steroid elution results in long-term reduction in energy consumption with maintenance of stimulation thresholds, lead impedance values, and sensing thresholds.^{23,24}

The stimulation threshold typically has a circadian pattern, generally increasing during sleep and decreasing during the day, probably reflecting changes in autonomic tone. The stimulation threshold may also rise after eating; during hyperglycemia, hypoxemia or acute viral illnesses; or as a result of electrolyte fluctuations. These changes, as well as the circadian variation in stimulation threshold, are usually minimal. Certain drugs used in patients with cardiac disease may also increase pacing thresholds (see Chapter 8: Programming).

The inflammatory reaction and subsequent fibrosis that occur after lead implantation may act as an insulating shield around the electrode. These processes effectively increase the distance between the electrode and the excitable tissue, allowing the stimulus to disperse partially before reaching the excitable cells. These changes result in an increased threshold for stimulation and attenuate the amplitude and slew rate of the endocardial signal being sensed. This is a process termed "lead maturation." Improvements in electrode design and materials have reduced the severity of the inflammatory reaction and thus improved lead maturation rates.^{19,25} When the capture threshold exceeds the programmed output of the pacemaker, exit block will occur; loss of capture will result if the capture threshold exceeds the programmed output of the pacemaker.^{17,26} Exit block, a consequence of lead matu-

ration, results from the progressive rise in thresholds over time.^{17,26} This phenomenon occurs despite initial satisfactory lead placement and implantation thresholds, often but not always occurs in parallel in the atrium and ventricle, and usually recurs with placement of subsequent leads. Steroid-eluting leads prevent exit block in most, but not all patients (Fig. 1.7).

Sensing

The first pacemakers functioned as fixed-rate, VOO devices. All contemporary devices offer demand-mode pacing, which pace only when the intrinsic rate is below the programmed rate. For such devices to function as programmed, accurate and consistent sensing of the native rhythm was essential.

Intrinsic cardiac electrical signals are produced by the wave of electrical current through the myocardium (Fig. 1.8). As the wavefront of electrical energy approaches an endocardial electrode, the electrode becomes positively charged relative to the depolarized region, recorded as a positive deflection in the intracardiac electrogram. As the wavefront passes directly under the electrode, the outside of the cell abruptly becomes negatively charged, and a sharp negative deflection is recorded, which is referred to as the intrinsic deflection.²⁷ It is considered to occur at the moment the advancing wavefront passes directly underneath the electrode. Smaller positive and negative deflections preceding and following the intrinsic deflection represent activation of surrounding myocardium. Ventricular electrograms typically are much larger than atrial electrograms because the ventricular mass is greater. The maximum frequency densities of atrial and ventricular electrograms have generally been found to be in the range of 80–100 Hz in the atrium and 10–30 Hz in the ventricle (these frequencies may differ slightly with newer leads/technologies). Based on these frequencies, filtering systems of pulse generators were designed to attenuate signals outside these ranges. Filtering and use of blanking and refractory periods have markedly reduced unwanted sensing, although myopotential frequencies (ranging from 10 to 200 Hz) considerably overlap with those generated by atrial and ventricular depolarization and are difficult to filter out, especially during sensing in a unipolar configuration.^{28–30} Shortening of the tip-to-ring spacing has also improved atrial sensing and rejection of far-field R waves.

Another component of the intracardiac electrogram is the slew rate, i.e. the peak slope of the devel-

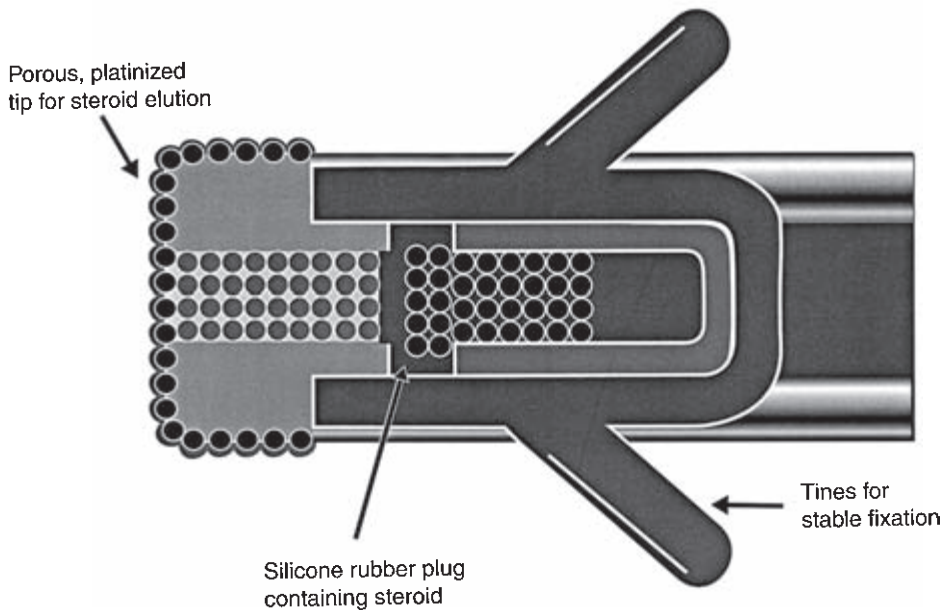


Fig. 1.7 Diagram of a steroid-eluting passive fixation lead. The electrode has a porous, platinized tip. A silicone rubber plug is impregnated with 1 mg of dexamethasone sodium.

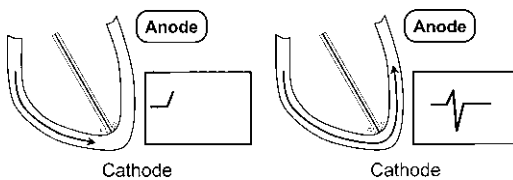


Fig. 1.8 Schema of the relationship of the pacing lead to the recorded electrogram with unipolar sensing. Left, As the electrical impulse moves toward the cathode (lead tip), a positive deflection is created in the electrogram. Right, As the electrical impulse passes the cathode, the deflection suddenly becomes downward, and as the impulse moves away from the cathode, a negative deflection occurs.

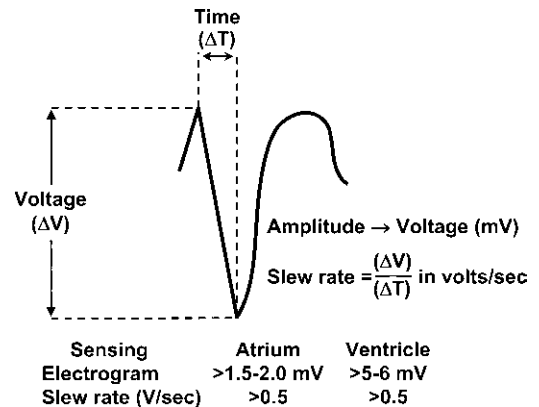


Fig. 1.9 In the intracardiac electrogram, the difference in voltage recorded between two electrodes is the amplitude, which is measured in millivolts. The slew rate is volts per second and should be at least 0.5.

oping electrogram³¹ (Fig. 1.9). The slew rate represents the maximal rate of change of the electrical potential between the sensing electrodes and is the first derivative of the electrogram (dV/dt). An acceptable slew rate should be at least 0.5V/s in both the atrium and the ventricle. In general, the higher the slew rate, the higher the frequency content and the more likely the signal will be sensed. Slow, broad signals, such as those generated by the T wave, are much less likely to be sensed because of a low slew rate and lower frequency density.

Polarization also affects sensing function. After termination of the pulse stimulus, an excess of positive

charge surrounds the cathode, which then decays until electrically neutral. Afterpotentials can be sensed with inappropriate inhibition or delay of the subsequent pacing pulse (Fig. 1.10). The amplitude of afterpotentials is directly related to both the amplitude and the duration of the pacing pulse; thus, they are most likely to be sensed when the pacemaker is programmed to high voltage and long pulse duration in combination

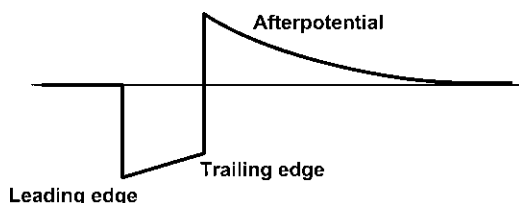


Fig. 1.10 Diagram of a pacing pulse, constant-voltage, with leading edge and trailing edge voltage and an afterpotential with opposite polarity. As described in the text, afterpotentials may result in sensing abnormalities.

with maximal sensitivity.³¹ The use of programmable sensing refractory and blanking periods has helped to prevent the pacemaker from reacting to afterpotentials, although in dual-chamber systems, atrial afterpotentials of sufficient strength and duration to be sensed by the ventricular channel may result in inappropriate ventricular inhibition (crosstalk), especially in unipolar systems.^{32,33} Afterpotentials may be a source of problems in devices with automatic threshold measurement and capture detection; the use of leads designed to minimize afterpotentials may increase the effectiveness of such algorithms.³⁴

“Source impedance” is a term used to describe the voltage drop that occurs from the site of the origin of the intracardiac electrogram to the proximal portion of the lead.³⁵ Components include the resistance between the electrode and the myocardium, the resistance of the lead conductor material, and the effects of polarization. The resistance between the electrode and the myocardium, as well as polarization, is inversely related to the surface area of the electrode; thus, the effects of both can be minimized by a large electrode surface area. The electrogram actually seen by the pulse generator is determined by the ratio between the sensing amplifier (input impedance) and the lead (source impedance). Less attenuation of the signal from the myocardium occurs when there is a greater ratio of input impedance to source impedance. Clini-

cally, impedance mismatch is seen with insulation or conductor failure, which results in sensing abnormalities or failure.

Lead design

Pacing lead components include the electrode and fixation device, the conductor, the insulation, and the connector pin (Figs 1.11 and 1.12). Leads function in a harsh environment *in vivo*. They must be constructed of materials that provide both mechanical stability and flexibility; they must have satisfactory electrical conductive and resistive properties; the insulating material must be durable but ideally have a low friction coefficient to facilitate implantation; and the electrode must provide good mechanical and electrical contact with the myocardium. Industry continues to modify and improve lead design, but the “ideal” lead remains a constant goal.

As previously discussed, optimal stimulation and sensing thresholds favor an electrode with a small radius and a large surface area. Electrode shape and surface composition have evolved over time. Early models utilized a round spherical shape with a smooth metal surface. Electrodes with an irregular, textured surface allow for increased surface area without an increase in electrode radius.^{16,34,36} To achieve increased electrode surface area, manufacturers have used a variety of designs, including microscopic pores, coatings of microspheres, and wire filament mesh.

Unfortunately, relatively few conductive materials have proven to be satisfactory for use in pacing electrodes. Ideally, electrodes are biologically inert, resist degradation over time, and do not elicit a marked tissue reaction at the myocardium–electrode interface. Certain metals, such as zinc, copper, mercury, nickel, lead and silver, are associated with toxic reactions with the myocardium. Stainless steel alloys are susceptible to corrosion. Titanium, tantalum, platinum and iridium oxide acquire a surface coating of

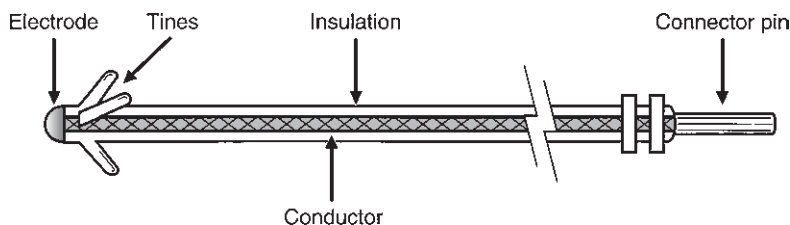


Fig. 1.11 Basic components of a passive fixation pacing lead with tines.

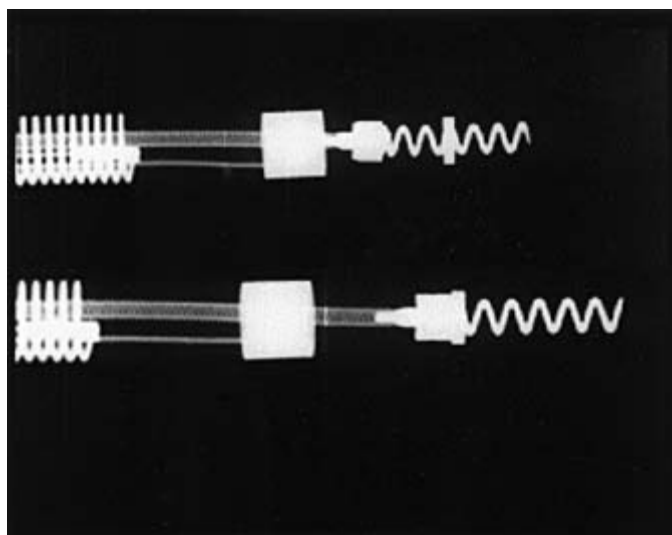


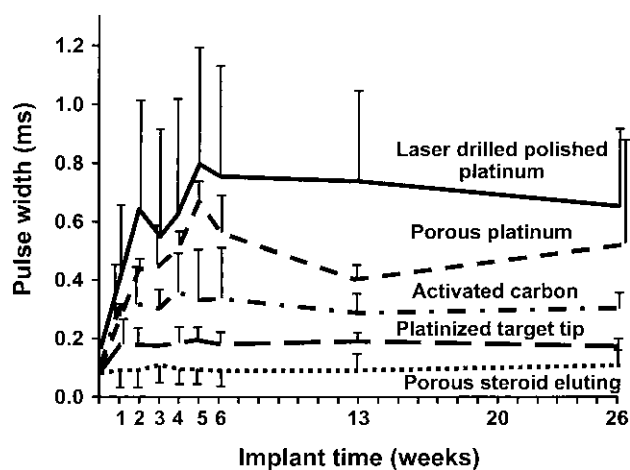
Fig. 1.12 Radiographic example of an active fixation screw-in lead with a retractable screw rather than a screw that is always extended. The screw is extended in the lower image but not in the upper image.

oxides that impedes current transfer. Materials currently in use are platinum-iridium, platinized titanium-coated platinum, iridium oxide, and platinum (Fig. 1.13). Carbon electrodes seem to be least susceptible to corrosion; they have also been improved by a process known as activation, which roughens the surface to increase the surface area and allow for tissue ingrowth.³⁷

Lead fixation may be active or passive. Passive fixation endocardial leads usually incorporate tines at the tip that become ensnared in trabeculated tissue in the right atrium or ventricle, providing lead stability. Leads designed for coronary venous placement usually incorporate a design that wedges the lead against

the wall of the coronary vein. Active fixation leads almost exclusively utilize screw mechanisms to embed in the myocardium to provide lead stability. Some leads incorporate screws that are electrically inactive, and in others the screw is electrically active. There are advantages and disadvantages to each design, and the clinical situation and preference of the operator are important considerations when a lead is chosen. Considerable myocardial and fibrous tissue enveloping the tip typically develops with both active and passive fixation leads. However, the encasement of the tines of a passive fixation lead by fibrous tissue often makes the extraction of passive fixation leads more difficult than that of active fixation leads. Active fixation leads are

Fig. 1.13 Capture thresholds from implantation to 26 weeks from a variety of unipolar leads with similar geometric surface area electrodes. From top to bottom, the curves represent laser-drilled polished platinum; porous-surface platinum; activated carbon; platinized target tip; and porous steroid-eluting leads. (From Stokes KB, Kay GN. Artificial electric cardiac stimulation. In: Ellenbogen KA, Kay GN, Wilkoff BL, eds. *Clinical cardiac pacing*. Philadelphia: WB Saunders Co., 1995:3–37. By permission of the publisher.)



often preferable in patients with distorted anatomy, such as those with congenital cardiac defects or those with surgically amputated atrial appendages. Active fixation leads are also preferable in patients with high right-sided pressures. As alternative site pacing has evolved, i.e. the placements of leads outside the right atrial appendage and right ventricular apex, screw-in leads have become more popular and necessary for long-term stability.

There are various types of mechanism used to keep the screw unexposed until it is placed in an optimal site for fixation. One example is a system in which the screw is extendable and retractable from the pacemaker lead tip. This allows the operator to designate the precise location and timing to extend the screw from the tip. Another example involves covering a fixed helix screw in a material that dissolves in the blood stream in a time period that is advantageous for lead positioning. For example, screws can be covered by a mannitol compound that dissolves over time in the blood stream. Since the mannitol covers the screw, it prevents it from catching on tissue, allowing easier lead placement.

New technologies have emerged to assist in the placement of leads to targeted anatomical sites. Catheter-delivered systems use a deflectable catheter that is braided to allow the simultaneous ability to torque the catheter. A second technology developed to reach difficult anatomical targets is to use an over-the-wire lead delivery system, mainly used with placement of coronary venous leads for left ventricular stimulation. With this system the lead can be advanced to a stable position, a guidewire then being advanced to navigate tortuous regions similar to techniques used extensively for coronary angiography, followed by advancement of the lead over the wire. This approach not only improves access to target sites, but decreases injury to coronary venous structures. By combining these technologies, access to target sites has improved greatly, in particular, coronary vein subselection for left ventricular lead placement.

Conductors are commonly of a multifilament design to facilitate tensile strength and reduce resistance to metal fatigue (Fig. 1.14). Alloys such as MP35N (cobalt, nickel, chromium and molybdenum) and nickel-silver are typically used in modern pacing leads. Bipolar leads may be of coaxial design, with an inner coil extending to the distal electrode and an outer coil terminating at the proximal electrode (Fig. 1.15). This design requires that the conductor coils be separated

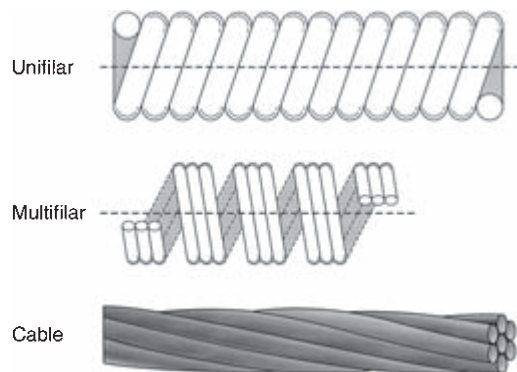


Fig. 1.14 Conductor coils may be of unifilar, multifilar, or cable design. The multifilar and cable designs allow the conductor to be more flexible and more resistant to fracture.

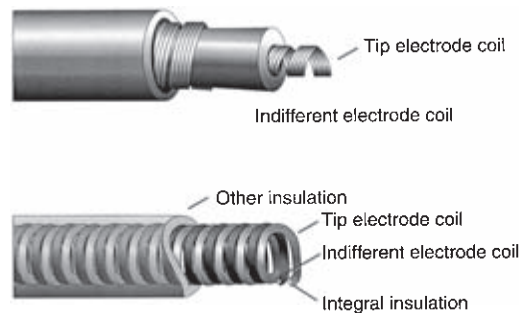


Fig. 1.15 Varieties of conductor construction. Top, bipolar coaxial design with an inner multifilar coil surrounded by insulation (inner), an outer multifilar coil, and outer insulation. Bottom, individually coated wires wound together in a single multifilar coil for bipolar pacing.

by a layer of inner insulation. Coaxial designs remain commonly used in the treatment of bradyarrhythmias. Some bipolar leads are coradial, or “parallel-wound”; that is, two insulated coils are wound next to each other. Leads may also be constructed with the conductor coils parallel to each other (multiluminal), again separated by insulating material (Fig. 1.16). This type of design is typically used for tachyarrhythmia leads. Additionally, leads may use a combination of coils and cables. The coil facilitates the passage of a stylet for lead implantation, and the cable allows a smaller lead body.

Two materials have predominated in lead insulation: silicone and polyurethane. Each has its respective advantages and disadvantages, but the overall performance of both materials has been excellent.³⁸ Table 4.2 in

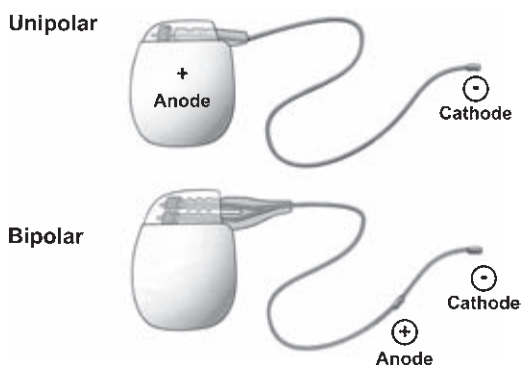


Fig. 1.16 In a unipolar configuration, the pacemaker case serves as the anode, or (+), and the electrode lead tip as the cathode, or (-). In a bipolar configuration, the anode is located on the ring, often referred to as the “ring electrode,” proximal to the tip, or cathode. The distance between tip and ring electrode varies among manufacturers and models.

Chapter 4 compares the advantages and disadvantages of these two insulating materials.

The two grades of polyurethane that have had the widest use are Pellathane 80A and Pellathane 55D. Early after the introduction of polyurethane as an insulating material, it became clear that clinical failure rates with specific leads were higher than acceptable; further investigation revealed that the failures were occurring primarily in leads insulated with the P80A polymer.^{36,39} Microscopic cracks developed in the P80A polymer, initially occurring as the heated polymer cooled during manufacture; with additional environmental stress, these cracks propagated deeper into the insulation, resulting in failure of the lead insulation.

Polyurethane may also undergo oxidative stress in contact with conductors containing cobalt and silver chloride, resulting in degradation of the lead from the inside and subsequent lead failure. Some current leads use silicone with a polyurethane coating, incorporating the strength and durability of silicone with the ease of handling of polyurethane while maintaining a satisfactory external lead diameter. Silicone rubber is well known to be susceptible to abrasion wear, cold flow due to cyclic compression, and wear from lead-to-lead and lead-to-can contact. Current silicone leads have surface modifications that improve lubricity and reduce friction in blood. Second, preliminary studies have suggested that a hybrid coating of silicone and polyurethane may offer improved wear.⁴⁰ Despite

lead improvements, laboratory testing and premarketing, clinical trials have been inadequate to predict the long-term performance of leads, so that clinicians implanting the devices or performing follow-up in patients with pacing systems must vigilantly monitor lead status.

Contemporary leads and connectors are standardized to conform to international guidelines (IS-1 Standard), which mandate that leads have a 3.2-mm diameter in-line bipolar connector pin.⁴¹ These standards were established many years ago because some leads and connector blocks were incompatible, requiring the development of multiple adaptors. Some patients who have functioning leads of the older 5- or 6-mm diameter unipolar design require lead adaptors when the pulse generator is replaced.

Coronary venous lead connectors were initially developed to accommodate patients with heart failure who had previously implanted pacemakers for other reasons and were considered eligible for an upgrade to biventricular pacing. For these patients, the ventricular output of the pacemaker generator was divided via a “Y” connector from one bipolar output to two separate outputs (usually a unipolar left ventricle and a bipolar right ventricle or a bipolar left ventricle and a bipolar right ventricle) to accommodate the left ventricular lead. However, this approach can lead to atrial oversensing, improper measurement of left ventricular thresholds, and inappropriate shocks.^{42,43} Currently, most left ventricular leads are connected to the pacemaker independently. The left ventricular leads are either bipolar or unipolar with a steroid eluting tip.

Bipolar vs. unipolar pacing and sensing

In unipolar pacing systems, the lead tip functions as the cathode and the pulse generator functions as the anode (Fig. 1.16). In bipolar systems, the lead tip functions as the cathode and the lead ring functions as the anode (Fig. 1.16). Unipolar leads are of simpler design and have a smaller external diameter. Unipolar leads have historically demonstrated greater durability than bipolar leads. In recent years the difference in durability has been less distinct. Unipolar leads do not offer the option of bipolar function. Although unipolar and bipolar leads are readily available, present usage of transvenous leads is almost exclusively bipolar in the USA. This is in contrast to epicardial leads, of which there is a lower percentage of bipolar leads in use. Bipolar leads may function in the unipolar mode if the pace-

maker is so programmed. They are available in several designs, generally coaxial or multiluminal. Regardless of design, the external diameter of a bipolar lead is usually greater than that of unipolar leads because each coil must be electrically separated by insulating material. Bipolar pacing and sensing are preferred over unipolar because bipolar pacing cannot cause extracardiac stimulation at the pulse generator, which may occasionally occur with unipolar pacing due to current returning to the generator. Also, bipolar sensing is less likely to detect myopotentials, far-field signals and electromagnetic interference.⁴⁴

There are long-standing controversies regarding unipolar vs. bipolar pacing and sensing configuration and which, if either, are superior.⁴⁴ Advocates of unipolar configuration argue that improvements in sensing circuitry and pacemaker filtering capabilities have minimized unipolar oversensing of extracardiac signals. The design of unipolar leads is often more simple and therefore the lead size may be less. They also argue that bipolar leads have a historically higher failure rate than unipolar leads. Although this is true, if the specific failures of Pellathane 80A and 55D that occurred many years ago are removed from the analysis, the failure rate between unipolar and bipolar lead designs does not differ significantly and varies between different manufacturers.⁴⁵ Unipolar leads are often considered safer because they do not short circuit significantly when there are insulation breaches, although they may be susceptible to significant external interference. Nevertheless, a lead that is malfunctioning in the bipolar mode may function satisfactorily when programmed to the unipolar configuration (see Chapter 8: Programming).

Most pulse generators offer independently programmable pacing and sensing in each channel; however, bipolar programming of a device attached to a unipolar lead results in no output. Bipolar leads can function in the unipolar mode; the converse is not true.

Left ventricular leads

Cardiac resynchronization therapy with biventricular pacing is an established treatment for patients with severe congestive heart failure, low left ventricular ejection fraction, and New York Heart Association class III or IV heart failure.⁴⁶ In order to pace the left ventricle, a pacing lead is implanted transvenously through the coronary sinus and coronary vein to stimulate the left ventricular free wall. Resynchronization is obtained by stimulating both ventricles to contract with mini-

mal intraventricular delay, thereby improving the left ventricular performance.⁴⁷ Modifications of the tip geometry have improved the stability of the passive lead over time. Tissue ingrowth can be a major impediment to the removal of defibrillation leads implanted in the coronary sinus. Coating these leads with polytetrafluoroethylene and backfilling the coil with medical adhesive facilitates transvenous lead removal.⁴⁸

Pulse generators

All pulse generators include a power source, an output circuit, a sensing circuit, a timing circuit, and a header with a standardized connector (or connectors) to attach a lead (or leads) to the pulse generator.⁴⁹ Essentially, all devices are capable of storing some degree of diagnostic information that can be retrieved at a later time. Most pacemakers incorporate a rate-adaptive sensor. Despite increasing complexity, device size has continued to decrease. This has led to a variable effect on the potential longevity.

Many power sources have been used for pulse generators over the years. Lithium iodine cells have been the energy source for almost all contemporary pulse generators. Newer pacemakers and implantable cardioverter-defibrillators (ICDs) that can support higher current drains for capacitor charging and high-rate antitachycardia pacing use lithium-silver-oxide-vanadium chemistries. Lithium is the anodal element and provides the supply of electrons; iodine is the cathodal element and accepts the electrons. The cathodal and anodal elements are separated by an electrolyte, which serves as a conductor of ionic movement but a barrier to the transfer of electrons. The circuit is completed by the external load, i.e. the leads and myocardium. The battery voltage of the cell depends on the chemical composition of the cell; at the beginning of life for the lithium iodine battery, the cell generates approximately 2.8V, which decreases to 2.4V when approximately 90% of the useable battery life has been reached. The voltage then exponentially declines to 1.8V as the battery reaches end-of-life. However, the voltage at which the cell reaches a certain depth of discharge is load dependent. The elective replacement indicated voltages were chosen based on the shape of the discharge curves under expected operating conditions. When the battery is at end-of-service, most devices lose telemetry and programming capabilities, frequently reverting to a fixed high-output mode to attempt to maintain

patient safety. This predictable depletion characteristic has made lithium-based power cells common in current devices. Nickel-cadmium technology is being used once again in at least one investigational implantable device.

The battery voltage can be telemetered from the pulse generator; most devices also provide battery impedance (which increases with battery depletion) for additional information about battery life. The battery life can also be estimated by the magnet rate of the device, which changes with a decline in battery voltage. Unfortunately, the magnet rates are not standardized, and rate change characteristics vary tremendously among manufacturers and even among devices produced by the same manufacturer. Therefore, it is important to know the magnet rate characteristics of a given device before using this feature to determine battery status.

The longevity of any battery is determined by several factors, including chemical composition of the battery, size of the battery, external load (pulse duration and amplitude, stimulation frequency, total pacing lead impedance, and amount of current required to operate device circuitry and store diagnostic information), amount of internal discharge, and voltage decay characteristics of the cell. The basic formula for longevity determination is $114 \times [\text{battery capacity (A-HR)} / \text{Current Drain } (\mu\text{A})] = \text{longevity in years}$. However, this formula is subject to how the power cell's ampere-hours is specified by the manufacturer, thus the longevity will vary somewhat by company. High-performance leads, automatic capture algorithms and programming options that minimize pacing should further enhance device longevity.^{50,51}

The pacing pulse is generated first by charging of an output capacitor and discharge of the capacitor to the pacing cathode and anode. Since the voltage of a lithium iodine cell is fixed, obtaining multiple selectable pulse amplitudes requires the use of a voltage amplifier between the battery and the output capacitor. Contemporary pulse generators are constant-voltage (rather than constant-current) devices, implying delivery of a constant-voltage pulse throughout the pulse duration. In reality, some voltage drop occurs between the leading and the trailing edges of the impulse; the size of this decrease depends on the pacing impedance and pulse duration. The lower the impedance, the greater the current flow from the fixed quantity of charge on the capacitor and the greater the voltage drop throughout the pulse duration.⁵² The voltage drop is also depend-

ent on the capacitance value of the capacitor and the time of longer pulse duration.

The output waveform is followed by a low-amplitude wave of opposite polarity, the afterpotential. The afterpotential is determined by the polarization of the electrode at the electrode-tissue interface; formation is due to electrode characteristics as well as to pulse amplitude and duration. The sensing circuit may sense afterpotentials of sufficient amplitude, especially if the sensitivity threshold is low. Newer pacemakers use the output circuit to discharge the afterpotential quickly, thus lowering the incidence of afterpotential sensing. The afterpotential also helps to prevent electrode corrosion.

The intracardiac electrogram is conducted from the myocardium to the sensing circuit via the pacing leads, where it is then amplified and filtered. As noted above, the input impedance must be significantly larger than the sensing impedance to minimize attenuation of the electrogram. A bandpass filter attenuates signals on either side of a center frequency, which varies among manufacturers (generally ranging from 20 to 40 Hz).^{53,54} After filtering, the electrogram signal is compared with a reference voltage, the sensitivity setting; signals with an amplitude of this reference voltage or higher are sensed as true intracardiac events and are forwarded to the timing circuitry, whereas signals with an amplitude below the reference amplitude are categorized as noise, extracardiac or other cardiac signal, such as T waves.

Sensing circuitry also incorporates noise reversion circuits that cause the pacemaker to revert to a noise reversion mode (asynchronous pacing) whenever the rate of signal received by the sensing circuit exceeds the noise reversion rate. This feature is incorporated to prevent inhibition of pacing when the device is exposed to electromagnetic interference. Pulse generators also use Zener diodes designed to protect the circuitry from high external voltages, which may occur, for example, with defibrillation. When the input voltage presented to the pacemaker exceeds the Zener voltage, the excess voltage is shunted back through the leads to the myocardium.

The timing circuit of the pacemaker is a crystal oscillator that regulates the pacing cycle length, refractory periods, blanking periods and AV intervals with extreme accuracy. The output from the oscillator (as well as signals from the sensing circuitry) is sent to a timing and logic control board that operates the inter-

nal clocks, which in turn regulate all the various timing cycles of the pulse generator. The timing and logic control circuitry also contains an absolute maximal upper rate cut-off to prevent “runaway pacing” in the event of random component failure.^{55,56}

Each new generation of pacemakers contains more microprocessor capability. The circuitry contains a combination of read-only memory (ROM) and random-access memory (RAM). ROM is used to operate the sensing and output functions of the device, and RAM is used in diagnostic functions. Larger RAM capability has allowed devices to store increased amounts of retrievable diagnostic information, with the potential to allow downloading of new features externally into an implanted device.

External telemetry is included in all implantable devices. The pulse generator can receive information from the programmer and send information back by radiofrequency signals. Each manufacturer’s programmer and pulse generator operate on an exclusive radiofrequency, preventing the use of one manufacturer’s programmer with a pacemaker from another manufacturer. Through telemetry, the programmer can retrieve both diagnostic information and real-time information on battery status, lead impedance, current, pulse amplitude and pulse duration. Real-time electrograms and marker channels can also be obtained with most devices. The device can also be directed to operate within certain limits and to store specific types of diagnostic information via the programmer.

The most recent change in telemetry is that of “remote” capability. Information exchange has traditionally occurred by placing and leaving the programming

‘head’ of the programmer over the pulse generator for the duration of the interrogation and programming changes. New telemetry designs allow the programming ‘head’ or ‘wand’ to be placed briefly over the pulse generator to establish identity of the specific model and pulse generator and then complete the bi-directional informational exchange at a distance, i.e. the ‘wand’ does not need to be kept in a position directly over the pulse generator. Finally, even the use of a wand for certain pulse generators is not required for remote programming.

Pacemaker nomenclature

A lettered code to describe the basic function of pacing devices, initially developed by the American Heart Association and the American College of Cardiology, has since been modified and updated by the members of the North American Society of Pacing and Electrophysiology and the British Pacing and Electrophysiology Group (currently the Heart Rhythm Society).⁵⁷ This code has five positions to describe basic pacemaker function, although it obviously cannot incorporate all of the various special features available on modern devices (Table 1.1).

The first position describes the chamber or chambers in which electrical stimulation occurs. A reflects pacing in the atrium, V implies pacing in the ventricle, D signifies pacing in both the atrium and the ventricle, and O is used when the device has antitachycardia pacing (ATP) or cardioversion-defibrillation capability but no bradycardia pacing capability.

The second position describes the chamber or chambers in which sensing occurs. The letter code is

Table 1.1 NBG* code

I	II	III	IV	V
Chamber(s) paced	Chamber(s) sensed	Response to sensing	Programmability, rate modulation	Multisite pacing
O = None	O = None	O = None	O = None	O = None
A = Atrium	A = Atrium	T = Triggered	P = Simple programmable	A = Atrium
V = Ventricle	V = Ventricle	I = Inhibited	M = Multiprogrammable	V=Ventricle
D = Dual (A + V)	D = Dual (A + V)	D = dual (T + I)	C = Communicating	D= Dual (A + V)

*The North American Society of Pacing and Electrophysiology and the British Pacing and Electrophysiology Group. Modified from Bernstein *et al.*⁵⁷ By permission of Futura Publishing Company.

the same as that in the first position, except that an **O** in this position represents lack of sensing in any chamber, i.e. fixed-rate pacing. (Manufacturers may use an **S** in both the first and the second positions to indicate single-chamber capability that can be used in either the atrium or the ventricle.)

The third position designates the mode of sensing, i.e. how the device responds to a sensed event. **I** indicates that the device inhibits output when an intrinsic event is sensed and starts a new timing interval. **T** implies that an output pulse is triggered in response to a sensed event. **D** indicates that the device is capable of dual modes of response (applicable only in dual-chamber systems).

The fourth position reflects both programmability and rate modulation. **O** indicates that none of the pacemaker settings can be changed by noninvasive programming, **P** suggests “simple” programmability (i.e. one or two variables can be modified), **M** indicates multiprogrammability (three or more variables can be modified) and **C** indicates that the device has telemetry capability and can communicate noninvasively with the programmer (which also implies multiprogrammability). Finally, an **R** in the fourth position designates rate-responsive capability. This means that the pacemaker has some type of sensor to modulate the heart rate independent of the intrinsic heart rate. All modern devices are multiprogrammable and have telemetry capability; therefore, the **R** to designate rate-responsive capability is the most commonly used currently.

The fifth position was originally used to identify antitachycardia treatment functions. However, this has been changed, and antitachycardia options are no longer included in the nomenclature. The fifth position now indicates whether multisite pacing is not present (**O**), or present in the atrium (**A**), ventricle (**V**) or both (**D**). Multisite pacing is defined for this purpose as stimulation sites in both atria, both ventricles, more than one stimulation site in any single chamber, or any combination of these.

All pacemaker functions (whether single- or dual-chamber) are based on timing cycles. Even the function of the most complex devices can be readily understood by applying the principles of pacemaker timing intervals. This understanding is critical to accurate interpretation of pacemaker electrocardiograms, especially during troubleshooting. Pacemaker timing cycles are described in detail in Chapter 7: Timing Cycles.

Defibrillation basics

In 1899, Prevost and Battelli⁵⁸ noted that the “fibrillatory tremulations produced in the dog” could be arrested with the reestablishment of the normal heartbeat if one submitted the animal “to passages of current of high voltage.” Despite these early observations, decades elapsed before broad clinical applicability fueled interest in more widespread investigation of the mechanism underlying defibrillation. With the development of internal defibrillators in the late 1970s came a greater need to quantify defibrillation effectiveness, to understand the factors governing waveform and lead design, and to determine the effect of pharmacological agents on defibrillation. Remarkably, much of this work was done without a complete understanding of the fundamental mechanism of defibrillation.

This section reviews the emerging insights to the electrophysiological effects of shocks and how they are related to defibrillation. It also reviews the means of assessing the efficacy of defibrillation (the “defibrillation threshold”) and the important effects of waveform, lead design and placement, and pharmacological agents on defibrillation, with an emphasis on those principles pertaining to clinical practice.

Electrophysiological effects of defibrillation shocks; antitachycardia pacing

Despite great strides made in understanding the technology required for defibrillation (e.g. lead design and position, waveform selection), the basic underlying mechanisms have not been definitively determined. A few contemporary theories accounting for how an electric shock terminates fibrillation coexist with some overlapping: critical mass, upper limit of vulnerability, progressive depolarization, and virtual electrode depolarization. These are discussed below in brief.

First, a brief review of the cardiac action potential will be useful to facilitate discussion of the effects of defibrillation. The surface electrocardiogram and intracardiac electrogram, common in clinical practice, are the result of extracellular potentials generated by myocardial action potential propagation. An action potential is the transmembrane voltage in a single myocyte over time (Fig. 1.17). The action potential upstroke (phase 0, or depolarization) is mediated by sodium ion flow through voltage-sensitive selective channels, and during ventricular activation it is registered on the sur-

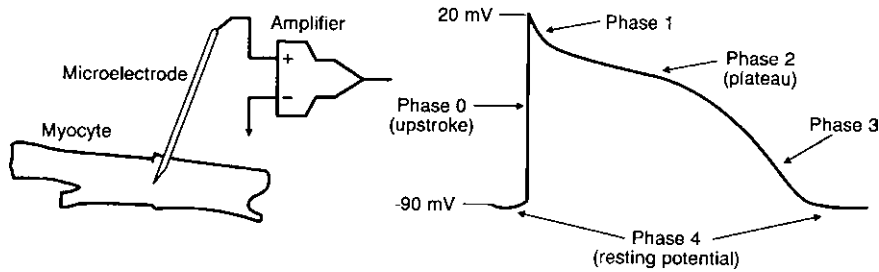


Fig. 1.17 The cardiac action potential. Left, Impalement of a single myocyte by a microelectrode. This permits recording of the change in voltage potential over time in a single cell. Right, On the graph, voltage (in millivolts) is on the ordinate, time on the abscissa. The action potential in

ventricular myocytes begins with a rapid upstroke (phase 0), which is followed by transient early repolarization (phase 1), a plateau (phase 2), and terminal repolarization (phase 3), which returns the membrane potential back to the resting value.

face electrocardiogram as the QRS complex (Fig. 1.18). Repolarization (phase 3) of ventricular myocardium generates the surface electrocardiographic T wave. In its resting state, the myocardium is excitable, and a pacing stimulus, or current injected by the depolarization of a neighboring myocyte, can bring the membrane potential to a threshold value, above which a new action potential ensues. The ability of the action potential of a myocyte to depolarize adjacent myocardium results in propagation of electrical activity through cardiac tissue. Importantly, immediately after depolarization, the myocardium is refractory and cannot be stimulated to produce another action potential until it has recovered excitability (Fig. 1.19). The interval immediately after an action potential, during which another action potential cannot be elicited by a pacing stimulus, is referred to as the “refractory period.”

Ventricular fibrillation (VF) is the most common cause of sudden death. VF results when an electrical wavebreak induces re-entry and results in a cascade of new wavebreaks. In patients with a structurally abnormal or diseased heart, the underlying tissue hetero-

geneity results in a predisposition to wavebreak, then re-entry, and finally fibrillation.⁵⁹ These wandering wavelets are self-sustaining once initiated. In the 1940s, Gurvich and Yuniev⁶⁰ predicted that electric shocks led to premature tissue stimulation in advance of propagating wavefronts, preventing continued progression of the wavefront. This concept of defibrillation as a large-scale stimulation remains a central tenet of many of the currently held theories of defibrillation.

Critical mass

The critical mass theory proposed that shocks need only eliminate fibrillatory wavelets in a critical amount of myocardium to extinguish the arrhythmia. Experiments in canine models found that injection of potassium chloride (which depolarizes myocardium, rendering it unavailable for fibrillation) into the right coronary artery or the left circumflex artery failed to terminate VF as often as injection into both the left circumflex and the left anterior descending arteries together. Similarly, electrical shocks of equal magnitude terminated fibrillation most frequently when the electrodes were

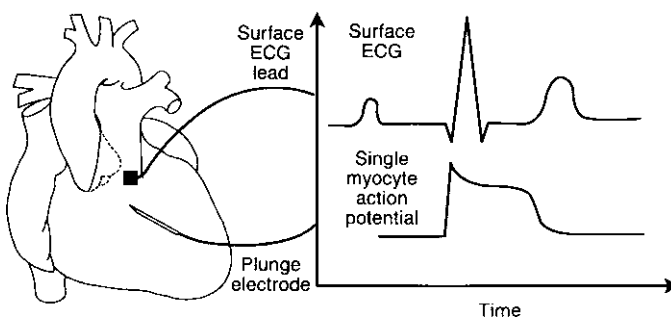


Fig. 1.18 Correlation of cellular and clinical electrical activity. The QRS complex of the surface electrocardiogram (ECG) is generated by the action potential upstroke (phase 0) of ventricular myocytes and the propagation of the upstroke through the ventricular myocardium. Similarly, the T wave is the result of ventricular repolarization (phase 3).

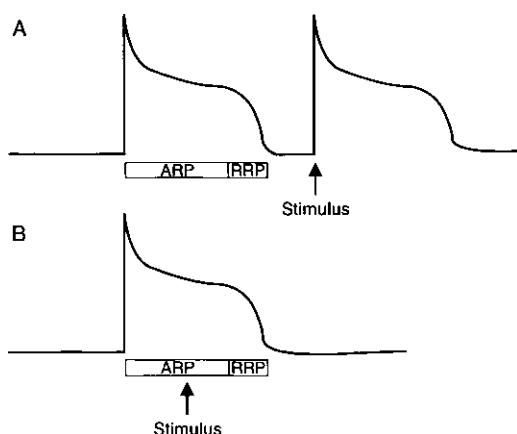


Fig. 1.19 Refractory periods. Myocytes can be stimulated to generate new action potentials, except in their absolute refractory period (ARP). In (A), a stimulus occurs after the myocyte has fully recovered from the preceding action potential, and a new action potential ensues. In contrast, in (B), the same stimulus is delivered earlier, the myocyte remains in its absolute refractory period because of the preceding action potential, and no new action potential is elicited. RRP, relative refractory period.

positioned at the right ventricular apex and the posterior left ventricle, as opposed to two right ventricular electrodes. Thus, it was concluded that if a “critical mass” of myocardium was rendered unavailable for VF either by potassium injection or by defibrillatory shock, the remaining excitable tissue was insufficient to support the wandering wavelets, and the arrhythmia terminated.⁶¹ However, it was not critical to depolarize every ventricular cell to terminate fibrillation.

Upper limit of vulnerability

Studies mapping electrical activation after failed shocks led to several observations not accounted for by the critical mass hypothesis, giving rise to the upper limit of vulnerability theory. First, an isoelectric interval (an electrical pause) was seen after failed shocks before resumption of fibrillation. The relatively long pause suggested that VF was terminated by the shock and then secondarily regenerated by it (Fig. 1.20).⁶² The concept that failed shocks are unsuccessful because they give rise to a new focus of fibrillation rather than because they fail to halt continuing wavelets was further buttressed by a second observation—that postshock conduction patterns were not the continuation of preshock wavefronts.⁶³ If a failed shock resulted from the inability to

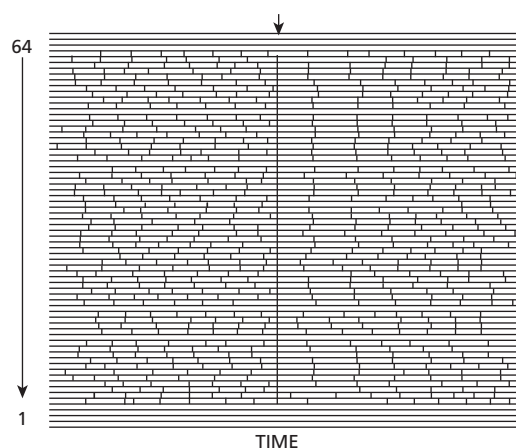


Fig. 1.20 Isoelectric interval after failed shock. Tracings show recordings from 64 electrodes evenly distributed over the epicardial surfaces of both ventricles. At the arrow, an unsuccessful 1-J defibrillation shock is delivered. Note that an isoelectric interval (i.e. flat line without activations) immediately follows the shock, that temporal clustering of the first activation follows the failed shock, and that rapid degeneration back to fibrillation then occurs. (Modified from Chen *et al.*⁶² By permission of American Society for Clinical Investigation.)

halt continuing fibrillation, the assumption was that the postshock wavefronts should be a continuation of the propagating wavefronts present before shock delivery and that new wavefronts at sites remote from the preshock wavefronts would not be expected. Furthermore, VF was frequently reinitiated in the regions of lowest shock intensity, suggesting that these low-intensity regions were responsible for reinitiating fibrillation.

Elegant mapping studies demonstrated that shocks with potential gradients less than a minimum critical value—termed the upper limit of vulnerability (ULV) (6V/cm for monophasic shocks, 4V/cm for biphasic shocks)—could induce fibrillation when applied to myocardium during its vulnerable period. Low-energy shocks did so by creating regions of functional block in vulnerable myocardium at “critical points” that initiated re-entry and subsequent fibrillation.⁶⁴ Figure 1.21 depicts the vulnerable zone during normal sinus rhythm. In sinus rhythm, low-energy shocks delivered during the T wave induce VF; higher energy shocks—with energy above the ULV—do not. Since at any given time during fibrillation a number of myocardial regions are repolarizing and thus vulnerable, a shock with a potential gradient below the ULV may create a

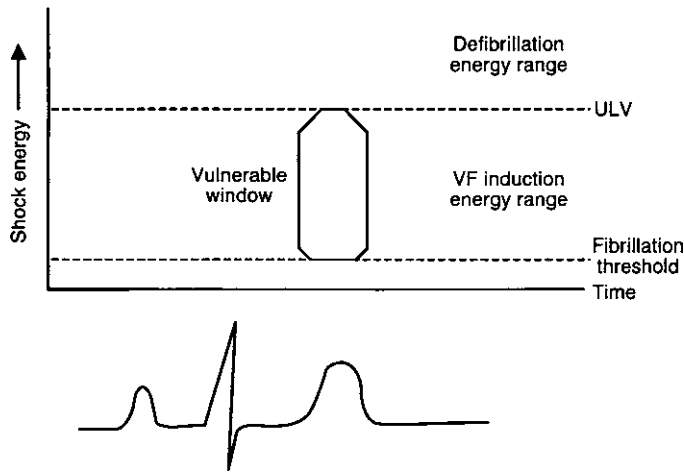


Fig. 1.21 Window of vulnerability during sinus rhythm. During sinus rhythm, the ventricles are vulnerable to ventricular fibrillation (VF) when a shock is delivered on the T wave, in the vulnerable window. To induce fibrillation, the shock energy must be greater than the fibrillation threshold and below the upper limit of vulnerability (ULV). Shocks with energy above the upper limit of vulnerability do not induce fibrillation. Since during VF there is

dyssynchrony of activation, at any given instant a number of regions are repolarizing (equivalent to the T wave in sinus rhythm), so that a shock with a gradient that is less than the ULV can reinduce fibrillation in these regions. In contrast, shocks with energy above the ULV throughout the myocardium cannot reinitiate VF and are successful. The ULV is correlated with the defibrillation threshold. Further details appear in the text.

critical point and reinitiate fibrillation. Conversely, a shock with a gradient above the ULV across the entire myocardium does not reinduce VF and should therefore succeed. During defibrillator testing, shocks are intentionally delivered in the vulnerable zone to induce fibrillation (Fig. 1.22), and the zone of vulnerability has been defined in humans.⁶⁵ The fact that the vulnerable zone exists and that the ULV has been correlated with the defibrillation threshold supports the ULV hypothesis as a mechanism of defibrillation.⁶⁶

Progressive depolarization

A third theory of defibrillation, the progressive depolarization theory (also referred to as the “refractory period extension theory”) incorporates some elements of both critical mass and ULV theories. Using voltage-sensitive optical dyes, Dillon and Kwaku⁶⁷ have demonstrated that shocks of sufficient strength were able to elicit active responses, even from supposedly refractory myocardium. Thus, as seen in Fig. 1.23A, the duration of an action potential can be prolonged (and the refractory period extended) despite refractory myocardium when a sufficiently strong shock is applied.⁶⁸ This phenomenon may result from sodium channel reactivation by the shock. The degree of ad-

ditional depolarization time is a function of both shock intensity and shock timing.⁶⁹ Since the shock stimulates new action potentials in myocardium that is late in repolarization and produces additional depolarization time when the myocardium is already depolarized, myocardial resynchronization occurs. This is manifested by myocardial repolarization at a constant time after the shock (second dashed line in Fig. 1.23, labeled “constant repolarization time”). Thus, the shock that defibrillates extends overall ventricular refractoriness, limiting the excitable tissue available for fibrillation. It thus extinguishes continuing wavelets and resynchronizes repolarization, so that distant regions of myocardium become excitable simultaneously, preventing dispersion of refractoriness and renewed re-entry. Experimental evidence has demonstrated that shocks with a potential gradient above the ULV result in time-dependent extension of the refractory period. In contrast, lower-energy shocks may result in a graded response that could create transient block and a critical point, thereby reinducing fibrillation.⁶⁹

Virtual electrode depolarization

More recently, optical signal measurements of trans-

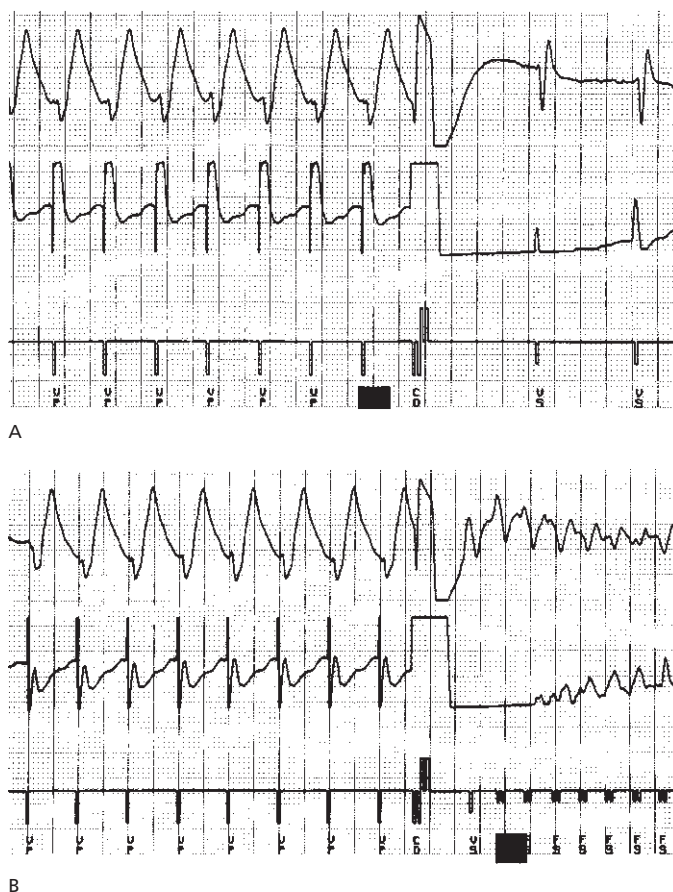


Fig. 1.22 Induction of ventricular fibrillation by a T-wave shock during testing of an implantable defibrillator. In (A), a 1-J shock is delivered 380 ms after the last paced beat. Fibrillation is not induced, because this shock is delivered outside the window of vulnerability. In (B), the timing of the shock is adjusted to 300 ms after the last paced complex, so that it is delivered more squarely on the T wave, in the window of vulnerability, and fibrillation is induced. The window of vulnerability is defined by both shock energy and timing. CD, charge delivered; FS, fibrillation sense; VP, ventricular pacing; VS, ventricular sensing.

membrane potentials have demonstrated the concept of the “virtual electrode.”⁷⁰ The virtual electrode effect makes the defibrillation electrode effectively much larger than the physical electrode. In the virtual electrode, the anode cells are brought close to their resting potential, increasing their responsiveness to stimulation. More importantly, the region of depolarization or hyperpolarization near the physical electrode is surrounded by regions with opposite polarity. Anodal shocking produces a wavefront which begins at the boundary of positively charged regions and then spreads in the direction of the negatively charged region of physical anode.⁷¹ This produces “collapsing” wavefronts that frequently collide and neutralize one another and thereby are less likely to result in a sustained arrhythmia (Fig. 1.24).⁷² This theory incorporates many aspects of the above-mentioned mechanisms.

To summarize and to put defibrillation theory into clinical perspective, the effects of the application of a voltage gradient across myocardium are a function

of field strength and timing. Although the biological effects of shocks may overlap, this concept is summarized in Fig. 1.25. Extremely low energy pulses may have no effect on the myocardium. Stronger pulses (in the microjoule range), such as those used for cardiac pacing, result in action potential generation in non-refractory myocardium, which leads to a propagating impulse. With increasing electric field strength (to the 1-J area), VF can be induced with shocks delivered during the vulnerable period. Increasing the shock strength above the ULV (and above the defibrillation threshold) puts the shock in the defibrillation zone. Very high-energy shocks can lead to toxic effects, including disruption of cell membranes, postshock block, mechanical dysfunction and new tachyarrhythmias.⁶⁹

Antitachycardia pacing

The concepts of basic myocardial function also explain the mechanism of arrhythmia termination with ATP.

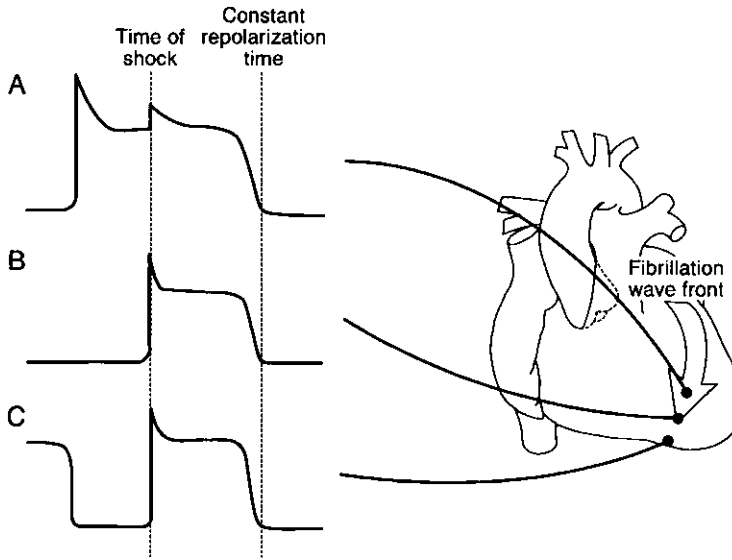


Fig. 1.23 Progressive depolarization. A fibrillatory wavefront is depicted by the arrow, and the action potential response to a defibrillatory shock is demonstrated at several points surrounding the wavefront. The fibrillatory wavefront has just passed through a myocyte at point A when the shock is delivered. The myocyte is in its plateau (phase 2), when it would ordinarily be refractory to additional stimulation. However, when a sufficiently strong shock is delivered, the myocyte can generate an active response with prolongation of the action potential and of the refractory period. The response is referred to as “additional depolarization time.” The

tissue at point B is at the leading edge of the fibrillatory wavefront. The shock strikes this myocardium at the time of the upstroke (phase 0) and has little effect on the action potential. The tissue at point C is excitable (it is the excitable gap that the fibrillatory wave front was about to enter) when the shock is delivered. The shock elicits a new action potential in this excitable tissue. Despite the different temporal and anatomical locations of the three action potentials depicted, after the shock there is resynchronization by the “constant repolarization time.” This resynchronization helps prevent continuation of fibrillation.

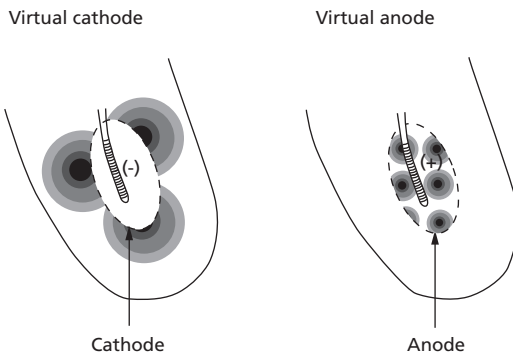


Fig. 1.24 The cathodal shocks (left) produce wavefronts that expand and propagate away from the right ventricular coil. In comparison, anodal shocks (right) produced wavefronts that collapse and propagate towards the right ventricular coil (Adapted with permission from Figure 4, Kroll *et al.*⁷⁰ Present understanding of shock polarity for internal defibrillation: the obvious and non-obvious clinical implications).

As an example, in monomorphic ventricular tachycardia (VT) late after myocardial infarction, a re-entrant circuit utilizing abnormal tissue adjacent to an infarct is responsible for the arrhythmia (Fig. 1.26). For the re-entrant circuit to perpetuate itself, the tissue immediately in front of the leading edge of the wavefront must have recovered excitability so that it can be depolarized (Fig. 1.26). Thus, an excitable gap of tissue must be present in advance of the leading tachycardia wavefront or the arrhythmia will terminate. ATP—delivered as a short burst of pacing impulses at a rate slightly greater than the tachycardia rate—can terminate VT by depolarizing the tissue in the excitable gap, so that the tissue in front of the advancing VT wavefront becomes refractory, preventing further arrhythmia propagation (Fig. 1.26B). The ability of a train of impulses to travel to the site of the re-entrant circuit and interrupt VT depends on several factors,