

ACC/AHA/NASPE 2002 Guideline Update for Implantation of Pacemakers and Antiarrhythmia Devices

These guidelines have been reviewed over the course of the past 4 years since their publication (Full Text—*J Am Coll Cardiol* 1998;31:1175-1209; Executive Summary—*Circulation* 1998;97:1325-1335). This update is based on the most significant advances for implantation of cardiac pacemakers and antiarrhythmia devices that have been published during that time frame. These guidelines are available on the Web sites of the American College of Cardiology, the American Heart Association, and the North American Society of Pacing and Electrophysiology. Deleted text is indicated by ~~strikeout~~, and revised text is underlined.

Copies of the full-text guideline incorporating the revisions (not showing ~~strikeout~~ and underlined text) will be available on the ACC, AHA, and NASPE Web sites in the near future. A summary article highlighting the changes to the guideline from 1997 to 2002 will be published in the October 15 issue of *Circulation* and the November 6 issue of the *Journal of the American College of Cardiology* and is also available for download on the ACC, AHA, and NASPE Web sites. See below for the full text of the guideline.

ACC/AHA/NASPE PRACTICE GUIDELINES—FULL TEXT

ACC/AHA/NASPE 2002 Guideline Update for Implantation of Cardiac Pacemakers and Antiarrhythmia Devices

A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (ACC/AHA/NASPE Committee on Pacemaker Implantation)

COMMITTEE MEMBERS

Gabriel Gregoratos, MD, FACC, FAHA, *Chair*

Jonathan Abrams, MD, FACC, FAHA
Andrew E. Epstein, MD, FACC, FAHA
Roger A. Freedman, MD, FACC
David L. Hayes, MD, FACC, FAHA
Mark A. Hlatky, MD, FACC, FAHA

Richard E. Kerber, MD, FACC, FAHA
Gerald V. Naccarelli, MD, FACC, FAHA
Mark H. Schoenfeld, MD, FACC, FAHA
Michael J. Silka, MD, FACC
Stephen L. Winters, MD, FACC

TASK FORCE MEMBERS

Raymond J. Gibbons, MD, FACC, FAHA, *Chair*
Elliott M. Antman, MD, FACC, FAHA, *Vice Chair*

Joseph S. Alpert, MD, FACC, FAHA
David P. Faxon, MD, FACC, FAHA
Valentin Fuster, MD, PhD, FACC, FAHA

Gabriel Gregoratos, MD, FACC, FAHA
Loren F. Hiratzka, MD, FACC, FAHA
Alice K. Jacobs, MD, FACC, FAHA

Sidney C. Smith, Jr., MD, FACC, FAHA

This document was approved by the American College of Cardiology Foundation Board of Trustees in September 2002, by the American Heart Association Science Advisory and Coordinating Committee in August 2002, and by the North American Society for Pacing and Electrophysiology in August 2002.

When citing this document, the American College of Cardiology Foundation, the American Heart Association, and the North American Society of Pacing and Electrophysiology would appreciate the following citation format: Gregoratos G, Abrams J, Epstein AE, Freedman RA, Hayes DL, Hlatky MA, Kerber RE, Naccarelli GV, Schoenfeld MH, Silka MJ, Winters SL. ACC/AHA/NASPE 2002 guideline update for implantation of cardiac pacemakers and antiarrhythmia devices: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (ACC/AHA/NASPE Committee on Pacemaker Implantation). 2002. Available at: www.acc.org/clinical/guidelines/pacemaker/pacemaker.pdf.

This document is available on the World Wide Web sites of the ACC (www.acc.org), the AHA (www.americanheart.org), and the NASPE (www.naspe.org). Copies of this document (the complete guidelines) are available for \$5 each by calling 800-253-4636 (US only) or writing the American College of Cardiology, Educational Services, 9111 Old Georgetown Road, Bethesda, MD 20814-1699 (ask for No. 71-0237). To obtain a reprint of the shorter version (summary article describing the changes to the guidelines) planned for subsequent publication in *J Am Coll Cardiol* and *Circulation*, ask for reprint No. 71-0236. To purchase additional reprints (specify version and reprint number): up to 999 copies, call 800-611-6083 (US only) or fax 413-665-2671; 1000 or more copies, call 214-706-1466, fax 214-691-6342, or e-mail pabauth@heart.org.

TABLE OF CONTENTS

Preamble	2
Introduction	3
I. Indications for Permanent Pacing.....	5
A. Pacing for Acquired Atrioventricular Block in Adults.....	5

B. Pacing for Chronic Bifascicular and Trifascicular Block.....	7
C. Pacing for Atrioventricular Block Associated With Acute Myocardial Infarction.....	8
D. Pacing in Sinus Node Dysfunction.....	9
E. Prevention and Termination of Tachyarrhythmias by Pacing.....	10
F. Pacing in Hypersensitive Carotid Sinus and Neurocardiogenic Syncope.....	11
G. Pacing in Children, Adolescents, and Patients With Congenital Heart Disease.....	12
H. Pacing in Specific Conditions.....	14
1. Hypertrophic Obstructive Cardiomyopathy.....	14
2. Idiopathic Dilated Cardiomyopathy.....	15
3. Cardiac Transplantation.....	16
I. Selection of Pacemaker Device.....	16
1. Newer Technical Innovations.....	17
2. Methodology of Comparing Different Pacing Modes.....	20
3. Pacing in Sinus Node Dysfunction.....	20
4. Pacing in Atrioventricular Block.....	22
5. Pacing in the Elderly.....	22
6. Optimizing Pacemaker Technology and Cost.....	23
J. Pacemaker Follow-up.....	23
1. Amount of Time Necessary for Verification.....	24
2. Length of Electrocardiographic Samples for Storage.....	24
3. Frequency of Transtelephonic Monitoring.....	24
II. Indications for Implantable Cardioverter-Defibrillator Therapy.....	25
A. Background.....	25
B. Clinical Efficacy of ICD Therapy.....	26

C. Alternatives to ICD Therapy.....	26
D. Comparison of Drug and Device Therapy for Secondary Prevention of Cardiac Arrest and Sustained Ventricular Tachycardia.....	27
E. Specific Disease States and Secondary Prevention of Cardiac Arrest or Sustained Ventricular Tachycardia.....	27
1. Coronary Artery Disease.....	28
2. Idiopathic Dilated Cardiomyopathy.....	28
3. Long-QT Syndrome.....	28
4. Idiopathic Ventricular Fibrillation.....	28
5. Idiopathic Ventricular Tachycardia.....	28
6. Hypertrophic Cardiomyopathy.....	28
7. Arrhythmogenic Right Ventricular Dysplasia/ Cardiomyopathy.....	29
8. Syncope With Inducible Sustained Ventricular Tachycardia.....	29
F. Pediatric Patients	29
G. Primary Prevention of Sudden Cardiac Death.....	30
1. Coronary Artery Disease.....	30
2. After Coronary Artery Bypass Surgery.....	30
3. As a Bridge to Heart Transplantation.....	30
4. Other Populations.....	30
H. Contraindications and Limitations of ICD Therapy.....	31
I. Cost-Effectiveness of ICD Therapy.....	31
J. Selection of ICD Generators.....	31
K. ICD Follow-up.....	32
1. Elements of ICD Follow-up.....	32
References	35

PREAMBLE

It is important that the medical profession play a significant role in critically evaluating the use of diagnostic procedures and therapies in the management or prevention of disease states. Rigorous and expert analysis of the available data documenting relative benefits and risks of those procedures and therapies can produce helpful guidelines that improve the effectiveness of care, optimize patient outcomes, and impact the overall cost of care favorably by focusing resources on the most effective strategies.

The American College of Cardiology (ACC) and the American Heart Association (AHA) have jointly engaged in the production of such guidelines in the area of cardiovascular disease since 1980. This effort is directed by the ACC/AHA Task Force on Practice Guidelines. Its charge is to develop and revise practice guidelines for important cardiovascular diseases and procedures. Experts in the subject under consideration are selected from both organizations to examine subject-specific data and write guidelines. The process includes additional representatives from other medical practitioner and specialty groups where appropriate. Writing groups are specifically charged to perform a formal literature review, weigh the strength of evidence for or against a particular treatment or procedure, and include estimates of expected health outcomes where data exist Patient-

specific modifiers, comorbidities, and issues of patient preference that might influence the choice of particular tests or therapies are considered, as well as frequency of follow-up and cost-effectiveness.

The ACC/AHA Task Force on Practice Guidelines makes every effort to avoid any actual or potential conflicts of interest that might arise as a result of an outside relationship or a personal interest of a member of the writing panel. Specifically, all members of the writing panel are asked to provide disclosure statements of all such relationships that might be perceived as real or potential conflicts of interest. These statements are reviewed by the parent task force, reported orally to all members of the writing panel at the first meeting, and updated as changes occur. (See Appendix for conflict of interest information for writing committee members.)

These practice guidelines are intended to assist physicians in clinical decision-making by describing a range of generally acceptable approaches for the diagnosis, management, or prevention of specific diseases or conditions. The guidelines attempt to define practices that meet the needs of most patients in most circumstances. The ultimate judgment regarding care of a particular patient must be made by the physician and patient in light of all of the circumstances presented by that patient.

The 1997 Committee on Pacemaker Implantation was chaired by Gabriel Gregoratos, MD, FACC, and included the following members: Melvin D. Cheitlin, MD, FACC; Alicia Conill, MD, FACP; Andrew E. Epstein, MD, FACC; Christopher Fellows, MD, FACC; T. Bruce Ferguson, Jr., MD, FACC; Roger A. Freedman, MD, FACC; Mark A. Hlatky, MD, FACC; Gerald V. Naccarelli, MD, FACC; Sanjeev Saksena, MD, MBBS, FACC; Robert C. Schlant, MD, FACC; and Michael J. Silka, MD, FACC. The document update used the 1997 work as its basis. The Committee to Update Guidelines on Cardiac Pacemaker Implantation and Antiarrhythmic Devices was chaired by Gabriel Gregoratos, MD, FACC, FAHA, and included the following members: Andrew E. Epstein, MD, FACC, FAHA; Roger A. Freedman, MD, FACC; David L. Hayes, MD, FACC, FAHA; Mark A. Hlatky, MD, FACC, FAHA; Richard E. Kerber, MD, FACC, FAHA; Gerald V. Naccarelli, MD, FACC, FAHA; Mark H. Schoenfeld, MD, FACC, FAHA; Michael J. Silka, MD, FACC; and Stephen L. Winters, MD, FACC.

The summary article is published in the October 15, 2002 issue of *Circulation* and in the November 6, 2002 issue of the *Journal of the American College of Cardiology*. The full text guideline is posted on the ACC, AHA, and NASPE Web sites. Copies of both the full text and the summary article are available from all three organizations.

Raymond J. Gibbons, MD, FACC, FAHA
 Chair, ACC/AHA Task Force on Practice Guidelines

Elliott M. Antman, MD, FACC, FAHA
 Vice Chair, ACC/AHA Task Force on Practice Guidelines

INTRODUCTION

This revision of the “ACC/AHA Guidelines for Implantation of Cardiac Pacemakers and Antiarrhythmia Devices” updates the previous versions published in 1984, 1991, and 1998. Revision of the statement was deemed necessary for two reasons: the publication of major studies that have advanced our knowledge of the natural history of bradyarrhythmias and tachyarrhythmias, which may be treated optimally with device therapy, and major advances in the technology of such devices.

The committee to revise the ACC/AHA Guidelines for Implantation of Cardiac Pacemakers and Antiarrhythmia Devices was composed of both university-affiliated and practicing physicians. It included experts in the area of device therapy and follow-up, senior clinicians skilled in cardiovascular care, a general internist, and a cardiothoracic surgeon. The committee included representatives of the American College of Physicians, NASPE, and the Society of Thoracic Surgeons. The 1998 document was reviewed by three outside reviewers nominated by the ACC, three outside reviewers nominated by the AHA, and individuals representing the American College of Physicians and NASPE. The section “Pacing in Children and Adolescents” was reviewed by additional reviewers with special expertise in pediatric electrophysiology. The 2002 update was reviewed by two outside reviewers nominated by the ACC, two outside reviewers nominated by the AHA, and two outside reviewers nominated by the NASPE. The committee thanks all the reviewers for their comments. Many of their suggestions were incorporated into the final document.

The recommendations listed in this document are, whenever possible, evidence based. Pertinent medical literature in the English language was identified through a search of library databases, and a large number of publications were reviewed by committee members during the course of their discussions. Additionally, the committee reviewed documents related to the subject matter previously published by the ACC, AHA, and NASPE. References selected and published in this document are representative and not all-inclusive.

The committee reviewed and ranked evidence supporting current recommendations with the weight of evidence ranked as level A if the data were derived from multiple *randomized* clinical trials involving a large number of individuals. The committee ranked available evidence as level B when data were derived from a limited number of trials involving a comparatively small number of patients or from well-designed data analyses of *nonrandomized* studies or *observational* data registries. Evidence was ranked as level C when the consensus of experts was the primary source of the recommendation. In the narrative portions of these guidelines, evidence is generally presented in chronological order of development. Studies are identified as *observational*, *randomized*, *prospective*, or *retrospective*. The committee emphasizes that for certain conditions for which no other therapy is available, the indications for device therapy are

based on expert consensus and years of clinical experience and are thus well supported, even though the evidence was ranked as level C. An analogous example is the use of penicillin in pneumococcal pneumonia where there are no *randomized* trials and only clinical experience. When indications at level C are supported by historical clinical data, appropriate references (e.g., case reports and clinical reviews) are cited if available. When level C indications are based strictly on committee consensus, no references are cited. In areas where sparse data were available (e.g., pacing in children and adolescents), a survey of current practices of major centers in North America was conducted to determine whether there was a consensus regarding specific pacing indications.

The final recommendations for indications for device therapy are expressed in the standard ACC/AHA format as follows:

Class I: Conditions for which there is evidence and/or general agreement that a given procedure or treatment is beneficial, useful, and effective.

Class II: Conditions for which there is conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of a procedure or treatment.

Class IIa: Weight of evidence/opinion is in favor of usefulness/efficacy.

Class IIb: Usefulness/efficacy is less well established by evidence/opinion.

Class III: Conditions for which there is evidence and/or general agreement that a procedure/treatment is not useful/effective and in some cases may be harmful.

The focus of these guidelines is the appropriate use of devices (pacemakers and implantable cardioverter-defibrillators [ICDs]), not the treatment of cardiac arrhythmias. The fact that use of a device for treatment of a particular condition is listed as a Class I indication (beneficial, useful, and effective) does not preclude the use of other therapeutic modalities that may be equally effective. As with all clinical practice guidelines, the recommendations in this document focus on treatment of an average patient with a specific disorder and may be modified by patient comorbidities, limitation of life expectancy because of coexisting diseases, and other situations that only the primary treating physician may evaluate appropriately.

These guidelines include expanded sections on selection of pacemakers and ICDs; optimization of technology; cost; and follow-up of implanted devices. The follow-up section is relatively brief and is included for the sake of completeness, since in many instances, the type and frequency of follow-up examinations are device specific. The importance of adequate follow-up, however, cannot be overemphasized, because optimal results from an implanted device can be

obtained only if the device is adjusted to changing clinical conditions.

The committee considered including a section on extraction of failed/unused leads, a topic of current interest, but elected not to do so in the absence of convincing evidence to support specific criteria for timing and methods of lead extraction. A policy statement on lead extraction from NASPE provides information on this topic (334). Similarly, the issue of when to discontinue long-term cardiac pacing or defibrillator therapy has not been studied sufficiently to allow formulation of appropriate guidelines despite the publication of isolated case reports (1). The committee therefore decided to defer inclusion of this topic until additional information is available.

The text accompanying the listed indications should be read carefully because it includes the rationale and supporting evidence for many of the indications, and in several instances, it includes a discussion of alternative acceptable therapies. Many of the indications are modified by the term “potentially reversible.” This term is used to indicate abnormal pathophysiology (e.g., complete heart block) that may be the result of reversible factors. Examples include complete heart block due to drug toxicity (digitalis), electrolyte abnormalities, diseases with inflammatory periaortioventricular node reaction (Lyme disease), and transient injury to the conduction system at the time of open heart surgery. When faced with a potentially reversible situation, the treating physician must decide how long a waiting period is justified before beginning device therapy. The committee recognizes that this statement does not address the issue of length of hospital stay *vis-à-vis* managed-care regulations. It is emphasized that these guidelines are not intended to address this issue, which falls strictly within the purview of the treating physician.

The term “symptomatic bradycardia” is used frequently throughout this document. Symptomatic bradycardia is defined as a documented bradyarrhythmia that is directly responsible for development of the clinical manifestations of frank syncope or near syncope, transient dizziness or lightheadedness, and confusional states resulting from cerebral hypoperfusion attributable to slow heart rate. Fatigue, exercise intolerance, and frank congestive failure may also result from bradycardia. These symptoms may occur at rest and/or with exertion. Definite correlation of symptoms with a bradyarrhythmia is required to fulfill the criteria that define symptomatic bradycardia. Caution should be exercised not to confuse physiologic sinus bradycardia (as occurs in highly trained athletes) with pathological bradyarrhythmias. Occasionally, symptoms may become apparent only in retrospect after antibradycardia pacing. Nevertheless, the universal application of pacing therapy to treat a specific heart rate cannot be recommended except in specific circumstances, as detailed subsequently.

In these guidelines, the terms “persistent,” “transient,” and “not expected to resolve” are frequently used. These terms are not specifically defined because the time element varies in different clinical conditions. The treating physician must use appropriate clinical judgment and available data in decid-

ing when a condition is persistent or when it can be expected to be transient. Section I-C, “Pacing for Atrioventricular Block Associated With Acute Myocardial Infarction,” overlaps with the “ACC/AHA Guidelines for the Management of Patients With Acute Myocardial Infarction” (2)(335) and includes expanded indications and stylistic changes. The statement “incidental finding at electrophysiologic study” is used several times in this document and does not mean that such a study is indicated. Appropriate indications for electrophysiologic studies have been published (3).

The section on indications for ICDs has been updated and enlarged to reflect the numerous new developments in this field and the voluminous literature related to the efficacy of these devices in the treatment of sudden cardiac death and malignant ventricular arrhythmias. Indications for ICDs are continuously changing and can be expected to change further as ongoing large-scale trials are reported. Thus, the ICD indications may require revision in the next 2 to 3 years. In this document, the term “mortality” is used to indicate all-cause mortality unless otherwise specified. The committee elected to use all-cause mortality because of the variable definition of sudden death and the developing consensus to use all-cause mortality as the most appropriate end point of clinical trials (4,5).

These guidelines are not designed to specify training or credentials required for physicians to use device therapy. Nevertheless, in view of the complexity of both cognitive and technical aspects of device therapy, only appropriately trained physicians should use device therapy. Appropriate training guidelines for physicians have been published previously (6,7,336).

The 2002 update reflects what the committee believes are the most relevant and significant advances in pacemaker/ICD therapy since the publication of these guidelines in the *Journal of the American College of Cardiology* and *Circulation* in 1998 (337,338). An extensive literature survey was conducted, and 113 new references have been added since the original publication of these guidelines in 1998. The new references are numbered 334 to 447 and are listed together at the end of the reference list.

In preparing this update, the committee was guided by the following principles:

1. Changes in recommendations and levels of evidence were made either because of new randomized trials or because of the accumulation of new clinical evidence and the development of clinical consensus.
2. The Committee is cognizant of the healthcare, logistic, and financial implications of recent trials and factored these considerations in arriving at the class level of certain recommendations.
3. Minor wording changes were made to render some of the original recommendations more precise.
4. The committee wishes to re-emphasize that the recommendations in this guideline apply to most patients but

may require modification by existing situations that only the primary treating physician can evaluate properly.

5. All of the listed recommendations for implantation of a device presume the absence of inciting causes that may be eliminated without detriment to the patient (e.g., nonessential drug therapy).
6. The committee endeavored to maintain consistency of recommendations in this and other previously published guidelines. In the section on atrioventricular (AV) block associated with acute myocardial infarction (AMI), the recommendations follow closely those in the ACC/AHA Guidelines for the Management of Patients With Acute Myocardial Infarction (335). However, because of the rapid evolution of pacemaker/ICD science, it has not always been possible to maintain consistency with other published guidelines. An example of such a discrepancy can be found in Section I-H, where the recommendation for biventricular pacing in selected patients with heart failure has been listed as Class IIa, whereas in the ACC/AHA Guidelines for the Evaluation and Management of Chronic Heart Failure in the Adult (339), biventricular pacing is cited as an investigational procedure.

The ACC/AHA/NASPE 2002 Guideline Update for Implantation of Cardiac Pacemakers and Antiarrhythmia Devices was approved for publication by the AHA Science and Advisory Coordinating Committee and the North American Society of Pacing and Electrophysiology in August 2002 and the ACC Board of Trustees in September 2002. These guidelines will be reviewed 1 year after publication and yearly thereafter and considered current unless the Task Force on Practice Guidelines revises or withdraws them from circulation.

I. INDICATIONS FOR PERMANENT PACING

A. Pacing for Acquired Atrioventricular Block in Adults

Atrioventricular (AV) block is classified as first-, second-, or third-degree (complete) block; anatomically, it is defined as supra-, intra-, or infra-His. First-degree AV block is defined as abnormal prolongation of the PR interval. Second-degree AV block is subclassified as type I and type II. Type I second-degree AV block is characterized by progressive prolongation of the PR interval before a blocked beat and is usually associated with a narrow QRS complex. Type II second-degree AV block is characterized by fixed PR intervals before and after blocked beats (no progressive prolongation of PR interval before a blocked beat) and is usually associated with a wide QRS complex. When AV conduction occurs in a 2:1 pattern, block cannot be unequivocally classified as type I or type II, although the width of the QRS can be suggestive as just described. Advanced second-degree AV block refers to the block of two or more consecutive P waves but with some conducted beats, indicating some preservation of AV con-

duction. Third-degree AV block (complete heart block) is defined as absence of AV conduction.

Patients with abnormalities of AV conduction may be asymptomatic or may experience serious symptoms related to bradycardia, ventricular arrhythmias, or both. Decisions regarding the need for a pacemaker are influenced importantly by the presence or absence of symptoms directly attributable to bradycardia. Furthermore, many of the indications for pacing have evolved over ~~30~~40 years based on experience without the benefit of comparative *randomized* clinical trials, in part because no acceptable alternative options exist to treat most bradycardias.

Nonrandomized studies strongly suggest that permanent pacing does improve survival in patients with third-degree AV block, especially if syncope has occurred (8-13). Although there is little evidence to suggest that pacemakers improve survival in patients with isolated first-degree AV block (14), it is now recognized that marked (PR more than 300 milliseconds) first-degree AV block can lead to symptoms even in the absence of higher degrees of AV block (15). Such marked first-degree AV block may follow catheter ablation of the fast AV nodal pathway with resultant slow pathway conduction. When marked first-degree AV block for any reason causes atrial systole in close proximity to the preceding ventricular systole and produces hemodynamic consequences usually associated with retrograde (ventriculoatrial) conduction, signs and symptoms similar to the pacemaker syndrome may occur (16). Marked first-degree AV block for any reason may also be associated with a pseudopacemaker syndrome (16) secondary to close proximity of atrial systole to the preceding ventricular systole that produces hemodynamic consequences similar to those associated with retrograde (ventriculoatrial) conduction. With marked first-degree AV block, atrial contraction occurs before complete atrial filling, ventricular filling is compromised, and an increase in pulmonary capillary wedge pressure and a decrease in cardiac output follow. Small, uncontrolled trials have suggested some symptomatic and functional improvement by pacing of patients with PR intervals more than 0.30 seconds by decreasing the time for AV conduction (15). Finally, a long PR interval may identify a subgroup of patients with left ventricular (LV) dysfunction, some of whom may benefit from dual-chamber pacing with a short(er) AV delay (17). These same principles also may be applied to patients with type I second-degree AV block who experience hemodynamic compromise due to loss of AV synchrony, even without bradycardia. Consideration should be given to demonstrating hemodynamic improvement by Although echocardiographic or invasive techniques may be used to assess hemodynamic improvement ~~assessment~~ before permanent pacemaker implantation, such studies are not required.

Type I second-degree AV block is usually due to delay in the AV node irrespective of QRS width. Because progression to advanced AV block in this situation patients with type I second-degree AV block, when due to delay in the AV node, is uncommon (18-20), pacing is usually not indicated unless

the patient is symptomatic. Nevertheless, controversy exists, and pacemaker implantation has been advocated for this finding (21-23). On the other hand, type II second-degree AV block is usually infranodal (either intra- or infra-His), especially when the QRS is wide. In these patients, symptoms are frequent, prognosis is compromised, and progression to third-degree AV block is common (18,20,24). Thus, type II second-degree AV block and a wide QRS indicate diffuse conduction system disease and constitute an indication for pacing even in the absence of symptoms. However, it is not always possible to determine the site of AV block without electrophysiologic evaluation, because type I second-degree AV block can be infranodal even when the QRS is narrow (340-342). If type I second-degree AV block with a narrow or wide QRS is found to be intra- or infra-His at electrophysiologic study, pacing should be considered.

Because it may be difficult for both patients and their physicians to attribute ambiguous symptoms such as fatigue to bradycardia, special vigilance must be exercised to acknowledge the patient's concerns that may be caused by a slow heart rate. Thus, in a patient with third-degree AV block, permanent pacing should be considered strongly even when the ventricular rate is more than 40 beats per minute (bpm), because the choice of a 40 bpm cutoff in these guidelines was not determined from clinical trial data. Indeed, it is not the escape rate that is necessarily critical for safety, but rather the site of origin of the escape rhythm (i.e., in the AV node, the His bundle, or infra-His).

AV block can sometimes be provoked by exercise. If not secondary to myocardial ischemia, AV block in this circumstance usually is due to disease in the His-Purkinje system and is associated with a poor prognosis. Thus, pacing is indicated (343,344). Conversely, long sinus pauses and AV block can occur during sleep apnea. In the absence of symptoms, these abnormalities are reversible and do not require pacing (345). If symptoms are present, pacing is indicated as in other conditions.

Recommendations for permanent pacemaker implantation in patients with AV block in AMI, congenital AV block, and AV block associated with enhanced vagal tone are discussed in separate sections. Neurocardiogenic ~~mechanisms etiologies~~ in young patients with AV block should be assessed before proceeding with permanent pacing. Physiologic AV block in the presence of supraventricular tachyarrhythmias does not constitute an indication for pacemaker implantation except as specifically defined in the recommendations that follow.

In general, the decision regarding implantation of a pacemaker must be considered with respect to whether or not AV block will be permanent. Reversible causes of AV block, such as electrolyte abnormalities, should be corrected first. Some diseases may follow a natural history to resolution (e.g., Lyme disease), and some AV block can be expected to reverse (e.g., hypervagotonia due to recognizable and avoidable physiologic factors stimuli, perioperative AV block due to hypothermia, or inflammation near the AV conduction system after surgery ~~for arrhythmias~~ in this region).

Conversely, some conditions may warrant pacemaker implantation owing to the possibility anticipated adverse consequences of disease progression even if the AV block reverses transiently (e.g., sarcoidosis, amyloidosis, and neuromuscular diseases). Finally, permanent pacing for AV block after valve surgery follows a variable natural history, and therefore the decision for permanent pacing is at the physician's discretion (346).

Recommendations for Permanent Pacing in Acquired Atrioventricular Block in Adults

Class I

- 1. Third-degree and advanced second-degree AV block at any anatomic level, associated with any one of the following conditions:**
 - a. Bradycardia with symptoms (including heart failure) presumed to be due to AV block. (Level of Evidence: C)**
 - b. Arrhythmias and other medical conditions that require drugs that result in symptomatic bradycardia. (Level of Evidence: C)**
 - c. Documented periods of asystole greater than or equal to 3.0 seconds (25) or any escape rate less than 40 bpm in awake, symptom-free patients (26,27). (Level of Evidence: B, C)**
 - d. After catheter ablation of the AV junction. (Level of Evidence: B, C) There are no trials to assess outcome without pacing, and pacing is virtually always planned in this situation unless the operative procedure is AV junction modification (28,29).**
 - e. Postoperative AV block that is not expected to resolve after cardiac surgery. (Level of Evidence: C) (30,30a,346)**
 - f. Neuromuscular diseases with AV block, such as myotonic muscular dystrophy, Kearns-Sayre syndrome, Erb's dystrophy (limb-girdle), and peroneal muscular atrophy, with or without symptoms, because there may be unpredictable progression of AV conduction disease. (Level of Evidence: B) (31-37)**
- 2. Second-degree AV block regardless of type or site of block, with associated symptomatic bradycardia. (Level of Evidence: B) (19)**

Class IIa

- 1. Asymptomatic third-degree AV block at any anatomic site with average awake ventricular rates of 40 bpm or faster, especially if cardiomegaly or LV dysfunction is present. (Level of Evidence: B, C)**
- 2. Asymptomatic type II second-degree AV block with a narrow QRS. When type II second-degree AV block occurs with a wide QRS, pacing becomes a Class I recommendation (see next section regarding Pacing for Chronic Bifascicular and Trifascicular Block). (Level of Evidence: B) (21,23)**

3. **Asymptomatic type I second-degree AV block at intra- or infra-His levels found ~~incidentally~~ at electrophysiologic study performed for other indications. (Level of Evidence: B) (19,21-23)**
4. **~~First- or second-degree AV block with symptoms suggestive similar to those of pacemaker syndrome and documented alleviation of symptoms with temporary AV pacing. (Level of Evidence: B) (15,16)~~**

Class IIb

1. **Marked first-degree AV block (more than 0.30 seconds) in patients with LV dysfunction and symptoms of congestive heart failure in whom a shorter AV interval results in hemodynamic improvement, presumably by decreasing left atrial filling pressure. (Level of Evidence: C) (17)**
2. **Neuromuscular diseases such as myotonic muscular dystrophy, Kearns-Sayre syndrome, Erb's dystrophy (limb-girdle), and peroneal muscular atrophy with any degree of AV block (including first-degree AV block), with or without symptoms, because there may be unpredictable progression of AV conduction disease. (Level of Evidence: B) (31-37)**

Class III

1. **Asymptomatic first-degree AV block. (Level of Evidence: B) (14) (See also "Pacing for Chronic Bifascicular and Trifascicular Block.")**
2. **Asymptomatic type I second-degree AV block at the supra-His (AV node) level or not known to be intra- or infra-Hisian. (Level of Evidence: B, C) (19)**
3. **AV block expected to resolve and/or unlikely to recur (38) (e.g., drug toxicity, Lyme disease, or during hypoxia in sleep apnea syndrome in absence of symptoms). (Level of Evidence: B)**

B. Pacing for Chronic Bifascicular and Trifascicular Block

~~Bifascicular and trifascicular~~ block refers to electrocardiographic (ECG) evidence of impaired conduction below the AV node in two ~~or three~~ fascicles of the right and left bundles. Alternating bundle-branch block (also known as bilateral bundle-branch block) refers to situations in which clear ECG evidence for block in all three fascicles is seen on successive ECGs. Examples are right bundle-branch block and left bundle-branch block on successive ECGs, or right bundle-branch block with associated left anterior fascicular block on one ECG and associated left posterior fascicular block on another ECG. A strict definition of trifascicular block is block documented in all three fascicles whether simultaneously or at different times. Alternating bundle-branch block also fulfills this criterion. This term has also been used to describe first-degree AV block in association with bifascicular block. Patients with such ECG abnormalities ~~there is convincing evidence that~~ and symptomatic, advanced AV block ~~is associated with~~ have a high mortality

rate and a significant incidence of sudden death (9,39). Although third-degree AV block is most often preceded by bifascicular block, there is ~~impressive~~ evidence that the rate of progression of bifascicular block to third-degree AV block is slow (347). Furthermore, no single clinical or laboratory variable, including bifascicular block, identifies patients at high risk of death from a future bradyarrhythmia due to bundle-branch block (48).

Syncope is common in patients with bifascicular block. Although syncope may be recurrent, it is not associated with an increased incidence of sudden death (40-52). Although pacing relieves the transient neurological symptoms, it does not reduce the ~~frequency~~ occurrence of sudden death (46). Electrophysiologic study may be helpful to evaluate and direct the treatment of inducible ventricular arrhythmias (53,54) that are common in patients with bifascicular and trifascicular block. There is convincing evidence that in the presence of permanent or transient third-degree AV block, syncope is associated with an increased incidence of sudden death regardless of the results of electrophysiologic study (9,54,55). Finally, if the cause of syncope in the presence of bifascicular or trifascicular block cannot be determined with certainty or if treatments used (such as drugs) may exacerbate AV block, prophylactic permanent pacing is indicated, especially if syncope may have been due to transient third-degree AV block (40,52).

Of the many laboratory variables, the PR and HV intervals have been identified as possible predictors of third-degree AV block and sudden death. Although PR interval prolongation is common in patients with bifascicular block, the delay is often at the level of the AV node. There is no correlation between the PR and HV intervals or between the length of the PR interval, progression to third-degree AV block, and sudden death (43,45,49). Although most patients with chronic or intermittent third-degree AV block demonstrate prolongation of the HV interval during anterograde conduction, some investigators (50,51) have suggested that asymptomatic patients with bifascicular block and a prolonged HV interval should be considered for permanent pacing, especially if the HV interval is greater than or equal to 100 milliseconds (49). The evidence indicates that although the prevalence of prolonged HV is high, the incidence of progression to third-degree AV block is low. Because HV prolongation accompanies advanced cardiac disease and is associated with increased mortality, death is often not sudden or due to AV block but rather due to the underlying heart disease itself and nonarrhythmic cardiac causes (43,46-49,51,54-56).

Atrial pacing at electrophysiologic study in asymptomatic patients as a means of identifying patients at increased risk of future high- or third-degree AV block is ~~probably not justified~~ controversial. The probability of inducing block distal to the AV node (i.e., intra- or infra-His) with rapid atrial pacing is low (47,50,51,57-60). Failure to induce distal block cannot be taken as evidence that the patient will not develop third-degree AV block in the future. However, if atrial pac-

ing induces nonphysiologic infra-His block, some consider this an indication for pacing (57).

Recommendations for Permanent Pacing in Chronic Bifascicular and Trifascicular Block

Class I

1. **Intermittent third-degree AV block. (Level of Evidence: B) (8-13,39)**
2. **Type II second-degree AV block. (Level of Evidence: B) (18,20,24,348)**
3. **Alternating bundle-branch block. (Level of Evidence: C) (349)**

Class IIa

1. **Syncope not proveddemonstrated to be due to AV block when other likely causes have been excluded, specifically ventricular tachycardia (VT). (Level of Evidence: B) (40-51,53-58)**
2. **Incidental finding at electrophysiologic study of markedly prolonged HV interval (greater than or equal to 100 milliseconds) in asymptomatic patients. (Level of Evidence: B) (49)**
3. **Incidental finding at electrophysiologic study of pacing-induced infra-His block that is not physiologic. (Level of Evidence: B) (57)**

Class IIb

None. Neuromuscular diseases such as myotonic muscular dystrophy, Kearns-Sayre syndrome, Erb's dystrophy (limb-girdle), and peroneal muscular atrophy with any degree of fascicular block, with or without symptoms, because there may be unpredictable progression of AV conduction disease. (Level of Evidence: C) (31-37)

Class III

1. **Fascicular block without AV block or symptoms. (Level of Evidence: B) (43,45,48,49)**
2. **Fascicular block with first-degree AV block without symptoms. (Level of Evidence: B) (43,45,48,49)**

C. Pacing for Atrioventricular Block Associated With Acute Myocardial Infarction

Indications for permanent pacing after myocardial infarction (MI) in patients experiencing AV block are related in large measure to the presence of intraventricular conduction defects. Unlike some other indications for permanent pacing, the criteria for patients with MI and AV block do not necessarily depend on the presence of symptoms. Furthermore, the requirement for temporary pacing in AMI does not by itself constitute an indication for permanent pacing [see ACC/AHA Guidelines for Management of Patients With Acute Myocardial Infarction (2335)].

The long-term prognosis for survivors of AMI who have had AV block is related primarily to the extent of myocardial injury and the character of intraventricular conduction dis-

turbances rather than the AV block itself (11,61-64). Patients with AMI who have intraventricular conduction defects, with the exception of isolated left anterior fascicular block, have an unfavorable short- and long-term prognosis and an increased risk of sudden death (11,24,61,63). This unfavorable prognosis is not necessarily due to development of high-grade AV block, although the incidence of such block is higher in postinfarction patients with abnormal intraventricular conduction (61,65,350).

When AV or intraventricular conduction block complicates AMI, the type of conduction disturbance, location of infarction, and relation of electrical disturbance to infarction must be considered if permanent pacing is contemplated. Even with data available, the decision is not always straightforward, because the reported incidence and significance of various conduction disturbances vary widely (66). Despite the use of thrombolytic therapy and primary angioplasty, which have decreased the incidence of AV block in AMI, mortality remains high if AV block occurs (67-70).

Although more severe disturbances in conduction are in general associated with greater arrhythmic and nonarrhythmic mortality (61-66), the impact of pre-existing bundle-branch block on mortality after AMI is controversial (52,66). A particularly ominous prognosis is associated with left bundle-branch block combined with advanced second- or third-degree AV block and with right bundle-branch block combined with left anterior or left posterior fascicular block (41,52,62,64). Irrespective of whether the infarction is anterior or inferior, the development of an intraventricular conduction delay reflects extensive myocardial damage rather than an electrical problem in isolation (64). Although AV block that occurs during inferior MI can be associated with a favorable long-term clinical outcome, in-hospital survival is impaired, irrespective of temporary or permanent pacing in this situation (67,68,71,72). Furthermore, pacemakers should not be implanted if the peri-infarctional AV block is expected to resolve or to not negatively impact long-term prognosis, as in the case of inferior MI (69).

Recommendations for Permanent Pacing After the Acute Phase of Myocardial Infarction*

Class I

1. **Persistent second-degree AV block in the His-Purkinje system with bilateral bundle-branch block or third-degree AV block within or below the His-Purkinje system after AMI. (Level of Evidence: B) (24,61-65)**
2. **Transient advanced (second- or third-degree) infranodal AV block and associated bundle-branch block. If the site of block is uncertain, an electrophysiologic study may be necessary. (Level of Evidence: B) (61,62)**
3. **Persistent and symptomatic second- or third-degree AV block. (Level of Evidence: C)**

Class IIb

Persistent second- or third-degree AV block at the AV node level. (Level of Evidence: B) (23)

Class III

1. **Transient AV block in the absence of intraventricular conduction defects. (Level of Evidence: B) (61)**
2. **Transient AV block in the presence of isolated left anterior fascicular block. (Level of Evidence: B) (63)**
3. **Acquired left anterior fascicular block in the absence of AV block. (Level of Evidence: B) (61)**
4. **Persistent first-degree AV block in the presence of bundle-branch block that is old or age indeterminate. (Level of Evidence: B) (61)***

*These recommendations generally follow the ACC/AHA Guidelines for the Management of Patients With Acute Myocardial Infarction (2335).

D. Pacing in Sinus Node Dysfunction

Sinus node dysfunction (sick sinus syndrome) constitutes a spectrum of cardiac arrhythmias, including sinus bradycardia, sinus arrest, sinoatrial block, and paroxysmal supraventricular tachyarrhythmias alternating with periods of bradycardia or even asystole. Patients with this condition may be symptomatic from paroxysmal tachycardia or bradycardia or both. Correlation of symptoms with the above arrhythmias by use of an ECG, ambulatory ECG monitoring, or an event recorder is essential. This correlation may be difficult because of the intermittent nature of the episodes. In the electrophysiology laboratory, abnormal sinus node function may be confirmed by demonstration of prolonged corrected sinus node recovery times or prolonged sinoatrial conduction times. However, utility of electrophysiologic studies for sinus node dysfunction is limited by issues of sensitivity and specificity.

Sinus node dysfunction may express itself as chronotropic incompetence in which there is an inadequate sinus response to exercise or stress. Rate-responsive pacemakers have clinically benefited patients by restoring physiologic heart rate during physical activity (73-75).

Sinus bradycardia is accepted as a physiologic finding in trained athletes, who not uncommonly have a heart rate of 40 to 50 bpm while at rest and awake and may have a sleeping rate as slow as 30 bpm, with sinus pauses or type I second-degree AV block producing asystolic intervals as long as 2.8 seconds (76-78). These findings are due to increased vagal tone.

Although sinus node dysfunction is frequently the primary indication for implantation of permanent pacemakers (73), permanent pacing in patients with sinus node dysfunction may not necessarily result in improved survival time (26,79), although symptoms related to bradycardia may be relieved (27,80) (see Section I, Selection of Pacemaker Devices). ~~Nonrandomized observational studies suggest that dual-chamber pacing may improve survival, improve quality of life and decrease morbidity (stroke and atrial fibrillation) compared with ventricular pacing (81-83). However, one randomized prospective study (84) of 225 patients with sinus node disease and intact AV nodal conduction followed for a mean of 40 months demonstrated no difference in overall or~~

~~cardiac mortality between the groups receiving atrial versus ventricular pacing. Multiple small studies suggest that dual-chamber pacing improves quality of life and decreases morbidity (atrial fibrillation, stroke). Multiple prospective trials are ongoing to assess the superiority of dual-chamber versus ventricular-based pacing systems in this population (84a). During monitoring, pauses are sometimes observed during sleep. Duration of sinus pauses and their clinical significance is uncertain. If due to sleep apnea, apnea should be treated. A small retrospective trial of atrial overdrive pacing in the treatment of sleep apnea demonstrated a decrease "in episodes of central or obstructive sleep apnea without reducing the total sleep time" (447). Although this initial trial is encouraging, it is premature to propose pacing guidelines until a larger body of data is available. Otherwise, there is not sufficient evidence to distinguish physiologic from pathologic nocturnal bradycardia.~~

Recommendations for Permanent Pacing in Sinus Node Dysfunction

Class I

1. **Sinus node dysfunction with documented symptomatic bradycardia, including frequent sinus pauses that produce symptoms. In some patients, bradycardia is iatrogenic and will occur as a consequence of essential long-term drug therapy of a type and dose for which there are no acceptable alternatives. (Level of Evidence: C) (27,73,79)**
2. **Symptomatic chronotropic incompetence. (Level of Evidence: C) (27,73-75,79)**

Class IIa

1. **Sinus node dysfunction occurring spontaneously or as a result of necessary drug therapy, with heart rate less than 40 bpm when a clear association between significant symptoms consistent with bradycardia and the actual presence of bradycardia has not been documented. (Level of Evidence: C) (26,27,73,78-80)**
2. **Syncope of unexplained origin when major abnormalities of sinus node function are discovered or provoked in electrophysiologic studies. (Level of Evidence: C) (351,352)**

Class IIb

In minimally symptomatic patients, chronic heart rate less than ~~30~~40 bpm while awake. (Level of Evidence: C) (26,27,73,78-80)

Class III

1. **Sinus node dysfunction in asymptomatic patients, including those in whom substantial sinus bradycardia (heart rate less than 40 bpm) is a consequence of long-term drug treatment.**
2. **Sinus node dysfunction in patients with symptoms suggestive of bradycardia that are clearly documented as not associated with a slow heart rate.**

3. Sinus node dysfunction with symptomatic bradycardia due to nonessential drug therapy.

E. Prevention and Termination of Tachyarrhythmias by Pacing

Under certain circumstances, an implanted pacemaker may be useful for treating patients with recurrent symptomatic ventricular and supraventricular tachycardias (85-94). Pacing can be useful in preventing and terminating arrhythmias. Re-entrant rhythms including atrial flutter, paroxysmal re-entrant supraventricular tachycardia, and VT may be terminated by a variety of pacing patterns, including programmed stimulation and short bursts of rapid pacing (95,96). These antitachyarrhythmia devices may detect tachycardia and automatically activate a pacing sequence, or they may respond only to an external instruction (for example, application of a magnet).

Prevention of arrhythmias by pacing has been demonstrated in certain situations. In some patients with the long-QT syndrome, recurrent pause-dependent VT may be prevented by continuous pacing (97). A combination of pacing and beta-blockade has been reported to shorten the QT interval and help prevent sudden cardiac death (98,99). ICD therapy in combination with overdrive suppression pacing should be considered in high-risk patients.

Atrial synchronous ventricular pacing may prevent recurrences of re-entrant supraventricular tachycardia (100) although this technique is rarely used given the availability of catheter ablation and other alternative therapies. Although ventricular ectopic activity may be suppressed by such pacing in other conditions, serious or symptomatic arrhythmias are rarely prevented (101). In some patients with bradycardia-dependent atrial fibrillation, atrial pacing may be effective in reducing the frequency of recurrences (92). In the Mode Selection Trial (MOST), 2010 patients with sinus node dysfunction were randomized between DDDR and VVIR pacing. After a mean follow-up of 33 months, there was a 21% lower risk of atrial fibrillation ($p = 0.008$) in the DDDR group than in the VVIR group (353). Other trials are under way to assess the efficacy of atrial overdrive pacing algorithms and algorithms that react to premature atrial complexes in preventing atrial fibrillation, but data to date are sparse. Dual-site right atrial pacing or alternate single-site atrial pacing from nonconventional sites (e.g., septal or Bachmann's bundle) may offer additional benefits to single-site right atrial pacing from the appendage in patients with symptomatic drug-refractory atrial fibrillation and concomitant bradyarrhythmias (93). In patients with sick sinus syndrome and intra-atrial block (P wave more than 180 milliseconds), biatrial pacing may lower recurrence rates of atrial fibrillation (94).

Potential recipients of antitachyarrhythmia devices that interrupt arrhythmias should undergo extensive testing before implantation to ensure that the devices safely and reliably terminate the ectopic mechanism without accelerating the tachycardia or inducing ventricular fibrillation (VF). Patients for whom an antitachycardia pacemaker has been

prescribed have usually been unresponsive to antiarrhythmic drugs or were receiving agents that could not control their cardiac arrhythmias. When permanent antitachycardia pacemakers detect and interrupt supraventricular tachycardia, all pacing should be done in the atrium, because adverse interactions have been reported (85,102) with use of ventricular pacing to interrupt supraventricular arrhythmias. Permanent antitachycardia pacing as monotherapy for VT is not appropriate given that antitachycardia pacing algorithms are available in tiered-therapy ICDs that have the capability of cardioversion and defibrillation in cases when antitachycardia pacing is ineffective or causes acceleration of the treated tachycardia.

Recommendations for Permanent Pacemakers That Automatically Detect and Pace to Terminate Tachycardias

Class I

None.

~~Class I~~

- ~~1. Symptomatic recurrent supraventricular tachycardia that is reproducibly terminated by pacing after drugs and catheter ablation fail to control the arrhythmia or produce intolerable side effects. (Level of evidence: C) (86-88, 90, 91)~~**
- ~~2. Symptomatic recurrent sustained VT as part of an automatic defibrillator system. (Level of evidence: B) (103-105)~~**

Class IIa

Symptomatic recurrent supraventricular tachycardia that is reproducibly terminated by pacing in the unlikely event that catheter ablation and/or drugs fail to control the arrhythmia or produce intolerable side effects. (Level of Evidence: C) (86-88,90,91)

Class IIb

Recurrent supraventricular tachycardia or atrial flutter that is reproducibly terminated by pacing as an alternative to drug therapy or ablation. (Level of Evidence: C) (85-88,90,91)

Class III

- Tachycardias frequently accelerated or converted to fibrillation by pacing.**
- The presence of accessory pathways with the capacity for rapid anterograde conduction whether or not the pathways participate in the mechanism of the tachycardia.**

Pacing Recommendations to Prevent Tachycardia

Class I

Sustained pause-dependent VT, with or without prolonged QT, in which the efficacy of pacing is thoroughly documented. (Level of Evidence: C) (97,98)

Class IIa

High-risk patients with congenital long-QT syndrome. (Level of Evidence: C) (97,98)

Class IIb

1. **AV re-entrant or AV node re-entrant supraventricular tachycardia not responsive to medical or ablative therapy. (Level of Evidence: C) (87,88,92)**
2. ~~Prevention of symptomatic, drug-refractory, recurrent atrial fibrillation. (Level of evidence: C) (93,94)~~
2. **Prevention of symptomatic, drug-refractory, recurrent atrial fibrillation in patients with coexisting sinus node dysfunction. (Level of Evidence: B) (93,94,354,355)**

Class III

1. **Frequent or complex ventricular ectopic activity without sustained VT in the absence of the long-QT syndrome.**
2. ~~Long-QT syndrome-Torsade de Pointes VT due to reversible causes.~~

F. Pacing in Hypersensitive Carotid Sinus and Neurocardiogenic Syncope Syndromes

The hypersensitive carotid sinus syndrome is defined as syncope or presyncope resulting from an extreme reflex response to carotid sinus stimulation. It is an uncommon cause of syncope. There are two components of the reflex:

1. *Cardioinhibitory*, resulting from increased parasympathetic tone and manifested by slowing of the sinus rate or prolongation of the PR interval and advanced AV block, alone or in combination.
2. *Vasodepressor*, secondary to a reduction in sympathetic activity resulting in loss of vascular tone and hypotension. This effect is independent of heart rate changes.

Before concluding that permanent pacing is clinically indicated, the physician should determine the relative contribution of the two components of carotid sinus stimulation to the individual patient's symptom complex. Hyperactive response to carotid sinus stimulation is defined as asystole due to either sinus arrest or AV block of more than 3 seconds, or a substantial symptomatic decrease in systolic blood pressure, or both (106). Pauses up to 3 seconds during carotid sinus massage are considered to be within normal limits. Such heart rate and hemodynamic responses may occur in normal subjects and patients with coronary artery disease. The cause-and-effect relation between the hypersensitive carotid sinus and the patient's symptoms must be made with great caution (107). Spontaneous syncope reproduced by carotid sinus stimulation should alert the physician to the presence of this syndrome. Minimal pressure on the carotid sinus in elderly patients or patients receiving digitalis may result in marked changes in heart rate and blood pressure yet not be of clinical significance. Permanent pacing for patients with pure

excessive cardioinhibitory response to carotid stimulation is effective in relieving symptoms (108,109). Because 10% to 20% of patients with this syndrome may have an important vasodepressor component of their reflex response, it is desirable to define this component before concluding that all symptoms are related to asystole alone. Among patients whose reflex response includes both cardioinhibitory and vasodepressor components, attention to the latter is essential for effective therapy in patients undergoing pacing.

Evidence has emerged that suggests that elderly patients who have sustained otherwise unexplained falls may have carotid sinus hypersensitivity (356). In a subsequent study, 175 elderly patients who had fallen without loss of consciousness and had pauses greater than 3 seconds during carotid sinus massage (thus fulfilling the diagnosis of carotid sinus hypersensitivity) were randomized to pacing or non-pacing therapy. The paced group had a significantly lower likelihood of subsequent falling episodes during follow-up (357).

~~Neurally mediated syncope accounts for 10% to 40% of syncope patients. Neurocardiogenic syncope and neurocardiogenic syndromes refer to a variety of clinical scenarios in which triggering of a neural reflex results in a usually self-limited episode of systemic hypotension characterized by both bradycardia and peripheral vasodilation (110). Neurocardiogenic syncope accounts for 10% to 40% of syncope episodes. Vasovagal syncope is a term used to denote one of the most common clinical scenarios within the category of neurocardiogenic syncopal syndromes. Patients classically have a prodrome of nausea and diaphoresis (often absent in the elderly), and there may be a positive familial history of the condition. Spells may be triggered by pain, anxiety, stress, or crowded conditions. Typically, no evidence of structural heart disease is present. Other causes of syncope such as LV outflow obstruction, bradyarrhythmias, and tachyarrhythmias should be excluded. Head-up tilt-table testing may be diagnostic.~~

The role of permanent pacing in refractory neurocardiogenic syncope associated with significant bradycardia or asystole is controversial. Approximately 25% of patients have a predominant vasodepressor reaction without significant bradycardia (111). An additional large percentage of patients will have a mixed vasodepressor/vasoinhibitory component of their symptoms. While one group of investigators have noted some benefit of pacing in these patients (112,113), another study using a pacing rate 20% higher than the resting heart rate demonstrated that pacing did not prevent syncope any better than pharmacotherapy (106). Because most individuals with neurocardiogenic syncope have a slowing of heart rate after the fall in blood pressure, pacing may be ineffective in most patients. Dual-chamber pacing, carefully prescribed on the basis of tilt-table test results, may be effective in reducing symptoms if the patient has a significant cardioinhibitory component to the cause of their symptoms (114). Results from a *randomized trial* ~~(115)~~ (358,359) in highly symptomatic patients with bradycardia demonstrated that permanent pacing increased the

time to first syncopal event ($P < .0007$). In one of these trials (358), the actuarial rate of recurrent syncope at 1 year was 18.5% for pacemaker patients and 59.7% for control patients. The specific modality of pacing under these circumstances is under active investigation. One study demonstrated that DDD pacing with rate-drop response function was more effective than beta-blockade in preventing recurrent syncope in highly symptomatic patients with vasovagal syncope and relative bradycardia during tilt-table testing (360). Although spontaneous or provoked prolonged pauses are a concern in this population, the prognosis without pacing is excellent (116). Several investigators have concluded that some patients with syncope of undetermined origin may benefit from pacing if findings strongly suggestive of bradycardic etiology are discovered or provoked at electrophysiologic study (117,118,361).

The evaluation of patients with syncope of undetermined origin should take into account clinical status and not overlook other, more serious causes of syncope such as ventricular tachyarrhythmias.

Recommendations for Permanent Pacing in Hypersensitive Carotid Sinus Syndrome and Neurocardiogenic Syncope

Class I

Recurrent syncope caused by carotid sinus stimulation; minimal carotid sinus pressure induces ventricular asystole of more than 3 seconds' duration in the absence of any medication that depresses the sinus node or AV conduction. (Level of Evidence: C) (108,109)

Class IIa

1. **Recurrent syncope without clear, provocative events and with a hypersensitive cardioinhibitory response. (Level of Evidence: C) (108,109)**
2. ~~Syncope of unexplained origin when major abnormalities of sinus node function or AV conduction are discovered or provoked in electrophysiologic studies. (Level of evidence: C)~~
23. **Significantly symptomatic and recurrent neurocardiogenic syncope associated with bradycardia documented spontaneously or at the time of tilt-table testing. (Level of Evidence: B) (358-360,362)**

Class IIb

~~Neurally mediated syncope with significant bradycardia reproduced by a head-up tilt with or without isoproterenol or other provocative maneuvers. (Level of evidence: B) (112-115)~~

Class III

1. **A hyperactive cardioinhibitory response to carotid sinus stimulation in the absence of symptoms or in the presence of vague symptoms such as dizziness, lightheadedness, or both. (Level of Evidence: C)**

2. ~~A hyperactive cardioinhibitory response to carotid sinus stimulation in the presence of vague symptoms such as dizziness, lightheadedness, or both.~~
32. **Recurrent syncope, lightheadedness, or dizziness in the absence of a hyperactive cardioinhibitory response. (Level of Evidence: C)**
43. **Situational vasovagal syncope in which avoidance behavior is effective. (Level of Evidence: C)**

G. Pacing in Children, Adolescents, and Patients With Congenital Heart Disease

The indications for permanent cardiac pacemaker implantation in the child, adolescent, or young adult with congenital heart disease may be considered broadly as 1) symptomatic sinus bradycardia, 2) the recurrent bradycardia-tachycardia syndromes, 3) congenital third-degree AV block, and 4) advanced second- or third-degree AV block, either surgical or acquired. Although the general indications for pacemaker implantation in children are similar to those in adults, there are several important considerations in young patients. First, an increasing number of patients are surviving complex surgical procedures for congenital heart disease that result in palliation rather than correction of circulatory physiology. The residua of impaired ventricular function and abnormal physiology may result in symptomatic bradycardia at rates that do not produce symptoms in persons with normal cardiovascular physiology. Hence, the indications for pacemaker implantation in these patients need to be based on the correlation of symptoms with relative bradycardia rather than absolute heart rate criteria. Second, the clinical significance of bradycardia is age dependent; whereas a heart rate of 45 bpm may be a normal finding in an adolescent, the same rate in a newborn or infant indicates profound bradycardia.

Bradycardia and associated symptoms in children are often transient (e.g., paroxysmal AV block or sinus arrest) and difficult to document. Although sinus node dysfunction (sick sinus syndrome) is increasingly recognized in pediatric patients, it is not itself an indication for pacemaker implantation. In the young patient with sinus bradycardia, the primary criterion for a pacemaker is the concurrent observation of a symptom (e.g., syncope) with bradycardia (e.g., heart rate less than 35 to 40 bpm or asystole more than 3 seconds) (25,27,119). In general, correlation of symptoms with bradycardia is determined by 24-hour ambulatory or transtelephonic electrocardiography. Symptomatic bradycardia (as defined) is considered an indication for pacemaker implantation, provided that other causes of the symptom(s) have been excluded. Alternative causes to be considered include seizures, breath holding, apnea, or neurocardiogenic mechanisms.

The bradycardia-tachycardia syndrome (sinus bradycardia alternating with atrial flutter or re-entrant atrial tachycardia) is an increasingly frequent problem in young patients following surgery for congenital heart disease. Substantial morbidity and mortality have been observed in young patients with recurrent or chronic atrial flutter, with the loss of sinus

rhythm an independent risk factor for subsequent development of atrial flutter (120,121). Thus, both long-term atrial pacing at physiologic rates as well as atrial antitachycardia pacing have been reported for treatment of sinus bradycardia and prevention or termination of recurrent episodes of tachycardia (122,123). To date, the results of pacing for the bradycardia-tachycardia syndrome in children have been equivocal and the source of considerable controversy (124,125). It is clear that long-term drug therapy (e.g., ~~sotalol~~~~propranolol~~ or amiodarone) deemed essential for the control of atrial flutter may result in symptomatic bradycardia in some patients, whereas the use of other antiarrhythmic agents (e.g., quinidine) may potentially increase the risk of ventricular arrhythmias or sudden death in the presence of profound bradycardia. Thus, in young patients with recurrent arrhythmias associated with the bradycardia-tachycardia syndrome, permanent pacing should be considered as an adjunctive form of therapy. As an alternative therapy to antiarrhythmic medications that result in profound bradycardia and the need for pacemaker implantation, radiofrequency catheter ablation may modify the anatomic substrate of tachycardia in select patients with congenital heart disease.

Indications for permanent pacing in young patients with congenital complete AV block continue to evolve, based on improved definition of the natural history of the disease as well as advances in pacemaker technology and diagnostic methods. In several studies it has been observed that pacemaker implantation may improve long-term survival and prevent syncopal episodes among asymptomatic patients with congenital complete AV block (126,127). Periodic evaluation of ventricular function is required in patients with congenital AV block, even after pacemaker implantation (363). Several criteria (average heart rate, pauses in the intrinsic rate, associated structural heart disease, prolonged QT interval, and exercise tolerance) must be considered in the asymptomatic patient with congenital complete AV block (128-130).

The use of cardiac pacing with beta-blockade for prevention of symptoms in patients with the congenital long-QT syndrome is supported by ~~observational~~~~recent~~ studies (98,131,364). The primary benefit of pacemaker therapy may be in patients with pause-dependent initiation of ventricular tachyarrhythmias (132) or those with sinus bradycardia or advanced AV block in association with the congenital long-QT syndrome (133,134). Although pacemaker implantation may reduce the incidence of symptoms in these patients, long-term benefit on risk of sudden cardiac arrest remains to be determined (98,131,133).

A poor prognosis has been established for patients with permanent postsurgical AV block who do not receive permanent pacemakers for rate support (135). The presence of advanced second- or third-degree AV block persisting for 7 to 14 days after cardiac surgery is considered a Class I indication for pacemaker implantation (136). The need for pacing in patients with transient advanced AV block with residual bifascicular block is less certain, whereas patients in whom AV conduction returns to normal generally have a favorable prognosis (137).

Additional details that need to be considered in pacemaker implantation in young patients include risk of paradoxical embolism ~~with~~due to thrombus formation on an endocardial lead system in the presence of residual intracardiac defects and the lifelong need for permanent cardiac pacing (138,139). Decisions about pacemaker implantation must also take into account implantation technique (transvenous versus epicardial) and long-term vascular access.

Recommendations for Permanent Pacing in Children, Adolescents, and Patients With Congenital Heart Disease

Class I

- 1. Advanced second- or third-degree AV block associated with symptomatic bradycardia, ~~congestive heart failure~~ventricular dysfunction, or low cardiac output. (Level of Evidence: C)**
- 2. Sinus node dysfunction with correlation of symptoms during age-inappropriate bradycardia. The definition of bradycardia varies with the patient's age and expected heart rate. (Level of Evidence: B) (25,27,119)**
- 3. Postoperative advanced second- or third-degree AV block that is not expected to resolve or persists at least 7 days after cardiac surgery. (Level of Evidence: B, C) (~~135,136~~)(365,366)**
- 4. Congenital third-degree AV block with a wide QRS escape rhythm, complex ventricular ectopy, or ventricular dysfunction. (Level of Evidence: B) (127,129,363)**
- 5. Congenital third-degree AV block in the infant with a ventricular rate less than 50 to 55 bpm or with congenital heart disease and a ventricular rate less than 70 bpm. (Level of Evidence: B, C) (129,130)**
- 6. Sustained pause-dependent VT, with or without prolonged QT, in which the efficacy of pacing is thoroughly documented. (Level of Evidence: B) (97,98,131,132)**

Class IIa

- 1. Bradycardia-tachycardia syndrome with the need for long-term antiarrhythmic treatment other than digitalis. (Level of Evidence: C) (123,124)**
- 2. Congenital third-degree AV block beyond the first year of life with an average heart rate less than 50 bpm, abrupt pauses in ventricular rate that are two or three times the basic cycle length, or associated with symptoms due to chronotropic incompetence. (Level of Evidence: B) (128)**
- 3. Long-QT syndrome with 2:1 AV or third-degree AV block. (Level of Evidence: B) (133,134)**
- 4. Asymptomatic sinus bradycardia in the child with complex congenital heart disease with resting heart rate less than ~~35~~40 bpm or pauses in ventricular rate more than 3 seconds. (Level of Evidence: C)**
- 5. Patients with congenital heart disease and impaired hemodynamics due to sinus bradycardia or loss of AV**

synchrony. (Level of Evidence: C)

Class IIb

1. Transient postoperative third-degree AV block that reverts to sinus rhythm with residual bifascicular block. (Level of Evidence: C) (137)
2. Congenital third-degree AV block in the asymptomatic infant, neonate, child, or adolescent, or young adult with an acceptable rate, narrow QRS complex, and normal ventricular function. (Level of Evidence: B) (126,127)
3. Asymptomatic sinus bradycardia in the adolescent with congenital heart disease with resting heart rate less than 3540 bpm or pauses in ventricular rate more than 3 seconds. (Level of Evidence: C)
4. Neuromuscular diseases with any degree of AV block (including first-degree AV block), with or without symptoms, because there may be unpredictable progression of AV conduction disease.

Class III

1. Transient postoperative AV block with return of normal AV conduction within 7 days. (Level of Evidence: B) (136,137)
2. Asymptomatic postoperative bifascicular block with or without first-degree AV block. (Level of Evidence: C)
3. Asymptomatic type I second-degree AV block. (Level of Evidence: C)
4. Asymptomatic sinus bradycardia in the adolescent with longest RR interval less than 3 seconds and minimum heart rate more than 40 bpm. (Level of Evidence: C) (140)

H. Pacing in Specific Conditions

1. Hypertrophic Obstructive Cardiomyopathy

Early *observational* studies suggested that pacing the right ventricular apex would reduce the LV outflow gradient. In patients with severely symptomatic hypertrophic cardiomyopathy, implantation of a dual-chamber pacemaker with a short AV delay has been shown to decrease the magnitude of LV outflow obstruction and alleviate symptoms (141-143). These findings come from *nonrandomized unblinded* studies. The mechanisms by which pacing improves the LV outflow gradient are not completely understood. Pacing therapy can change the ventricular contraction pattern by prematurely activating part of the ventricle, creating a regional dyssynchrony. This early paced portion of the ventricle faces low chamber pressure and stress and contracts against a lower afterload (144). Altered LV activation causes disordered ventricular contractility with late septal activation, increases LV systolic dimension, and reduces systolic anterior motion of the mitral valve. Thus, LV outflow obstruction is reduced and the atrial contribution to LV filling is maintained. Selection of an optimal AV delay appears to be critical in achieving an optimal hemodynamic result (142,145). The optimal AV

delay appears to be the longest AV interval that consistently results in a completely paced QRS morphology (146). Some patients with too short a native AV delay may benefit from AV junction ablation so that the paced and sensed AV delay can be optimized (147). Pacing may cause thinning of the LV wall and decrease outflow obstruction (142, 148). Two recent *observational* studies have suggested that a decrease in LV outflow gradient produced by temporary dual-chamber pacing may have adverse effects on ventricular filling and cardiac output (149, 150). Another small *observational* study of dual-chamber pacing in hypertrophic cardiomyopathy patients without outflow obstruction failed to show significant hemodynamic or short-term benefit (151).

One study (142) demonstrated that dual-chamber pacing eliminated or ameliorated symptoms in 74 of 88 patients. Patients in this study were not required to have a beneficial hemodynamic response to temporary pacing as a selection criterion for permanent pacing. A recent *randomized* study (152) demonstrated that DDD pacing reduced outflow tract gradient and improved New York Heart Association (NYHA) functional class. Early *nonrandomized* studies demonstrated a fall in the LV outflow gradient with dual-chamber pacing and a short AV delay and symptomatic improvement in some patients with hypertrophic obstructive cardiomyopathy (141-143,154). One long-term study (153) in eight patients supported the long-term benefit of dual-chamber pacing in this group of patients. The outflow gradient was reduced even after cessation of pacing, suggesting that some ventricular remodeling had occurred consequent to pacing. Two randomized trials (152,154) demonstrated subjective improvement in approximately 50% of study participants but there was no correlation with gradient reduction, and a significant placebo effect was present. A third randomized trial (367) failed to demonstrate any overall improvement in quality of life with pacing, although there was a suggestion that elderly patients (aged more than 65 years) may derive more benefit from pacing. Although these data are encouraging, a recent randomized, double-blind crossover study (154) of 19 patients demonstrated no significant subjective or exercise capacity improvement in the paced versus nonpaced group at 2 to 3 months of follow-up, despite a significant decrease in LV outflow gradient.

In a small group of patients with symptomatic, hypertensive cardiac hypertrophy with cavity obliteration, VDD pacing with premature excitation statistically improved exercise capacity, cardiac reserve, and clinical symptoms (368). However, several individual patients in this study demonstrated symptomatic and hemodynamic improvement from dual-chamber pacing. Dual-chamber pacing may improve symptoms and LV outflow gradient in pediatric patients. However, rapid atrial rates, rapid AV conduction, and congenital mitral valve abnormalities may preclude effective pacing in some patients (155).

The lack of large, *prospective*, placebo-controlled data makes this indication for permanent pacing controversial. There are currently no data available to support the contention that pacing alters the clinical course of the disease or

improves survival or quality of life. Therefore, routine implantation of dual-chamber pacemakers should not be advocated in all patients with symptomatic hypertrophic obstructive cardiomyopathy. Patients who may benefit the most are those with significant gradients (more than 30 mm Hg at rest or more than 50 mm Hg provoked (154,369-371). In highly symptomatic patients, septal myectomy or percutaneous septal alcohol ablation should be considered instead of dual-chamber pacing (372). For the patient with hypertrophic obstructive cardiomyopathy who is at high risk for sudden death and has a definite indication for pacemaker implantation, the clinician should weigh the long-term advantages of implantation instead an ICD, even if the patient's condition might not warrant an ICD implant at that point in time (see Section II-E).

Pacing Recommendations for Hypertrophic Cardiomyopathy

Class I

Class I indications for sinus node dysfunction or AV block as described previously. (Level of Evidence: C)

Class IIb

Medically refractory, symptomatic hypertrophic cardiomyopathy with significant resting or provoked LV outflow obstruction. (Level of Evidence: C_A) (142,145,146,152,154,367)

Class III

1. Patients who are asymptomatic or medically controlled.
2. Symptomatic patients without evidence of LV outflow obstruction.

2. Idiopathic Dilated Cardiomyopathy

Several *observational* studies have shown limited improvement in patients who have symptomatic dilated cardiomyopathy refractory to medical therapy with dual-chamber pacing with a short AV delay (156-159). Theoretically, a short AV delay may optimize the timing of mechanical AV synchrony and ventricular filling time. In patients with prolonged PR intervals more than 200 milliseconds, diastolic filling time may be improved by dual-chamber pacing with a short AV delay (17). In one study (157), cardiac output was increased 38% by shortening AV delay when the average PR interval was 283 milliseconds before pacing. When the PR interval was shorter, no benefit of pacing was noted. Permanent pacing in symptomatic patients with drug-refractory dilated cardiomyopathy and a prolonged PR interval may be useful if short-term benefit is demonstrated in acute studies. At this time no long-term data are available, and there is no consensus for this indication. The mechanisms by which dual-chamber pacing might benefit patients with dilated cardiomyopathy are poorly understood. One hypothesis is that a well-timed atrial contraction primes the ventricles and

decreases mitral regurgitation, thus augmenting stroke volume and arterial pressure. Several studies have not demonstrated improvement in cardiac output with dual-chamber pacing in patients with congestive heart failure (160, 161). One randomized controlled trial of 12 patients showed no significant benefit of VDD pacing through a range of PR intervals despite the presence of both tricuspid and mitral regurgitation (160). One study (162) in 89 patients with LV dysfunction suggested that VVI pacing in the right ventricular outflow tract (simulating a normal high to low ventricular activation) improved cardiac output by 18.8% when compared with pacing the right ventricular apex.

Thirty to fifty percent of patients with congestive heart failure have intraventricular conduction defects (373,374). These conduction abnormalities progress over time, lead to disorganized contraction of an already hemodynamically compromised ventricle, and are an independent predictor of mortality (375). Delayed activation of the LV during right ventricular pacing also leads to significant dyssynchrony in both LV contraction and relaxation. Biventricular pacing can provide a more coordinated pattern of ventricular contraction, reduce the QRS duration, and reduce intraventricular and interventricular asynchrony. Biventricular pacing was initially demonstrated to improve cardiac index acutely, decrease systemic vascular resistance and pulmonary capillary wedge pressure, increase systolic blood pressure, and lower V-wave amplitude compared with right ventricular or AAI pacing in several trials (376-378). Advances in lead design have allowed the insertion of endocardial leads into distal branches of the coronary sinus to pace the LV. These advances have led to several small and large *prospective* trials to study the efficacy of biventricular pacing in patients with congestive heart failure and intraventricular conduction defects. Auricchio *et al.* (379) demonstrated that pacing in the mid-lateral LV augments positive pulse pressure changes more than pacing other areas. In the Pacing Therapies for Congestive Heart Failure trial (380), increases in LV dP/dt and pulse pressure were significantly better with biventricular than with right ventricular pacing. Convincing recent data from several *prospective, randomized* trials (381-384) support the hemodynamic and subjective improvement that was noted in multiple previous anecdotal and smaller trials (385-387). These trials demonstrate that in patients with New York Heart Association (NYHA) class III or IV congestive heart failure, decreased ejection fraction, and prolonged QRS duration, biventricular pacing decreases QRS duration and improves 6-minute walk distance, NYHA class, and quality-of-life scores. In the Multisite Stimulation in Cardiac Insufficiency trial (381), rehospitalizations from congestive heart failure were also reduced. No data exist demonstrating that biventricular pacing improves survival, although early data suggest trends in improvement in decreasing spontaneous ventricular ectopy and ICD shocks (388-390). Ongoing studies will determine whether a combination of biventricular pacing with an ICD will result in an improvement in subjective symptoms plus improved survival. Preliminary data (163, 164) suggest that simultaneous biven-

~~tricular pacing may improve cardiac hemodynamics and thus lead to subjective and objective symptom improvement. Prospective controlled trials are under way to confirm these initial findings and further define the benefit of biventricular pacing in patients with symptomatic, drug-refractory dilated cardiomyopathy. Overall there are sparse long-term data to show improvement in hemodynamics, symptom relief, or survival for pacing in dilated cardiomyopathy. Even less data exist in patients with ischemic cardiomyopathy.~~

Pacing Recommendations for Dilated Cardiomyopathy

Class I

Class I indications for sinus node dysfunction or AV block as described previously. (Level of Evidence: C)

Class IIa

~~None. Biventricular pacing in medically refractory, symptomatic NYHA class III or IV patients with idiopathic dilated or ischemic cardiomyopathy, prolonged QRS interval (greater than or equal to 130 milliseconds), LV end-diastolic diameter greater than or equal to 55 mm, and ejection fraction less than or equal to 35%. (Level of Evidence: A) (381,383)~~

Class IIb

~~Symptomatic, drug-refractory dilated cardiomyopathy with prolonged PR interval when acute hemodynamic studies have demonstrated hemodynamic benefit of pacing. (Level of evidence: C)(17, 156-158)~~

Class III

1. Asymptomatic dilated cardiomyopathy.
2. Symptomatic dilated cardiomyopathy when patients are rendered asymptomatic by drug therapy.
3. Symptomatic ischemic cardiomyopathy when the ischemia is amenable to intervention.

3. Cardiac Transplantation

The incidence of bradyarrhythmias after cardiac transplantation varies from 8% to 23% (165-167). The majority of bradyarrhythmias are associated with sinus node dysfunction. Because of symptoms and impaired recovery and rehabilitation, some transplant programs recommend more liberal use of cardiac pacing for persistent postoperative bradycardia. About 50% of patients show improvement/resolution of the bradyarrhythmia within 6 to 12 months, and long-term pacing is often unnecessary in a large number of patients (168-170). Significant bradyarrhythmias and asystole have been associated with reported cases of sudden death (171). No predictive factors have been identified to indicate which patients will develop post-transplantation bradyarrhythmias. In some patients, the need for pacing may be transient. The benefits of the atrial contribution to cardiac output and chronotropic competence may optimize the patient's functional status. Attempts to treat the bradycardia temporarily

with measures such as theophylline (172) may minimize the need for pacing. Post-transplant patients who have irreversible sinus node dysfunction or AV block with previously stated Class I indications should have permanent pacemakers.

Pacing Recommendations After Cardiac Transplantation

Class I

Symptomatic bradyarrhythmias/chronotropic incompetence not expected to resolve and other Class I indications for permanent pacing. (Level of Evidence: C)

Class IIb

Symptomatic bradyarrhythmias/chronotropic incompetence that, although transient, may persist for months and require intervention. (Level of Evidence: C)

Class III

Asymptomatic bradyarrhythmias after cardiac transplantation.

I. Selection of Pacemaker Device

Once the decision has been made to implant a pacemaker in a given patient, the clinician must decide among a large number of available pacemaker generators and leads. Generator choices include single- versus dual-chamber devices, unipolar versus bipolar configuration, presence and type of sensor for rate response, advanced features such as automatic mode switching, size, battery capacity, and cost. Lead choices include polarity, type of insulation material, fixation mechanism (active versus passive), and presence of steroid elution, and typical pacing impedance. Some lead models typically show low (300-500 Ohms) and some high (greater than 1000 Ohms) pacing impedance, and this can have implications with regard to the generator's battery longevity. Other factors that importantly influence the choice of pacemaker system components include the capabilities of the pacemaker programmer, which provides the link between the pacemaker system and the physician, and local availability of technical support.

Even after selecting and implanting the pacing system, the physician has a number of options for programming the device. In modern single-chamber pacemakers, programmable features include pacing mode, lower rate, pulse width and amplitude, sensitivity, and refractory period. Dual-chamber pacemakers have the same programmable features, as well as maximum tracking rate, AV delay, and others. Rate-responsive pacemakers require programmable features to regulate the relation between sensor output and pacing rate and to limit the maximum sensor-driven pacing rate. ~~These programmable parameters must be individually adjusted for each patient, and the choice of one programmable parameter will often depend on the availability of another parameter. For example, in a patient with complete AV block and parox-~~

~~ysmal atrial fibrillation, a dual-chamber pacemaker without mode-switching capability most appropriately might be programmed to DDIR* mode, whereas in the same patient, a pacemaker with mode-switching capability most appropriately might be programmed to DDDR mode with mode switching. In recent years, w~~With the advent of more sophisticated pacemaker generators, optimal programming of pacemakers has become increasingly complex and device-specific and requires specialized knowledge on the part of the physician.

Many of these considerations are beyond the scope of this document. The discussion below focuses on the most fundamental choice the clinician has with respect to the pacemaker prescription: ~~those that have the greatest impact on procedural time and complexity, follow-up, patient outcome, and cost:~~ (1) the choice among single-chamber ventricular pacing, single-chamber atrial pacing, and dual-chamber pacing, and (2) whether or not to use a generator that incorporates a sensor for rate responsive pacing.

Table 1 gives brief guidelines on the appropriateness of different pacemakers for the most commonly encountered indications for pacing. Figure 1 is a decision tree for selecting a pacing system in a patient with AV block. Figure 2 is a decision tree for selecting a pacing system in a patient with sinus node dysfunction.

An important challenge in selecting a pacemaker system is anticipating progression of abnormalities of automaticity and conduction and selecting a system that will best accommodate these developments. Thus, it is reasonable to select a pacemaker with more extensive capabilities than needed at the time of implantation but that may prove useful in the future. Some patients with sinus node dysfunction and paroxysmal atrial fibrillation, for example, may develop AV block in the future (as a result of natural progression of disease, drug therapy, or catheter ablation) and may ultimately benefit from a dual-chamber pacemaker with mode-switching capability. ~~Patients who are likely to develop ventricular tachyarrhythmias, for which an ICD would be warranted, should receive a pacemaker that is compatible with ICDs.~~

1. Newer Technical Innovations

Rate-Responsive Pacemakers

An increasing percentage of pacemakers implanted in the United States incorporate sensors to detect states of exercise and trigger accelerations in pacing rate. Approximately 97% of all generators implanted in the United States in 2000 had rate response as a programmable option (Morgan Stanley Dean Witter, Equity Research, North America, Healthcare: Pharmaceuticals, Hospital Supplies & Medical, July 26, 2000). An industrywide survey in 1996 indicates that 83% of all generators implanted in 1996 in the United States had rate response as a programmable option. In pacemaker patients who are chronotropically incompetent (i.e., unable to increase sinus node rate appropriately with exercise), rate-responsive pacemakers allow for increases in pacing rates

with exercise and have been shown to improve exercise capacity and quality of life.

In the United States, the vast majority of sensors incorporated into rate-responsive implantable pacemakers are piezoelectric crystals or accelerometers that detect motion, vibration, ~~pressure,~~ or acceleration. Other technologies using sensors that measure minute ventilation or QT interval may provide a heart rate response more proportional to exercise than piezoelectric sensors or accelerometers. An advantage of all of these sensor technologies is that they do not require specialized pacemaker leads, although minute ventilation sensing requires a bipolar lead. ~~An older technique that measured circulating blood temperature has largely been abandoned.~~

Pacemaker generators that incorporate two rate-responsive sensors are now available. These dual-sensor pacemakers incorporate one sensor that rapidly responds to exercise (i.e., piezoelectric crystal or accelerometer) and one that responds more proportionately to increasing levels of exercise (i.e., minute ventilation or QT interval). Studies have shown more appropriate rate response to various types of exercise when information from two sensors is used than when a single sensor is used (391,392). Studies are lacking that demonstrate an improvement in quality of life resulting from dual-sensor pacemakers compared with single-sensor pacemakers.

The challenge of adjusting the response of these generators to exercise appropriately in individual patients is increasingly becoming recognized. To facilitate optimal programming of rate-response capability, ~~recently introduced many current~~ generators incorporate procedures for initial programming of rate-response parameters, subsequent automatic adjustment of these parameters, and retrievable diagnostic data (such as heart rate histograms or heart rate plots) to assess the appropriateness of the rate response.

Single-Lead VDD Pacemaker Systems

Despite advances in rate-responsive pacemakers, it is widely appreciated that the best signal to guide heart rate response to exercise (and other forms of physiologic stress) is a normally functioning sinus node. Most commonly, dual-chamber pacemakers incorporating separate atrial and ventricular leads are used to detect atrial depolarization. Single-lead transvenous pacing systems that are capable of sensing atrial depolarization are available. The distal end of the lead is positioned in the right ventricle for ventricular pacing and sensing; a pair of electrodes is incorporated in the more proximal portion of the lead body lying within the right atrial cavity for atrial sensing. With current technology, single-lead VDD* pacing systems are not capable of atrial pacing. The atrial signal sensed by single-lead VDD pacemakers has a less consistent amplitude than that typically sensed by conventional dual-chamber pacemakers and varies significantly with posture, but sensing performance is generally satisfactory (174). Single-lead VDD pacemaker systems are an ~~rea-~~

*This and other three- or four-letter notations conform to the NASPE/BPEG generic pacemaker code (173).

Table 1. Guidelines for Choice of Pacemaker Generator in Selected Indications for Pacing

	Sinus Node Dysfunction	AV Block	Neurally Mediated Syncope or Carotid Sinus Hypersensitivity
Single-chamber atrial pacemaker	<ul style="list-style-type: none"> No suspected abnormality of AV conduction and not at increased risk for future AV block Maintenance of AV synchrony during pacing desired Rate response available if desired 	<ul style="list-style-type: none"> Not appropriate 	<ul style="list-style-type: none"> Not appropriate (unless AV block systematically excluded)
Single-chamber ventricular pacemaker	<ul style="list-style-type: none"> Maintenance of AV synchrony during pacing not necessary Rate response available if desired 	<ul style="list-style-type: none"> Chronic atrial fibrillation or other atrial tachyarrhythmia or maintenance of AV synchrony during pacing not necessary Rate response available if desired 	<ul style="list-style-type: none"> Chronic atrial fibrillation or other atrial tachyarrhythmia Rate response available if desired
Dual-chamber pacemaker	<ul style="list-style-type: none"> AV synchrony during pacing desired Suspected abnormality of AV conduction or increased risk for future AV block Rate response available if desired 	<ul style="list-style-type: none"> Rate response available if desired Rate response available if desired AV synchrony during pacing desired Atrial pacing desired Rate response available if desired 	<ul style="list-style-type: none"> Sinus mechanism present Rate response available if desired
Single-lead, atrial-sensing ventricular pacemaker	<ul style="list-style-type: none"> Not appropriate 	<ul style="list-style-type: none"> Normal sinus node function and no need for atrial pacing Desire to limit the number of pacemaker leads 	<ul style="list-style-type: none"> Not appropriate

AV = atrioventricular.

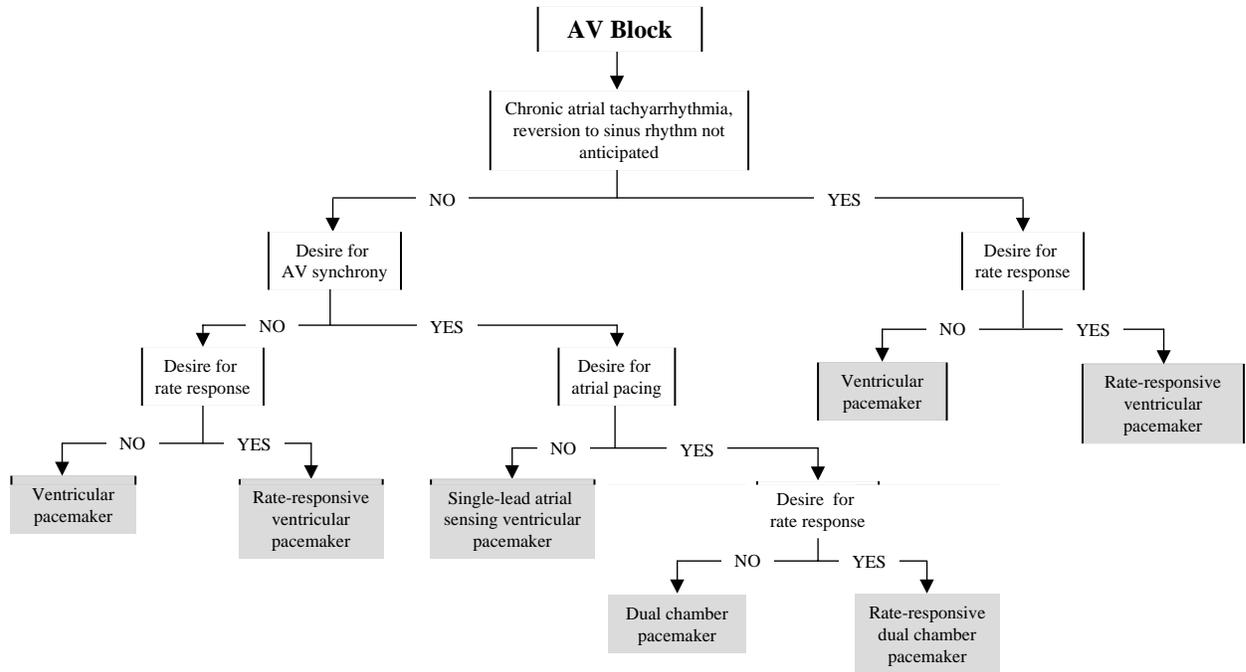


Figure 1. Selection of pacemaker systems for patients with atrioventricular (AV) block.

reasonable alternative to dual-chamber lead pacemakers in patients with AV block in whom atrial pacing is not required and in whom simplicity of implantation or avoidance of two leads is desired.

Automatic Mode Switching

When nonphysiologic atrial tachyarrhythmias, such as atrial fibrillation or flutter, occur paroxysmally in a patient with a dual-chamber pacemaker programmed to conventional DDD or DDDR mode, the tachyarrhythmia will generally be tracked near the programmed maximum tracking rate, lead-

ing to an undesirable acceleration of ventricular pacing rate. Newer dual-chamber generators incorporate algorithms for detecting rapid, nonphysiologic atrial rates and automatically switch modes to one that does not track atrial activity, such as DDI or DDIR. When the atrial tachyarrhythmia terminates, the pacemaker automatically reverts back to the DDD or DDDR mode. This automatic mode switch feature is especially helpful in patients with AV block and paroxysmal atrial fibrillation and expands the usefulness of dual-chamber pacemakers in such patients. Virtually all dual-chamber pacemakers now implanted in the United States incorporate automatic mode switching as a programmable option.

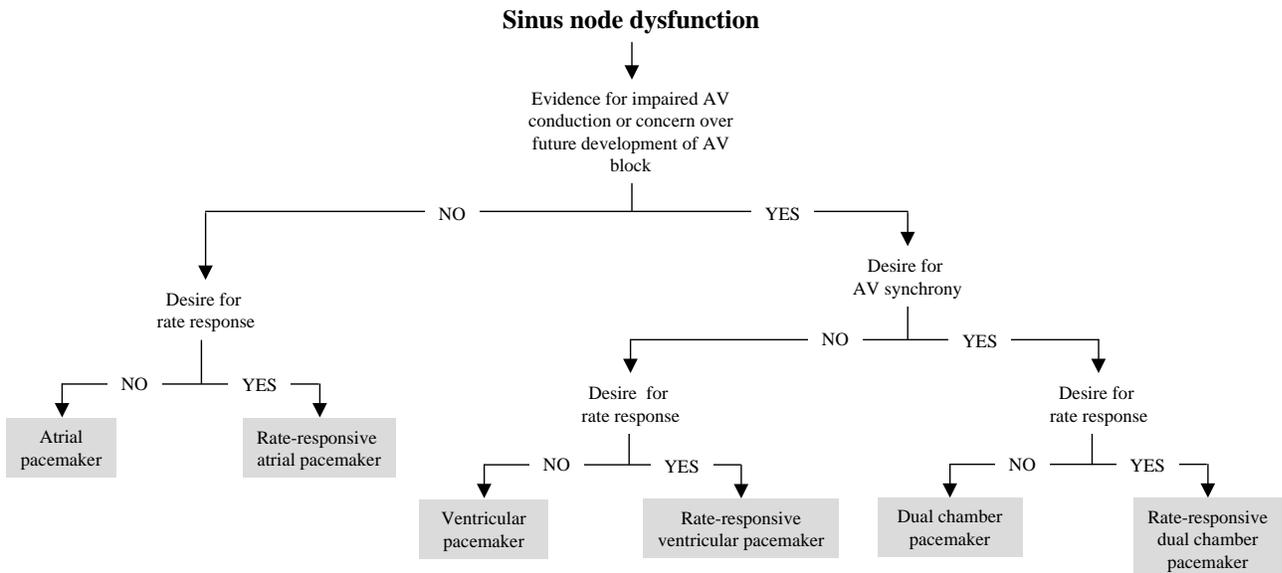


Figure 2. Selection of pacemaker systems for patients with sinus node dysfunction. AV indicates atrioventricular.

Rate-Drop Response for Neurocardiogenic Syncope

A programmable feature of some dual-pacemaker generators is automatic acceleration of pacing rate (e.g., to 100 bpm) for up to several minutes after detection of a sudden fall in intrinsic heart rate, such as would typically occur in patients with neurocardiogenic syncope. Of the two randomized studies showing a benefit of implanted pacemakers in patients with neurocardiogenic syncope in decreasing the recurrence of syncope in such patients, one of them (358) used pacemakers with rate-drop response, whereas the other (359) used pacemakers programmed to a more conventional hysteresis function. A large prospective, randomized multicenter trial is under way that will assess the specific benefit of rate-drop response in patients with neurocardiogenic syncope (393).

Pacemaker Leads

The vast majority of implanted pacemakers use transvenous endocardial leads, with the remainder using epicardial leads. Transvenous leads may be bipolar or unipolar in configuration. Bipolar configurations have the advantage of avoiding myopotential inhibition and skeletal muscle stimulation, and an increasingly important advantage is that unlike most unipolar pacing systems, they are compatible with concomitantly implanted ICDs. However, some manufacturers' bipolar leads have higher failure rates than their unipolar leads.

The insulation material used in pacemaker leads is either silicone rubber or polyurethane. ~~Polyurethane insulated leads have a thinner diameter and better handling characteristics than silicone insulated leads. However,~~ Historically, some bipolar lead models with polyurethane insulation have shown unacceptably high failure rates due to degradation of the insulation. ~~More recently introduced—~~Many current polyurethane leads, using different polymers and different manufacturing processes, appear to be avoiding these unacceptably high failure rates.

Active fixation leads, in which the distal tip of the lead incorporates a small helical screw for fixation to the endocardium, are an alternative to passive fixation leads. Active fixation leads allow for more alternatives in the site of endocardial attachment. For instance, whereas a passive fixation ventricular lead generally must be positioned in the right ventricular apex, an active fixation lead may be positioned in the apex, outflow tract, or inflow tract of the right ventricle. Active fixation leads have an additional advantage of greater ease of extraction after long-term implantation. A disadvantage of active fixation leads is that they generally have higher chronic capture thresholds than do passive fixation leads, although this difference is minimized with the incorporation of steroid elution (see below).

An important advance in pacemaker leads is the development of leads with lower capture thresholds, which result in reduced battery consumption during pacing. Steroid-eluting leads incorporate at their distal tip a small reservoir of corticosteroid that slowly elutes into the interface between the lead electrode and the endocardium, reducing the inflammation and fibrosis that normally occur at this interface. As a

result, steroid-eluting leads have significantly lower long-term capture thresholds than leads not incorporating steroid. The benefit of steroid elution was originally demonstrated in passive fixation transvenous leads (175); the benefit has also been demonstrated in active fixation transvenous leads (176) and epicardial leads (177). Similar improvements in capture thresholds have been achieved with modification in electrode shape, size, and composition (178)(394).

2. Methodology of Comparing Different Pacing Modesemaker Generators and Configurations

Two or more pacemaker modes can be compared with respect to exercise capacity, quality of life, clinical end points (such as death, heart failure, atrial fibrillation, and stroke), and cost. For end points such as exercise capacity or quality of life, pacemaker modes can be compared using a *randomized* crossover study design, provided that the patients have pacing systems that can be programmed to each of these modes. (For example, dual-chamber, rate-responsive pacemakers can be crossed over between VVIR and DDDR pacing.)

Studies that compare clinical end points require long-term follow-up without crossover. In long-term studies, patients can be randomly assigned to receive different types of pacemakers (e.g., hardware randomization, single-chamber ventricular pacemakers versus single-chamber atrial pacemakers), or all patients may receive a single type of pacemaker system (e.g., dual-chamber, rate-responsive) and be randomly assigned to different modes (e.g., software randomization, VVIR versus DDDR).

Quality-of-life measures have been emphasized as important end points when comparing different modes of pacing, and there are important considerations in the choice of the instrument used to measure quality of life (179-181,395). Although the quality of life experienced with different modes of pacing may be compared using short-term crossover studies, long-term studies that include quality-of-life end points may reflect effects of chronic adaptation to stimulation not detectable in short-term comparisons. Several reported or ongoing long-term *randomized* comparisons of pacing modes have quality-of-life end points (83,395,396).

An important consideration in the assessment of trials that compare pacing modes is the percent of pacing among the study patients. For example, a patient who is paced only for very infrequent sinus pauses will probably have a similar outcome with ventricular pacing compared with dual-chamber pacing, regardless of the potential physiologic benefits of dual-chamber pacing. Several older studies comparing pacing modes do not include data on the frequency of pacing (84,84a,397,398), but newer studies do (355,399).

3. Pacing in Sinus Node Dysfunction

Short-Term Outcomes

Short-term crossover studies in patients with sinus node dysfunction have shown improved quality of life with atrial-based (i.e., atrial or dual chamber) pacing versus ventricular

pacing, with or without rate response (180,182,395). There are conflicting data regarding any improvement in maximum exercise performance in rate-responsive atrial-based pacing compared with rate-responsive ventricular pacing in patients with sinus node dysfunction (~~482,183,395~~).

Long-Term Outcomes

Over the past decade, a number of *nonrandomized observational* studies have been published comparing atrial-based pacing (~~either atrial pacemakers or dual-chamber pacemakers~~) with ventricular pacing in patients with sinus node dysfunction. These studies have been reviewed extensively (83,184,185,395,396). The incidences of atrial fibrillation, stroke, heart failure, and total mortality appear to be consistently lower in patients receiving atrial-based pacing than in those receiving ventricular pacing (395). ~~A consistent finding is that the incidence of atrial fibrillation is lower in patients receiving atrial-based pacemakers than in those receiving ventricular pacemakers; atrial-based pacing is associated with a reduction in risk of atrial fibrillation averaging 74% (185). The findings of the studies were mixed with regard to mortality end points: some studies showed a lower mortality in atrial-based pacemaker patients and some showed no significant difference.~~ The studies suffer from limitations common to all *nonrandomized* studies (most importantly, uncertainty as to the clinical equivalence of the patient groups). In some of these studies, the patient groups appear to be well matched, whereas in others, there is insufficient information to assess their comparability.

Andersen *et al.* (84,84a) published the first randomized study comparing pacemaker modes with long-term follow-up in patients with sinus node dysfunction. Two hundred twenty-five patients were assigned randomly to atrial and ventricular pacing. After mean follow-up of 5.5 years, the patients assigned to atrial pacing had significantly lower incidences of atrial fibrillation, thromboembolic events, heart failure, cardiovascular mortality, and total mortality compared with the ventricular paced patients. ~~During a mean of 40 months of follow up, there were significantly fewer thromboembolic events in the atrial paced patients. There was a trend toward less atrial fibrillation in the atrial paced group, but it did not reach statistical significance. The study was not powered to detect a mortality difference between the two patient groups. However, when follow up was extended to 8 years, atrial pacing was associated with significantly decreased "all-cause" and "cardiovascular" mortality compared to ventricular pacing (84a).~~

Connolly *et al.* (398) published a *randomized comparison of ventricular pacemaker implantation versus atrial-based pacemaker implantation in patients with a variety of indications for pacing*. Among all patients, there was no significant difference in the combined incidence of stroke or death or in the likelihood of a heart failure hospitalization between the two treatment groups. There was, however, a statistically significant decrease in the incidence of atrial fibrillation in the patients with atrial-based pacemakers compared with ventricular pacemakers, which became apparent only after 2-

year follow-up. The reduction in atrial fibrillation was seen both in patients paced for sinus node dysfunction and in those paced for AV block (345). A subgroup analysis of patients paced for sinus node dysfunction did not show any trends toward particular mortality or stroke benefit from atrial-based pacing in these patients.

The results of the MOST trial, in which 2010 patients with sinus node dysfunction were randomized between DDDR and VVIR pacing (355,395,396), have been reported (353). After mean follow-up of 33 months, there was no significant difference in the incidence of death or stroke between the two groups, but there was a 21% lower risk of atrial fibrillation ($p = 0.008$), lower heart failure scores ($p = 0.0001$), 27% lower risk of heart failure hospitalizations ($p = 0.02$), and improved quality of life in the DDDR group compared with the VVIR group. Of the patients randomized to VVIR pacing, 37.7% crossed over to DDDR, most commonly for pacemaker syndrome.

In summary, studies consistently demonstrate that in patients with sinus node dysfunction, the incidence of atrial fibrillation in patients receiving atrial or dual-chamber pacemakers is lower than in patients receiving ventricular pacemakers. Published data are mixed regarding stroke, heart failure, and mortality benefit with atrial-based pacing compared with ventricular pacing. Pacemaker syndrome is common in patients with sinus node dysfunction treated with ventricular pacing. ~~In summary, available data suggest that in patients with sinus node dysfunction, the incidence of atrial fibrillation in patients receiving atrial or dual-chamber pacemakers may be lower than in patients receiving ventricular pacemakers. Published studies do not adequately address the issues of other clinical end points, such as heart failure, mortality, or quality of life.~~

Role of Single-Chamber Atrial Pacemakers

Single-chamber atrial pacemakers offer the advantages of atrial-based pacing without the added complexity and cost of dual-chamber pacemakers. Such pacing systems, with rate-responsive capability if appropriate, have been advocated for patients with sinus node dysfunction but no evidence of AV block (21,179,186-188). Use of single-chamber atrial pacemakers is limited by concerns about subsequent development of AV block. The risk of developing significant AV block after atrial pacemaker implantation for sinus node dysfunction has been estimated to be 0.6% to ~~3-05.0%~~ per year (186,188,189). Pre-existing bundle-branch block, but not AV Wenckebach rate, is predictive of a higher likelihood of subsequent development of AV block (~~486,187,189,190~~). In selected patients with sinus node dysfunction, use of single-chamber atrial pacemakers is an acceptable approach that maintains normal AV synchrony, ~~without the added cost and extra lead of a dual-chamber pacemaker system~~ but there is a small risk of subsequent development of AV block requiring pacemaker revision. With rate-responsive atrial pacemakers, the risk of developing hemodynamically significant first-degree AV block during rate accelerations has not been extensively studied but may be important (191).

~~A randomized study of DDDR versus VVIR pacing in patients with sinus node dysfunction is ongoing, with end points of total mortality, atrial fibrillation, stroke, heart failure, quality of life, and cost (83).~~

4. Pacing in Atrioventricular Block

Short-Term Outcomes

A number of short-term crossover studies have compared pacing modes in patients with AV block with respect to quality of life and exercise capacity. These studies have been reviewed in depth (83,180,395,396). Studies comparing dual-chamber pacing with non-rate-responsive ventricular pacing have shown improved exercise capacity and symptomatology with dual-chamber pacing. Studies comparing rate-responsive ventricular pacing with non-rate-responsive ventricular pacing have shown similar advantages with rate-responsive ventricular pacing. However, studies comparing dual-chamber pacing (with or without rate response) with rate-responsive ventricular pacing have shown modest or no significant difference in exercise capacity; with respect to symptoms, most but not all of the studies have shown an advantage of dual-chamber pacing. It is likely that the symptomatic advantage of dual-chamber pacing over rate-responsive ventricular pacing is derived from the maintenance of AV association during rest and low-level activity.

Gillis et al. (399) examined atrial fibrillation recurrences in patients with paroxysmal atrial fibrillation who received pacemakers after AV ablation. Patients were crossed over between 6-month periods of DDDR pacing and VDD pacing; the principal difference between the two pacing modes was the lack of atrial pacing support and the possibility of asynchronous ventricular pacing during VDD pacing. No significant difference was seen in the time to atrial fibrillation recurrences between the two modes of pacing. However, nearly 15% of patients originally randomized to VDD pacing prematurely crossed over to DDDR pacing because of symptoms presumably related either to asynchronous ventricular pacing or atrial fibrillation.

Long-Term Outcomes

Two *nonrandomized observational* studies comparing patients with AV block who received dual-chamber pacemakers or ventricular pacemakers have shown improved survival associated with implantation of dual-chamber pacemakers among those patients with heart failure but no difference in survival between the two pacing modes among patients without heart failure (74,192). In the randomized studies of Connolly et al. (398) and Skanes et al. (400), the subgroup of patients implanted for AV block showed trends toward lower cardiovascular mortality or stroke and atrial fibrillation with physiologic pacing over ventricular pacing, but these did not reach statistical significance. In an ongoing study, patients with AV block are randomly assigned to receive a ventricular pacemaker or a dual-chamber pacemaker; the primary end point is total mortality (83).

5. Pacing in the Elderly

More than 85% of pacemaker recipients are at least 64 years old (193). Elderly pacemaker patients are the rule, not the exception.

It has been suggested that elderly patients requiring pacing should be considered for less sophisticated devices, e.g., single-chamber ventricular pacemakers or non-rate-responsive pacemakers. However, studies in elderly patients show improved exercise capacity and alleviated symptoms with rate-responsive ventricular pacing or dual-chamber pacing compared with non-rate-responsive ventricular pacing (75,194). A *retrospective* analysis of 36,312 elderly Medicare patients receiving pacemakers suggested that dual-chamber pacing is associated with improved survival compared with ventricular pacing, even after correction for confounding variables (195).

Lamas et al. conducted a *prospective, randomized* long-term comparison of rate-responsive ventricular pacing and rate-responsive dual-chamber pacing in elderly patients aged 65 years or older, with the principal end points being quality-of-life parameters (355). Overall, pacemaker implantation regardless of pacing mode was associated with large improvements in quality of life. In the intention-to-treat analysis, dual-chamber pacing showed modest quality-of-life advantages over ventricular pacing, primarily in the patients paced for sinus node dysfunction. However, the most striking finding of the study was that 26% of patients randomized to ventricular pacing crossed over to dual-chamber pacing because of symptoms of pacemaker syndrome, with improvement in quality-of-life indices after crossing over. has recently been completed G.A. Lamas, PACE Study, unpublished data, 1997). The primary end point of the trial was quality of life measures; only transient improvement in a minority of the quality of life measures was found to be associated with rate responsive dual-chamber pacing compared with rate responsive ventricular pacing.

On the basis of these studies, ~~rate-responsive ventricular pacing and dual-chamber pacing~~ appears to offer benefits over ~~fixed-rate~~ ventricular pacing with respect to quality of life in elderly patients, ~~but there may not be any benefit of dual-chamber pacing over rate-responsive ventricular demand pacing.~~ It does not appear appropriate to withhold use of dual-chamber or rate-responsive pacemakers uniformly in the elderly, although such a decision may be appropriate in any patient who is extremely sedentary or has a limited life expectancy.

In an ongoing large, multicenter, randomized study of elderly (aged 70 years or older) patients undergoing pacemaker implantation for AV block (UKPACE, United Kingdom Pacing and Cardiovascular Events), patients are randomly assigned to receive a ventricular pacemaker or a dual-chamber pacemaker. The study's primary end point is total mortality, and secondary end points are morbidity, exercise capacity, and quality of life (83,395,396).

6. Optimizing Pacemaker Technology and Cost

The cost of a pacemaker system increases with its degree of complexity and sophistication. For example, the cost of a dual-chamber pacemaker system exceeds that of a single-chamber system with respect to the cost of the generator (additional \$1000), the second lead (approximately \$900), additional implantation time and supplies, and additional follow-up. The implant costs and complication rate of dual-chamber pacemakers also exceed those of single-chamber pacemakers (398). Some pacemaker models offer more extensive diagnostics than others, at a premium cost. Similarly, the cost of a rate-responsive generator exceeds that of a non-rate-responsive generator by \$500 to \$1000. Against these additional costs are the potential benefits of the more sophisticated systems with respect to quality of life, morbidity, and mortality. Furthermore, the additional diagnostic information available from more sophisticated generators may eliminate the need for additional diagnostic testing, such as ambulatory monitoring or exercise electrocardiography, that would otherwise be necessary occasionally in selected pacemaker patients. Little is known about the cost-effectiveness of the additional features of more complex pacemaker systems. Several ongoing trials assessing the clinical benefits of dual-chamber ~~or rate-responsive~~ pacing include economic analyses to estimate the incremental cost-effectiveness of these features (83,395,396).

Approximately 16% of pacemaker implantations are for replacement of generators; of those, 76% are replaced because their batteries have reached end of service (193). Hardware and software (i.e., programming) features of pacemaker systems that prolong useful battery longevity may improve the cost-effectiveness of pacing. Optimal programming of output voltages, pulse widths, and AV delays can markedly decrease battery drain; a study showed that expert programming of pacemaker generators can have a major impact on longevity, prolonging it by an average of 4.2 years compared with nominal settings (196). Extensive diagnostic capabilities, ~~which typically add \$500 to \$1000 to the cost of a pacemaker generator, may~~ allow for optimal programming by the experienced physician with regard to improved device longevity. Newer lead designs, such as those incorporating steroid elution or high pacing impedance, allow for less current drain; ~~the cost of such leads is approximately \$125 greater than that of conventional leads.~~ Generators that automatically determine whether a pacing impulse results in capture allow for programming outputs closer to threshold values than conventional generators, and this new technology may also have a major impact on device longevity. Although all of these features arguably should prolong generator life, there are other constraints on the useful life of a pacemaker generator, including battery drain not directly related to pulse generation and the limited life expectancy of many pacemaker recipients; rigorous studies supporting the overall cost-effectiveness of advanced pacing features are lacking.

The cost of pacemaker implantation may vary between different locations within a hospital (e.g., cardiac catheteriza-

tion laboratory versus operating room); costs can be minimized by selecting the most economical site for implantation that preserves excellent patient outcome. One study comparing hospital charges for pacemaker implants in the catheterization laboratory versus the operating room within a single hospital showed a 45% lower charge for implants in the catheterization laboratory (401). There has been a trend to shorter hospital stays for pacemaker implantations, and some implantations are now being performed on an outpatient basis.

Reuse of explanted pacemakers, not currently performed to any extent in the United States, may eventually add significantly to the cost-effectiveness of cardiac pacing (197). Reports from Canada and Sweden indicate the safety and cost savings of selective pacemaker reuse (197,402).

J. Pacemaker Follow-up

After implantation of a pacemaker, careful follow-up and continuity of care are required. The committee considered the advisability of extending the scope of these guidelines to include recommendations for follow-up and device replacement ~~but deferred this decision given other published statements and guidelines on this topic. These are listed below as a matter of information. No endorsement is implied. In general, follow-up is dictated by the patient's disease substrate, the device used, and evolving technology.~~ NASPE has published a ~~comprehensive~~ series of reports on antibradycardia pacemaker follow-up (198-200). The Canadian Working Group in Cardiac Pacing has also published a consensus statement on pacemaker follow-up (403). In addition, the Health Care Financing Administration (HCFA; currently the Centers for Medicare and Medicaid Services) has established guidelines for monitoring of patients covered by Medicare who have antibradycardia pacemakers (201). ~~These documents are endorsed by this writing group.~~

Many of the same considerations are relevant to both pacemaker and ICD follow-up. Programming undertaken at implantation should be reviewed before discharge and changed accordingly at subsequent follow-up visits as indicated by interrogation, testing, and patient needs. With careful attention to programming pacing amplitude, pulse width, and diagnostic functions, battery life can be enhanced significantly without compromising patient safety. Taking advantage of programmable options also allows optimization of pacemaker function for the individual patient.

The frequency and method of follow-up is dictated by multiple factors, including other cardiovascular or medical problems managed by the physician involved, the age of the pacemaker, and geographic accessibility of the patient to medical care, and the results of transtelephonic testing. Some centers may prefer to use transtelephonic monitoring (TTM) as the mainstay of follow-up, with intermittent clinic evaluations. Others may prefer to do the majority or all of the patient follow-up in clinic. Automatic features such as automatic threshold assessment have been incorporated increasingly into newer devices and facilitate follow-up for patients who

live far from follow-up clinics (404). These automatic functions are not, however, universal and need not and cannot supplant the benefits of direct patient contact, particularly with regard to history taking and physical examination. Clinic In patients who are pacemaker dependent, clinical evaluation may be more frequent than for those who are not pacemaker dependent. In general, follow-up usually includes assessment of the clinical status of the patient, battery status, pacing threshold and pulse width, sensing function, and lead integrity, as well as optimization of sensor-driven rate response. The schedule for clinic follow-up should be at the discretion of the caregivers providing pacemaker follow-up. As a guideline, the 1984 HCFA document suggests the following: for single-chamber pacemakers, twice in the first 6 months after implant and then once every 12 months; for dual-chamber pacemakers, twice in the first 6 months, then once every 6 months.

Guidelines for TTM of permanent pacemakers have evolved clinically based on evolution of pacemaker and transtelephonic technology. Legislation regarding TTM has not been revised since 1984 (MED-MANUAL, MED-GUIDE ¶27,201, Coverage Issue Manual §50-1 Cardiac Pacemaker Evaluation Services [effective date: October 1, 1984]). Clearly stated guidelines are necessary and should be written in such a way as to mandate TTM that achieves specific clinical goals.

Appropriate clinical goals of TTM should be divided into those pieces of information obtainable during nonmagnet (free-running) ECG assessment and assessment of the ECG tracing obtained during magnet application. The same goals should be achieved whether the service is being provided by a commercial or noncommercial monitoring service.

Goals of TTM nonmagnet ECG assessment are as follows:

- Determine whether the patient displays intrinsic rhythm or is intermittently or continuously pacing at the programmed settings.
- Characterize the patient's underlying atrial mechanism, e.g., sinus versus atrial fibrillation.
- If intrinsic rhythm is displayed, determine that normal (appropriate) sensing is present for one or both chambers depending on whether it is a single- or dual-chamber pacemaker and programmed pacing mode.

Goals of TTM ECG assessment during magnet application are as follows:

- Verify effective capture of the appropriate chamber(s) depending on whether it is a single- or dual-chamber pacemaker and programmed pacing mode.
- Assess magnet rate. Once magnet rate is determined, the value should be compared to value(s) obtained on previous transmissions to determine whether any change has occurred. The person assessing the TTM should also be aware of the magnet rate that indicates elective replacement indicators for that pacemaker.

- If the pacemaker is one in which pulse width is an indicator of elective replacement indicators, the pulse width should also be assessed and compared to previous values.
- If the pacemaker has some mechanism to allow transtelephonic assessment of threshold, i.e., Threshold Margin Test (TMT™), and that function is programmed "on," the results of this test should be demonstrated and analyzed.
- If a dual-chamber pacemaker is being assessed and magnet application results in a change in AV interval during magnet application, that change should be demonstrated and verified.

1. Amount of Time Necessary for Verification

The amount of time spent during TTM should not be specified in terms of actual seconds or minutes but in terms of verification of the above clinical parameters. Whatever length of time is necessary to verify the points listed above during "free running" and "magnet," obtained ECG assessment should be sufficient.

2. Length of Electrocardiographic Samples for Storage

It is important that the caregiver(s) providing TTM assessment be able to refer to a paper copy or computer-archived copy of the transtelephonic assessment for subsequent care. The length of the ECG sample saved should, once again, be predicated based on the clinical information that is required, i.e., the points listed above. It is the experience of personnel trained in TTM that an ECG sample of 6 to 9 seconds that is of quality and is carefully selected can demonstrate all of the points for each of the categories listed above, i.e., a 6- to 9-second strip of nonmagnet and 6- to 9-second strip of magnet-applied ECG tracing.

Historically, there may have been some reason to collect another nonmagnet ECG example after the sample had been obtained during magnet application. In very early pacemakers, it may have been that magnet application would rarely result in a "stuck" reed switch, and a subsequent nonmagnet tracing would verify that function was indeed normal. However, with contemporary pacemakers, there is no logical clinical reason to obtain another nonmagnet tracing.

Because the indications for device implantation are evolving and some of the original indications for a particular patient may have been controversial, future replacement decisions may be more or less certain and must be individualized.

3. Frequency of Transtelephonic Monitoring

The follow-up schedule for TTM varies between centers, and there is no absolute schedule that need be mandated. Regardless of any of the following schedules to which the center may adhere, TTM may be necessary at unscheduled times if, for example, the patient experiences symptoms

Table 2. HCFA Guidelines for Transtelephonic Monitoring (1984)

Guideline I				
	Months Pacemaker Implanted			
Single Chamber	1st Every 2 weeks	2nd to 36th Every 8 weeks	37th to Failure Every 4 weeks	
Dual Chamber	1st Every 2 weeks	2nd to 6th Every 4 weeks	7th to 36th Every 8 weeks	37th to Failure Every 4 weeks
Guideline II				
	Months Pacemaker Implanted			
Single Chamber	1st Every 2 weeks	2nd to 48th Every 12 weeks	49th to Failure Every 4 weeks	
Dual Chamber	1st Every 2 weeks	2nd to 30th Every 12 weeks	31st to 48th Every 8 weeks	49th to Failure Every 4 weeks

potentially reflecting an alteration in rhythm or device function.

The majority of centers with TTM services follow the schedule allowed by HCFA. In the 1984 HCFA guidelines, there are two broad categories for follow-up (as shown in Table 2): guideline I, which was thought to apply to the majority of pacemakers in use at that time, and guideline II, which would apply to pacemaker systems for which sufficient long-term clinical information exists to ensure that they meet the standards of the Inter-Society Commission for Heart Disease Resources for longevity and end-of-life decay. The standards to which they referred are 90% cumulative survival at 5 years after implant and an end-of-life decay of less than a 50% drop of output voltage and less than a 20% deviation of magnet rate, or a drop of 5 bpm or less, over a period of 3 months or more. As of 2000, it would appear that most pacemakers would meet the specifications in guideline II.

There is no federal or clinical mandate that these TTM guidelines be followed. The ACC, AHA, and NASPE have not officially endorsed these HCFA guidelines. Nevertheless, they may be useful as a framework for TTM. An experienced center may choose to do less frequent TTM and supplement it with in-clinic evaluations as stated previously.

II. INDICATIONS FOR IMPLANTABLE CARDIOVERTER-DEFIBRILLATOR THERAPY

A. Background

ICDs were originally developed and have been most frequently used for to prevent sudden cardiac death in patients who have experienced life-threatening ventricular arrhythmias such as sustained VT or VF (202-205). Epidemiological studies report high rates of recurrence of these life-threatening arrhythmias (30% to 50% in 2 years) during follow-up. Early observational reports documented efficacy in reversion of sustained VT and VF (103-105,202,203,205-215,405-407). have now been supplemented by Large prospective, and sometimes randomized single center and multicenter studies with long term outcome data have established the effect of the ICD on long-term outcomes (204,216-221).

Enrollment in these trials has included patients with coronary and noncoronary heart diseases with a wide range of ventricular function and coexisting disorders.

These studies uniformly document sudden cardiac death recurrence rates that average 1% to 2% annually after device implantation in these populations. Simultaneously, rapid technological evolution of ICD systems has occurred. The ICD has evolved from a short-lived nonprogrammable device requiring a thoracotomy for lead insertion into a multiprogrammable antiarrhythmia device implanted almost exclusively without thoracotomy, now capable of treating bradycardia, VT, VF, and atrial tachycardia (222-224, 408,409). Clinical studies registries have recorded major improvements in implant risk, system longevity, symptoms associated with arrhythmia recurrences, quality of life, and diagnosis and management of inappropriate device therapy (103,216-218,225-229).

Implantation, follow-up, and replacement of these devices is a complex process requiring familiarity with device capabilities, adequate case volume, continuing education, and skill in the management of ventricular arrhythmias, therefore mandating involvement of a trained electrophysiologist (230,410,411) to provide an optimal personnel team for patient safety and device management.

A substantial new body of information has emerged regarding the clinical outcome of patients with VT or VF treated with currently available antiarrhythmic therapies. There are currently three major therapeutic options to reduce or prevent VT or VF in patients at risk for these arrhythmias. These are:

1. Antiarrhythmic drug therapy. selected by electrophysiologic study or ambulatory monitoring or prescribed empirically.
2. For VT, ablative techniques applied at cardiac surgery or percutaneously using catheter techniques.
3. Implantation of a cardioverter-defibrillator device system.

A combination of ICD therapy with drugs or ablation is also frequently used. Currently, the largest clinical experience is with combined antiarrhythmic drug and ICD therapy.

B. Clinical Efficacy of ICD Therapy

ICD devices have been extensively evaluated in *prospective* clinical trials and ~~clinical experience now exceeds device registries~~ 100,000 implants worldwide since the inception of this therapy (103-105,202-221). ~~ICDs have been clearly documented to revert~~ Single-chamber nonthoracotomy systems can be implanted with a procedural mortality rate of 0.5% (217) to 0.8% (216). The ICD has been shown to terminate VF successfully in 98.8% (217) and 98.6% (216) of episodes. ~~They effectively terminate sustained ventricular tachyarrhythmias, including by pace or shock termination of sustained VT, and shock reversion termination of VF. Large series have shown that single-chamber nonthoracotomy systems can be implanted with an average a procedural mortality of 0.5% (217) to 0.8% (216). The ICD has been shown to terminate VF successfully in 98.8% (217) and 98.6% (216) of episodes. VT has been converted with antitachycardia pacing in 89.4% (216) to 91.2% (217) of episodes, with further successful conversions (98%) using shock therapy. Inappropriate therapy, typically for atrial fibrillation with a rapid ventricular response, has been noted in 5% to 11% of patients.~~

~~Early retrospective reports showed significant improvements in survival with the defibrillator (205,208,231). The study design tended to overestimate benefits by using device therapies (antitachycardia pacing and shocks) as surrogate mortality events. In a large body of subsequent experience, the sudden death rate reported in virtually all series ranges from 1% to 2% per year with a cumulative incidence of #10% at 5 years (105,205,207,210,211,213,215,217,232). Higher sudden death rates have been reported in patients with severe LV dysfunction (233,234). Dilution of the survival benefit conferred by sudden death reduction in ICD patients by non-arrhythmic mortality and its impact on overall survival is patient population dependent (232,233).~~

~~Device therapy delivery cannot be used as a surrogate mortality end point because arrhythmias other than VT/VF can activate the device, and recurrent VT is not invariably fatal. Symptomatic ICD activations alone underestimate antiarrhythmic benefits of ICD therapy. More recently, firmer estimates of benefits from ICD therapy using devices with event memory capabilities have become possible in the absence of placebo-controlled studies (225,227,235,236). In these studies ICD patients had successful reversion (>98%) of VT with circulatory collapse or VF, with a significant projected survival benefit compared with untreated populations (235). This benefit is incremental and continues to increase over longer periods (3 to 4 years). A similar benefit exists in patients with sustained VT (236).~~

There has been controversy about the appropriate end point for evaluation of ICD efficacy. Many studies have used sudden death, but classification of the cause of death is often difficult and imprecise. Consequently, it is now accepted that total mortality is the appropriate primary end point for judging ICD efficacy (237). Rates of sudden death and ICD discharges provide useful information, but they should be con-

sidered as secondary end points. Total mortality varies significantly between reports due to differences in the disease status of the population under study and LV function. The presence of concomitant cardiac disease is a major determinant of survival (233,238,239). Survival of ICD recipients is influenced by LV function. ~~Patients with LV ejection fractions <30% have reduced survival compared with those with higher ejection fractions at 3 years (233,234). However, both populations appear to derive a significant survival benefit (221). Patients with reduced LV systolic function appear to benefit the most from ICD therapy (412,413). A retrospective analysis indicated that patients thought to have had a reversible cause for their life-threatening arrest were still at substantial risk of death (414).~~

C. Alternatives to ICD Therapy

Pharmacological options for ~~guided~~ antiarrhythmic therapy include drugs in classes I, II, and III. Therapy can be guided by Holter monitoring or serial electrophysiologic testing or given empirically. High arrhythmia recurrence rates and moderate sudden death rates are observed with Class I agents (240). By contrast, Class III agents are associated with significantly lower arrhythmia recurrences, sudden death, and total mortality (240-243).

~~β-Blocking agents have also demonstrated efficacy in reducing mortality after AMI (244,245). However, their value in a population of patients with sustained ventricular tachyarrhythmias is not well established. Suppression of inducible VT as well as control of spontaneous VT is often not achieved (246). Although the overall survival of cardiac arrest patients treated empirically with beta-blockers and Class I agents may be comparable, patients given Class I agents on serial electrophysiologic testing have a better outcome than those treated with empiric beta-blocker therapy (247). Current data do not support a significant role for monotherapy with beta-blockers in this condition.~~

In the post-myocardial infarction patient, empiric amiodarone therapy reduces arrhythmic mortality, but benefit with respect to total mortality in such patients ~~with ventricular dysfunction is less clear~~ has been less consistently demonstrated in individual studies (248-251). In cardiac arrest survivors treated empirically with amiodarone, patients with a reduced ejection fraction (<40%) continue to exhibit high arrhythmia recurrence and sudden death rates (252). Similarly, patients with congestive heart failure may show little to no mortality reduction with empiric amiodarone therapy (253,254). Quantitative overviews of amiodarone use in randomized trials, however, demonstrate a significant reduction in total mortality (415,416).

Long-term maintenance of effective antiarrhythmic drug therapy remains problematic. Discontinuation for drug intolerance is high for Class I agents and sotalol at initiation of therapy and during long-term administration (240). Amiodarone therapy is also frequently discontinued for adverse effects during long-term administration (243).

Ablative therapy has been most often used for patients with sustained monomorphic VT induced at cardiac surgery or electrophysiologic study and mapped to a specific ventricular site(s). Intraoperative ablation is accomplished mechanically or with physical energy sources (cryothermia or laser), whereas catheter-based energy delivery (direct-current shock, radiofrequency, microwaves, or laser) is used during electrophysiologic procedures (255-258). These methods are applicable to a select population of patients with malignant ventricular tachyarrhythmias that have reproducibly inducible monomorphic VT suitable for cardiac mapping. ~~Surgical experience is more extensive and favorable in patients with coronary heart disease than noncoronary disease. Perioperative mortality is now lower and averages <5% in more recent experience, particularly when preoperative LV systolic function is preserved. Intraoperative map-guided ablation—now performed infrequently—is associated with low arrhythmia recurrence (less than 10% at 2 years) and minimal sudden death rates (256-258) during long-term follow-up, making it an important therapeutic alternative in this subgroup.~~ among patients with preserved LV function.

Catheter ablation approaches are still in technological evolution (259,260). ~~Hemodynamically stable VT is usually required for mapping, and radiofrequency energy is currently used for ablation (261,262). Procedural complication rates are moderate with modest arrhythmia control (261,262), often in conjunction with previously ineffective drug therapy in patients with coronary artery disease.~~ Higher efficacy rates are observed in patients with right ventricular outflow tract tachycardia, idiopathic left septal VT, and bundle-branch re-entrant VT in whom ablation may be the preferred therapy (263-265). Although acute success rates of 71% have been reported in patients with structural heart disease, recurrence rates of 33% have subsequently occurred (417). Multiple VT morphologies, polymorphic VT, and progressive cardiomyopathy, when present, are less amenable to a favorable result with ablative intervention (255,256). Nonetheless, catheter ablation of recurrent VT associated with frequent ICD therapy may be associated with a marked reduction in the occurrence of shocks and an overall improved quality of life (418). Newer electroanatomic (419) and noncontact (420) mapping technologies may improve the outcomes of such procedures.

D. Comparison of Drug and Device Therapy for Secondary Prevention of Cardiac Arrest and Sustained Ventricular Tachycardia

A significant body of information ~~from prospective, randomized trials now exists~~ comparing these two therapeutic options. ICD and drug therapy is now available. ~~Direct comparison of drug and device therapy has been performed in several retrospective nonrandomized reports and fewer in prospective randomized studies. In comparison with concurrently medically treated but nonrandomized populations receiving amiodarone, a significant mortality benefit was noted in the patients with ICDs over the first 3 years of follow-up (206,209). This benefit may dissipate with follow-up~~

~~beyond 5 years in some reports (209). In similar nonrandomized comparisons in sudden death survivors discharged either on electrophysiologically guided antiarrhythmic therapy using Class I or III drugs or on an ICD-based regimen, the survival of the ICD patients was superior, both in patients with early or advanced LV dysfunction (210). In such analyses, the use of an ICD in the treatment regimen was the strongest predictor of long-term survival. ICD recipients also show improved survival in such comparisons with patients receiving guided sotalol therapy (266).~~

~~Information from randomized trials comparing drug and device therapy also suggests. These trials demonstrate survival benefits with ICD therapy in this population compared with electrophysiologically guided drug therapy using Class I agents, propafenone, or sotalol (267,268). The first reported large prospective, randomized study comparing ICD therapy with Class III antiarrhythmic drug therapy, predominantly empiric amiodarone, in survivors of cardiac arrest and hemodynamically unstable VT revealed greater survival with ICD therapy (221). Unadjusted survival estimates for the ICD and drug therapy, respectively, were 89.3% versus 82.3% at 1 year, 81.6% versus 74.7% at 2 years, and 75.4% versus 64.1% at 3 years. Estimated relative risk reduction with ICD therapy was 39% at 1 year and 31% at 3 years. Two other reports of large prospective trials in similar patient groups have shown similar trends (406,407). A pooling of these three studies shows a 27% reduction in total mortality with ICD therapy (421).~~

~~Implementation of ICD therapy has been directly compared for safety with antiarrhythmic drug therapy in large systematic trials. Prospective observational data demonstrate a low perioperative mortality (0.4% to 1.8%) for primary nonthoracotomy implants (105,216-218). Similar mortality estimates in large prospective antiarrhythmic drug trials range from 3.2% to 13.0% (221,240,243). However, these populations may not be directly comparable. During long-term therapy, drug discontinuation rates have ranged from 7% to 32%, the lowest being with sotalol in reported data (240). In a large prospective trial, 98% of randomly assigned patients could be maintained on ICD therapy, with 25.4% requiring the addition of drug therapy by 2 years (221). Withdrawal of device therapy is infrequent and rarely exceeds 2% of implants (216-218). The addition of an antiarrhythmic drug in selected patients with ICDs may improve quality of life by reducing arrhythmia recurrences and the need for shock therapy (266,269).~~

E. Specific Disease States and Secondary Prevention of Cardiac Arrest or Sustained Ventricular Tachycardia

Prior guidelines do not relate the decision to implant an ICD device to the underlying cardiac disease (270). Current information suggests that the underlying disease state may have an important impact on patient prognosis and will influence the decision to implant an ICD earlier or later in the treatment algorithm.

1. Coronary Artery Disease

Patients with coronary artery disease represent the majority of patients receiving devices in most reports. Device implantation is widely accepted as improving the outcome of these patients. Patients with reduced LV function may experience greater benefit with ICD therapy than with drug therapy (208,210,267,412,413). To limit patient risk during defibrillation efficacy testing (270,271), assessment for the presence of active ischemia should precede implementation of device therapy. Furthermore, optimal anti-ischemic therapy (including, where possible, a beta-blocker) will further enhance survival. ~~Measurement of ventricular function is recommended, although poor function is not necessarily a contraindication to device implantation.~~ Abbreviated defibrillation threshold testing, however, may be desirable in patients with elevated pulmonary capillary wedge pressures or severely compromised cardiac output (271).

2. Idiopathic Dilated Cardiomyopathy

Dilated cardiomyopathy is associated with a high mortality within 2 years of diagnosis, with a minority of patients surviving 5 years (272). Approximately one-half of these deaths are sudden and unexpected (273). The combination of poor LV function and frequent episodes of nonsustained VT in these patients is associated with an increased risk of sudden death (274). Moreover, although useful in patients with unlike in ischemic coronary heart disease, the value of electrophysiologic studies in patients with nonischemic cardiomyopathies is limited (275). Furthermore, the efficacy of drug therapy is low in the presence of impaired LV function and difficult to predict on the basis of invasive or noninvasive testing. ICD implantation may be preferred for treatment of patients with VT or VF and this condition. In one large *prospective* study, this population represented 10% of the study group and showed survival benefits with ICD rather than empiric amiodarone therapy similar to the entire study cohort (221).

3. Long-QT Syndrome

The long-QT syndromes represent a spectrum of electrophysiologic disorders characterized by a propensity for development of malignant ventricular arrhythmias, especially polymorphic VT (239,276-278). Because this is a primary electrical disorder, usually with no evidence of structural heart disease or LV dysfunction, the long-term prognosis is excellent if arrhythmia is controlled. Long-term treatment with beta-blockers, permanent pacing, or left cervicothoracic sympathectomy is frequently effective (277). ICD implantation is recommended for selected patients in whom recurrent syncope, sustained ventricular arrhythmias, or sudden cardiac death occurs despite drug therapy (276). Furthermore, use of the ICD as primary therapy should be considered in certain patients, such as those in whom aborted sudden cardiac death is the initial presentation of the long-QT syndrome, where there is a strong family history of sudden car-

diac death, or when compliance or intolerance to drugs is a concern (276,422).

4. Idiopathic Ventricular Fibrillation

It has been estimated that in 10% of young patients resuscitated from cardiac arrest, the origin of VF is not determined despite extensive evaluation (279,280). Electrophysiologic testing in these patients with "idiopathic VF" usually reveals polymorphic VT or VF that is often suppressible ~~with~~ by Class IA drugs administered during the electrophysiologic testing (279). However, the long-term efficacy of drug therapy remains unknown. Given the guarded prognosis even with effective drug therapy (the annual rate of sudden cardiac death is estimated to be as high as 11%), the limited clinical data available appear to support the use of ICDs in such patients (279-281).

Brugada Syndrome

Individuals with syncope and/or a family history of unexplained sudden cardiac death who have variants of right bundle-branch block QRS morphology and ST-segment elevations in leads V1 through V3 have the Brugada syndrome. Because of the high incidence of VF, ICD therapy should be recommended in such individuals (423). However, ICD therapy is not recommended in individuals with these ECG findings alone, because the specificity of this finding in the absence of the historical details noted above is very low (424). Catheter ablation should be considered before ICD insertion in patients with idiopathic right or left VT (263).

5. Idiopathic Ventricular Tachycardia

Ventricular tachycardia may arise in structurally normal hearts from the right ventricular outflow tract or the LV. These arrhythmias should be treated pharmacologically or with catheter ablation, if amenable, before an ICD is considered for these patients (263).

6. Hypertrophic Cardiomyopathy

Hypertrophic cardiomyopathy should be suspected and is often identified as the cause of sudden death in young people, including trained athletes (239,282). Ventricular tachyarrhythmias are a common mechanism of sudden death in this condition (283). Sudden death may also be the first manifestation of the disease in a previously asymptomatic individual. Criteria to stratify these patients according to risk are not well defined. ~~In contrast with other cardiomyopathies, electrophysiologic testing may be of prognostic value because inducible sustained ventricular arrhythmias appear to be associated with cardiac arrest and syncope in some studies (284)~~The most prominent characteristics of patients with hypertrophic cardiomyopathy who may be at high risk for experiencing sudden death include the following: 1) prior cardiac arrest or sustained VT; 2) a history of a first-degree relative who has experienced sudden cardiac death; 3) LV hypertrophy with a wall thickness greater than 30 mm (425);

4) syncope, if exertional, repetitive, or in a young patient if no other cause is documented; and 5) nonsustained VT on ECG monitoring if frequent, repetitive, and prolonged. Studies of patients resuscitated from cardiac arrest indicate that many patients will experience another event. Prophylactic pharmacological therapy in the form of beta-blockers or calcium channel antagonists has frequently been used, but efficacy in sudden death prevention has not been established. Empiric use of amiodarone has been reported to be associated with improved survival in one observational study with historical controls (282). However, prediction of drug efficacy remains difficult and controversial. Sudden death survivors should be considered for ICD therapy in preference to or in conjunction with drug therapy (285). Because these patients are often young, drug compliance is frequently an issue. Long-term protection for these patients may be better afforded by treatment with an ICD. Other data support automatic defibrillator implantation as the preferred therapy in high-risk patients with hypertrophic cardiomyopathy to decrease sudden cardiac death, in preference to or in conjunction with drug therapy (285,426).

7. Arrhythmogenic Right Ventricular Dysplasia/ Cardiomyopathy

Arrhythmogenic right ventricular dysplasia can be an important cause of congestive heart failure and ventricular arrhythmias in some patients (286). Drug therapy is often used as primary therapy but is often ineffective. Nonpharmacological options for treatment of significant arrhythmias include catheter ablation of the sites of tachycardia, surgical disarticulation of the right ventricle, and ICDs. In patients with drug-refractory malignant arrhythmias, the ICD provides prophylaxis against syncope due to hemodynamically unstable VT and sudden death (287,288).

8. Syncope With Inducible Sustained Ventricular Tachycardia

Patients with syncope of undetermined etiology in whom clinically relevant VT/VF is induced at electrophysiologic study may be candidates for ICD therapy. In these patients, the induced arrhythmia is presumed to be the cause of syncope (289-291). Cardiovascular mortality averages 20% annually, with a large proportion of it sudden. In some patients, antiarrhythmic treatment is limited by inefficacy, intolerance, or noncompliance. ICD therapy is often used in sustained VT populations with comparable results (292). In patients with hemodynamically significant and symptomatic inducible sustained VT, ICD therapy can be a primary treatment option. The documentation of appropriate ICD therapy of VT and VF from review of event counters and stored electrograms in such patients lends support to use of ICD therapy as a primary treatment option in those who have experienced syncope (414,427).

F. Pediatric Patients

~~Pediatric experience with ICDs represents less than 1% of all implantations (239,293). Special considerations such as the need for lifelong pharmacological therapy with its associated problems of noncompliance and side effects make the ICD an important treatment option for young patients.~~

Fewer than 1% of all ICD implantations are performed in pediatric patients (239,293). However, special considerations, such as the need for lifelong pharmacological therapy with its associated problems of noncompliance and side effects, make the ICD an important treatment option for young patients.

Sudden cardiac death is uncommon in childhood but is associated with three principal forms of cardiovascular disease: 1) congenital heart disease, 2) cardiomyopathy, and 3) primary electrical disease (239,294). Patients with pre-existing heart disease are more likely to experience ventricular tachyarrhythmias as the immediate cause of sudden death than are those with normal hearts (295). However, a lower percentage of children undergoing resuscitation survive to hospital discharge compared with adults (296).

Indications for ICD therapy for pediatric patients are similar to those for arrhythmias in adults. However, the data used for risk stratification in adults with coronary artery disease may have less positive predictive value in pediatric patients with a variety of underlying diseases (297). The risk of unexpected sudden death is greater in young patients with diseases such as hypertrophic cardiomyopathy or long-QT syndrome than in adults; therefore, a family history of sudden death may influence the decision to use an ICD in a pediatric patient (277,282). A limited experience with ICDs implanted in young patients with hypertrophic cardiomyopathies or long-QT syndromes after resuscitation has been encouraging (285,293,301,302,351,428).

In patients with congenital heart disease, sudden death has been estimated to occur in 1.5% to 2.5% of patients per decade after repair of tetralogy of Fallot (298). A higher risk has been identified for patients with transposition of the great arteries and aortic stenosis, with most cases presumed to be due to a malignant ventricular arrhythmia associated with ischemia, ventricular dysfunction, or a rapid response to atrial flutter (120,299). An ischemic substrate for arrhythmias leading to sudden cardiac death also exists in congenital coronary anomalies or after Kawasaki disease.

ICD therapy may be preferable to antiarrhythmic drugs in patients with dilated cardiomyopathy or other causes of impaired ventricular function who experience syncope or sustained ventricular arrhythmias because of concern about drug-induced proarrhythmia and myocardial depression. ICDs may also be considered as a bridge to orthotopic heart transplantation in pediatric patients with ventricular arrhythmias whose anomalies are not amenable to surgical correction, particularly given the longer times to donor procurement in younger patients (300). Young patients with hypertrophic cardiomyopathy have a higher annual sudden cardiac death event rate than adults (282,301). A limited experience

with ICDs implanted in this population after resuscitation has been encouraging (285,293,302).

G. Primary Prevention of Sudden Cardiac Death

1. Coronary Artery Disease

Nonsustained VT in patients with prior MI and LV dysfunction is associated with a 2-year mortality estimated at 30% (303,304). Approximately one-half of this is believed to be arrhythmic in origin. Antiarrhythmic drug therapy has been widely prescribed in patients after MI with and without ventricular arrhythmia, but evidence of improved survival with this approach is not forthcoming. Increased mortality in coronary disease patients with and without nonsustained VT has actually been noted with specific Class I agents (305). Empiric amiodarone therapy has shown inconsistent survival benefit in large *prospective randomized* trials (250,251), although quantitative overviews (meta-analyses) suggest total mortality may be reduced compared with other medical therapies (241,306). In this population, electrophysiologic testing has identified a subgroup with inducible sustained ventricular tachyarrhythmias that is at high risk for sudden death (307). While arrhythmia-related symptoms and repeated MIs may help identify such patients, asymptomatic persons post-MI may also be at high risk (304,307,308). ~~Survival of patients treated with drugs that suppressed induced arrhythmias improved in comparison with historically untreated or drug-refractory patients (307).~~ In the first prospective randomized trial conducted in such a patient population, improved survival was documented after implantation of ICDs in patients with inducible and nonsuppressible ventricular tachyarrhythmias when compared with conventional drug therapy, including amiodarone (220). Results of another prospective, randomized trial showed reduced mortality with therapy for patients with low ejection fraction, nonsustained VT on Holter monitoring, and inducible sustained ventricular tachyarrhythmias at electrophysiologic study (405). Most of this benefit appeared to be due to ICD placement. The results of a study of 1232 patients after myocardial infarction with an LV ejection fraction of less than or equal to 30% randomized to ICD therapy or not in a 3:2 fashion without the requirement for electrophysiologic screening for inducible ventricular tachyarrhythmia were reported during this publication's review process (429). At a mean follow-up of 20 months, the mortality rate was 14.2% in the individuals who had ICDs and 19.8% in the conventionally treated group, a 5.6% absolute and 31% relative risk reduction for death. In this study, the survival curves did not begin to separate until 9 months after randomization. Of potential importance, ICD therapy was not implemented until at least 1 month after myocardial infarction and 3 months after coronary artery revascularization surgery. The cost impact, as well as a thorough analysis of the impact of other variables (e.g., risk stratification potential of programmed stimulation performed through the ICDs) has not been fully analyzed and reported. Also of note was an observed increased incidence of new or worsened heart fail-

ure in the ICD-treated patients compared with those in the conventional treatment arm. As one editorial suggested, the extent to which ICD therapy actually extends life in given patients is not fully known, and more refined screening techniques even in such patients are needed (430). Although such patients merit consideration of ICD therapy, this approach requires consideration of the patient's overall health and life expectancy. Additional risk stratification studies are needed to better define which patient subgroups will benefit more or less from ICD therapy than that demonstrated in the above-referenced population. Further preliminary data presented at the May 2002 Scientific Session of NASPE as a "late-breaking clinical trial" analyzed the effects of ICD therapy in patients stratified on the basis of various noninvasive ECG criteria. A standard ECG QRS duration longer than 0.12 seconds was found to be the strongest predictor of such patients who benefit most from ICD therapy. In the Cox proportional hazard model analysis, individuals with a QRS duration greater than 0.12 seconds had a 63% reduction in mortality relative to conventionally treated patients ($p = 0.004$). Atrial fibrillation as the baseline rhythm was the only other independent predictor of ICD therapy benefit in such patients. Whether the recommendation to implant ICDs in post-myocardial infarction patients with LV ejection fractions of 30% or less should be limited to individuals with these high-risk variables awaits further clarification.

2. After Coronary Artery Bypass Surgery

Routine ICD insertion does not improve survival in patients with coronary artery disease undergoing bypass surgery who are believed to be at high risk of sudden death based on QRS duration and severe LV dysfunction. In one *randomized* study, no benefit was noted over placebo (309) in patients with ejection fractions less than 35% and a positive signal-averaged ECG who were undergoing surgical revascularization.

3. As a Bridge to Heart Transplantation

Orthotopic heart transplantation has emerged as an acceptable therapeutic alternative for selected patients with congestive heart failure caused by severe ventricular dysfunction. About 20% of patients requiring transplantation die awaiting a donor organ, with a significant incidence of sudden death. ~~ICDs effectively prevent~~ ICDs have been associated with a lower risk of sudden death in these patients (310,311). This benefit is diluted by mortality due to heart failure in some patients (310-312).

4. Other Populations

Other high-risk populations under study for similar benefits include asymptomatic patients, from the standpoint of ventricular tachyarrhythmias, who have impaired LV systolic function and congestive heart failure (431) or idiopathic dilated cardiomyopathy (432), but no recommendations can yet be made with respect to these patients owing to insuffi-

cient data. Randomized trials of the ICD are ongoing in these populations. Patients with advanced structural heart disease and syncope of unknown origin may benefit from an ICD even if electrophysiologic evaluation is negative (433).

H. Contraindications and Limitations of \pm ICD Therapy

ICD therapy is not recommended for ~~the conditions listed below. The first major group, which can be identified by invasive and noninvasive preimplantation testing, includes those~~ patients in whom a reversible triggering factor for VT/VF can be definitely identified, such as ventricular tachyarrhythmias in evolving AMI or electrolyte abnormalities. Another population in whom ICD therapy is not routinely recommended is coronary disease patients without inducible or spontaneous VT undergoing routine coronary bypass surgery (309). Similarly, patients with Wolff-Parkinson-White syndrome presenting with VF secondary to atrial fibrillation should undergo catheter or surgical ablation if their accessory pathways are amenable to such treatment.

Patients with terminal illnesses, NYHA class IV drug-refractory congestive heart failure who are not candidates for cardiac transplantation, or with a life expectancy not exceeding 6 months are likely to obtain limited benefit—if any—from ICD therapy. Thus, ICD therapy is discouraged in such individuals. Significant behavioral disorders, including anxiety, device dependence, or social withdrawal, have been described (316,317). A history of psychiatric disorders, including uncontrolled depression and substance abuse that interfere with the meticulous care and follow-up needed by these patients, is a relative contraindication to device therapy.

Patients who have frequent tachyarrhythmias that may trigger shock therapy, such as sustained VT not responsive to antitachycardia pacing or pharmacological therapy, are not suitable candidates for a device because these events would cause frequent device activation and multiple shocks. Alternative therapies, such as combining drugs or ablation with ICD insertion, should be considered.

I. Cost-Effectiveness of ICD Therapy

Several studies have addressed the cost-effectiveness of ICD therapy. The cost-effectiveness ratio compares the total cost of ICD therapy with the total cost of an alternative management strategy such as amiodarone or guided serial drug testing. The overall costs of the ICD have been reduced as the result of nonthoracotomy implantation methods and improvements in ICD reliability and longevity that reduce cost of device replacement and modification. Significant reductions in initial costs have been realized, with newer treatment algorithms eliminating prolonged drug testing (318,319).

The early studies of ICD cost-effectiveness were based on mathematical models and relied on *nonrandomized* studies to estimate clinical efficacy and cost. These studies found cost-effectiveness ratios of \$17,000 (320), \$18,100 (321), and \$29,200 per year of life saved (322). Another model incor-

porated costs of nonthoracotomy ICDs and efficacy estimates based on *randomized* trials and found ICD cost-effectiveness was between \$27,300 and \$54,000 per life-year gained, corresponding to risk reduction of 40% and 20%, respectively (323).

Several completed and ongoing *randomized* clinical trials have measured cost as well as clinical outcomes and thus can directly estimate ICD cost-effectiveness. ~~A preliminary analysis of the MADIT (324) trial found the ICD to have a cost-effectiveness ratio of \$27,000 per life-year gained. The Multicenter Automatic Defibrillator Implantation Trial (MADIT) found a 54% reduction in total mortality and a cost-effectiveness ratio of \$27,000 per life-year added (434). The Canadian Implantable Defibrillator Trial (CIDS), by contrast, found a 20% reduction in total mortality and a cost-effectiveness ratio of \$139,000 per life-year added (406,435). The cost-effectiveness ratio from the Antiarrhythmics Versus Implantable Defibrillators (AVID) trial was \$66,677 per life-year added (436). This range of results is primarily due to different estimates of the effectiveness of the ICD in reducing mortality, because all showed similar increases in the cost of care among ICD recipients. When the results of all clinical trials were used in a model that projected the full gain in life expectancy and lifetime costs (323), the cost-effectiveness of the ICD was \$31,500 per life-year added. All studies suggest that ICD implantation in appropriately selected patients has a cost effectiveness ratio comparable to other cardiovascular therapies as well as comparable to widely accepted noncardiac therapies such as renal dialysis (\$30,000 to \$50,000 per year of life saved). The cost-effectiveness of the ICD is more favorable in patients with high risk of arrhythmic death but low risk of other causes of death an ejection fraction below 35%. In principle, the device is most cost-effective in patients at high risk of arrhythmic death and at low risk of other causes of death. Cost-effectiveness of the ICD would be improved by lowering the cost of the device itself and further improving its reliability and longevity.~~

J. Selection of ICD Generators

All ICDs currently marketed in the United States incorporate a number of advanced features, including multiple tachycardia zones, with rate detection criteria and tiered therapy (including low-energy cardioversion and high-energy defibrillation shocks) independently programmable for each zone. Furthermore, all devices incorporate programmable ventricular demand pacing, antitachycardia pacing, and extensive diagnostics, including stored electrograms of rhythms immediately before and after tachycardia detection and therapy. ~~The principal feature distinguishing some ICDs from others is the availability of antitachycardia pacing as a programmable therapy option. The addition of antitachycardia pacing increases the cost of the device by 5% to 10% compared with similar ICDs without this feature.~~ The vast majority of devices are small enough for pectoral new implantations. Larger devices suitable for abdominal implants are available primarily as replacement generators in patients with pre-

existing lead systems but are being phased out by manufacturers; these larger devices are available at a cost savings of approximately 10% to 25% compared with the smaller devices.

Antitachycardia pacing appears to be a useful feature in the majority of patients receiving ICDs. In one study (325), antitachycardia pacing was activated in 68% of patients receiving ICDs with such a capability, despite the fact that the efficacy of antitachycardia pacing was tested with the device in only 53% of the patients in whom it was activated; in the remainder, antitachycardia pacing algorithms were programmed empirically. In the patients with activated antitachycardia pacing, 96% of all detected episodes of ventricular tachyarrhythmias were terminated with pacing (325). Acceleration of VT by antitachycardia pacing remains a concern, with most series reporting an incidence of antitachycardia pacing acceleration of an episode of VT ranging from 3% to 6% (326). Patients whose only clinical arrhythmia detected before ICD implantation was VF have a lower likelihood of having VT subsequently detected by the ICD than do patients with a prior history of VT (327). However, the incidence of subsequent VT in those with a history of only VF before device implantation is not inconsiderable [18% during 14 months of follow-up in one study (327)], so it is reasonable to select a device with assess activation of antitachycardia pacing even in such patients.

Defibrillators incorporating an atrial lead are now available. Such devices not only provide dual-chamber pacing but also use the pattern of sensed atrial depolarization to distinguish supraventricular from ventricular arrhythmias. A dual-chamber pacemaker-ventricular defibrillator device is an appropriate choice for an ICD candidate who has a concomitant need for dual-chamber pacing or a patient with supraventricular tachycardia thought likely to lead to inappropriate ICD therapies.

Early reports have documented that the time required for detection of VF during acute testing at the time of implantation is not impaired with the addition of atrial leads (437,438). However, hemodynamic benefits of dual-chamber pacing in such devices have been documented in few patients followed up for relatively short-term intervals only (439). Furthermore, data on long-term benefits of dual-chamber ICDs are lacking despite their widespread dissemination. One center's reported experience has been associated with a 2.8% complication rate in their first 95 implants. A worrisome infection rate of 8.8% was observed in patients who had previously implanted single-chamber ICDs upgraded to dual-chamber systems (440). Expected incremental benefits of the use of atrial electrograms together with ventricular electrograms to evaluate stored arrhythmic events have been documented (441). Studies are ongoing to further assess efficacy benefits that dual-chamber ICD therapy may have over single-chamber ICD therapy.

Atrial defibrillation therapy for recurrent AF has been evaluated in stand-alone implantable atrioverters (408) and in conjunction with conventional dual-chamber ICDs (409,442). Although clinically available as complementary

features with some dual-chamber ICDs, the indications and role of such therapy are unclear and must await further reports and results of additional studies.

K. ICD Follow-up

All patients with ICDs require periodic and meticulous follow-up to ensure safety and optimal device performance. The goals of ICD follow-up include monitoring of device system function; optimizing performance for maximal clinical effectiveness and system longevity; minimizing complications; anticipating replacement of system components; ensuring timely intervention for clinical problems; patient tracking, education, and support; and maintenance of ICD system records. The need for device surveillance and management should be discussed *a priori* with patients before insertion of an ICD. Compliance with device follow-up is an important element in evaluating appropriate candidates for device therapy and obtaining the best long-term result. ICD follow-up is best achieved in an organized program analogous to pacemaker follow-up at outpatient clinics (198).

Institutions performing implantation of these devices should also maintain these facilities for inpatient and outpatient use. Such facilities should obtain and maintain implantation and follow-up support devices for all ICDs used at that facility. The facility should be staffed or supported by a fully trained clinical cardiac electrophysiologist (328) who may work in conjunction with trained associated professionals (198,328,329). Access to these services should be available as far as is feasible on both a regularly scheduled and emergent 24-hour-per-day basis. The implantation and/or follow-up facility should be able to locate and track patients who have received ICDs or who have entered the follow-up program.

1. Elements of ICD Follow-up

The follow-up of an ICD patient must be individualized in accordance with the patient's clinical status and conducted by a fully trained clinical cardiac electrophysiologist. In general, device programming is initiated at implantation and should be reviewed at predischarge and/or subsequent post-operative electrophysiologic testing. Devices should be followed at 1- to 4-month intervals, depending on the device model and the patient's clinical status. Manufacturer guidelines for device follow-up vary with individual models and should be available. Transtelephonic follow-up (if available) should always be supplemented by clinic visits at a minimum of 4-month intervals for patient and device evaluation (330,410).

It is often necessary to reprogram the initially selected parameters either in the outpatient clinic or by electrophysiologic testing. When device function or concomitant antiarrhythmic therapy is modified, electrophysiologic testing can be and often is required to evaluate sensing, pacing, or defibrillation functions of the device. Particular attention should be given to review of sensing parameters, programmed defibrillation and pacing therapies, device activation, and event

logs. Technical elements requiring review include battery status, lead system parameters, and elective replacement indicators. Intervening evaluation of device function is often necessary. In general, in patients experiencing device activation, with or without therapy, delivery should be evaluated shortly after the event until a regular acceptable pattern of patient symptomatology and tolerance for such events is established and device behavior is deemed reliable, safe, and effective.

After insertion of a device, its performance should be reviewed, limitations on the patient's specific physical activities established, and registration accomplished. Current policies on driving advise the patient with an ICD to avoid operating a motor vehicle for ~~a minimum of 3 months and preferably 6 months~~ after the last symptomatic arrhythmic event to determine the pattern of recurrent VT/VF (331,332). Interactions with electromagnetic interference sources, impact on employment, and prophylaxis for device infections should be discussed. ICD recipients should be encouraged to carry proper identification and information about their device at all times. Patients receiving these devices can experience transient or sustained emotional disturbances. Education and psychological support before, during, and after ICD insertion are highly desirable and can improve the patient's quality of life (316,317).

Recommendations for ICD Therapy

Class I

1. **Cardiac arrest due to VF or VT not due to a transient or reversible cause.** (*Level of Evidence: A*) (103-105,202,203,205-211,216,217,219,221,238,260,267,269,406,407)
2. **Spontaneous sustained VT in association with structural heart disease.** (*Level of Evidence: B*) (103-105,202,203,205-211,216,217,219)
3. **Syncope of undetermined origin with clinically relevant, hemodynamically significant sustained VT or VF induced at electrophysiologic study when drug therapy is ineffective, not tolerated, or not preferred.** (*Level of Evidence: B*) (204,213,215,219,227,228,266,406)
4. **Nonsustained VT in patients with coronary disease, prior MI, LV dysfunction, and inducible VF or sustained VT at electrophysiologic study that is not suppressible by a Class I antiarrhythmic drug.** (*Level of Evidence: BA*) (220,308,405)
5. **Spontaneous sustained VT in patients without structural heart disease not amenable to other treatments.** (*Level of Evidence: C*)

Class IIa

Patients with left ventricular ejection fraction of less than or equal to 30% at least 1 month post myocardial infarction and 3 months post coronary artery revascularization surgery. (*Level of Evidence: B*) (429)

Class IIb

1. **Cardiac arrest presumed to be due to VF when electrophysiologic testing is precluded by other medical conditions.** (*Level of Evidence: C*) (211,218,267,276)
2. **Severe symptoms (e.g., syncope) attributable to ventricular tachyarrhythmias in patients awaiting cardiac transplantation.** (*Level of Evidence: C*) (310,311)
3. **Familial or inherited conditions with a high risk for life-threatening ventricular tachyarrhythmias such as long-QT syndrome or hypertrophic cardiomyopathy.** (*Level of Evidence: B*) (8,41,277,282,284,288,300-302)
4. **Nonsustained VT with coronary artery disease, prior MI, LV dysfunction, and inducible sustained VT or VF at electrophysiologic study.** (*Level of Evidence: B*) (103,205,212,217,220,307,308)
5. **Recurrent syncope of undetermined origin in the presence of ventricular dysfunction and inducible ventricular arrhythmias at electrophysiologic study when other causes of syncope have been excluded.** (*Level of Evidence: C*)
6. **Syncope of unexplained origin or family history of unexplained sudden cardiac death in association with typical or atypical right bundle-branch block and ST-segment elevations (Brugada syndrome).** (*Level of Evidence: C*) (443,444)
7. **Syncope in patients with advanced structural heart disease in whom thorough invasive and noninvasive investigations have failed to define a cause.** (*Level of Evidence: C*)

Class III

1. **Syncope of undetermined cause in a patient without inducible ventricular tachyarrhythmias and without structural heart disease.** (*Level of Evidence: C*)
2. **Incessant VT or VF.** (*Level of Evidence: C*)
3. **VF or VT resulting from arrhythmias amenable to surgical or catheter ablation; for example, atrial arrhythmias associated with the Wolff-Parkinson-White syndrome, right ventricular outflow tract VT, idiopathic left ventricular tachycardia, or fascicular VT.** (*Level of Evidence: C*) (259-263)
4. **Ventricular tachyarrhythmias due to a transient or reversible disorder (e.g., AMI, electrolyte imbalance, drugs, or trauma) when correction of the disorder is considered feasible and likely to substantially reduce the risk of recurrent arrhythmia.** (*Level of Evidence: CB*) (414,445,446)
5. **Significant psychiatric illnesses that may be aggravated by device implantation or may preclude systematic follow-up.** (*Level of Evidence: C*) (316,317)
6. **Terminal illnesses with projected life expectancy less than 6 months.** (*Level of Evidence: C*)
7. **Patients with coronary artery disease with LV dysfunction and prolonged QRS duration in the absence of spontaneous or inducible sustained or nonsustained**

Appendix 1. ACC/AHA/NASPE Committee to Update the 1998 Guidelines for Implantation of Cardiac Pacemakers and Antiarrhythmias Devices—Conflict of Interest

Committee Member Name	Research Grant	Speakers Bureau	Stock Ownership	Committee Member	Advisory Committee	Honoraria	Consultant
Dr. Gabriel Gregoratos	None	None	None	None	None	None	None
Dr. Jonathan Abrams	None	None	None	None	None	None	None
Dr. Andrew Epstein	Biotronik Cordis-Webster Daig Guidant HMR Medtronic St. Jude	Berlex Guidant Medtronic	None	Guidant	None	None	None
Dr. Roger Freedman	Guidant St. Jude	None	None	None	None	None	None
Dr. David Hayes	None	ELA	Guidant Medtronic St. Jude	None	ELA Guidant Medtronic	Guidant Medtronic St. Jude	None
Dr. Mark Hlatky	None	None	None	None	None	None	None
Dr. Richard Kerber	Agilent	None	None	None	None	None	None
Dr. Gerald Naccarelli	Guidant Knoll Proctor & Gamble Sanofi Solvay Wyeth Ayerst	None	None	None	None	None	Berlex Guidant Knoll Medtronic Pfizer Wyeth Ayerst
Dr. Mark Schoenfeld	None	None	None	None	None	None	None
Dr. Michael Silka	None	None	None	None	None	None	None
Dr. Stephen Winters	Medtronic St. Jude Wyeth Ayerst	Berlex Pfizer	Medtronic Transneuronix	None	None	None	None

This table represents the actual or potential conflicts of committee members with industry that were reported orally at the initial writing committee meeting on November 1, 2000 and updated in conjunction with all meetings and conference calls of this writing committee. It does not reflect any actual or potential conflicts at the time of publication.

VT who are undergoing coronary bypass surgery. (Level of Evidence: B) (309)

- 8. NYHA Class IV drug-refractory congestive heart failure in patients who are not candidates for cardiac transplantation. (Level of Evidence: C)**

APPENDIX 1

See Appendix 1 on page 34 for conflict of interest information.

STAFF

American College of Cardiology

Christine W. McEntee, Chief Executive Officer
Victoria Furnelli, MA, Research Analyst
Sharyn L. Vitrano, Project Manager
Gwen C. Pigman, MLS, Librarian

American Heart Association

M. Cass Wheeler, Chief Executive Officer
Sidney C. Smith, Jr., MD, Chief Science Officer
Kathryn A. Taubert, PhD, Vice President
Science and Medicine

North American Society of Pacing and Electrophysiology

James H. Youngblood, Chief Executive Officer
Stephanie Mascetta, RN, Clinical Documents
Project Manager

REFERENCES

1. Iskos D, Lurie KG, Sakaguchi S, Benditt DG. Termination of implantable pacemaker therapy: experience in 5 patients. *Ann Intern Med* 1997;126:787-90.
2. Ryan TJ, Anderson JL, Antman EM, et al. ACC/AHA guidelines for the management of patients with acute myocardial infarction: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on Management of Acute Myocardial Infarction). *J Am Coll Cardiol* 1996;28:1328-428. Deleted during update.
3. Zipes DP, DiMarco JP, Gillette PC, et al. Guidelines for clinical intracardiac electrophysiological and catheter ablation procedures: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on Clinical Intracardiac Electrophysiological and Catheter Ablation Procedures), developed in collaboration with the North American Society of Pacing and Electrophysiology. *J Am Coll Cardiol* 1995;26:555-73.
4. Epstein AE, Carlson MD, Fogoros RN, Higgins SL, Venditti FJ. Classification of death in antiarrhythmia trials. *J Am Coll Cardiol* 1996;27:433-42.
5. Kim SG, Fogoros RN, Furman S, et al. Standardized reporting of ICD patient outcome: the report of a North American Society of Pacing and Electrophysiology Policy Conference, February 9-10, 1993. *PACE Pacing Clin Electrophysiol* 1993;16:1358-62.
6. Hayes DL, Naccarelli GV, Furman S, Parsonnet V. Report of the NASPE policy conference on training requirements for permanent pacemaker selection, implantation, and follow-up. North

- American Society of Pacing and Electrophysiology. *PACE Pacing Clin Electrophysiol* 1994;17:6-12.
7. Josephson ME, Maloney JD, Barold SS, et al. ACC Core Cardiology Training Symposium (COCATS): guidelines for training in adult cardiovascular medicine. June 27-28, 1994. Task Force 6: training in specialized electrophysiology, cardiac pacing and arrhythmia management. *J Am Coll Cardiol* 1995;25:23-6. Deleted during update.
 8. Freidberg CK, Donoso E, Stein WG. Nonsurgical acquired heart block. *Ann NY Acad Sci* 1964;111:835-47.
 9. Gadboys HL, Wisoff BG, Litwak RS. Surgical treatment of complete heart block: an analysis of 36 cases. *JAMA* 1964;189:97-102.
 10. Johansson BW. Complete heart block: a clinical, hemodynamic and pharmacological study in patients with and without an artificial pacemaker. *Acta Med Scand* 1966;180(Suppl 451):1-127.
 11. Hindman MC, Wagner GS, JaRo M, et al. The clinical significance of bundle branch block complicating acute myocardial infarction: indications for temporary and permanent pacemaker insertion. *Circulation* 1978;58:689-99.
 12. Donmoyer TL, DeSanctis RW, Austen WG. Experience with implantable pacemakers using myocardial electrodes in the management of heart block. *Ann Thorac Surg* 1967;3:218-27.
 13. Edhag O, Swahn A. Prognosis of patients with complete heart block or arrhythmic syncope who were not treated with artificial pacemakers: a long-term follow-up study of 101 patients. *Acta Med Scand* 1976;200:457-63.
 14. Mymin D, Mathewson FA, Tate RB, Manfreda J. The natural history of primary first-degree atrioventricular heart block. *N Engl J Med* 1986;315:1183-7.
 15. Barold SS. Indications for permanent cardiac pacing in first-degree AV block: class I, II, or III? *PACE Pacing Clin Electrophysiol* 1996;19:747-51.
 16. Kim YH, O'Nunain S, Trouton T, et al. Pseudopacemaker syndrome following inadvertent fast pathway ablation for atrioventricular nodal reentrant tachycardia. *J Cardiovasc Electrophysiol* 1993;4:178-82.
 17. Brecker SJD, Xiao HB, Sparrow J, Gibson DG. Effects of dual chamber pacing with short atrioventricular delay in dilated cardiomyopathy. *Lancet* 1992;340:1308-12.
 18. Dhingra RC, Denes P, Wu D, Chuquimia R, Rosen KM. The significance of second degree atrioventricular block and bundle branch block: observations regarding site and type of block. *Circulation* 1974;49:638-46.
 19. Strasberg B, Amat-Y-Leon F, Dhingra RC, et al. Natural history of chronic second-degree atrioventricular nodal block. *Circulation* 1981;63:1043-9.
 20. Donoso E, Adler LN, Friedberg CK. Unusual forms of second-degree atrioventricular block, including Mobitz type-II block, associated with the Morgagni-Adams-Stokes syndrome. *Am Heart J* 1964;67:150-7.
 21. Recommendations for pacemaker prescription for symptomatic bradycardia: report of a working party of the British Pacing and Electrophysiology Group. *Br Heart J* 1991;66:185-91.
 22. Connelly DT, Steinhaus DM. Mobitz type I atrioventricular block: an indication for permanent pacing? *PACE Pacing Clin Electrophysiol* 1996;19:261-4.
 23. Shaw DB, Kekwick CA, Veale D, Gowers J, Whistance T. Survival in second degree atrioventricular block. *Br Heart J* 1985; 53:587-93.
 24. Ranganathan N, Dhurandhar R, Phillips JH, Wigle ED. His Bundle electrogram in bundle-branch block. *Circulation* 1972; 45:282-94.

25. Ector H, Rolies L, De Geest H. Dynamic electrocardiography and ventricular pauses of 3 seconds and more: etiology and therapeutic implications. *PACE Pacing Clin Electrophysiol* 1983;6:548-51.
26. Shaw DB, Holman RR, Gowers JI. Survival in sinoatrial disorder (sick-sinus syndrome). *Br Med J* 1980;280:139-41.
27. Kay R, Estioko M, Wiener I. Primary sick sinus syndrome as an indication for chronic pacemaker therapy in young adults: incidence, clinical features, and long-term evaluation. *Am Heart J* 1982;103:338-42.
28. Gallagher JJ, Svenson RH, Kasell JH, et al. Catheter technique for closed-chest ablation of the atrioventricular conduction system. *N Engl J Med* 1982;306:194-200.
29. Langberg JJ, Chin MC, Rosenqvist M, et al. Catheter ablation of the atrioventricular junction with radiofrequency energy. *Circulation* 1989;80:1527-35.
30. Kastor JA. Atrioventricular block (first of two parts). *N Engl J Med* 1975;292:462-5.
- 30a. Glikson M, Dearani JA, Hyberger LK, Schaff HV, Hammill SC, Hayes DL. Indications, effectiveness, and long-term dependency in permanent pacing after cardiac surgery. *Am J Cardiol* 1997; 80:1309-13.
31. Perloff JK, Stevenson WG, Roberts NK, Cabeen W, Weiss J. Cardiac involvement in myotonic muscular dystrophy (Steinert's disease): a prospective study of 25 patients. *Am J Cardiol* 1984;54:1074-81.
32. Hiromasa S, Ikeda T, Kubota K, et al. Myotonic dystrophy: ambulatory electrocardiogram, electrophysiologic study, and echocardiographic evaluation. *Am Heart J* 1987;113:1482-8.
33. Stevenson WG, Perloff JK, Weiss JN, Anderson TL. Facioscapulohumeral muscular dystrophy: evidence for selective, genetic electrophysiologic cardiac involvement. *J Am Coll Cardiol* 1990;15:292-9.
34. James TN, Fisch C. Observations on the cardiovascular involvement in Friedreich's ataxia. *Am Heart J* 1963;66:164-75.
35. Roberts NK, Perloff JK, Kark RAP. Cardiac conduction in the Kearns-Sayre syndrome (a neuromuscular disorder associated with progressive external ophthalmoplegia and pigmentary retinopathy): report of 2 cases and review of 17 published cases. *Am J Cardiol* 1979;44:1396-1400.
36. Charles R, Holt S, Kay JM, Epstein EJ, Rees JR. Myocardial ultrastructure and the development of atrioventricular block in Kearns-Sayre syndrome. *Circulation* 1981;63:214-9.
37. James TN. Observations on the cardiovascular involvement, including the conduction system, in progressive muscular dystrophy. *Am Heart J* 1962;63:48-56.
38. McAlister HF, Klementowicz PT, Andrews C, Fisher JD, Feld M, Furman S. Lyme carditis: an important cause of reversible heart block. *Ann Intern Med* 1989;110:339-45.
39. Penton GB, Miller H, Levine SA. Some clinical features of complete heart block. *Circulation* 1956;13:801-24.
40. Kulbertus H, Collignon P. Association of right bundle-branch block with left superior or inferior intraventricular block: its relation to complete heart block and Adams-Stokes syndrome. *Br Heart J* 1969;31:435-40.
41. DePasquale NP, Bruno MS. Natural history of combined right bundle branch block and left anterior hemiblock (bilateral bundle branch block). *Am J Med* 1973;54:297-303.
42. Dhingra RC, Denes P, Wu D, et al. Syncope in patients with chronic bifascicular block: significance, causative mechanisms, and clinical implications. *Ann Intern Med* 1974;81:302-6.
43. Scheinman MM, Peters RW, Modin G, Brennan M, Mies C, O'Young J. Prognostic value of infranodal conduction time in patients with chronic bundle branch block. *Circulation* 1977; 56:240-4.
44. Denes P, Dhingra RC, Wu D, Wyndham CR, Amat-Y-Leon F, Rosen KM. Sudden death in patients with chronic bifascicular block. *Arch Intern Med* 1977;137:1005-10.
45. McAnulty JH, Kauffman S, Murphy E, Kassebaum DG, Rahimtoola SH. Survival in patients with intraventricular conduction defects. *Arch Intern Med* 1978;138:30-5.
46. Peters RW, Scheinman MM, Modin C, O'Young J, Somelofski CA, Mies C. Prophylactic permanent pacemakers for patients with chronic bundle branch block. *Am J Med* 1979;66:978-85.
47. Fisch GR, Zipes DP, Fisch C. Bundle branch block and sudden death. *Prog Cardiovasc Dis* 1980;23:187-224.
48. McAnulty JH, Rahimtoola SH, Murphy E, et al. Natural history of "high-risk" bundle-branch block: final report of a prospective study. *N Engl J Med* 1982;307:137-43.
49. Scheinman MM, Peters RW, Suavé MJ, et al. Value of the H-Q interval in patients with bundle branch block and the role of prophylactic permanent pacing. *Am J Cardiol* 1982;50:1316-22.
50. Morady F, Higgins J, Peters RW, et al. Electrophysiologic testing in bundle branch block and unexplained syncope. *Am J Cardiol* 1984;54:587-91.
51. Click RL, Gersh BJ, Sugrue DD, et al. Role of invasive electrophysiologic testing in patients with symptomatic bundle branch block. *Am J Cardiol* 1987;59:817-23.
52. Lie KL, Wellens HJJ, Schuilenburg RM. Bundle branch block and acute myocardial infarction. In: Wellens HJJ, Lie KI, Janse MD, editors. *The Conduction System of the Heart: Structure, Function and Clinical Implications*. Philadelphia (PA): Lea & Febiger, 1976:662-72.
53. Ezri M, Lerman BB, Marchlinski FE, Buxton AE, Josephson ME. Electrophysiologic evaluation of syncope in patients with bifascicular block. *Am Heart J* 1983;106:693-7.
54. Twidale N, Heddle WF, Ayres BF, Tonkin AM. Clinical implications of electrophysiology study findings in patients with chronic bifascicular block and syncope. *Aust N Z J Med* 1988;18:841-7.
55. Englund A, Bergfeldt L, Rehnqvist N, Aström H, Rosenqvist M. Diagnostic value of programmed ventricular stimulation in patients with bifascicular block: a prospective study of patients with and without syncope. *J Am Coll Cardiol* 1995;26:1508-15.
56. Probst P, Pachinger O, Akbar Murad A, Leisch F, Kaindl F. The HQ time in congestive cardiomyopathies. *Am Heart J* 1979;97:436-41.
57. Dhingra RC, Wyndham C, Bauernfeind R, et al. Significance of block distal to the His bundle induced by atrial pacing in patients with chronic bifascicular block. *Circulation* 1979;60:1455-64.
58. Cheng TO. Atrial pacing: its diagnostic and therapeutic applications. *Prog Cardiovasc Dis* 1971;14:230-47.
59. Gupta PK, Lichstein E, Chadda KD. Intraventricular conduction time (H-V interval) during antegrade conduction in patients with heart block. *Am J Cardiol* 1973;32:27-31.
60. Altschuler H, Fisher JD, Furman S. Significance of isolated H-V interval prolongation in symptomatic patients without documented heart block. *Am Heart J* 1979;97:19-26.
61. Col JJ, Weinberg SL. The incidence and mortality of intraventricular conduction defects in acute myocardial infarction. *Am J Cardiol* 1972;29:344-50.
62. Ritter WS, Atkins JM, Blomqvist CG, Mullins CB. Permanent pacing in patients with transient trifascicular block during acute myocardial infarction. *Am J Cardiol* 1976;38:205-8.
63. Ginks WR, Sutton R, Oh W, Leatham A. Long-term prognosis after acute anterior infarction with atrioventricular block. *Br Heart J* 1977;39:186-9.

64. Domenighetti G, Perret C. Intraventricular conduction disturbances in acute myocardial infarction: short- and long-term prognosis. *Eur J Cardiol* 1980;11:51-9.
65. Lamas GA, Muller JE, Turi ZG, et al. A simplified method to predict occurrence of complete heart block during acute myocardial infarction. *Am J Cardiol* 1986;57:1213-9.
66. Juma Z, Castellanos A, Myerburg RJ. Prognostic significance of the electrocardiogram in patients with coronary heart disease. In: Wellens HJJ, Kulbertus HE, editors. *What's New in Electrocardiography*. The Hague: Martinus Nijhoff Publishers, 1981:5-22.
67. Clemmensen P, Bates ER, Califf RM, et al. Complete atrioventricular block complicating inferior wall acute myocardial infarction treated with reperfusion therapy. *Am J Cardiol* 1991;67:225-30.
68. Goldberg RJ, Zevallos JC, Yarzebski J, et al. Prognosis of acute myocardial infarction complicated by complete heart block (the Worcester Heart Attack Study). *Am J Cardiol* 1992;69:1135-41.
69. Behar S, Zissman E, Zion M, et al. Prognostic significance of second-degree atrioventricular block in inferior wall acute myocardial infarction. *Am J Cardiol* 1993;72:831-4.
70. Berger PB, Ruocco NA, Ryan TJ, et al. Incidence and prognostic implications of heart block complicating inferior myocardial infarction treated with thrombolytic therapy: results from TIMI II. *J Am Coll Cardiol* 1992;20:533-40.
71. Nicod P, Gilpin E, Ditttrich H, Polikar R, Henning H, Ross J Jr. Long-term outcome in patients with inferior myocardial infarction and complete atrioventricular block. *J Am Coll Cardiol* 1988;12:589-94.
72. Dubois C, Piérard LA, Smeets JP, Carlier J, Kulbertus HE. Long-term prognostic significance of atrioventricular block in inferior acute myocardial infarction. *Eur Heart J* 1989;10:816-20.
73. Kusumoto FM, Goldschlager N. Cardiac pacing. *N Engl J Med* 1996;334:89-97.
74. Linde-Edelstam C, Nordlander R, Pehrsson SK, Ryden L. A double-blind study of submaximal exercise tolerance and variation in paced rate in atrial synchronous compared to activity sensor modulated ventricular pacing. *PACE Pacing Clin Electrophysiol* 1992;15:905-15.
75. Gammage M, Schofield S, Rankin I, Bennett M, Coles P, Pentecost B. Benefit of single setting rate responsive ventricular pacing compared with fixed rate demand pacing in elderly patients. *PACE Pacing Clin Electrophysiol* 1991;14:174-80.
76. Meytes I, Kaplinsky E, Yahini JH, Hanne-Paparo N, Neufeld HN. Wenckebach A-V block: a frequent feature following heavy physical training. *Am Heart J* 1975;90:426-30.
77. Talan DA, Bauernfeind RA, Ashley WW, Kanakis CJ, Rosen KM. Twenty-four hour continuous ECG recordings in long-distance runners. *Chest* 1982;82:19-24.
78. Dreifus LS, Michelson EL, Kaplinsky E. Bradyarrhythmias: clinical significance and management. *J Am Coll Cardiol* 1983;1:327-38.
79. Rasmussen K. Chronic sinus node disease: natural course and indications for pacing. *Eur Heart J* 1981;2:455-9.
80. Rubenstein JJ, Schulman CL, Yurchak PM, DeSanctis RW. Clinical spectrum of the sick sinus syndrome. *Circulation* 1972;46:5-13.
81. Rosenqvist M, Brandt J, Schuller H. Long-term pacing in sinus node disease: effects of stimulation mode on cardiovascular morbidity and mortality. *Am Heart J* 1988;116:16-22.
82. Santini M, Alexidou G, Ansalone G, Cacciari G, Cini R, Turitto G. Relation of prognosis in sick sinus syndrome to age, conduction defects and modes of permanent cardiac pacing. *Am J Cardiol* 1990;65:729-35.
83. Connolly SJ, Kerr C, Gent M, Yusuf S. Dual-chamber versus ventricular pacing: critical appraisal of current data. *Circulation* 1996;94:578-83.
84. Andersen HR, Thuesen L, Bagger JP, Vesterlund T, Thomsen PE. Prospective randomised trial of atrial versus ventricular pacing in sick-sinus syndrome. *Lancet* 1994;344:1523-8.
- 84a. Andersen HR, Nielsen JC, Thomsen PEB, et al. Long-term follow up of patients from a randomised trial of atrial versus ventricular pacing for sick-sinus syndrome. *Lancet* 1997;350:1210-6.
85. Spurrell RA, Nathan AW, Camm AJ. Clinical experience with implantable scanning tachycardia reversion pacemakers. *PACE Pacing Clin Electrophysiol* 1984;7:1296-1300.
86. Peters RW, Scheinman MM, Morady F, Jacobson L. Long-term management of recurrent paroxysmal tachycardia by cardiac burst pacing. *PACE Pacing Clin Electrophysiol* 1985;8:35-44.
87. Fisher JD, Johnston DR, Furman S, Mercado AD, Kim SG. Long-term efficacy of antitachycardia pacing for supraventricular and ventricular tachycardias. *Am J Cardiol* 1987;60:1311-6.
88. Den Dulk K, Bertholet M, Brugada P, et al. Clinical experience with implantable devices for control of tachyarrhythmias. *PACE Pacing Clin Electrophysiol* 1984;7:548-56.
89. Herre JM, Griffin JC, Nielsen AP, et al. Permanent triggered anti-tachycardia pacemakers in the management of recurrent sustained ventricular tachycardia. *J Am Coll Cardiol* 1985;6:206-14.
90. Saksena S, Pantopoulos D, Parsonnet V, Rothbart ST, Hussain SM, Gielchinsky I. Usefulness of an implantable antitachycardia pacemaker system for supraventricular or ventricular tachycardia. *Am J Cardiol* 1986;58:70-4.
91. Barold SS, Wyndham CR, Kappenberger LL, Abinader EG, Griffin JC, Falkoff MD. Implanted atrial pacemakers for paroxysmal atrial flutter: long-term efficacy. *Ann Intern Med* 1987;107:144-9.
92. Attuel P, Pellerin D, Mugica J, Coumel P. DDD pacing: an effective treatment modality for recurrent atrial arrhythmias. *PACE Pacing Clin Electrophysiol* 1988;11:1647-54.
93. Saksena S, Prakash A, Hill M, et al. Prevention of recurrent atrial fibrillation with chronic dual-site right atrial pacing. *J Am Coll Cardiol* 1996;28:687-94.
94. Daubert C, Mabo P, Berder V. Arrhythmia prevention by permanent atrial resynchronization in advanced intra-atrial block. *Eur Heart J* 1990;11:237-42.
95. Ward DE, Camm AJ, Spurrell RA. The response of regular re-entrant supraventricular tachycardia to right heart stimulation. *PACE Pacing Clin Electrophysiol* 1979;2:586-95.
96. Naccarelli GV, Zipes DP, Rahilly GT, Heger JJ, Prystowsky EN. Influence of tachycardia cycle length and antiarrhythmic drugs on pacing termination and acceleration of ventricular tachycardia. *Am Heart J* 1983;105:1-5.
97. Eldar M, Griffin JC, Abbott JA, et al. Permanent cardiac pacing in patients with the long QT syndrome. *J Am Coll Cardiol* 1987;10:600-7.
98. Eldar M, Griffin JC, Van Hare GF, et al. Combined use of beta-adrenergic blocking agents and long-term cardiac pacing for patients with the long QT syndrome. *J Am Coll Cardiol* 1992;20:830-7.
99. Moss AJ, Robinson J. Clinical features of the idiopathic long QT syndrome. *Circulation* 1992;85(suppl I):I-140-4.
100. Naccarelli GV, Dougherty AH, Jalal S, Shih HT, Wolbrette D. Paroxysmal supraventricular tachycardia: comparative role of therapeutic methods—drugs, devices and ablation. In: Saksena S, Luderitz B, editors. *Interventional Electrophysiology: A Textbook*. Armonk (NY): Futura Publishing Co Inc, 1996:381-90.

101. Fisher JD, Teichman SL, Ferrick A, Kim SG, Waspe LE, Martinez MR. Antiarrhythmic effects of VVI pacing at physiologic rates: a crossover controlled evaluation. *PACE Pacing Clin Electrophysiol* 1987;10:822-30.
102. Lau CP, Cornu E, Camm AJ. Fatal and nonfatal cardiac arrest in patients with an implanted antitachycardia device for the treatment of supraventricular tachycardia. *Am J Cardiol* 1988;61:919-21.
103. Mehta D, Saksena S, Krol RB, Makhija V. Comparison of clinical benefits and outcome in patients with programmable and nonprogrammable implantable cardioverter defibrillators. *PACE Pacing Clin Electrophysiol* 1992;15:1279-90.
104. Saksena S, Poczbott-Johanos M, Castle LW, et al, for the Guardian Multicenter Investigators Group. Long-term multicenter experience with a second-generation implantable pacemaker-defibrillator in patients with malignant ventricular tachyarrhythmias. *J Am Coll Cardiol* 1992;19:490-9.
105. Bardy GH, Troutman C, Poole JE, et al. Clinical experience with a tiered-therapy, multiprogrammable antiarrhythmia device. *Circulation* 1992;85:1689-98.
106. Sra JS, Jazayeri MR, Avitall B, et al. Comparison of cardiac pacing with drug therapy in the treatment of neurocardiogenic (vasovagal) syncope with bradycardia or asystole. *N Engl J Med* 1993;328:1085-90.
107. Sugrue DD, Gersh BJ, Holmes DR, Wood DL, Osborn MJ, Hammill SC. Symptomatic "isolated" carotid sinus hypersensitivity: natural history and results of treatment with anticholinergic drugs or pacemaker. *J Am Coll Cardiol* 1986;7:158-62.
108. Peretz DI, Gerein AN, Miyagishima RT. Permanent demand pacing for hypersensitive carotid sinus syndrome. *Can Med Assoc J* 1973;108:1131-4.
109. Brignole M, Menozzi C, Gianfranchi L, Oddone D, Lolli G, Bertulla A. Neurally mediated syncope detected by carotid sinus massage and head-up tilt test in sick sinus syndrome. *Am J Cardiol* 1991;68:1032-6.
110. Benditt DG, Ferguson DW, Grubb BP, et al. Tilt table testing for assessing syncope. American College of Cardiology. *J Am Coll Cardiol* 1996;28:263-75.
111. Sutton R, Petersen M, Brignole M, Raviele A, Menozzi C, Giani P. Proposed classification for tilt-induced vasovagal syncope. *Eur J Cardiac Pacing Electrophysiol* 1992;2:180-3.
112. Kenny RA, Ingram A, Bayliss J, Sutton R. Head-up tilt: a useful test for investigating unexplained syncope. *Lancet* 1986;1:1352-5.
113. Fitzpatrick A, Sutton R. Tilting towards a diagnosis in recurrent unexplained syncope. *Lancet* 1989;1:658-60.
114. Petersen ME, Chamberlain-Webber R, Fitzpatrick AP, Ingram A, Williams T, Sutton R. Permanent pacing for cardioinhibitory malignant vasovagal syndrome. *Br Heart J* 1994;71:274-81.
115. Connolly SJ, Sheldon RS, Gent M, Roberts RS, VPS Investigators. A randomized trial of cardiac pacing for recurrent fainting: the Vasovagal Pacemaker Study (VPS). Presented at: North American Society of Pacing and Electrophysiology 18th Annual Scientific Session; May 1997; New Orleans, La.
116. Grubb BP, Gerard G, Roush K, et al. Differentiation of convulsive syncope and epilepsy with head up tilt testing. *Ann Intern Med* 1991;115:871-6.
117. Fisher JD. Role of electrophysiologic testing in the diagnosis and treatment of patients with known and suspected bradycardias and tachycardias. *Prog Cardiovasc Dis* 1981;24:25-90.
118. Reiffel JA, Kuehnert MJ. Electrophysiological testing of sinus node function: diagnostic and prognostic application—including updated information from sinus node electrograms. *PACE Pacing Clin Electrophysiol* 1994;17:349-65.
119. Mackintosh AF. Sinuatrial disease in young people. *Br Heart J* 1981;45:62-6.
120. Garson A Jr, Bink-Boelkens M, Hesslein PS, et al. Atrial flutter in the young: a collaborative study of 380 cases. *J Am Coll Cardiol* 1985;6:871-8.
121. Gelatt M, Hamilton RM, McCrindle BW, et al. Arrhythmia and mortality after the Mustard procedure: a 30-year single-center experience. *J Am Coll Cardiol* 1997;29:194-201.
122. Silka MJ, Manwill JR, Kron J, McAnulty JH. Bradycardia-mediated tachyarrhythmias in congenital heart disease and responses to chronic pacing at physiologic rates. *Am J Cardiol* 1990;65:488-93.
123. Gillette PC, Zeigler VL, Case CL, Harold M, Buckles DS. Atrial antitachycardia pacing in children and young adults. *Am Heart J* 1991;122:844-9.
124. Rhodes LA, Walsh EP, Gamble WJ, Triedman JK, Saul JP. Benefits and potential risks of atrial antitachycardia pacing after repair of congenital heart disease. *PACE Pacing Clin Electrophysiol* 1995;18:1005-16.
125. Kugler JD, Danford DA. Pacemakers in children: an update. *Am Heart J* 1989;117:665-79.
126. Sholler GF, Walsh EP. Congenital complete heart block in patients without anatomic cardiac defects. *Am Heart J* 1989;118:1193-8.
127. Michaelsson M, Jonzon A, Riesenfeld T. Isolated congenital complete atrioventricular block in adult life: a prospective study. *Circulation* 1995;92:442-9.
128. Dewey RC, Capeless MA, Levy AM. Use of ambulatory electrocardiographic monitoring to identify high-risk patients with congenital complete heart block. *N Engl J Med* 1987;316:835-9.
129. Pinsky WW, Gillette PC, Garson A Jr, McNamara DG. Diagnosis, management, and long-term results of patients with congenital complete atrioventricular block. *Pediatrics* 1982;69:728-33.
130. Michaelsson M, Engle MA. Congenital complete heart block: an international study of the natural history. *Cardiovasc Clin* 1972;4:85-101.
131. Moss AJ, Liu JE, Gottlieb S, Locati EH, Schwartz PJ, Robinson JL. Efficacy of permanent pacing in the management of high-risk patients with long QT syndrome. *Circulation* 1991;84:1524-9.
132. Viskin S, Alla SR, Barron HV, et al. Mode of onset of torsade de pointes in congenital long QT syndrome. *J Am Coll Cardiol* 1996;28:1262-8.
133. Trippel DL, Parsons MK, Gillette PC. Infants with long-QT syndrome and 2:1 atrioventricular block. *Am Heart J* 1995;130:1130-4.
134. Solti F, Szatmary L, Vecsey T, Renyi-Vamos FJ, Bodor E. Congenital complete heart block associated with QT prolongation. *Eur Heart J* 1992;13:1080-3.
135. Lillehei CW, Sellers RD, Bonnanbeau RC, Eliot RS. Chronic postsurgical complete heart block with particular reference to prognosis, management, and a new P-wave pacemaker. *J Thorac Cardiovasc Surg* 1963;46:436-56.
136. Kertesz N, McQuinn T, Collins E, Friedman R. Surgical atrioventricular block in 888 congenital heart operations: new implications for early implantation of a permanent pacemaker [abstract]. *PACE Pacing Clin Electrophysiol* 1996;19:613.
137. Krongrad E. Prognosis for patients with congenital heart disease and post-operative intraventricular conduction defects. *Circulation* 1978;57:867-70.
138. Silka MJ, Rice MJ. Paradoxical embolism due to altered hemodynamic sequencing following transvenous pacing. *PACE Pacing Clin Electrophysiol* 1991;14:499-503.
139. Lau YR, Gillette PC, Buckles DS, Zeigler VL. Actuarial survival of transvenous pacing leads in a pediatric population. *PACE*

- Pacing Clin Electrophysiol 1993;16:1363-7.
140. Greenspan AM, Kay HR, Berger BC, Greenberg RM, Greenspan AJ, Gaughan MJ. Incidence of unwarranted implantation of permanent cardiac pacemakers in a large medical population. *N Engl J Med* 1988;318:158-63.
 141. McDonald K, McWilliams E, O'Keefe B, Maurer B. Functional assessment of patients treated with permanent dual chamber pacing as a primary treatment for hypertrophic cardiomyopathy. *Eur Heart J* 1988;9:893-8.
 142. Fananapazir L, Epstein ND, Curiel RV, Panza JA, Tripodi D, McAreavey D. Long-term results of dual-chamber (DDD) pacing in obstructive hypertrophic cardiomyopathy: evidence for progressive symptomatic and hemodynamic improvement and reduction of left ventricular hypertrophy. *Circulation* 1994;90:2731-42.
 143. Fananapazir L, Cannon RO, Tripodi D, Panza JA. Impact of dual-chamber permanent pacing in patients with obstructive hypertrophic cardiomyopathy with symptoms refractory to verapamil and beta-adrenergic blocker therapy. *Circulation* 1992;85:2149-61.
 144. Prinzen FW, Cheriex EC, Delhaas T, et al. Asymmetric thickness of the left ventricular wall resulting from asynchronous electric activation: a study in dogs with ventricular pacing and in patients with left bundle branch block. *Am Heart J* 1995;130:1045-53. Deleted during update.
 145. Nishimura RA, Hayes DL, Ilstrup DM, Holmes DR, Tajik AJ. Effect of dual-chamber pacing on systolic and diastolic function in patients with hypertrophic cardiomyopathy: acute Doppler echocardiographic and catheterization hemodynamic study. *J Am Coll Cardiol* 1996;27:421-30.
 146. Nishimura RA, Symanski JD, Hurrell DG, Trusty JM, Hayes DL, Tajik AJ. Dual-chamber pacing for cardiomyopathies: a 1996 clinical perspective. *Mayo Clin Proc* 1996;71:1077-87.
 147. Jeanrenaud X, Schlapper J, Fromer M, Aebischer N, Kappenberger L. Dual chamber pacing in hypertrophic obstructive cardiomyopathy: beneficial effect of atrioventricular junction ablation of optimal left ventricular capture and filling. *PACE Pacing Clin Electrophysiol* 1997;20:293-300. Deleted during update.
 148. Spirito P, McKenna WJ, Schultheiss HP. DDD pacing in obstructive HCM. *Circulation* 1995;92:1670-3. Deleted during update.
 149. Slade AK, Sadoul N, Shapiro L, et al. DDD pacing in hypertrophic cardiomyopathy: a multicentre clinical experience. *Heart* 1996;75:44-9. Deleted during update.
 150. Betocehi S, Losi MA, Piscione F, et al. Effects of dual chamber pacing in hypertrophic cardiomyopathy on left ventricular outflow tract obstruction and on diastolic function. *Am J Cardiol* 1996;77:498-502. Deleted during update.
 151. Cannon RO, Tripodi D, Dilsizian V, Panza JA, Fananapazir L. Results of permanent dual chamber pacing in symptomatic nonobstructive hypertrophic cardiomyopathy. *Am J Cardiol* 1994;73:571-6. Deleted during update.
 152. Kappenberger L, Linde C, Daubert C, et al. Pacing in hypertrophic obstructive cardiomyopathy (PIC): a randomized crossover study. *Eur Heart J* 1997;18:1249-56.
 153. Jeanrenaud X, Goy JJ, Kappenberger L. Effects of dual-chamber pacing in hypertrophic obstructive cardiomyopathy. *Lancet* 1992;339:1318-23.
 154. Nishimura RA, Trusty JM, Hayes DL, et al. Dual-chamber pacing for hypertrophic cardiomyopathy: a randomized, double-blind, crossover trial. *J Am Coll Cardiol* 1997;29:435-41.
 155. Rishi F, Hulse JE, Auld DO, et al. Effects of dual-chamber pacing for pediatric patients with hypertrophic obstructive cardiomyopathy. *J Am Coll Cardiol* 1997;29:734-40.
 156. Nishimura RA, Hayes DL, Holmes DR, Tajik AJ. Mechanism of hemodynamic improvement by dual-chamber pacing for severe left ventricular dysfunction: an acute Doppler and catheterization hemodynamic study. *J Am Coll Cardiol* 1995;25:281-8.
 157. Hochleitner M, Hortnagl H, Fridrich L, Gschnitzer F. Long-term efficacy of physiologic dual-chamber pacing in the treatment of end-stage idiopathic dilated cardiomyopathy. *Am J Cardiol* 1992;70:1320-5.
 158. Auricchio A, Sommariva L, Salo RW, Scafuri A, Chiariello L. Improvement of cardiac function in patients with severe congestive heart failure and coronary artery disease by dual chamber pacing with shortened AV delay. *PACE Pacing Clin Electrophysiol* 1993;16:2034-43.
 159. Linde C, Gadler F, Edner M, Nordlander R, Rosenqvist M, Ryden L. Results of atrioventricular synchronous pacing with optimized delay in patients with severe congestive heart failure. *Am J Cardiol* 1995;75:919-23.
 160. Gold MR, Feliciano Z, Gottlieb SS, Fisher ML. Dual chamber pacing with a short atrioventricular delay in congestive heart failure: a randomized study. *J Am Coll Cardiol* 1995;26:967-73. Deleted during update.
 161. Innes D, Leitch JW, Fletcher PJ. VDD pacing at short atrioventricular intervals does not improve cardiac output in patients with dilated heart failure. *PACE Pacing Clin Electrophysiol* 1994;17:959-65. Deleted during update.
 162. Giudici MC, Thornburg GA, Buck DL, et al. Comparison of right ventricular outflow tract and apical lead permanent pacing on cardiac output. *Am J Cardiol* 1997;79:209-12. Deleted during update.
 163. Saxon LA, Cahalan MK, Merriek SH, et al. Effects of multi-site ventricular pacing in dilated cardiomyopathy [abstract]. *PACE Pacing Clin Electrophysiol* 1996;19:641. Deleted during update.
 164. Cazauc S, Ritter P, Lazarus A, Gras D, Mujica J. Multisite pacing for congestive heart failure [abstract]. *PACE Pacing Clin Electrophysiol* 1996;19:568. Deleted during update.
 165. DiBiase A, Tse TM, Schnittger I, Wexler L, Stinson EB, Valentine HA. Frequency and mechanism of bradycardia in cardiac transplant recipients and need for pacemakers. *Am J Cardiol* 1991;67:1385-9.
 166. Heinz G, Hirschl M, Buxbaum P, Laufer G, Gasic S, Laczkovics A. Sinus node dysfunction after orthotopic cardiac transplantation: postoperative incidence and long-term implications. *PACE Pacing Clin Electrophysiol* 1992;15:731-7.
 167. Scott CD, Dark JH, McComb JM. Sinus node function after cardiac transplantation. *J Am Coll Cardiol* 1994;24:1334-41.
 168. Scott CD, Omar I, McComb JM, Dark JH, Bexton RS. Long-term pacing in heart transplant recipients is usually unnecessary. *PACE Pacing Clin Electrophysiol* 1991;14:1792-6.
 169. Montero JA, Anguita M, Concha M, et al. Pacing requirements after orthotopic heart transplantation: incidence and related factors. *J Heart Lung Transplant* 1992;11:799-802.
 170. Payne ME, Murray KD, Watson KM, et al. Permanent pacing in heart transplant recipients: underlying causes and long-term results. *J Heart Lung Transplant* 1991;10:738-42.
 171. Grinstead WC, Smart FW, Pratt CM, et al. Sudden death caused by bradycardia and asystole in a heart transplant patient with coronary arteriopathy. *J Heart Lung Transplant* 1991;10:931-6.
 172. Bertolet BD, Eagle DA, Conti JB, Mills RM Jr, Belardinelli L. Bradycardia after heart transplantation: reversal with theophylline. *J Am Coll Cardiol* 1996;28:396-9.
 173. Bernstein AD, Camm AJ, Fletcher RD, et al. The NASPE/BPEG generic pacemaker code for antibradyarrhythmia and adaptive-rate pacing and antitachyarrhythmia devices. *PACE Pacing Clin*

- Electrophysiol 1987;10:794-9.
174. Toivonen L, Lommi J. Dependence of atrial sensing function on posture in a single-lead atrial triggered ventricular (VDD) pacemaker. *PACE Pacing Clin Electrophysiol* 1996;19:309-13.
 175. Mond H, Stokes K, Helland J, et al. The porous titanium steroid eluting electrode: a double blind study assessing the stimulation threshold effects of steroid. *PACE Pacing Clin Electrophysiol* 1988;11:214-9.
 176. Crossley GH, Reynolds D, Kay GN, et al, for the Model 4068 Investigators. Treatment of patients with prior exit block using a novel steroid-eluting active fixation lead. *PACE Pacing Clin Electrophysiol* 1994;17:2042-6.
 177. Karpawich PP, Hakimi M, Arciniegas E, Cavitt DL. Improved chronic epicardial pacing in children: steroid contribution to porous platinized electrodes. *PACE Pacing Clin Electrophysiol* 1992;15:1151-7.
 178. ~~Mond HG, Helland JR. Engineering and clinical aspects of pacing leads. In: Ellenbogen KA, Kay GN, Wilkoff BL, editors. *Clinical Cardiac Pacing*. Philadelphia (PA): WB Saunders, 1995:69-90. Deleted during update.~~
 179. Ovshyshcher IE. Matching optimal pacemaker to patient: do we need a large scale clinical trial of pacemaker mode selection? *PACE Pacing Clin Electrophysiol* 1995;18:1845-52.
 180. Linde C. How to evaluate quality-of-life in pacemaker patients: problems and pitfalls. *PACE Pacing Clin Electrophysiol* 1996;19:391-7.
 181. Van Hemel NM. Pacemakers and quality of life. *Eur J Cardiac Pacing Electrophysiol* 1993;1:27-28.
 182. Adornato E, Bacca F, Polimeni RM. Ventricular single-chamber RR pacing in comparison to dual-chamber RR pacing: preliminary results of an Italian multicenter trial [abstract]. *PACE Pacing Clin Electrophysiol* 1993;16:1147.
 183. Barrington WW, Windle JR, Easley AA, Rundlett R, Eisenger G. Clinical comparison of acute single to dual chamber pacing in chronotropically incompetent patients with left ventricular dysfunction. *PACE Pacing Clin Electrophysiol* 1995;18:433-40.
 184. Brandt J, Schuller H. Pacing for sinus node disease: a therapeutic rationale. *Clin Cardiol* 1994;17:495-8.
 185. Lamas GA, Estes NM, Schneller S, Flaker GC. Does dual chamber or atrial pacing prevent atrial fibrillation? The need for a randomized controlled trial. *PACE Pacing Clin Electrophysiol* 1992;15:1109-13.
 186. Rosenqvist M, Obel IW. Atrial pacing and the risk for AV block: is there a time for change in attitude? *PACE Pacing Clin Electrophysiol* 1989;12:97-101.
 187. Brandt J, Anderson H, Fahraeus T, Schuller H. Natural history of sinus node disease treated with atrial pacing in 213 patients: implications for selection of stimulation mode. *J Am Coll Cardiol* 1992;20:633-9.
 188. Katritsis D, Camm AJ. AAI pacing mode: when is it indicated and how should it be achieved? *Clin Cardiol* 1993;16:339-43.
 189. Sutton R, Kenny RA. The natural history of sick sinus syndrome. *PACE Pacing Clin Electrophysiol* 1986;9:1110-4.
 190. Haywood GA, Ward J, Ward DE, Camm AJ. Atrioventricular Wenckebach point and progression to atrioventricular block in sinoatrial disease. *PACE Pacing Clin Electrophysiol* 1990;13:2054-8.
 191. Mabo P, Pouillot C, Kermarrec A, Lelong B, Lebreton H, Daubert C. Lack of physiological adaptation of the atrioventricular interval to heart rate in patients chronically paced in the AAIR mode. *PACE Pacing Clin Electrophysiol* 1991;14:2133-42.
 192. Alpert MA, Curtis JJ, Sanfelippo JF, et al. Comparative survival after permanent ventricular and dual chamber pacing for patients with chronic high degree atrioventricular block with and without preexistent congestive heart failure. *J Am Coll Cardiol* 1986;7:925-32.
 193. Bernstein AD, Parsonnet V. Survey of cardiac pacing and defibrillation in the United States in 1993. *Am J Cardiol* 1996;78:187-96.
 194. Channon KM, Hargreaves MR, Cripps TR, Gardner M, Ormerod OJ. DDD vs. VVI pacing in patients aged over 75 years with complete heart block: a double-blind crossover comparison. *QJM* 1994;87:245-51.
 195. Lamas GA, Pashos CL, Normand SL, McNeil B. Permanent pacemaker selection and subsequent survival in elderly Medicare pacemaker recipients. *Circulation* 1995;91:1063-9.
 196. Crossley GH, Gayle DD, Simmons TW, Haisty WK, Bailey JR, Davis-O'Brien K. Reprogramming pacemakers enhances longevity and is cost-effective. *Circulation* 1996;94(Suppl II):II-245-7.
 197. McGregor M. The reuse of cardiac pacemakers. *Can J Cardiol* 1992;8:697-701.
 198. Bernstein AD, Irwin ME, Parsonnet V, et al. Report of the NASPE Policy Conference on antibradycardia pacemaker follow-up: effectiveness, needs, and resources. *PACE Pacing Clin Electrophysiol* 1994;17:1714-29.
 199. Levine PA, Belott PH, Bilitch M, et al. Recommendations of the NASPE policy conference on pacemaker programmability and follow-up programs. *PACE Pacing Clin Electrophysiol* 1983;6:1222-3.
 200. Levine PA. Proceedings of the policy conference of the North American Society of Pacing and Electrophysiology on programmability and pacemaker follow-up programs. *Clin Prog Pacing Electrophysiol* 1984;2:145-91.
 201. Medicare Coverage Issues Manual. Baltimore (MD): US Dept of Health and Human Services, Health Care Financing Administration; 1990. HCFA publication 6 Thur Rev. 42.
 202. Mirowski M, Reid PR, Mower MM, et al. Termination of malignant ventricular arrhythmias with an implanted automatic defibrillator in human beings. *N Engl J Med* 1980;303:322-4.
 203. Lehmann MH, Steinman RT, Schuger CD, Jackson K. The automatic implantable cardioverter defibrillator as antiarrhythmic treatment modality of choice for survivors of cardiac arrest unrelated to acute myocardial infarction. *Am J Cardiol* 1988;62:803-5.
 204. Saksena S, Breithardt G, Dorian P, Greene HL, Madan N, Block M. Nonpharmacological therapy for malignant ventricular arrhythmias: implantable defibrillator trials. *Prog Cardiovasc Dis* 1996;38:429-44.
 205. Tchou 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 ventricular arrhythmias. *Ann Intern Med* 1988;109:529-34.
 206. Fogoros RN, Fiedler SB, Elson JJ. The automatic implantable cardioverter-defibrillator in drug-refractory ventricular tachyarrhythmias. *Ann Intern Med* 1987;107:635-41.
 207. 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.
 208. Fogoros RN, Elson JJ, Bonnet CA, Fiedler SB, Burkholder JA. Efficacy of the automatic implantable cardioverter-defibrillator in prolonging survival in patients with severe underlying cardiac disease. *J Am Coll Cardiol* 1990;16:381-6.
 209. Newman D, Sauve MJ, Herre J, et al. Survival after implantation of the cardioverter defibrillator. *Am J Cardiol* 1992;69:899-903.
 210. Powell AC, Fuchs T, Finkelstein DM, et al. Influence of implantable cardioverter-defibrillators on the long-term prognosis

- of survivors of out-of-hospital cardiac arrest. *Circulation* 1993;88:1083-92.
211. Crandall BG, Morris CD, Cutler JE, et al. Implantable cardioverter-defibrillator therapy in survivors of out-of-hospital sudden cardiac death without inducible arrhythmias. *J Am Coll Cardiol* 1993;21:1186-92.
212. Mehta D, Saksena S, Krol RB, et al. Device use patterns and clinical outcome of implantable cardioverter defibrillator patients with moderate and severe impairment of left ventricular function. *PACE Pacing Clin Electrophysiol* 1993;16:179-85.
213. Nisam S, Kaye SA, Mower MM, Hull M. AICD automatic cardioverter defibrillator clinical update: 14 years experience in over 34,000 patients. *PACE Pacing Clin Electrophysiol* 1995;18:142-7.
214. Porterfield JG, Porterfield LM, Smith BA, Bray L. Experience with three different third-generation cardioverter-defibrillators in patients with coronary artery disease or cardiomyopathy. *Am J Cardiol* 1993;72:301-4.
215. Axtell K, Tchou P, Akhtar M. Survival in patients with depressed left ventricular function treated by implantable cardioverter defibrillator. *PACE Pacing Clin Electrophysiol* 1991;14:291-6.
216. Saksena S, for the PCD Investigators. Clinical outcome of patients with malignant ventricular tachyarrhythmias and a multiprogrammable implantable cardioverter-defibrillator implanted with or without thoracotomy: an international multicenter study. *J Am Coll Cardiol* 1994;23:1521-30.
217. Zipes DP, Roberts D, for the Pacemaker-Cardioverter-Defibrillator Investigators. Results of the international study of the implantable pacemaker cardioverter-defibrillator: a comparison of epicardial and endocardial lead systems. *Circulation* 1995;92:59-65.
218. Bardy GH, Yee R, Jung W, for the Active Can Investigators. Multicenter experience with a pectoral unipolar implantable cardioverter-defibrillator. *J Am Coll Cardiol* 1996;28:400-10.
219. Wever EF, Hauer RN, Schrijvers G, et al. Cost-effectiveness of implantable defibrillator as first-choice therapy versus electrophysiologically guided, tiered strategy in postinfarct sudden death survivors: a randomized study. *Circulation* 1996;93:489-96.
220. Moss AJ, Hall WJ, Cannom DS, et al. Improved survival with an implanted defibrillator in patients with prior myocardial infarction, low ejection fraction and asymptomatic non-sustained ventricular tachycardia. *N Engl J Med* 1996;335:1933-40.
221. The 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.
222. Saksena S, Krol RB, Kaushik RR. Innovations in pulse generators and lead systems: balancing complexity with clinical benefit and long-term results. *Am Heart J* 1994;127:1010-21.
223. Timmis GC. The development of implantable cardioversion defibrillation systems: the clinical chronicle of defibrillation leads. *Am Heart J* 1994;127:1003-9.
224. Jung W, Manz M, Luderitz B. New technology for implantable cardioverter-defibrillators: capacitors, lead systems, shock waveforms. In: Saksena S, Luderitz B, editors. *Interventional Electrophysiology*. 2nd ed. Armonk (NY): Futura Publishing Co; 1996:257-81.
225. Grimm W, Flores BF, Marchlinski FE. Symptoms and electrocardiographically documented rhythm preceding spontaneous shocks in patients with implantable cardioverter-defibrillator. *Am J Cardiol* 1993;71:1415-8.
226. Song SL. Performance of implantable cardiac rhythm management devices. *PACE Pacing Clin Electrophysiol* 1994;17:692-708.
227. Hook BG, Marchlinski FE. Value of ventricular electrogram recordings in the diagnosis of arrhythmias precipitating electrical device shock therapy. *J Am Coll Cardiol* 1991;17:985-90.
228. Leitch JW, Gillis AM, Wyse DG, et al. Reduction in defibrillator shocks with an implantable device combining antitachycardia pacing and shock therapy. *J Am Coll Cardiol* 1991;18:145-51.
229. Luderitz B, Jung W, Deister A, Manz M. Quality of life in multiprogrammable ICD recipients. In: Saksena S, Luderitz B, editors. *Interventional Electrophysiology*. 2nd ed. Armonk (NY): Futura Publishing Co, 1996:305-13.
230. Flowers NC, Abildskov JA, Armstrong WF, et al, for the Electrophysiology/Electrocardiography Subcommittee, American College of Cardiology. ACC policy statement: recommended guidelines for training in adult clinical cardiac electrophysiology. *J Am Coll Cardiol* 1991;18:637-40.
231. Mirowski M, Reid PR, Winkle RA, et al. Mortality in patients with implanted automatic defibrillators. *Ann Intern Med* 1983;98:585-8.
232. Saksena S, Camm AJ. Implantable defibrillators for prevention of sudden death: technology at a medical and economic crossroad. *Circulation* 1992;85:2316-21. Deleted during update.
233. Mehta D, Saksena S, Krol RB. Survival of implantable cardioverter defibrillator recipients: role of left ventricular function and its relationship to device use. *Am Heart J* 1992;124:1608-14. Deleted during update.
234. Kim SG, Fisher JD, Choue CW, et al. Influence of left ventricular function on outcome of patients treated with implantable defibrillators. *Circulation* 1992;85:1304-10. Deleted during update.
235. Boeker D, Block M, Isbruch F, et al. Do patients with an implantable defibrillator live longer? *J Am Coll Cardiol* 1993; 21:1638-44. Deleted during update.
236. Boeker D, Block M, Isbruch F, et al. Benefits of treatment with implantable cardioverter defibrillators in patients with stable ventricular tachycardia without cardiac arrest. *Br Heart J* 1995; 73:158-63. Deleted during update.
237. Kim SG. Implantable defibrillator therapy: does it really prolong life? How can we prove it? *Am J Cardiol* 1993;71:1213-8.
238. Borggreffe M, Chen X, Martinez-Rubio A, et al. The role of implantable cardioverter defibrillators in dilated cardiomyopathy. *Am Heart J* 1994;127:1145-50.
239. Silka MJ, Kron J, Dunnigan A, Dick M II, for the Pediatric Electrophysiology Society. Sudden cardiac death and the use of implantable cardioverter-defibrillators in pediatric patients. *Circulation* 1993;87:800-7.
240. Mason JW, for the Electrophysiologic Study versus Electrocardiographic Monitoring Investigators. A comparison of seven antiarrhythmic drugs in patients with ventricular tachyarrhythmias. *N Engl J Med* 1993;329:452-8.
241. Teo KK, Yusuf S, Furburg CD. Effects of prophylactic antiarrhythmic drug therapy in acute myocardial infarction: an overview of results from randomized controlled trials. *JAMA* 1993;270:1589-95.
242. Mitchell LB, Duff HJ, Gillis AM, Ramadan D, Wyse DG. A randomized clinical trial of the noninvasive and invasive approaches to drug therapy for ventricular tachycardia: long-term follow-up of the Calgary trial. *Prog Cardiovasc Dis* 1996;38:377-84.
243. Cardiac Arrest in Seattle: Conventional versus Amiodarone Drug Evaluation (the CASCADE study). *Am J Cardiol* 1991;67:578-84.
244. Yusuf S, Peto R, Lewis J, Collins R, Sleight P. Beta blockade during and after myocardial infarction: an overview of the randomized trials. *Prog Cardiovasc Dis* 1985;27:335-71. Deleted during update.
245. A randomized trial of propranolol in patients with acute myocar-

- dial infarction, I: mortality results. *JAMA* 1982;247:1707-14. Deleted during update.
246. ~~Munsif AN, Saksena S. Efficacy of nadolol alone or in combination with a type IA antiarrhythmic drug in sustained ventricular tachycardia: a prospective study. *PACE Pacing Clin Electrophysiol* 1989;12:1816-26. Deleted during update.~~
247. Steinbeck G, Andresen D, Bach P, et al. A comparison of electrophysiologically guided antiarrhythmic drug therapy with beta-blocker therapy in patients with symptomatic, sustained ventricular tachyarrhythmias. *N Engl J Med* 1992;327:987-92.
248. Ceremuzynski L, Kleczar E, Krzeminska-Pakula M, et al. Effect of amiodarone on mortality after myocardial infarction: a double-blind, placebo-controlled, pilot study. *J Am Coll Cardiol* 1992;20:1056-62.
249. Burkart F, Pfisterer M, Kiowski W, Follath F, Burckhardt D. Effect of antiarrhythmic therapy on mortality in survivors of myocardial infarction with asymptomatic complex ventricular arrhythmias: Basel Antiarrhythmic Study of Infarct Survival (BASIS). *J Am Coll Cardiol* 1990;16:1711-8.
250. Julian DG, Camm AJ, Frangin G, et al, for the European Myocardial Infarct Amiodarone Trial Investigators. Randomized trial of effect of amiodarone on mortality in patients with left-ventricular dysfunction after recent myocardial infarction: EMIAT. *Lancet* 1997;349:667-74.
251. Cairns JA, Connolly SJ, Roberts R, Gent M, for the Canadian Amiodarone Myocardial Infarction Arrhythmia Trial Investigators. Randomised trial of outcome after myocardial infarction in patients with frequent or repetitive ventricular premature depolarisations: CAMIAT. *Lancet* 1997;349:675-82.
252. ~~Olson PJ, Woelfel A, Simpson RJ, Foster JR. Stratification of sudden death risk in patients receiving long term amiodarone treatment for sustained ventricular tachycardia or ventricular fibrillation. *Am J Cardiol* 1993;71:823-6. Deleted during update.~~
253. ~~Singh SN, Fletcher RD, Fisher SG, et al. Amiodarone in patients with congestive heart failure and asymptomatic ventricular arrhythmia. Survival Trial of Antiarrhythmic Therapy in Congestive Heart Failure. *N Engl J Med* 1995;333:77-82. Deleted during update.~~
254. ~~Doval HC, Nul DR, Grancelli HO, Perrone SV, Bortman GR, Curiel R. Randomised trial of low dose amiodarone in severe congestive heart failure. Grupo de Estudio de la Sobrevida en la Insuficiencia Cardiaca en Argentina (GESICA). *Lancet* 1994;20:489-90. Deleted during update.~~
255. Ferguson TB Jr. The future of arrhythmia surgery. *J Cardiovasc Electrophysiol* 1994;5:621-34.
256. Saksena S, Gielchinsky I, Tullo NG. Argon laser ablation of malignant ventricular tachycardia associated with coronary artery disease. *Am J Cardiol* 1989;64:1298-1304.
257. Svenson RH, Littmann L, Gallagher JJ, et al. Termination of ventricular tachycardia with epicardial laser photocoagulation: a clinical comparison with patients undergoing successful endocardial photocoagulation alone. *J Am Coll Cardiol* 1990;15:163-70.
258. Borggrefe M, Podczek A, Ostermeyer J, Breithardt G, The Surgical Ablation Registry. Long-term results of electrophysiologically guided antitachycardia surgery in ventricular tachyarrhythmias: a collaborative report on 665 patients. In: Breithardt G, Borggrefe M, Zipes DP, editors. *Nonpharmacological Therapy of Tachyarrhythmias*. Mount Kisco (NY): Futura Publishing Inc, 1987:109-32.
259. Stevenson WG, Khan H, Sager P, et al. Identification of reentry circuit sites during catheter mapping and radiofrequency ablation of ventricular tachycardia late after myocardial infarction. *Circulation* 1993;88:1647-70.
260. Morady F, Harvey M, Kalbfleisch SJ, el-Atassi R, Calkins H, Langberg JJ. Radiofrequency catheter ablation of ventricular tachycardia in patients with coronary artery disease. *Circulation* 1993;87:363-72.
261. Gonska BD, Cao K, Schaumann A, Dorszewski A, von zur Muhlen F, Kreuzer H. Catheter ablation of ventricular tachycardia in 136 patients with coronary artery disease: results and long-term follow-up. *J Am Coll Cardiol* 1994;24:1506-14.
262. Hindricks G, for the Multicentre European Radiofrequency Survey (MERFS) Investigators of the Working Group on Arrhythmias of the European Society of Cardiology. The Multicentre European Radiofrequency Survey (MERFS): complications of radiofrequency catheter ablation of arrhythmias. *Eur Heart J* 1993;14:1644-53.
263. Klein LS, Shih HT, Hackett FK, Zipes DP, Miles WM. Radiofrequency catheter ablation of ventricular tachycardia in patients without structural heart disease. *Circulation* 1992;85:1666-74.
264. Blanck Z, Dhala A, Deshpande S, Sra J, Jazayeri M, Akhtar M. Bundle branch reentrant ventricular tachycardia: cumulative experience in 48 patients. *J Cardiovasc Electrophysiol* 1993;4:253-62.
265. Leclercq JF, Chouty F, Cauchemez B, Leenhardt A, Coumel P, Slama R. Results of electrical fulguration in arrhythmogenic right ventricular disease. *Am J Cardiol* 1988;62:220-4.
266. Bocker D, Haverkamp W, Block M, Borggrefe M, Hammel D, Breithardt G. Comparison of D,L-sotalol and implantable defibrillators for treatment of sustained ventricular tachycardia or fibrillation in patients with coronary artery disease. *Circulation* 1996;94:151-7.
267. Wever EF, Hauer RN, van Capelle FL, et al. Randomized study of implantable defibrillator as first-choice therapy versus conventional strategy in postinfarct sudden death survivors. *Circulation* 1995;91:2195-2203.
268. Siebels J, Kuck KH. Implantable cardioverter defibrillator compared with antiarrhythmic drug treatment in cardiac arrest survivors (the Cardiac Arrest Study Hamburg). *Am Heart J* 1994; 127:1139-44.
269. Krol RB, Saksena S. Clinical trials of antiarrhythmic drugs in recipients of implantable cardioverter-defibrillators. In: Saksena S, Luderitz B, editors. *Interventional Electrophysiology*. 2nd ed. Armonk (NY): Futura Publishing Co, 1996:365-75.
270. Lehmann MH, Saksena S, for the NASPE Policy Conference Committee. Implantable cardioverter defibrillators in cardiovascular practice: report of the Policy Conference of the North American Society of Pacing and Electrophysiology. *PACE Pacing Clin Electrophysiol* 1991;14:969-79.
271. Steinbeck G, Dorwarth U, Matke S, et al. Hemodynamic deterioration during ICD implant: predictors of high-risk patients. *Am Heart J* 1994;127:1064-7.
272. Fuster V, Gersh BJ, Giuliani ER, Tajik AJ, Brandenburg RO, Frye RL. The natural history of idiopathic dilated cardiomyopathy. *Am J Cardiol* 1981;47:525-31.
273. Johnson RA, Palacios I. Dilated cardiomyopathies of the adult (first of two parts). *N Engl J Med* 1982;307:1051-8.
274. Follansbee WP, Michelson EL, Morganroth J. Nonsustained ventricular tachycardia in ambulatory patients: characteristics and association with sudden cardiac death. *Ann Intern Med* 1980;92:741-7.
275. Milner PG, DiMarco JP, Lerman BB. Electrophysiological evaluation of sustained ventricular tachyarrhythmias in idiopathic dilated cardiomyopathy. *PACE Pacing Clin Electrophysiol* 1988;11:562-8.
276. Groh WJ, Silka MJ, Oliver RP, Halperin BD, McAnulty JH, Kron

- J. Use of implantable cardioverter-defibrillators in the congenital long QT syndrome. *Am J Cardiol* 1996;78:703-6.
277. Garson AJ, Dick MI, Fournier A, et al. The long QT syndrome in children: an international study of 287 patients. *Circulation* 1993;87:1866-72.
278. Schwartz PJ. Idiopathic long QT syndrome: progress and questions. *Am Heart J* 1985;109:399-411.
279. Topaz O, Perin E, Cox M, Mallon SM, Castellanos A, Myerburg RJ. Young adult survivors of sudden cardiac arrest: analysis of invasive evaluation of 22 subjects. *Am Heart J* 1989;118:281-7.
280. Viskin S, Belhassen B. Idiopathic ventricular fibrillation. *Am Heart J* 1990;120:661-71.
281. Wellens HJ, Lemery R, Smeets JL, et al. Sudden arrhythmic death without overt heart disease. *Circulation* 1992;85(Suppl I):I-92-7.
282. McKenna WJ, Franklin RC, Nihoyannopoulos P, Robinson KC, Deanfield JE. Arrhythmia and prognosis in infants, children and adolescents with hypertrophic cardiomyopathy. *J Am Coll Cardiol* 1988;11:147-53.
283. Nicod P, Polikar R, Peterson KL. Hypertrophic cardiomyopathy and sudden death. *N Engl J Med* 1988;318:1255-7.
284. Fananapazir L, Epstein SE. Hemodynamic and electrophysiologic evaluation of patients with hypertrophic cardiomyopathy surviving cardiac arrest. *Am J Cardiol* 1991;67:280-7.
285. Hamilton RM, Dorian P, Gow RM, Williams WG. Five-year experience with implantable defibrillators in children. *Am J Cardiol* 1996;77:524-6.
286. Marcus FI, Fontaine GH, Guiraudon G, et al. Right ventricular dysplasia: a report of 24 adult cases. *Circulation* 1982;65:384-98.
287. Breithardt G, Wichter T, Haverkamp W, et al. Implantable cardioverter defibrillator therapy in patients with arrhythmogenic right ventricular cardiomyopathy, long QT syndrome, or no structural heart disease. *Am Heart J* 1994;127:1151-8.
288. Wichter T, Block M, Bocker D, Borggrefe G, Breithardt G. Cardioverter-defibrillator therapy in a high-risk subgroup of patients with arrhythmogenic right ventricular disease [abstract]. *J Am Coll Cardiol* 1993;21:127A.
289. Krol RB, Morady F, Flaker GC, et al. Electrophysiologic testing in patients with unexplained syncope: clinical and noninvasive predictors of outcome. *J Am Coll Cardiol* 1987;10:358-63.
290. DiMarco JP, Garan H, Harthorne JW, Ruskin JN. Intracardiac electrophysiologic techniques in recurrent syncope of unknown case. *Ann Intern Med* 1981;95:542-8.
291. Akhtar M, Shenasa M, Denker S, Gilbert CJ, Rizwi N. Role of cardiac electrophysiologic studies in patients with unexplained recurrent syncope. *PACE Pacing Clin Electrophysiol* 1983;6:192-201.
292. Akhtar M, Garan H, Lehmann MH, Troup PJ. Sudden cardiac death: management of high-risk patients. *Ann Intern Med* 1991;114:499-512.
293. Kron J, Silka MJ, Ohm OJ, et al. Preliminary experience with nonthoracotomy implantable cardioverter defibrillators in young patients. *PACE Pacing Clin Electrophysiol* 1994;17:26-31.
294. Driscoll DJ, Edwards WD. Sudden unexpected death in children and adolescents. *J Am Coll Cardiol* 1985;5(Suppl 6):118B-21B.
295. Walsh CK, Krongrad E. Terminal cardiac electrical activity in pediatric patients. *Am J Cardiol* 1983;51:557-61.
296. Eisenberg M, Bergner L, Hallstrom A. Epidemiology of cardiac arrest and resuscitation in children. *Ann Emerg Med* 1983;12:672-4.
297. Silka MJ, Kron J, Cutler JE, McNulty JH. Analysis of programmed stimulation methods in the evaluation of ventricular arrhythmias in patients 20 years old and younger. *Am J Cardiol* 1990;66:826-30.
298. Garson AJ. Ventricular arrhythmias after repair of congenital heart disease: who needs treatment? *Cardiol Young* 1991;1:177-81.
299. Keane JF, Driscoll DJ, Gersony WM, et al. Second natural history study of congenital heart defects: results of treatment of patients with aortic valvular stenosis. *Circulation* 1993;87(Suppl I):I-16-27.
300. Evans RW, Manninen DL, Dong FB, Frist WH, Kirklin JK. The medical and surgical determinants of heart transplantation outcomes: the results of a consensus survey in the United States. *J Heart Lung Transplant* 1993;12:42-5.
301. Maron BJ, Fananapazir L. Sudden cardiac death in hypertrophic cardiomyopathy. *Circulation* 1992;85(Suppl I):I-57-63.
302. Kaminer SJ, Pickoff AS, Dunnigan A, Sterba R, Wolff GS. Cardiomyopathy and the use of implanted cardio-defibrillators in children. *PACE Pacing Clin Electrophysiol* 1990;13:593-7.
303. Bigger JT, Fleiss JL, Kleiger R, Miller JP, Rolnitzky LM. The relationships among ventricular arrhythmias, left ventricular dysfunction, and mortality in the 2 years after myocardial infarction. *Circulation* 1984;69:250-8.
304. Buxton AE, Marchlinski FE, Waxman HL, Flores BT, Cassidy DM, Josephson ME. Prognostic factors in nonsustained ventricular tachycardia. *Am J Cardiol* 1984;53:1275-9.
305. Echt DS, Liebson PR, Mitchell LB, et al. Mortality and morbidity in patients receiving encainide, flecainide, or placebo: the Cardiac Arrhythmia Suppression Trial. *N Engl J Med* 1991;324:781-8.
306. Sim I, McDonald KM, Lavori PW, Norbutas CM, Hlatky MA. Quantitative overview of randomized trials of amiodarone to prevent sudden cardiac death. *Circulation* 1997;96:2823-9.
307. Wilber DJ, Olshansky B, Moran JF, Scanlon PJ. Electrophysiological testing and nonsustained ventricular tachycardia: use and limitations in patients with coronary artery disease and impaired ventricular function. *Circulation* 1990;82:350-8.
308. Saksena S, Moss AJ, Gorgeberidze I, et al. Factors associated with shock delivery in the Multicenter Automatic Defibrillator Implantation Trial (MADIT) [abstract]. *J Am Coll Cardiol* 1997;29(Suppl A):79A.
309. Bigger JT Jr, for the CABG-Patch Investigators. 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.
310. Grimm M, Wieselthaler G, Avanesian R, et al. The impact of implantable cardioverter-defibrillators on mortality among patients on the waiting list for heart transplantation. *J Thorac Cardiovasc Surg* 1995;110:532-9.
311. Sweeney MO, Ruskin JN, Garan H, et al. Influence of the implantable cardioverter/defibrillator on sudden death and total mortality in patients evaluated for cardiac transplantation. *Circulation* 1995;92:3273-81.
312. Bigger JT Jr. Why patients with congestive heart failure die: arrhythmias and sudden cardiac death. *Circulation* 1987;75(5 Pt 2):IV-28-35.
313. Defibrilat Study Group. Actuarial risk of sudden death while awaiting cardiac transplantation in patients with atherosclerotic heart disease. *Am J Cardiol* 1991;68:545-6.
314. Bigger JT Jr. Prophylactic use of implantable cardioverter defibrillators: medical, technical, economic considerations. *Pacing Clin Electrophysiol* 1991;14:376-80.
315. Stevenson WG, Stevenson LW, Middlekauff HR, Saxon LA. Sudden death prevention in patients with advanced ventricular dysfunction. *Circulation* 1993;88:2953-61.
316. Vlay SC, Olson LC, Fricchione GL, Friedman R. Anxiety and anger in patients with ventricular tachyarrhythmias: responses

- after automatic internal cardioverter defibrillator implantation. *PACE Pacing Clin Electrophysiol* 1989;12:366-73.
317. Luderitz B, Jung W, Deister A, Marneros A, Manz M. Patient acceptance of the implantable cardioverter defibrillator in ventricular tachyarrhythmias. *PACE Pacing Clin Electrophysiol* 1993;16:1815-21.
 318. O'Donoghue S, Platia EV, Brooks-Robinson S, Mispireta L. Automatic implantable cardioverter-defibrillator: is early implantation cost-effective? *J Am Coll Cardiol* 1990;16:1258-63.
 319. Kuppermann M, Luce BR, McGovern B, Podrid PJ, Bigger JT, Ruskin JN. An analysis of the cost effectiveness of the implantable defibrillator. *Circulation* 1990;81:91-100.
 320. Saksena S, Madan N, Lewis C. Implanted cardioverter-defibrillators are preferable to drugs as primary therapy in sustained ventricular tachyarrhythmias. *Prog Cardiovasc Dis* 1996;38:445-54.
 321. Kupersmith J, Hogan A, Guerrero P, et al. Evaluating and improving the cost-effectiveness of the implantable cardioverter-defibrillator. *Am Heart J* 1995;130:507-15.
 322. Larson GC, Manolis AS, Sonnenberg FA, et al. Cost-effectiveness of the implantable cardioverter-defibrillator: effect of improved battery life and comparison with amiodarone therapy. *J Am Coll Cardiol* 1992;19:1323-34.
 323. Owens DK, Sanders GD, 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.
 324. ~~Mushlin AL. Cost effectiveness of ICDs versus conventional therapy in the Multicenter Automatic Defibrillator Implantation Trial (MADIT). Presented at the North American Society of Pacing and Electrophysiology 18th Annual Scientific Sessions, May 1997; New Orleans, La. Deleted during update.~~
 325. Wood MA. Lessons learned from data logging in a multicenter clinical trial using a late-generation implantable cardioverter-defibrillator. *J Am Coll Cardiol* 1994;24:1692-9.
 326. Pinski SL, Fahy GJ. The proarrhythmic potential of implantable cardioverter-defibrillators. *Circulation* 1995;92:1651-64.
 327. Raitt MH, Dolack GL, Kudenchuk PJ, et al. Ventricular arrhythmias detected after transvenous defibrillator implantation in patients with a clinical history of only ventricular fibrillation. *Circulation* 1995;91:1996-2001.
 328. Scheinman MM, Akhtar M, Brugada P, et al. Teaching objectives for fellowship programs in clinical electrophysiology. *J Am Coll Cardiol* 1988;12:255-61.
 329. Faust M, Fraser J, Schurig L, et al. Educational guidelines for the clinically associated professional in cardiac pacing and electrophysiology. *PACE Pacing Clin Electrophysiol* 1990;13:1448-55.
 330. Fetter JG, Stanton MS, Benditt DG, Trusty J, Collins J. Transtelephonic monitoring and transmission of stored arrhythmia detection and therapy data from an implantable cardioverter defibrillator. *PACE Pacing Clin Electrophysiol* 1995;18:1531-9.
 331. 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.
 332. Jung W, Luderitz B. European policy on driving for patients with implantable cardioverter-defibrillators. *PACE Pacing Clin Electrophysiol* 1995;19:981-4.
 333. Maron BJ, Poliac LC, Kaplan JA, Mueller FO. Blunt impact to the chest leading to sudden death from cardiac arrest during sports activities. *N Engl J Med* 1995;333:337-42.
 334. Love CJ, Wilkoff BL, Byrd CL, et al, for the North American Society of Pacing and Electrophysiology Lead Extraction Conference Faculty. Recommendations for extraction of chronically implanted transvenous pacing and defibrillator leads: indications, facilities, training. *Pacing Clin Electrophysiol* 2000;23:544-51.
 335. Ryan TJ, Antman EM, Brooks NH, et al. 1999 update: ACC/AHA guidelines for the management of patients with acute myocardial infarction: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on Management of Acute Myocardial Infarction). *J Am Coll Cardiol* 1999;34:890-911.
 336. Beller GA, Bonow RO, Fuster V. ACC revised recommendations for training in adult cardiovascular medicine: Core Cardiology Training II (COCATS 2). (Revision of the 1995 COCATS training statement.) *J Am Coll Cardiol* 2002;39:1242-6.
 337. Gregoratos G, Cheitlin MD, Conill A, et al. ACC/AHA guidelines for implantation of cardiac pacemakers and antiarrhythmia devices: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on Pacemaker Implantation). *J Am Coll Cardiol* 1998;31:1175-209.
 338. Gregoratos G, Cheitlin MD, Conill A, et al. ACC/AHA guidelines for implantation of cardiac pacemakers and antiarrhythmia devices: executive summary—a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on Pacemaker Implantation). *Circulation* 1998;97:1325-35.
 339. Hunt SA, Baker DW, Chin MH, et al. ACC/AHA guidelines for the evaluation and management of chronic heart failure in the adult: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Revise the 1995 Guidelines for the Evaluation and Management of Heart Failure), developed in collaboration with the International Society for Heart and Lung Transplantation, endorsed by the Heart Failure Society of America. *J Am Coll Cardiol* 2001;38:2101-13.
 340. Zipes DP. Second-degree atrioventricular block. *Circulation* 1979;60:465-72.
 341. Narula OS, Samet P. Wenckebach and Mobitz type II A-V block due to block within the His bundle and bundle branches. *Circulation* 1970;41:947-65.
 342. Narula OS, Scherlag BJ, Samet P, Javier RP. Atrioventricular block: localization and classification by His bundle recordings. *Am J Med* 1971;50:146-65.
 343. Chokshi SK, Sarmiento J, Nazari J, Mattioni T, Zheutlin T, Kehoe R. Exercise-provoked distal atrioventricular block. *Am J Cardiol* 1990;66:114-6.
 344. Barold SS, Falkoff MD, Ong LS, Vaughn MJ, Heinle RA. Atrioventricular block: new insights. In: Barold SS, Mugica J, editors. *New Perspectives in Cardiac Pacing*. Mount Kisco (NY): Futura Publishing Co, 1991:23-52.
 345. Grimm W, Koehler U, Fus E, et al. Outcome of patients with sleep apnea-associated severe bradyarrhythmias after continuous positive airway pressure therapy. *Am J Cardiol* 2000;86:688-92, A9.
 346. Kim MH, Deeb GM, Eagle KA, et al. Complete atrioventricular block after valvular heart surgery and the timing of pacemaker implantation. *Am J Cardiol* 2001;87:649-51, A10.
 347. Fisch GR, Zipes DP, Fisch C. Bundle branch block and sudden death. *Prog Cardiovasc Dis* 1980;23:187-224.
 348. Dhingra RC, Denes P, Wu D, et al. Syncope in patients with chronic bifascicular block: significance, causative mechanisms, and clinical implications. *Ann Intern Med* 1974;81:302-6.
 349. Josephson ME. *Clinical Cardiac Electrophysiology: Techniques*

- and Interpretations. 2nd ed. Philadelphia (PA): Lea & Febiger, 1993:145.
350. Harthorne JW, Barold SS. Atherosclerosis, the conduction system, and cardiac pacing. In: Fuster V, Ross R, Topol EJ, editors. *Atherosclerosis and Coronary Artery Disease*. Philadelphia (PA): Lippincott-Raven Publishers, 1996:1013-30.
351. Fisher JD. Role of electrophysiologic testing in the diagnosis and treatment of patients with known and suspected bradycardias and tachycardias. *Prog Cardiovasc Dis* 1981;24:25-90.
352. Reiffel JA, Kuehnert MJ. Electrophysiological testing of sinus node function: diagnostic and prognostic application-including updated information from sinus node electrograms. *Pacing Clin Electrophysiol* 1994;17:349-65.
353. Lamas GA, Lee KL, Sweeney MO, et al. Ventricular pacing or dual-chamber pacing for sinus-node dysfunction. *N Engl J Med* 2002;346:1854-62.
354. Saksena S, Delfaut P, Prakash A, Kaushik RR, Krol RB. Multisite electrode pacing for prevention of atrial fibrillation. *J Cardiovasc Electrophysiol* 1998;9:S155-62.
355. Lamas GA, Lee K, Sweeney M, et al. The Mode Selection Trial (MOST) in sinus node dysfunction: design, rationale, and baseline characteristics of the first 1000 patients. *Am Heart J* 2000;140:541-51.
356. Bexton RS, Davies A, Kenny RA. The rate-drop response in carotid sinus syndrome: the Newcastle experience. *Pacing Clin Electrophysiol* 1997;20:840.
357. Kenny RA, Richardson DA, Steen N, Bexton RS, Shaw FE, Bond J. Carotid sinus syndrome: a modifiable risk factor for nonaccidental falls in older adults (SAFE PACE). *J Am Coll Cardiol* 2001;38:1491-6.
358. Connolly SJ, Sheldon R, Roberts RS, Gent M. The North American Vasovagal Pacemaker Study (VPS): a randomized trial of permanent cardiac pacing for the prevention of vasovagal syncope. *J Am Coll Cardiol* 1999;33:16-20.
359. Sutton R, Brignole M, Menozzi C, et al, for the Vasovagal Syncope International Study (VASIS) Investigators. Dual-chamber pacing in the treatment of neurally mediated tilt-positive cardioinhibitory syncope: pacemaker versus no therapy: a multicenter randomized study. *Circulation* 2000;102:294-9.
360. Ammirati F, Colivicchi F, Santini M. Permanent cardiac pacing versus medical treatment for the prevention of recurrent vasovagal syncope: a multicenter, randomized, controlled trial. *Circulation* 2001;104:52-7.
361. Benditt DG, Petersen M, Lurie KG, Grubb BP, Sutton R. Cardiac pacing for prevention of recurrent vasovagal syncope. *Ann Intern Med* 1995;122:204-9.
362. Sheldon R, Koshman ML, Wilson W, Kieser T, Rose S. Effect of dual-chamber pacing with automatic rate-drop sensing on recurrent neurally mediated syncope. *Am J Cardiol* 1998;81:158-62.
363. Moak JP, Barron KS, Hougen TJ, et al. Congenital heart block: development of late-onset cardiomyopathy, a previously underappreciated sequela. *J Am Coll Cardiol* 2001;37:238-42.
364. Dorostkar PC, Eldar M, Belhassen B, Scheinman MM. Long-term follow-up of patients with long-QT syndrome treated with beta-blockers and continuous pacing. *Circulation* 1999;100:2431-6.
365. Lillehei CW, Sellers RD, Bonnanbeau RC, Eliot RS. Chronic postsurgical complete heart block with particular reference to prognosis, management, and a new P-wave pacemaker. *J Thorac Cardiovasc Surg* 1963;46:436-56.
366. Kertesz N, McQuinn T, Collins E, Friedman R. Surgical atrioventricular block in 888 congenital heart operations: new implications for early implantation of a permanent pacemaker [abstract]. *Pacing Clin Electrophysiol* 1996;19:613.
367. Maron BJ, Nishimura RA, McKenna WJ, Rakowski H, Josephson ME, Kieval RS. Assessment of permanent dual-chamber pacing as a treatment for drug-refractory symptomatic patients with obstructive hypertrophic cardiomyopathy: a randomized, double-blind, crossover study (M-PATHY). *Circulation* 1999;99:2927-33.
368. Kass DA, Chen CH, Curry C, et al. Improved left ventricular mechanics from acute VDD pacing in patients with dilated cardiomyopathy and ventricular conduction delay. *Circulation* 1999;99:1567-73.
369. Symanski JD, Nishimura RA. The use of pacemakers in the treatment of cardiomyopathies. *Curr Probl Cardiol* 1996;21:385-443.
370. Hayes DL, Barold SS, Camm AJ, Goldschlager NF. Evolving indications for permanent cardiac pacing: an appraisal of the 1998 American College of Cardiology/American Heart Association Guidelines. *Am J Cardiol* 1998;82:1082-6, A6.
371. Erwin JP, Nishimura RA, Lloyd MA, Tajik AJ. Dual chamber pacing for patients with hypertrophic obstructive cardiomyopathy: a clinical perspective in 2000. *Mayo Clin Proc* 2000;75:173-80.
372. Ommen SR, Nishimura RA, Squires RW, Schaff HV, Danielson GK, Tajik AJ. Comparison of dual-chamber pacing versus septal myectomy for the treatment of patients with hypertrophic obstructive cardiomyopathy: a comparison of objective hemodynamic and exercise end points. *J Am Coll Cardiol* 1999;34:191-6.
373. Doval HC, Nul DR, Grancelli HO, Perrone SV, Bortman GR, Curiel R. Randomised trial of low-dose amiodarone in severe congestive heart failure: Grupo de Estudio de la Sobrevida en la Insuficiencia Cardiaca en Argentina (GESICA). *Lancet* 1994;344:493-8.
374. Singh SN, Fletcher RD, Fisher SG, et al. Amiodarone in patients with congestive heart failure and asymptomatic ventricular arrhythmia: Survival Trial of Antiarrhythmic Therapy in Congestive Heart Failure. *N Engl J Med* 1995;333:77-82.
375. Naccarelli GV, Luck JC, Wolbrette DL, et al. Pacing therapy for congestive heart failure: is it ready for prime time? *Curr Opin Cardiol* 1999;14:1-3.
376. Foster AH, Gold MR, McLaughlin JS. Acute hemodynamic effects of atrio-biventricular pacing in humans. *Ann Thorac Surg* 1995;59:294-300.
377. Blanc JJ, Etienne Y, Gilard M, et al. Evaluation of different ventricular pacing sites in patients with severe heart failure: results of an acute hemodynamic study. *Circulation* 1997;96:3273-7.
378. Leclercq C, Cazeau S, Le Breton H, et al. Acute hemodynamic effects of biventricular DDD pacing in patients with end-stage heart failure. *J Am Coll Cardiol* 1998;32:1825-31.
379. Auricchio A, Klein H, Tockman B, et al. Transvenous biventricular pacing for heart failure: can the obstacles be overcome? *Am J Cardiol* 1999;83:136D-42D.
380. Auricchio A, Stellbrink C, Block M, et al, for the Pacing Therapies for Congestive Heart Failure Study Group and the Guidant Congestive Heart Failure Research Group. Effect of pacing chamber and atrioventricular delay on acute systolic function of paced patients with congestive heart failure. *Circulation* 1999;99:2993-3001.
381. Cazeau S, Leclercq C, Lavergne T, et al. Effects of multisite biventricular pacing in patients with heart failure and intraventricular conduction delay. *N Engl J Med* 2001;344:873-80.
382. Stellbrink C, Breithardt OA, Franke A, et al. Impact of cardiac resynchronization therapy using hemodynamically optimized pacing on left ventricular remodeling in patients with congestive heart failure and ventricular conduction disturbances. *J Am Coll Cardiol* 2001;38:1957-65.
383. Abraham WT, Fisher WG, Smith AL, et al. Cardiac resynchro-

- nization in chronic heart failure. *N Engl J Med* 2002;346:1845-53.
384. Butter C, Auricchio A, Stellbrink C, et al. Effect of resynchronization therapy stimulation site on the systolic function of heart failure patients. *Circulation* 2001;104:3026-9.
385. Leclercq C, Cazeau S, Ritter P, et al. A pilot experience with permanent biventricular pacing to treat advanced heart failure. *Am Heart J* 2000;140:862-70.
386. Stellbrink C, Auricchio A, Diem B, et al. Potential benefit of biventricular pacing in patients with congestive heart failure and ventricular tachyarrhythmia. *Am J Cardiol* 1999;83:143D-50D.
387. Saxon LA, Boehmer JP, Hummel J, et al, for the VIGOR CHF and VENTAK CHF Investigators. Biventricular pacing in patients with congestive heart failure: two prospective randomized trials. *Am J Cardiol* 1999;83:120D-3D.
388. Walker S, Levy TM, Rex S, et al. Usefulness of suppression of ventricular arrhythmia by biventricular pacing in severe congestive cardiac failure. *Am J Cardiol* 2000;86:231-3.
389. Higgins SL, Yong P, Sheck D, et al, for the Ventak CHF Investigators. Biventricular pacing diminishes the need for implantable cardioverter defibrillator therapy. *J Am Coll Cardiol* 2000;36:824-7.
390. 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.
391. Leung SK, Lau CP, Tang MO. Cardiac output is a sensitive indicator of difference in exercise performance between single and dual sensor pacemakers. *Pacing Clin Electrophysiol* 1998;21:35-41.
392. Alt E, Combs W, Willhaus R, et al. A comparative study of activity and dual sensor: activity and minute ventilation pacing responses to ascending and descending stairs. *Pacing Clin Electrophysiol* 1998;21:1862-8.
393. Sheldon R. Role of pacing in the treatment of vasovagal syncope. *Am J Cardiol* 1999;84:26Q-32Q.
394. Mond. Engineering and clinical aspects of pacing leads. In: Ellenbogen K, Kay GN, Wilkoff BL, editors. *Clinical Cardiac Pacing and Defibrillation*. Philadelphia (PA): WB Saunders, 2000.
395. Barlow, et al. Survival, quality of life, and clinical aspects of pacing leads. In: Ellenbogen K, Kay GN, Wilkoff BL, editors. *Clinical Cardiac Pacing and Defibrillation*. Philadelphia (PA): WB Saunders, 2000.
396. Tang CY, Kerr CR, Connolly SJ. Clinical trials of pacing mode selection. *Cardiol Clin* 2000;18:1-23, vii.
397. Lamas GA, Orav EJ, Stambler BS, et al, for the Pacemaker Selection in the Elderly Investigators. Quality of life and clinical outcomes in elderly patients treated with ventricular pacing as compared with dual-chamber pacing. *N Engl J Med* 1998;338:1097-104.
398. Connolly SJ, Kerr CR, Gent M, et al, for the Canadian Trial of Physiologic Pacing Investigators. Effects of physiologic pacing versus ventricular pacing on the risk of stroke and death due to cardiovascular causes. *N Engl J Med* 2000;342:1385-91.
399. Gillis AM, Connolly SJ, Lacombe P, et al, for the Atrial Pacing Peri-Ablation for Paroxysmal Atrial Fibrillation (PA (3)) Study Investigators. Randomized crossover comparison of DDDR versus VDD pacing after atrioventricular junction ablation for prevention of atrial fibrillation. *Circulation* 2000;102:736-41.
400. Skanes AC, Krahn AD, Yee R, et al, for the CTOPP Investigators. Progression to chronic atrial fibrillation after pacing: the Canadian Trial of Physiologic Pacing. *J Am Coll Cardiol* 2001;38:167-72.
401. Yamamura KH, Kloosterman EM, Alba J, et al. Analysis of charges and complications of permanent pacemaker implantation in the cardiac catheterization laboratory versus the operating room. *Pacing Clin Electrophysiol* 1999;22:1820-4.
402. Linde CL, Bocray A, Jonsson H, Rosenqvist M, Radegran K, Ryden L. Re-used pacemakers: as safe as new? A retrospective case-control study [published erratum appears in *Eur Heart J* 1998;19:527]. *Eur Heart J* 1998;19:154-7.
403. Fraser JD, Gillis AM, Irwin ME, Nishimura S, Tyers GF, Philippon F. Guidelines for pacemaker follow-up in Canada: a consensus statement of the Canadian Working Group on Cardiac Pacing. *Can J Cardiol* 2000;16:355-76.
404. Schoenfeld MH, Markowitz HT. Device follow-up in the age of automaticity [editorial]. *Pacing Clin Electrophysiol* 2000;23:803-6.
405. Buxton AE, Lee KL, Fisher JD, Josephson ME, Prystowsky EN, Hafley G, for the Multicenter Unsustained Tachycardia Trial Investigators. A randomized study of the prevention of sudden death in patients with coronary artery disease. *N Engl J Med* 1999;341:1882-90.
406. 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.
407. 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.
408. Wellens HJ, Lau CP, Luderitz B, et al. Atrioverter: an implantable device for the treatment of atrial fibrillation. *Circulation* 1998;98:1651-6.
409. Swerdlow CD, Schls W, Dijkman B, et al, for the Worldwide Jewel AF Investigators. Detection of atrial fibrillation and flutter by a dual-chamber implantable cardioverter-defibrillator. *Circulation* 2000;101:878-85.
410. 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.
411. Curtis AB, Langberg JJ, Tracy CM. Clinical competency statement. implantation and follow-up of cardioverter-defibrillators. *J Cardiovasc Electrophysiol* 2001;12:280-4.
412. Domanski MJ, Sakseena S, Epstein AE, et al, for the AVID Investigators (Antiarrhythmics Versus Implantable Defibrillators). 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.
413. Moss AJ. Implantable cardioverter defibrillator therapy: the sickest patients benefit the most. *Circulation* 2000;101:1638-40.
414. Anderson JL, Hallstrom AP, Epstein AE, et al, for the AVID Investigators. Design and results of the Antiarrhythmics Vs Implantable Defibrillators (AVID) registry. *Circulation* 1999;99:1692-9.
415. Sim I, McDonald KM, Lavori PW, Norbutas CM, Hlatky MA. Quantitative overview of randomized trials of amiodarone to prevent sudden cardiac death. *Circulation* 1997;96:2823-9.
416. Amiodarone Trials Meta-Analysis Investigators. Effect of prophylactic amiodarone on mortality after acute myocardial infarction and in congestive heart failure: meta-analysis of individual data from 6500 patients in randomised trials. *Lancet* 1997;350:1417-24.
417. Stevenson WG, Friedman PL, Kocovic D, Sager PT, Saxon LA, Pavri B. Radiofrequency catheter ablation of ventricular tachycar-

- dia after myocardial infarction. *Circulation* 1998;98:308-14.
418. Strickberger SA, Man KC, Daoud EG, et al. A prospective evaluation of catheter ablation of ventricular tachycardia as adjuvant therapy in patients with coronary artery disease and an implantable cardioverter-defibrillator. *Circulation* 1997;96:1525-31.
419. Marchlinski FE, Callans DJ, Gottlieb CD, Zado E. Linear ablation lesions for control of unmappable ventricular tachycardia in patients with ischemic and nonischemic cardiomyopathy. *Circulation* 2000;101:1288-96.
420. Schilling RJ, Peters NS, Davies DW. Feasibility of a noncontact catheter for endocardial mapping of human ventricular tachycardia. *Circulation* 1999;99:2543-52.
421. Connolly SJ, Hallstrom AP, Cappato R, et al. Meta-analysis of the implantable cardioverter defibrillator secondary prevention trials: AVID, CASH and CIDS studies: Antiarrhythmics vs Implantable Defibrillator study, Cardiac Arrest Study Hamburg, Canadian Implantable Defibrillator Study. *Eur Heart J* 2000;21:2071-8.
422. Moss AJ. Clinical management of patients with the long QT syndrome: drugs, devices, and gene-specific therapy. *Pacing Clin Electrophysiol* 1997;20:2058-60.
423. Brugada P, Brugada R, Brugada J, Geelen P. Use of the prophylactic implantable cardioverter defibrillator for patients with normal hearts. *Am J Cardiol* 1999;83:98D-100D.
424. Hermida JS, Lemoine JL, Aoun FB, Jarry G, Rey JL, Quiet JC. Prevalence of the Brugada syndrome in an apparently healthy population. *Am J Cardiol* 2000;86:91-4.
425. Spirito P, Bellone P, Harris KM, Bernabo P, Bruzzi P, Maron BJ. Magnitude of left ventricular hypertrophy and risk of sudden death in hypertrophic cardiomyopathy. *N Engl J Med* 2000;342:1778-85.
426. Maron BJ, Shen WK, 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.
427. Link MS, Costeas XF, Griffith JL, Colburn CD, Estes NA, Wang PJ. High incidence of appropriate implantable cardioverter-defibrillator therapy in patients with syncope of unknown etiology and inducible ventricular arrhythmias. *J Am Coll Cardiol* 1997;29:370-5.
428. Wilson WR, Greer GE, Grubb BP. Implantable cardioverter-defibrillators in children: a single-institutional experience. *Ann Thorac Surg* 1998;65:775-8.
429. 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.
430. Bigger JT. Expanding indications for implantable cardiac defibrillators. *N Engl J Med* 2002;346:931-3.
431. 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-7D.
432. 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.
433. Knight BP, Goyal R, Pelosi F, et al. Outcome of patients with non-ischemic dilated cardiomyopathy and unexplained syncope treated with an implantable defibrillator. *J Am Coll Cardiol* 1999;33:1964-70.
434. Mushlin AI, Hall WJ, Zwanziger J, et al. The cost-effectiveness of automatic implantable cardiac defibrillators: results from MADIT: Multicenter Automatic Defibrillator Implantation Trial. *Circulation* 1998;97:2129-35.
435. O'Brien BJ, Connolly SJ, Goeree R, et al. Cost-effectiveness of the implantable cardioverter-defibrillator: results from the Canadian Implantable Defibrillator Study (CIDS). *Circulation* 2001;103:1416-21.
436. Larsen G, Hallstrom A, McAnulty J, et al. Cost-effectiveness of the implantable cardioverter-defibrillator versus antiarrhythmic drugs in survivors of serious ventricular tachyarrhythmias: results of the Antiarrhythmics Versus Implantable Defibrillators (AVID) economic analysis substudy. *Circulation* 2002;105:2049-57.
437. Capucci A, Villani GQ, Groppi F, Aschieri D, Hull M, Kuehl M. Comparison of therapy detection times between implantable cardioverter defibrillators with standard dual- and single-chamber pacing. *J Intervent Card Electrophysiol* 1999;3:329-33.
438. Kuhlkamp V, Mortensen P, Kirstein P, et al, for the Acute Ventak AV Investigator Group. A randomized controlled clinical trial comparing ventricular fibrillation detection time between two transvenous defibrillator models. *Pacing Clin Electrophysiol* 1999;22:990-8.
439. Trappe HJ, Achtelik M, Pfitzner P, Voigt B, Weismuller P. Single-chamber versus dual-chamber implantable cardioverter defibrillators: indications and clinical results. *Am J Cardiol* 1999;83:8D-16D.
440. Higgins SL, Pak JP, Barone J, et al. The first year experience with the dual chamber ICD. *Pacing Clin Electrophysiol* 2000;23:18-25.
441. Greenberg RM, Degeratu FT. Use of atrial and ventricular electrograms from a dual chamber implantable cardioverter defibrillator to elucidate a complex dysrhythmia. *Pacing Clin Electrophysiol* 1998;21:2002-4.
442. Kuhlkamp V, Dornberger V, Mewis C, Suchalla R, Bosch RF, 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.
443. Priori SG, Napolitano C, Gasparini M, et al. Natural history of Brugada syndrome: insights for risk stratification and management. *Circulation* 2002;105:1342-7.
444. Brugada J, Brugada R, Brugada P. Pharmacological and device approach to therapy of inherited cardiac diseases associated with cardiac arrhythmias and sudden death. *J Electrocardiol* 2000;33(Suppl):41-7.
445. Michaud GF, Sticherling C, Tada H, et al. Relationship between serum potassium concentration and risk of recurrent ventricular tachycardia or ventricular fibrillation. *J Cardiovasc Electrophysiol* 2001;12:1109-12.
446. Michaud GF, Strickberger SA. Should an abnormal serum potassium concentration be considered a correctable cause of cardiac arrest? *J Am Coll Cardiol* 2001;38:1224-5.
447. Garrigue S, Bordier P, Jais P, et al. Benefit of atrial pacing in sleep apnea syndrome. *N Engl J Med* 2002;346(6):404-12.