

REVIEW ARTICLE

MEDICAL PROGRESS

Implantable Cardioverter–Defibrillators

John P. DiMarco, M.D., Ph.D.

From the Electrophysiology Laboratory, Cardiovascular Division, Department of Medicine, University of Virginia Health System, Charlottesville. Address reprint requests to Dr. DiMarco at the Cardiovascular Division, Department of Medicine, University of Virginia Health System, P.O. Box 800158, Charlottesville, VA 22908-0158, or at jdimarco@virginia.edu.

N Engl J Med 2003;349:1836-47.
Copyright © 2003 Massachusetts Medical Society.

DESPITE ADVANCES IN EMERGENCY MEDICAL SYSTEMS AND IN TECHNIQUES of resuscitation, sudden death from cardiac arrest remains a major public health problem. Most persons who have an out-of-hospital cardiac arrest do not survive.^{1,2} Those who are resuscitated may have severe, long-term cognitive impairment and motor impairment due to delays before a stable rhythm could be restored. In the 1970s, motivated by the death of a colleague, Drs. Michel Mirowski and Morton Mower, and their colleagues, developed the concept of an implantable device that could automatically monitor and analyze cardiac rhythm and deliver defibrillating shocks when it detected ventricular fibrillation.^{3,4} After years of testing, in 1980 the first clinical implantation was performed in a young woman with recurrent ventricular fibrillation.⁵ Subsequently, the implantable cardioverter–defibrillator evolved from a therapy of last resort for patients with recurrent cardiac arrest to a management standard for use in primary prevention (the prevention of a first life-threatening event) and secondary prevention (prevention of a recurrence of a potentially fatal arrhythmia or cardiac arrest) in patients with coronary heart disease.

COMPONENTS AND FUNCTION

An implantable cardioverter–defibrillator system comprises a pulse generator and one or more leads for pacing and defibrillation electrodes (Fig. 1). The pulse generator has a number of components (Table 1).⁶ A sealed titanium can encloses a lithium–silver vanadium oxide battery, voltage converters and resistors, capacitors to store charges, microprocessors and integrated circuits to control the analysis of the rhythm and the delivery of the therapy, memory chips to store electrographic and other data, and a telemetry module. Technological advances have made possible a gradual reduction in the size of the pulse generator, permitting subcutaneous implantation of the defibrillator on the anterior chest wall in most patients.

The top of the pulse generator contains an epoxy resin header for connecting the pacing and defibrillation leads. The defibrillation leads must be capable of delivering high-energy shocks to the heart without damaging the myocardium. In the earliest defibrillators, epicardial patches were used, but transvenous leads are now standard. Each defibrillation lead contains one or two coils that dissipate heat during high-voltage discharges. In most systems, the pulse generator can serve as a part of the defibrillation pathway. The defibrillation lead also contains bipolar electrodes, which are used for ventricular pacing and sensing. If both pacing electrodes are independent of the defibrillation coils, they form what is called a dedicated bipole. If a defibrillation coil is linked to the ring electrode for sensing, it forms what is called an integrated bipole. Both systems are effective in most patients. Active-fixation (screw-in) and passive-fixation lead systems are in clinical use. Dual-chamber and biventricular devices also have ports for atrial or left ventricular electrodes, which are used for pacing and sensing.

DETECTION OF ARRHYTHMIA

The original implantable cardioverter–defibrillator was designed to detect only ventricular fibrillation, by means of a wave-form analysis termed a probability-density function. Use of this device indicated that therapy for organized ventricular tachycardia was also important. Subsequently, the rate of R waves detected by the defibrillator’s ventricular-sensing circuit became the standard measurement used to identify cardiac rhythm. In the present generation of defibrillators, the ventricular bipolar sensing circuit filters the incoming signal to eliminate unwanted low-frequency components (e.g., T waves and baseline drift) and high-frequency components (e.g., skeletal–muscle electrical activity). One or more tachycardia-detection zones may be programmed. The fastest rate, or ventricular-fibrillation zone, is treated by delivery of a shock. Zones with lower rate boundaries may be treated with antitachycardia pacing or low-energy synchronized shocks or, in some cases, just observed. Because the amplitude of the bipolar electrogram may be low or unstable during ventricular fibrillation, all implantable cardioverter–defibrillators allow sensitivity-gain adjustment during intervals when an R wave is not sensed, in order to detect low-amplitude signals when ventricular fibrillation does occur. In many cases, the rates of sinus tachycardia or of other supraventricular arrhythmias may be within the zones set for detection of ventricular tachycardia or ventricular fibrillation, which may result in inappropriate delivery of the therapy. Therefore, most implantable defibrillators can be programmed to enhance the discrimination between supraventricular and ventricular arrhythmias.⁷⁻⁹

Single-chamber devices most commonly can distinguish the sudden onset of sinus tachycardia from ventricular tachycardia. They can also identify the stability of cardiac-cycle lengths in order to detect atrial fibrillation and can characterize morphology and width in electrograms. In dual-chamber devices, information from the atrial electrogram may be included in the algorithm used to perform the analysis. Features that enhance detection are primarily used in ventricular-tachycardia zones, where even a transient inhibition of the delivery of the appropriate therapy is undesirable.⁹ Early models delivered therapy after the criteria for detecting arrhythmia had been met, which could lead to the delivery of unnecessary shocks when the arrhythmia was spontaneously terminated. Therefore, defibrillators

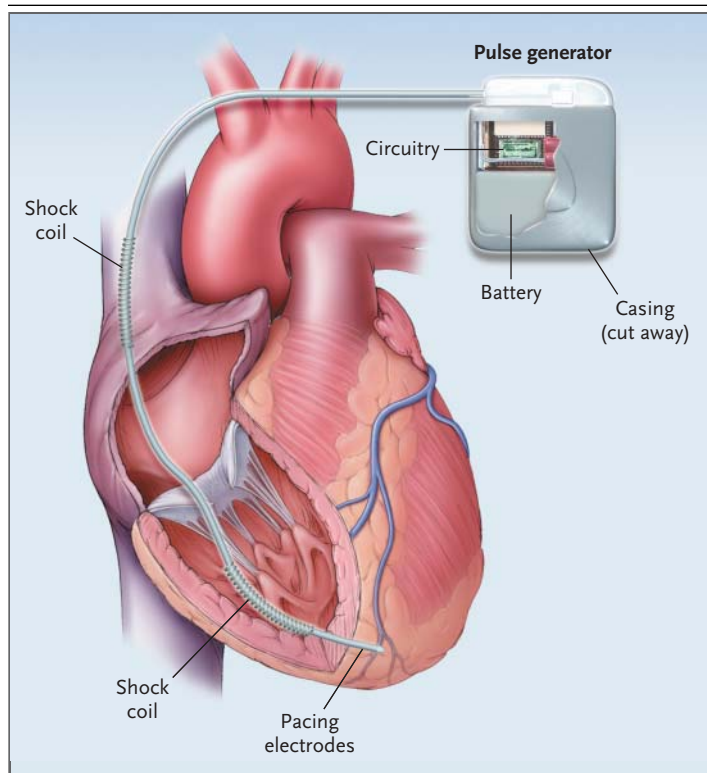


Figure 1. Diagram of a Single-Chamber Implantable Cardioverter–Defibrillator System.

The pulse generator is usually placed in a subcutaneous pocket in the pectoral region. It contains a header with ports for leads, the battery and capacitors, memory chips, integrated circuits and microprocessors, and the telemetry module. The transvenous right ventricular lead contains the shock coils and pacing electrodes. Additional leads may be connected for right atrial or left ventricular pacing.

now reanalyze the rhythm before delivering shocks and painlessly dump the stored charge when the criteria for detection are no longer met.

In an implanted cardioverter–defibrillator, two basic methods are used to terminate arrhythmias: antitachycardia pacing and direct-current shocks. Physicians select the method to be used first to deliver therapy in each tachycardia-detection zone. Antitachycardia pacing is a standard electrophysiological technique that is useful for terminating monomorphic tachycardias.¹⁰ The electrophysiologist can program the device to deliver one or more bursts of pacing in an attempt to terminate the tachycardia. The characteristics of the bursts can be programmed and may vary, depending on the detection zone. Antitachycardia pacing is painless for the patient and, because the capacitor does not need to be

Table 1. Specifications of Implantable Cardioverter–Defibrillators.*

Weight (g)	50–120
Volume (ml)	30–70
Battery	Lithium–silver vanadium oxide
Capacitors	Aluminum or aluminum chloride electrolytic
Generator can	Titanium
Leads	Transvenous defibrillation coils RA, RV, LV sensing and pacing electrodes Active can Epicardial or subcutaneous patches
Functions	
Ventricle	Shock, RV or BIV sensing, pacing
Atrium	Sensing, pacing (shock)
Estimated battery life (yr)	4 to 9
Estimated costs (\$)†	
Device	10,000–40,000 or more
Implantation	6,000–12,000

* RA denotes right atrial, RV right ventricular, LV left ventricular, and BIV biventricular.

† Systems that can be used for defibrillation and resynchronization are more expensive. The costs of the implantation procedure include only payments for the hospitalization and physicians' services.

charged, can be delivered rapidly. However, antitachycardia pacing is not always effective, and it can accelerate ventricular tachycardia or, if applied during a supraventricular rhythm, induce a ventricular arrhythmia. Thus, delivery of a shock is always included in the prescription for therapy when antitachycardia pacing is ineffective.

All implantable cardioverter–defibrillators can be programmed to deliver either synchronized, usually low-energy shocks (less than 5 J) or unsynchronized high-energy shocks. Low-energy shocks may have very short charge times, but they may accelerate ventricular tachycardia and, in spite of the low energy, are uncomfortable for the patient. High-energy shocks are used in the zone with the highest rate and in zones with lower rates, if antitachycardia pacing or low-energy shocks are either unsuccessful or not programmed. Traditionally, the energy of the first shock is set at least 10 J above the threshold of the last defibrillation measured. Early models used monophasic wave forms, but the use of biphasic wave forms improved defibrillation thresholds.¹¹ Defibrillation administered by transvenous systems that deliver up to about 30 J can be successful in most patients, but in rare cases, alternative lead configurations or high-energy devices may be necessary to deliver the therapy.

OTHER FUNCTIONS OF IMPLANTABLE DEFIBRILLATORS

In current models of implantable defibrillators there are a number of features that are not directly related to the analysis of or the delivery of therapy for ventricular arrhythmias. All models now have pacing modes similar to those in single- or dual-chamber pacemakers. All models routinely store electrograms for sensed arrhythmias, a feature that is extremely helpful during follow-up for analysis of the therapies delivered and for detection of many malfunctions that may occur in the device (Fig. 2). Information about battery voltage, lead impedance, and the time needed to charge the capacitor is stored for later analysis. Some models can detect atrial arrhythmia and deliver the appropriate therapy (shock or antitachycardia pacing). A dedicated atrial defibrillator has been developed and tested in limited clinical trials in patients with atrial fibrillation, but it is not yet available as a separate unit.^{12,13} The most recent major innovation in implantable cardioverter–defibrillators is implementation of biventricular pacing to achieve cardiac resynchronization in patients with advanced congestive heart failure and intraventricular conduction delays, especially left bundle-branch block.^{14,15}

CLINICAL TRIALS

From the time of its clinical introduction, the implantable cardioverter–defibrillator has been shown to recognize ventricular fibrillation and terminate the arrhythmia by delivering shocks. In early, uncontrolled studies, the delivery of a shock was assumed to represent a life saved.^{16,17} This analytic approach overestimated the benefit of a defibrillator, because not all shocks are appropriate, not every arrhythmia would prove fatal if not terminated, and death may still soon occur from other cardiac causes.¹⁸ Randomized clinical trials were therefore conducted to evaluate the effect of implanted defibrillators on mortality (Table 2).^{19–25} Secondary-prevention trials in which the subjects enrolled were survivors of cardiac arrest or had sustained ventricular tachycardia were conducted to compare the effect of defibrillator therapy and antiarrhythmic-drug therapy on mortality. The enrollment of an untreated control group was considered unethical. Primary-prevention trials in which the subjects enrolled were high-risk patients without a history of sustained ventricular arrhythmias compared the effects of no treat-

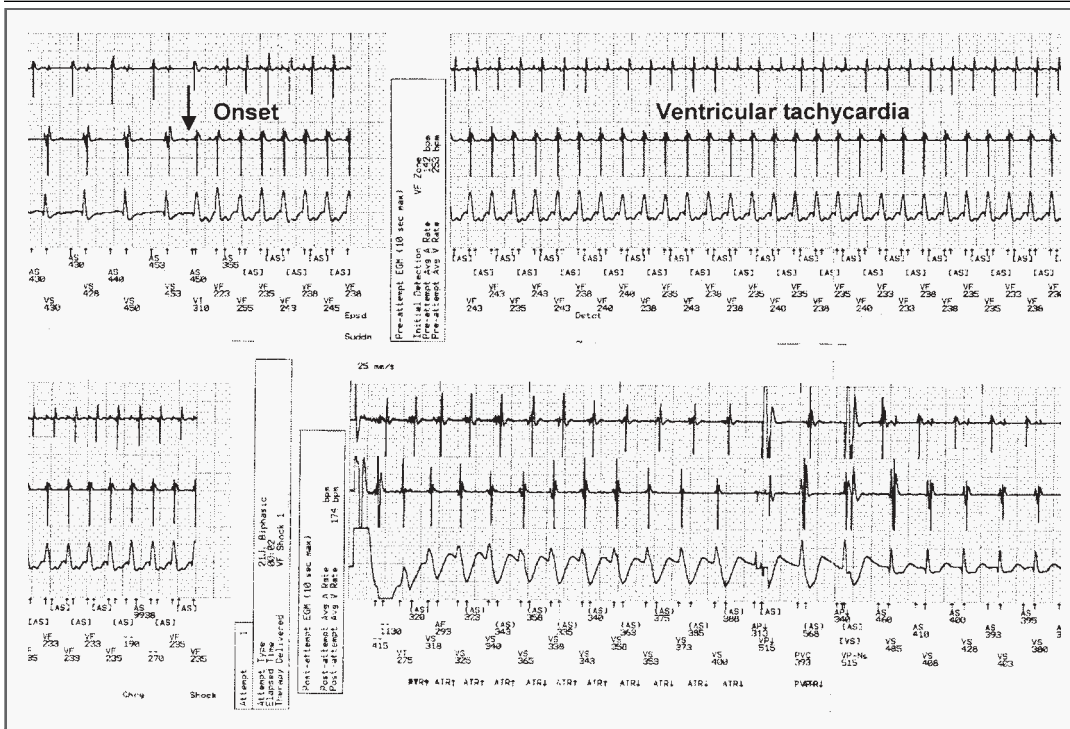


Figure 2. Normal Function of an Implantable Cardioverter–Defibrillator.

Stored data are shown from an episode of ventricular tachycardia after successful therapy in a 22-year-old woman with recurrent ventricular tachycardia. From top to bottom, the tracings represent electrograms from the atrial, ventricular, and shock leads and from an annotated marker channel. Ventricular activity (arrow) initiates the tachycardia, and a change occurs in the QRS complex on the shock-lead electrogram. The initial beat after the arrow is a fusion complex, which is followed by a wider complex during the rest of the episode. The first break in the rhythm strip denotes that criteria for the detection of tachycardia in the ventricular-fibrillation zone have been met. The ventricular tachycardia, with 1:1 retrograde conduction, continues. The second break corresponds to the delivery of a 21-J shock (not shown in the printout). After the shock, there are a few beats of a different ventricular rhythm that gradually slows and breaks. This phenomenon is frequently observed after a shock. By the end of the strip, sinus rhythm is restored.

ment, antiarrhythmic-drug therapy, or both with the effect of defibrillator therapy on mortality from cardiac arrhythmias.

SECONDARY-PREVENTION TRIALS

The Antiarrhythmics versus Implantable Defibrillators (AVID)¹⁹ trial enrolled 1016 subjects who had survived one or more episodes of ventricular fibrillation or symptomatic, sustained ventricular tachycardia. To be eligible for enrollment, subjects with ventricular tachycardia had to have a reduced left ventricular ejection fraction. The subjects were randomly assigned to receive either an implanted cardioverter–defibrillator or drug therapy. Although electrophysiologically guided therapy with sotalol, a beta-blocker with Vaughn Williams class III antiarrhythmia effects, was permitted, almost all of

those receiving drug therapy received amiodarone. The AVID trial was terminated early by the study’s data safety monitoring board when a relative reduction in mortality from all causes of 29 percent was noted in the defibrillator group.

The Canadian Implantable Defibrillator Study (CIDS)²⁰ compared the benefits of the implantable defibrillator with amiodarone therapy in a group of 659 subjects with a history of cardiac arrest, episodes of sustained ventricular tachycardia, or syncope with a depressed ejection fraction and inducible sustained ventricular arrhythmia. In the defibrillator group there was a relative decrease of mortality from all causes of 20 percent.

The Cardiac Arrest Study Hamburg (CASH)²¹ enrolled 288 subjects who had survived cardiac arrest and compared the benefits of implanted cardi-

Table 2. Selected Randomized, Clinical Trials of Implantable Cardioverter–Defibrillator (ICD) Therapy.*

Trial	No. of Patients	Age <i>yr</i>	Mean LVEF <i>%</i>	Follow-up <i>mo</i>	Control Therapy	Mortality		P Value
						Control	ICD	
						<i>%</i>		
Secondary-prevention trials								
AVID ¹⁹	1016	65±10	35	18±12	Amiodarone or sotalol	24.0	15.8	0.02
CIDS ²⁰	659	64±9	34	36	Amiodarone	29.6	25.3	0.14
CASH ²¹	288	58±11	45	57±34	Amiodarone or metoprolol	44.4	36.4	0.08
Primary-prevention trials								
MADIT ²²	196	63±9	26	27	Conventional	38.6	15.7	0.009
MADIT II ²³	1232	64±10	23	20	Conventional	19.8	14.2	0.007
CABG Patch ²⁴	900	64±9	27	32±16	No ICD	21.3	22.2	0.64
CAT ²⁵	104	52±11	24	66±26	No ICD	31.4	26.0	0.554

* Plus–minus values are means ±SD. LVEF denotes left ventricular ejection fraction, AVID Antiarrhythmics versus Implantable Defibrillators, CIDS Canadian Implantable Defibrillator Study, CASH Cardiac Arrest Study Hamburg, MADIT Multicenter Automatic Defibrillator Implantation Trial (first and second), CABG Patch Coronary Artery Bypass Graft Patch, and CAT Cardiomyopathy Trial.

ac defibrillators with antiarrhythmic-drug therapy (amiodarone, metoprolol, or propafenone). In comparison with the subjects in the AVID and CIDS trials, those in CASH had a higher mean ejection fraction and included a greater proportion of patients with defibrillators who had also received epicardial systems. Despite these differences, in CASH there was a relative decrease in total mortality of 23 percent in the defibrillator group, as compared with the amiodarone and metoprolol groups combined. Random assignment to propafenone was stopped early in the trial because of excess mortality.

Although the AVID trial enrolled the largest number of patients and the CIDS and CASH trials did not achieve statistical significance for the end point of total mortality, the average length of follow-up in the AVID trial was shorter than in either the CIDS or CASH trial. Connolly et al.²⁶ performed a meta-analysis of the results of AVID, CIDS, and CASH and concluded that the results of the three studies were consistent. Overall, the reduction in total mortality was 28 percent (95 percent confidence interval, 13 to 40 percent; $P=0.006$). Over an estimated follow-up period of 6 years, the mean increase in survival with defibrillator therapy, as compared with drug therapy, was 4.4 months.

The subgroup or data-base analysis reported by all three trials provided additional insights. The greatest benefit of implantable cardioverter–defibrillators occurs among patients with advanced heart

disease. In both the AVID trial²⁷ and the meta-analysis,²⁶ little advantage over drug therapy was seen in subjects with an ejection fraction that was greater than 35 percent. According to Sheldon et al.,²⁸ when the CIDS population was stratified according to age, ejection fraction, and functional status, defibrillator therapy was shown to improve survival primarily for patients in the quartile at highest risk. Patients with arrhythmias that were thought to be due to a transient or reversible cause were excluded from the AVID trial, but they continued to be at high risk,²⁹ presumably either because the transient cause was likely to explain a recurrence or because the patients had an underlying chronic instability. In the absence of any contraindication, such patients may therefore be considered candidates for treatment with an implantable defibrillator.

Electrophysiological studies performed after resuscitation were not significant predictors of recurrent arrhythmias during follow-up among the subjects in either the AVID trial³⁰ or CASH.²¹ Patients in whom clusters of shocks were delivered in a brief time — reflecting a phenomenon sometimes termed an electrical storm — have an increased risk of death in the next several months, but not of sudden death, even if, as is usually the case, they survive the acute episode.³¹ Defibrillator therapy and antiarrhythmic-drug treatment had similar effects on the quality of life among the subjects in the AVID trial³² and CIDS,³³ with a reduced quality of life as-

sociated with sporadic shocks in the defibrillator groups. The use of beta-adrenergic blocking drugs is associated with improved survival even among patients receiving amiodarone.¹⁹

DEFIBRILLATOR THERAPY PLUS DRUG THERAPY IN SECONDARY PREVENTION

The AVID, CIDS, and CASH secondary-prevention trials were designed to test the hypothesis that therapy with an implantable cardioverter-defibrillator was superior to antiarrhythmic-drug therapy. Patients in whom antiarrhythmic-drug therapy was thought to be required were excluded from all three trials. In actual practice, drug therapy is often used in conjunction with a defibrillator. Antiarrhythmic drugs may be needed early after resuscitation to stabilize the patient, or they may be needed to decrease the frequency of shocks, to terminate the arrhythmia along with antitachycardia pacing, or to treat atrial arrhythmias. Pacifico et al.³⁴ reported that long-term therapy with oral sotalol decreased the need for defibrillator shocks. Because some antiarrhythmic drugs may influence defibrillation thresholds or tachycardia sensing, physicians should be aware of the potential for interactions and should retest the function of the defibrillator when a harmful interaction is liable to occur.³⁵

PRIMARY-PREVENTION TRIALS

Even with advances in emergency medical systems, most persons who have an out-of-hospital cardiac arrest do not survive. Clinical trials of antiarrhythmic-drug therapy for the primary prevention of sudden death have had variable results, showing harm, no effect, or an inconsistent benefit.³⁶ Several clinical trials evaluating the implantable cardioverter-defibrillator for the primary prevention of sudden death have been reported. The first Multicenter Automatic Defibrillator Implantation Trial (MADIT)²² enrolled 196 subjects with coronary artery disease, spontaneous nonsustained ventricular tachycardia, an ejection fraction of 35 percent or less, and inducible ventricular tachycardia that was not suppressed with the use of intravenous procainamide. The subjects were randomly assigned to therapy with a defibrillator or "conventional" antiarrhythmic therapy, as prescribed by their primary care physicians, and they were followed for a mean of 27 months. There were 15 deaths in the defibrillator group, as compared with 39 deaths in the conventional-therapy group, for a relative reduction of 54 percent. Interestingly, the improvement in mortality was report-

ed for all causes of death: arrhythmic and nonarrhythmic cardiac, noncardiac, and unknown. Similar effects on deaths from noncardiac causes have not been seen in other trials.

The Coronary Artery Bypass Graft Patch (CABG Patch) trial²⁴ enrolled subjects with decreased ejection fractions (35 percent or less) and abnormalities on signal-averaged electrocardiography who were scheduled for coronary revascularization. Patients were randomly assigned in the operating room either to implantation of a defibrillator with epicardial leads or to no defibrillator therapy. The CABG Patch trial was terminated when an interim analysis of data from 900 subjects who were followed for more than a mean (\pm SD) of 32 ± 16 months showed no potential benefit in the defibrillator group. There were 101 deaths among the 454 patients who received defibrillators, and 95 deaths among the 446 control patients. The hazard ratio for death in the defibrillator group was 1.07 (95 percent confidence interval, 0.81 to 1.42).

Several possible explanations for this result have been proposed. Most of the deaths occurred in the hospital, with a large proportion of them occurring early in the postoperative period.³⁷ About 10 percent of the control group crossed over early to implantation of a defibrillator, and these patients may have been at the highest long-term risk for death from cardiovascular causes. The mortality rate was lower than anticipated, possibly owing to improvements in early surgical management and to the benefits of revascularization for patients with a low ejection fraction. Epicardial-lead systems were used in the patients who received defibrillators and may have had an adverse effect on early mortality.

The second Multicenter Automatic Defibrillator Implantation Trial (MADIT II)²³ enrolled 1232 patients with coronary artery disease, a history of myocardial infarction, and an ejection fraction of 30 percent or less. Documentation of spontaneous or inducible arrhythmias was not required. Patients were randomly assigned to either defibrillator therapy or conventional medical therapy. Antiarrhythmic therapy was used in less than 20 percent of patients in both groups. During an average of 20 months of follow-up, mortality from all causes was 19.8 percent in the control group and 14.2 percent in the defibrillator group. The hazard ratio for death in the defibrillator group was 0.69.

The Multicenter Unsustained Tachycardia Trial (MUSTT)^{38,39} enrolled a study population similar to that in the first MADIT. Patients with a history of

myocardial infarction, an ejection fraction of 40 percent or less, and spontaneous, nonsustained ventricular tachycardia underwent an electrophysiological study. Patients who did not have inducible ventricular tachycardia were followed in a registry. Patients with inducible ventricular tachycardia were randomly assigned to either no therapy or antiarrhythmic therapy, which was guided by serial electrophysiological studies, and could receive a defibrillator if one or more of the trial drugs were not beneficial. Although MUSTT has often been described as a defibrillator trial, it may be better described as a test of an electrophysiologically guided treatment strategy in which implantable cardioverter-defibrillators were prescribed at an investigator's discretion. The frequency of the prescription of an implantable defibrillator varied among centers and over time. However, at five years the mortality from all causes among the 161 subjects who received defibrillators during the initial hospitalization (24 percent) was much lower than among the 171 subjects who were treated with drugs (55 percent) and the 353 subjects who received no therapy (48 percent).

All the clinical trials cited above included patients who had had myocardial infarctions. The role of defibrillator therapy for the primary prevention of death from cardiac causes in patients with nonischemic cardiomyopathy has not yet been established. The Cardiomyopathy Trial²⁵ enrolled 104 subjects with nonischemic cardiomyopathy and an ejection fraction of 30 percent or less who were randomly assigned either to implantation of a defibrillator or to no therapy. No significant difference in survival was observed. As cited by Raj and Sheldon,⁴⁰ preliminary data from the Amiodarone versus Implantable Cardioverter-Defibrillator Trial (AMIOVIRT) showed no improvement in survival with implantation of a defibrillator as compared with amiodarone therapy in 103 patients with nonischemic dilated cardiomyopathy. Two large, ongoing trials, the Defibrillators in Nonischemic Cardiomyopathy Treatment Evaluation (DEFINITE)⁴¹ and the Sudden Cardiac Death in Heart Failure Trial (SCD-HEFT),⁴² may help to clarify the comparative benefits of these therapies in patients at high risk for sudden death from cardiac causes.

Ventricular arrhythmias that lead to sudden death can result from a number of congenital syndromes and acquired diseases that have been treated with implantable defibrillators. Some examples are hypertrophic cardiomyopathy,⁴³ the long-QT syn-

drome,⁴⁴ the Brugada syndrome,⁴⁵ sarcoidosis,⁴⁶ arrhythmogenic right ventricular dysplasia,⁴⁷ and certain congenital heart diseases.⁴⁸⁻⁵⁰ Since these conditions are relatively uncommon, it is unlikely that randomized trials of defibrillator therapy for them will be conducted.

On the basis of large completed trials, ongoing trials, and other clinical evidence, revised guidelines for therapy with implantable cardioverter-defibrillators have recently been published in the United States⁵¹ and Europe.⁵² The list of indications includes both primary prevention of sudden death in persons at high risk and secondary prevention, after an initial episode of sustained ventricular tachyarrhythmia, in most forms of cardiac disease (Table 3).

CARDIAC RESYNCHRONIZATION AND THE IMPLANTABLE CARDIOVERTER-DEFIBRILLATOR

Cardiac resynchronization is a recently developed technique in which biventricular pacing is used to improve ventricular function.⁵³ In patients with depressed ejection fractions, intraventricular conduction delay, and advanced heart failure (New York Heart Association [NYHA] functional class III or IV), cardiac resynchronization may improve hemodynamic function, increase exercise tolerance, and lower the NYHA functional class. Preliminary reports from two randomized trials^{54,55} indicate that combining cardiac resynchronization with defibrillator therapy may improve functional status and lower mortality.

COMPLICATIONS

The evolution of the implantable defibrillator from a large device that required an abdominal pocket and insertion of an epicardial lead system by thoracotomy to the present generation of smaller transvenous pectoral devices has markedly decreased the complications related to implantation (Table 4).⁵⁶⁻⁵⁸ The surgical complications are similar in type and frequency to those seen with routine pacemaker implantation. Infection occurs in 1 to 2 percent of cases after implantation and requires further surgery to remove the device. Malfunctions in a lead after implantation continue to be a problem. Fractures in a lead or failure in the insulation can cause false signals, which, when detected, prompt delivery of inappropriate shocks. Changes in the patient's condition, the addition of drug therapy, or abnormal-

ities in the levels of electrolytes may increase the defibrillation threshold. The unnecessary use of ventricular pacing may have led to an increased number of hospitalizations among the subjects in the second MADIT²³ and those in the Dual Chamber and VVI Implantable Defibrillator (DAVID) trial,⁵⁹ in which defibrillators that provide dual-chamber pacing were compared with defibrillators that provide ventricular backup pacing.

Frequent shocks, whether appropriately delivered during a ventricular arrhythmia or inappropriately delivered in the absence of an arrhythmia, are the most common complications encountered after implantation of a defibrillator. When the shocks are appropriate, antitachycardia pacing can be reprogrammed to improve its effectiveness, antiarrhythmic-drug therapy can be instituted or changed, or catheter ablation can be performed.⁶⁰ When shocks are inappropriately delivered because of supraventricular arrhythmias in the detection zone, reprogramming of the defibrillator to include an arrhythmia-discrimination algorithm, drug therapy, or an ablation procedure may be helpful.

Patients' psychological responses to implantation of a defibrillator are highly variable.⁶¹ In the AVID trial,³² patients who reported shocks during follow-up also reported reductions in their physical functioning and mental well-being and increased anxiety. In CIDS,³³ adverse effects on the quality of life were observed only in patients who received more than four shocks. In both of these studies, patients who reported having received no shocks also reported a quality of life similar or superior to that reported by subjects receiving antiarrhythmic drugs who had no adverse effects from the therapy.

FOLLOW-UP

Current implantable defibrillators automatically perform necessary periodic capacitor reformation and recharging of the battery to maintain electrical integrity. Patients should be seen at regular intervals to monitor the site of implantation, proper functioning of the leads and the device, arrhythmia detection, and the delivery of therapy.^{62,63} The interval between follow-up visits may range between one and six months, depending on the patient's condition and the length of time since implantation of the defibrillator. Primary follow-up should be conducted by or in coordination with an electrophysiologist with experience in defibrillator management. Manufacturers of implantable defibrillators have

Table 3. Major Indications and Contraindications for Implantable Cardioverter-Defibrillator (ICD) Therapy.*

Indications	Contraindications
Secondary prevention Cardiac arrest due to VT or VF Sustained VT, especially with structural heart disease Unexplained syncope with inducible sustained VT or VF or with advanced structural heart disease and no other identifiable cause	Unexplained syncope in the absence of structural heart disease or inducible VT or VF Incessant VT or VF VT or VF due to completely correctable cause
Primary prevention Coronary disease, LV dysfunction, inducible VT Chronic coronary disease, LVEF \leq 30 percent High-risk, inherited or acquired conditions (e.g., long-QT syndrome, Brugada's syndrome, hypertrophic cardiomyopathy)	Psychiatric illness potentially aggravated by ICD therapy Terminal illness Irreversible NYHA class IV congestive heart failure without option of cardiac transplantation
ICD therapy plus biventricular pacing Above indications with QRS \geq 130 msec, LV dilatation, LVEF \leq 35 percent, and advanced heart failure	Implantation at time of coronary-bypass surgery performed for primary prevention

* Modified from Gregoratos et al.,⁵¹ where a full list and description of indications can be found. VT denotes ventricular tachycardia, VF ventricular fibrillation, LV left ventricular, LVEF left ventricular ejection fraction, and NYHA New York Heart Association.

Web sites and other technical support services for physicians who have questions concerning patients with defibrillators.

Patients who report single shocks without sequelae can be evaluated by the physician during a routine office visit. Patients who have multiple shocks within a short period (24 to 48 hours) should contact their physicians within 24 hours. Patients and physicians should both be aware that strong electromagnetic fields may interfere with the function of a defibrillator. Malfunctions caused by diagnostic or therapeutic devices that generate electrical current or magnetic fields (e.g., cautery and magnetic resonance imaging) or by the use of motors, appliances, cellular phones, and security and anti-theft devices have been reported.^{64,65}

Driving should not be affected by an implanted defibrillator, but patients who have had episodes of severe symptoms or loss of consciousness within the previous six months, whether or not they have an implanted defibrillator, should be advised to refrain from driving.^{66,67} Many patients resume driving after an interval of less than six months during which they have been free of symptoms.⁶⁸ Patients must be warned of specific local legal restrictions

Table 4. Complications of Implantable Cardioverter–Defibrillator Therapy.**Device-related**

Infection or erosion
 Hematoma
 Pneumothorax
 Lead dislodgment
 Inadequate defibrillation threshold
 Connection problems
 Lead malfunctions or fractures
 Electromagnetic interference

Therapy-related

Frequent shocks, appropriate or inappropriate
 Acceleration of ventricular tachycardia
 Psychological reactions
 Longer or additional hospitalization (possibly for right ventricular pacing)

on driving. Driving is typically not restricted among patients who receive defibrillators for primary prevention, because such patients have no history of an arrhythmia that might cause loss of control of a vehicle.

FACTORS AFFECTING USE

Many factors affect the adoption of new medical devices.⁶⁹⁻⁷¹ Originally, the indication for implantable cardioverter–defibrillator therapy was recurrent life-threatening ventricular arrhythmias that were unresponsive to drug therapy. Now, implantable defibrillator therapy may also be indicated for the primary or secondary prevention of sudden death from cardiac causes in many groups of patients. The development of devices that combine cardiac resynchronization with standard defibrillator functions offers the possibility of improving the patient's functional status as well as prolonging life. In other countries, the acceptance of implantable cardioverter–defibrillator therapy for secondary and, especially, primary prevention has been uneven.^{70,71} The rate of defibrillator implantation per 1 million persons in the United States is five times as high as the rate in Western Europe, whereas the rate of implantation there far exceeds that elsewhere in the world. Possible reasons for these differences include social attitudes toward sudden death, the prevalence of heart disease in the population, differences in the organization and funding of medical care, the amount of resources available for such

high-technology devices, the availability of trained electrophysiologists, and market penetration by manufacturers of cardioverter–defibrillators.

Estimates of the costs of implantable-defibrillator therapy depend strongly on the design used in the analysis.⁷⁰ Implantable-defibrillator therapy has both a large up-front cost and considerable additional costs throughout the life of the device. If the estimates of costs and benefits used in a clinical trial are truncated at the close of the study, the result will overestimate the cost per year of life saved. Long-term data from the meta-analysis²⁶ of the results of the AVID, CASH, and CIDS trials suggest that the survival benefits of defibrillator therapy for secondary prevention, in comparison with those of drug therapy, decrease over time and are negligible after about six years. Long-term economic data from trials on the primary prevention of sudden death are not yet available.

Although complex models for the economic assessment of defibrillator therapy have been described, the results have varied, owing to the wide range of assumptions made regarding the risk of death from arrhythmias in the patient population and the relative effectiveness of the therapies examined.⁷²⁻⁷⁴ An economic analysis conducted by the CIDS investigators⁷⁵ suggested that the cost per year of life saved might be acceptable if implantable defibrillators were prescribed only for persons with at least two of the following risk factors: an age of 70 years or more, an ejection fraction of 35 percent or less, and advanced heart failure. Others have reported similar analyses.⁷⁶

In the United States, the greatest number of out-of-hospital deaths from cardiac causes and the highest ratios of out-of-hospital to in-hospital deaths from cardiac causes are seen in the oldest age groups; in 1999, 37.3 percent and 28.4 percent of 465,000 such deaths that occurred out-of-hospital or in emergency departments were in persons over 85 years of age and between 75 and 84 years of age, respectively.⁷⁷

The appropriate application of an intervention as expensive as implantable cardioverter–defibrillator therapy remains an unsettled issue, and one that is influenced by political, ethical, philosophical, social, economic, and medical factors. Although some have called on manufacturers to market low-cost implantable defibrillators,⁷⁸ such marketing would require a change in the current business model, which features competition among large manufac-

turers on the basis of technological innovation and intensive support to patients and physicians.⁷⁹

SUMMARY

Implantable cardioverter-defibrillator therapy has been established as an effective method of preventing sudden death from cardiac causes. Few other interventions have been shown as consistently to have equivalent absolute and relative effects on survival among high-risk patients. New models of cardio-

verter-defibrillators may improve the functional status and quality of life of selected patients who are likely to benefit from biventricular pacing. The implantable defibrillator, however, is invasive and expensive and may expose patients to complications. Optimal use of implantable defibrillators in populations and in individual patients will depend on careful decision making by managers of health care systems, clinicians, and patients.

Dr. DiMarco reports having received lecture fees from Medtronic and CPI/Guidant.

REFERENCES

- Zipes DP, Wellens HJJ. Sudden cardiac death. *Circulation* 1998;98:2334-51.
- Huikuri HV, Castellanos A, Myerburg RJ. Sudden death due to cardiac arrhythmias. *N Engl J Med* 2001;345:1473-82.
- Mirowski M, Mower MM. Transvenous automatic defibrillator as an approach to prevention of sudden death from ventricular fibrillation. *Heart Lung* 1973;2:867-9.
- Mirowski M, Mower MM, Langer A, Heilman MS, Schreibman J. A chronically implanted system for automatic defibrillation in active conscious dogs: experimental model for treatment of sudden death from ventricular fibrillation. *Circulation* 1978;58:90-4.
- Mirowski M, Reid PR, Mower MM, et al. Termination of malignant ventricular arrhythmias with an implantable automatic defibrillator in human beings. *N Engl J Med* 1980;303:322-4.
- Smith WM, Ideker RE. Automatic implantable cardioverter-defibrillators. *Annu Rev Biomed Eng* 1999;1:331-46.
- Swerdlow CD, Chen PS, Kass RM, Allard JR, Peter CT. Discrimination of ventricular tachycardia from sinus tachycardia and atrial fibrillation in a tiered-therapy cardioverter-defibrillator. *J Am Coll Cardiol* 1994;23:1342-55.
- Kühlkamp V, Dörnberger V, Mewis C, Suchalla R, Bosch RE, Seipel L. Clinical experience with the new detection algorithms for atrial fibrillation of a defibrillator with dual chamber sensing and pacing. *J Cardiovasc Electrophysiol* 1999;10:905-15.
- Swerdlow CD, Ahern T, Chen PS, et al. Underdetection of ventricular tachycardia by algorithms to enhance specificity in a tiered-therapy cardioverter-defibrillator. *J Am Coll Cardiol* 1994;24:416-24.
- Hammill SC, Packer DL, Stanton MS, Fetter J. Termination and acceleration of ventricular tachycardia with autodecremental pacing, burst pacing, and cardioversion in patients with an implantable cardioverter defibrillator. *Pacing Clin Electrophysiol* 1995;18:3-10.
- Wyse DG, Kavanagh KM, Gillis AM, et al. Comparison of biphasic and monophasic shocks for defibrillation using a nonthoracotomy system. *Am J Cardiol* 1993;71:197-202.
- Wellens HJJ, Lau CP, Lüderitz B, et al. Atrioverter: an implantable device for the treatment of atrial fibrillation. *Circulation* 1998;98:1651-6.
- Tse HF, Lau CP, Yu CM, et al. Effect of the implantable atrial defibrillator on natural history of atrial fibrillation. *J Cardiovasc Electrophysiol* 1999;10:1200-9.
- Kühlkamp V. Initial experience with an implantable cardioverter-defibrillator incorporating cardiac resynchronization therapy. *J Am Coll Cardiol* 2002;39:790-7.
- Lozano I, Bocchiardo M, Achtelik M, et al. Impact of biventricular pacing on mortality in a randomized crossover study of patients with heart failure and ventricular arrhythmias. *Pacing Clin Electrophysiol* 2000;23:1711-2.
- Mirowski M, Reid PR, Winkle RA, et al. Mortality in patients with implanted automatic defibrillators. *Ann Intern Med* 1983;98:585-8.
- Tehou PJ, Kadri N, Anderson J, Caceres JA, Jazayeri M, Akhtar M. Automatic implantable cardioverter defibrillators and survival of patients with left ventricular dysfunction and malignant arrhythmias. *Ann Intern Med* 1988;109:529-34.
- Winkle RA, Mead RH, Ruder MA, et al. Long-term outcome with the automatic implantable cardioverter-defibrillator. *J Am Coll Cardiol* 1989;13:1353-61.
- The Antiarrhythmic versus Implantable Defibrillators (AVID) Investigators. A comparison of antiarrhythmic-drug therapy with implantable defibrillators in patients resuscitated from near-fatal ventricular arrhythmias. *N Engl J Med* 1997;337:1576-83.
- Connolly SJ, Gent M, Roberts RS, et al. Canadian Implantable Defibrillator Study (CIDS): a randomized trial of the implantable cardioverter defibrillator against amiodarone. *Circulation* 2000;101:1297-302.
- Kuck KH, Cappato R, Siebels J, Ruppel R. Randomized comparison of antiarrhythmic drug therapy with implantable defibrillators in patients resuscitated from cardiac arrest: the Cardiac Arrest Study Hamburg (CASH). *Circulation* 2000;102:748-54.
- Moss AJ, Hall WJ, Cannom DS, et al. Improved survival with an implantable defibrillator in patients with coronary disease at high risk for ventricular arrhythmia. *N Engl J Med* 1996;335:1933-40.
- Moss AJ, Zareba W, Hall WJ, et al. Prophylactic implantation of a defibrillator in patients with myocardial infarction and reduced ejection fraction. *N Engl J Med* 2002;346:877-83.
- Bigger JT Jr. Prophylactic use of implanted cardiac defibrillators in patients at high risk for ventricular arrhythmias after coronary-artery bypass graft surgery. *N Engl J Med* 1997;337:1569-75.
- Bänsch D, Antz M, Boczor S, et al. Primary prevention of sudden death in idiopathic dilated cardiomyopathy: the Cardiomyopathy Trial (CAT). *Circulation* 2002;105:1453-8.
- Connolly SJ, Hallstrom AP, Cappato R, et al. Meta-analysis of the implantable cardioverter defibrillator secondary prevention trials: AVID, CASH and CIDS studies. *Eur Heart J* 2000;21:2071-8.
- Domanski MJ, Sakseena S, Epstein AE, et al. Relative effectiveness of the implantable cardioverter-defibrillator and antiarrhythmic drugs in patients with varying degrees of left ventricular dysfunction who have survived malignant ventricular arrhythmias. *J Am Coll Cardiol* 1999;34:1090-5.
- Sheldon R, Connolly S, Krahn A, Roberts R, Gent M, Gardner M. Identification of patients most likely to benefit from implantable cardioverter-defibrillator therapy: the Canadian Implantable Defibrillator Study. *Circulation* 2000;101:1660-4.
- Wyse DG, Friedman PL, Brodsky MA, et al. Life-threatening ventricular arrhythmias due to transient or correctable causes: high risk for death in follow-up. *J Am Coll Cardiol* 2001;38:1718-24.
- Brodsky MA, Mitchell LB, Halperin BD, Raitt MH, Hallstrom AP. Prognostic value of baseline electrophysiology studies in patients with sustained ventricular tachyarrhythmia: the Antiarrhythmics Versus Implantable Defibrillators (AVID) trial. *Am Heart J* 2002;144:478-84.
- Exner DV, Pinski SL, Wyse DG, et al. Electrical storm presages nonsudden death: the Antiarrhythmics Versus Implantable Defib-

- rillators (AVID) trial. *Circulation* 2001;103:2066-71.
32. Schron EB, Exner DV, Yao Q, et al. Quality of life in the Antiarrhythmics Versus Implantable Defibrillators trial: impact of therapy and influence of adverse symptoms and defibrillator shocks. *Circulation* 2002;105:589-94.
33. Irvine J, Dorian P, Baker B, et al. Quality of life in the Canadian Implantable Defibrillator Study (CIDS). *Am Heart J* 2002;144:282-9.
34. Pacifico A, Hohnloser SH, Williams JH, et al. Prevention of implantable-defibrillator shocks by treatment with sotalol. *N Engl J Med* 1999;340:1855-62.
35. Brode SE, Schwartzman D, Callans DJ, Gottlieb CD, Marchlinski FE. ICD-antiarrhythmic drug and ICD-pacemaker interactions. *J Cardiovasc Electrophysiol* 1997;8:830-42.
36. Naccarelli GV, Wolbrette DL, Dell'Orfano JT, Patel HM, Luck JC. A decade of clinical trial developments in postmyocardial infarction, congestive heart failure, and sustained ventricular tachyarrhythmia patients: from CAST to AVID and beyond. *J Cardiovasc Electrophysiol* 1998;9:864-91.
37. Bigger Jr JT, Whang W, Rottman JN, et al. Mechanisms of death in the CABG Patch trial: a randomized trial of implantable cardiac defibrillator prophylaxis in patients at high risk of death after coronary artery bypass graft surgery. *Circulation* 1999;99:1416-21.
38. Buxton AE, Lee KL, Fisher JD, Josephson ME, Prystowsky EN, Hafley G. A randomized study of the prevention of sudden death in patients with coronary artery disease. *N Engl J Med* 1999;341:1882-90. [Erratum, *N Engl J Med* 2000;342:1300.]
39. Buxton AE, Lee KL, DiCarlo L, et al. Electrophysiologic testing to identify patients with coronary artery disease who are at risk for sudden death. *N Engl J Med* 2000;342:1937-45.
40. Raj SR, Sheldon RS. The implantable cardioverter-defibrillator: does everybody need one? *Prog Cardiovasc Dis* 2001;44:169-94.
41. Kadish A, Quigg R, Schaechter A, Anderson KP, Estes M, Levine J. Defibrillators in nonischemic cardiomyopathy treatment evaluation. *Pacing Clin Electrophysiol* 2000;23:338-43.
42. Klein H, Auricchio A, Reek S, Geller C. New primary prevention trials of sudden cardiac death in patients with left ventricular dysfunction: SCD-HEFT and MADIT-II. *Am J Cardiol* 1999;83:91D-97D.
43. Maron BJ, Shen W-K, Link MS, et al. Efficacy of implantable cardioverter-defibrillators for the prevention of sudden death in patients with hypertrophic cardiomyopathy. *N Engl J Med* 2000;342:365-73.
44. Groh WJ, Silka MJ, Oliver RP, Halperin BD, McNulty JH, Kron J. Use of implantable cardioverter-defibrillators in the congenital long QT syndrome. *Am J Cardiol* 1996;78:703-6.
45. Priori SG, Napolitano C, Gasparini M, et al. Natural history of Brugada syndrome: insights for risk stratification and management. *Circulation* 2002;105:1342-7.
46. Paz HL, McCormick DJ, Kutalek SP, Patchefsky A. The automated implantable cardiac defibrillator: prophylaxis in cardiac sarcoidosis. *Chest* 1994;106:1603-7.
47. Tavernier R, Gevaert S, De Sutter J, et al. Long term results of cardioverter-defibrillator implantation in patients with right ventricular dysplasia and malignant ventricular tachyarrhythmias. *Heart* 2001;85:53-6.
48. Gradaus R, Hammel D, Kotthoff S, Bocker D. Nonthoracotomy implantable cardioverter defibrillator placement in children: use of subcutaneous array leads and abdominally placed implantable cardioverter defibrillators in children. *J Cardiovasc Electrophysiol* 2001;12:356-60.
49. Shannon K. Use of implantable cardioverter-defibrillators in pediatric patients. *Curr Opin Cardiol* 2002;17:280-2.
50. Chatrath R, Porter C, Ackerman MJ. Role of transvenous cardioverter-defibrillators in preventing sudden death in children, adolescents, and young adults. *Mayo Clin Proc* 2002;77:226-31.
51. Gregoratos G, Abrams A, Epstein AE, et al. ACC/AHA/NASPE 2002 guideline update for implantation of cardiac pacemakers and antiarrhythmia devices: summary article: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (AHA/ACC/NASPE Committee to Update the 1998 Pacemaker Guidelines). *Circulation* 2002;106:2145-61.
52. Hauer RN, Aliot E, Block M, et al. European Society of Cardiology Working Group on Arrhythmias and Working Group on Cardiac Pacing. Indications for implantable cardioverter defibrillators (ICD) therapy. *Eur Heart J* 2001;22:1074-81.
53. Abraham WT, Fisher WG, Smith AL, et al. Cardiac resynchronization in chronic heart failure. *N Engl J Med* 2002;346:1845-53.
54. Center for Devices and Radiological Health. InSync ICD model 7272 dual chamber implantable cardioverter defibrillator with cardiac resynchronization therapy and the model 9969 application software — P010031. Rockville, Md.: Food and Drug Administration, June 2002. (Accessed September 5, 2003, at <http://www.fda.gov/cdrh/pdf/p010031.pdf>.)
55. Bristow MR. Comparison of medical resynchronization and defibrillation therapies in heart failure (COMPANION) trial. Bethesda, Md.: American College of Cardiology, 2003. (Accessed September 5, 2003, at http://www.acc.org/media/session_info/late/ACC03/lbct_Monday.htm#bristow.)
56. Kennergren C. Impact of implant techniques on complications with current implantable cardioverter-defibrillator systems. *Am J Cardiol* 1996;78:Suppl 5A:15-20.
57. Kron J, Herre J, Renfro EG, et al. Lead and device-related complications in the Antiarrhythmics versus Implantable Defibrillators trial. *Am Heart J* 2001;141:92-8.
58. Pavia S, Wilkoff B. The management of surgical complications of pacemaker and implantable cardioverter-defibrillators. *Curr Opin Cardiol* 2001;16:66-71.
59. Wilkoff BL, Cook JR, Epstein AE, et al. Dual-chamber pacing or ventricular backup pacing in patients with an implantable defibrillator: the Dual-Chamber and VVI Implantable Defibrillator (DAVID) Trial. *JAMA* 2002;288:3115-23.
60. Miller JM, Hsia HH. Management of the patient with frequent discharges from implantable cardioverter defibrillator devices. *J Cardiovasc Electrophysiol* 1996;7:278-85.
61. Heller SS, Ormont MA, Lidagoster L, Sciacca RR, Steinberg S. Psychosocial outcome after ICD implantation: a current perspective. *Pacing Clin Electrophysiol* 1998;21:1207-15.
62. Winters SL, Packer DL, Marchlinski FE, et al. Consensus statement on indications, guidelines for use, and recommendations for follow-up of implantable cardioverter defibrillators. *Pacing Clin Electrophysiol* 2001;24:262-9.
63. Curtis AB, Langberg JJ, Tracy CM. Clinical competency statement: implantation and follow-up of cardioverter defibrillators. *J Cardiovasc Electrophysiol* 2001;12:280-4.
64. Glickson M, Friedman PA. The implantable cardioverter defibrillator. *Lancet* 2001;357:1107-17.
65. Greene HL. The implantable cardioverter-defibrillator. *Clin Cardiol* 2000;23:315-26.
66. Epstein AE, Miles WM, Benditt DG, et al. Personal and public safety issues related to arrhythmias that may affect consciousness: implications for regulation and physician recommendations: a medical/scientific statement from the American Heart Association and the North American Society of Pacing and Electrophysiology. *Circulation* 1996;94:1147-66.
67. Petch MC. Driving and heart disease. *Eur Heart J* 1998;19:1165-77.
68. Akiyama T, Powell JL, Mitchell LB, Ehlert FA, Baessler C. Resumption of driving after life-threatening ventricular tachyarrhythmia. *N Engl J Med* 2001;345:391-7.
69. Exner DV, Klein GJ, Prystowsky EN. Primary prevention of sudden death with implantable defibrillator therapy in patients with cardiac disease: can we afford to do it? (Can we afford not to?) *Circulation* 2001;104:1564-70.
70. Seidl K, Senges J. Geographic differences in implantable cardioverter defibrillator usage. *J Cardiovasc Electrophysiol* 2002;13:Suppl:S100-S105.
71. Camm AJ, Nisam S. The utilization of the implantable defibrillator — a European enigma. *Eur Heart J* 2000;21:1998-2004.
72. Morgan JM. Cost-effectiveness of implantable cardioverter-defibrillator therapy. *J Cardiovasc Electrophysiol* 2002;13:Suppl:S114-S117.
73. Sanders GD, Hlatky MA, Every NR, et al. Potential cost-effectiveness of prophylactic

use of the implantable cardioverter-defibrillator or amiodarone after myocardial infarction. *Ann Intern Med* 2001;135:870-83.

74. Owens DK, Sanders DG, Harris RA, et al. Cost-effectiveness of implantable cardioverter defibrillators relative to amiodarone for prevention of sudden cardiac death. *Ann Intern Med* 1997;126:1-12.

75. Sheldon R, O'Brien BJ, Blackhouse G, et al. Effect of clinical risk stratification on cost-effectiveness of the implantable cardiovert-

er-defibrillator: the Canadian Implantable Defibrillator Study. *Circulation* 2001;104:1622-6.

76. Owens DK, Sanders GD, Heidenreich PA, McDonald KM, Hlatky MA. Effect of risk stratification on cost-effectiveness of the implantable cardioverter defibrillator. *Am Heart J* 2002;144:440-8.

77. State-specific mortality from sudden cardiac death — United States, 1999. *MMWR Morb Mortal Wkly Rep* 2002;51:123-6. (Al-

so available at <http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5106a3.htm>.)

78. Zipes DP. Implantable cardioverter-defibrillator: a Volkswagen or a Rolls Royce: how much will we pay to save a life? *Circulation* 2001;103:1372-4.

79. Jeffrey K. *Machines in our hearts: the cardiac pacemaker, the implantable defibrillator, and American health care*. Baltimore: Johns Hopkins University Press, 2001.

Copyright © 2003 Massachusetts Medical Society.



El-Giza, Egypt

Maurizio Toso, M.D.