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CHAPTER 1

Indications for permanent cardiac pacing

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Introduction

Defects of cardiac impulse generation and conduction can occur at various levels in the cardiac conduction system. In general, intrinsic disease of the conduction system is often diffuse. For example, normal atrioventricular (AV) conduction cannot necessarily be assumed when a pacemaker is implanted for a disorder seemingly localized to the sinus node. Similarly, normal sinus node function cannot be assumed when a pacemaker is implanted in a patient with AV block. Conduction disorders that lead to important bradycardia or asystole may result from reversible or irreversible causes. Recognition of reversible causes is critical to avoid unnecessary commitment to long-term pacemaker therapy. This chapter reviews the common disorders that warrant cardiac pacing and lists the recommended indications set out by published guidelines.

Anatomy and physiology of the conduction system

For a complete understanding of rhythm generation and intracardiac conduction, and of their pathology, a brief review of the anatomy and physiology of the specialized conduction system is warranted.

Sinus node

The sinus node or sinoatrial (SA) node is a crescent-shaped subepicardial structure located at the junction of the right atrium and superior vena cava along the terminal crest. It measures 10–20 mm (with larger extension in some studies) and has abundant autonomic innervation and blood supply, with the sinus node artery commonly coursing through the body of the node. Endocardially, the crista terminalis overlies the nodal tissue, although the inferior aspect of the node has a more subendocardial course. Histologically, the sinus node comprises specialized nodal cells (P cells) packed within a dense matrix of connective tissue. At the periphery, these nodal cells intermingle with transitional cells and the atrial working myocardium, with radiations extending toward the superior vena cava, the crista terminalis, and the intercaval regions [1,2]. The absence of a distinct border and the presence of distal fragmentation explain the lack of a single breakthrough of the sinus node excitatory wavefront. The radiations of the node, although histologically distinct, are not insulated from the atrial myocardium. Hence, a clear anatomical SA junction is absent. The sinus node is protected from the hyperpolarizing effect of the surrounding atria, probably by its unique structure wherein electrical coupling between cells and

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expression of ion channels vary from the center of the node to the periphery. The pacemaker cells at the center of the node are more loosely coupled, while those at the periphery are more tightly coupled with higher density I_f (funny current, a mixed sodium and potassium current carried by the HCN channels) and I_{Na} currents [2].

The SA node has the highest rate of spontaneous depolarization (automaticity) in the specialized conduction system and is responsible for the generation of the cardiac impulse under normal circumstances, although normal human pacemaker activity may be widely distributed in the atrium. The unique location of the sinus node astride the large SA nodal artery provides an ideal milieu for continuous monitoring and instantaneous adjustment of heart rate to meet the body's changing metabolic needs.

Impulse generation in the sinus node remains incompletely understood. Sinus nodal cells have a low resting membrane potential of −50 to −60 mV. Spontaneous diastolic (phase 4) depolarizations are probably triggered by several currents, including I_f. The predominant inward current in the center of the node is I_{CaL} that generates a "slow" action potential. The action potentials spread peripherally into the musculature of the terminal crest. In the periphery of the node, I_{Na} is operative and necessary for providing sufficient inward current to depolarize the larger mass of atrial tissue. Defects of a number of molecular and biophysical factors that govern the ionic channels of the sinus node can lead to sinus node dysfunction (Figure 1.1).

Differential sensitivity to adrenergic and vagal inputs exists along the nodal pacemaker cells, such that superior sites tend to dominate during adrenergic drive while the inferior sites predominate during vagal stimulation [3]. Interventions including premature stimulation, autonomic stimulation, and drugs have been shown to induce pacemaker shifts (due to multicentric origins) with variable exit locations [4].

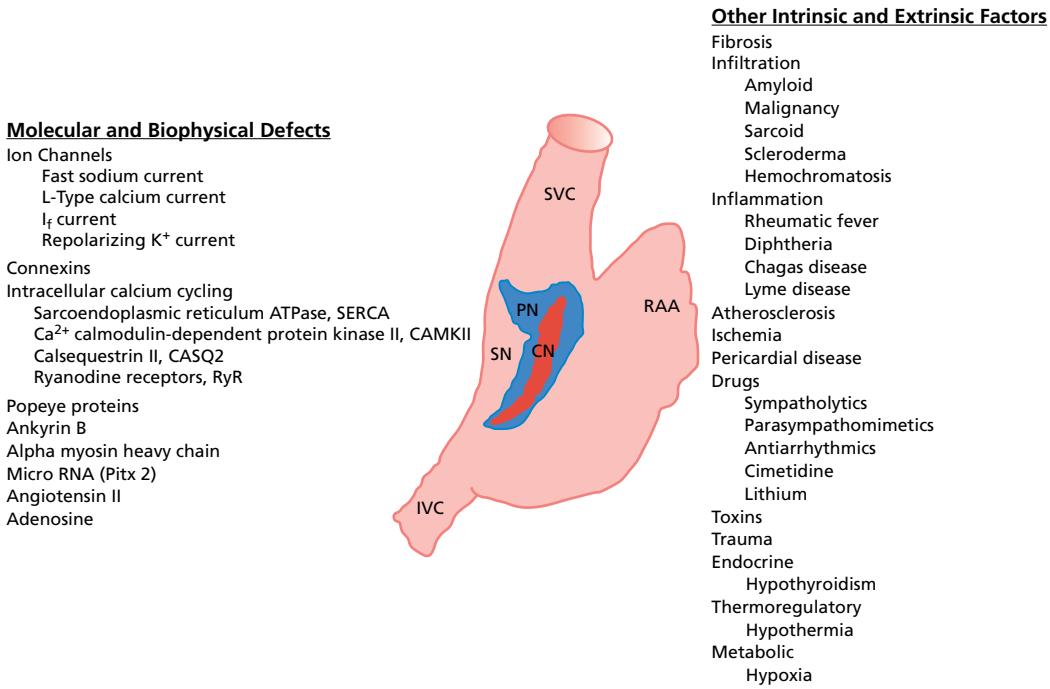

Figure 1.1 Summary of factors contributing to sinus node (SN) dysfunction. The central node (CN) shown in red is surrounded by the peripheral nodal (PN) structure in blue. RAA, right atrial appendage; SVC, superior vena cava; IVC, inferior vena cava. Source: modified from Monfredi O, Boyett MR. Sinus sinus syndrome and atrial fibrillation in older persons: a view from the sinoatrial nodal myocyte. *J Mol Cell Cardiol* 2015;83:88–100. Reproduced with permission of Elsevier.

Atrioventricular node

The compact AV node is a subendocardial structure situated within the triangle of Koch and measuring 5–7 mm in length and 2–5 mm in width [5,6]. On the atrial side, the node is an integral part of the atrial musculature, in contrast to the AV bundle which is insulated within the central fibrous body and merges with the His bundle. Based on action potential morphology in rabbit hearts, atrial (A), nodal (N), and His (H) cells have been defined. Intermediate cell types such as AN and NH define areas toward the atrial and His bundle ends of the compact node, respectively. Histologically, the mid nodal part has densely packed cells in a basket-like structure interposed between the His bundle and the loose atrial approaches to the node. The AN cells are composed primarily of transitional cells. Distinct electrical and morphological specialization is seen only in the progressively distal His fibers. Rightward and leftward posterior extensions of the AV node were described by Inoue and Becker [7]. These extensions have clinical implications for defining reentrant circuits that act as a substrate of AV nodal reentrant tachycardia.

The AV node has extensive autonomic innervation and an abundant blood supply from the large AV nodal artery, a branch of the right coronary artery, in 90% of patients, and from the left circumflex artery in 10% (Figure 1.2). AV nodal conduction is mediated via "slow" calcium-mediated action potential and demonstrates decremental conduction due to post-repolarization refractoriness as a result of delayed recovery of the slow inward currents. AV nodal tissue closer to the His bundle (NH and proximal His bundle area) generates junctional escape rhythms (Figure 1.3). Escape rates are dependent on the site of dominant pacemaker activity. Isoproterenol stimulation, for example, accelerates junctional escape and shifts the dominant activity to the transitional cells in the AN region and posterior extensions of the node [8–10].

His–Purkinje system

Purkinje fibers emerging from the area of the distal AV node converge gradually to form the His bundle, a narrow tubular structure that runs through or around the membranous septum to the crest of the muscular septum, where it divides into the bundle branches. The bulk of the His bundle cells contribute to the left bundle branch with a smaller contribution to the right bundle. Longitudinal strands of Purkinje fibers, divided into separate parallel compartments by a collagenous skeleton, can be discerned by histological examination of the His bundle [11]. The collagen sheathing minimizes lateral spread of impulses from the main body of the bundle branches. The rapid conduction of electrical impulses across the His–Purkinje system is responsible for the almost simultaneous activation of the right and left ventricles. The His bundle has relatively sparse autonomic innervation, although its blood supply is quite ample, emanating from both the AV nodal artery and the septal branches of the left anterior descending artery (Figure 1.2).

The bundle branch system is a complex network of interlaced Purkinje fibers that varies greatly among individuals. It generally starts as one or

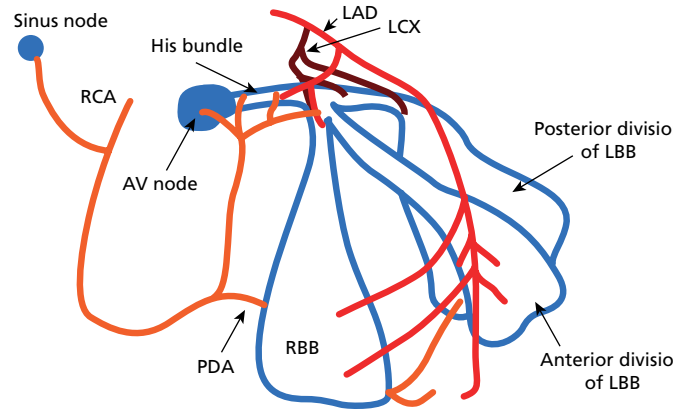

Figure 1.2 Schematic of the conduction system with arterial supply shown. LAD, left anterior descending coronary artery; LBB, left bundle branch; LCX, left circumflex coronary artery; RBB, right bundle branch; RCA, right coronary artery.

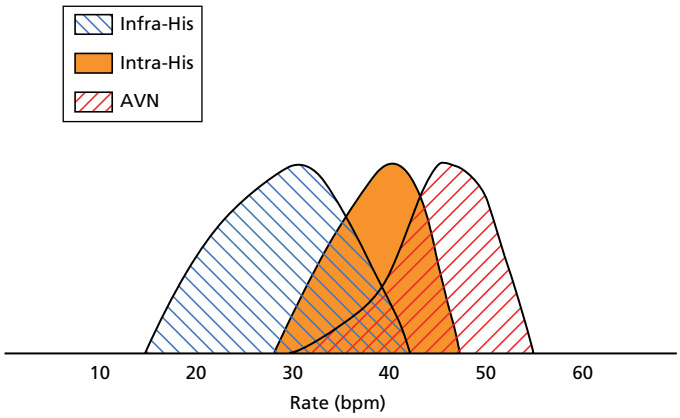

Figure 1.3 Rate of escape rhythm from various areas of the atrioventricular conduction system. AVN, atrioventricular node; infra-His, below the bundle of His; intra-His, within the bundle of His.

more large fiber bands that split and fan out across the ventricles until they finally terminate in a Purkinje network that interfaces with the myocardium (Figure 1.2). In some cases, the bundle branches clearly conform to a tri- or quadri-fascicular system. In other cases, however, detailed dissection of the conduction system has failed to delineate separate fascicles. The right bundle is usually a single discrete structure that extends down the right side of the interventricular septum to the base of the anterior papillary muscle, where it divides into three or more branches. The left bundle more commonly originates as a very broad band of interlaced fibers that spread out over the left ventricle, sometimes in two or three distinct fiber tracts. There is relatively little autonomic innervation of the bundle branch system, but the blood supply is extensive, with most areas receiving branches from both the right and left coronary systems.

His–Purkinje conduction disease may be relatively proximal in some patients and can potentially be overcome by pacing distal to the site of block. His bundle pacing is thus feasible in some patients with left bundle branch in order to normalize QRS complexes and synchronize ventricular contraction [12].

Indications for permanent pacemakers

Permanent pacing is considered in a number of clinical situations, some of which are unambiguous whereas others require a higher level of expertise for determination of potential benefit. The main factors that determine the need for cardiac pacing are (i) symptoms associated with a bradyarrhythmia, (ii) the site of conduction abnormality in the conduction system, and (iii) the presence of conditions associated with progressive AV conduction abnormalities (e.g. genetic cardiomyopathies). In addition, the determination will depend on whether the conduction disease is likely to be permanent or reversible, such as due to a drug effect or acute inflammatory or ischemic process. A permanent pacemaker is generally a lifelong commitment for a patient; the need for generator changes and surgical revisions for malfunction become important considerations in younger patients. Hence, the decision to implant a pacemaker is not to be taken lightly.

A joint committee of the American College of Cardiology (ACC) and the American Heart Association (AHA) was formed in the 1980s to provide uniform criteria for pacemaker implantation. A recent update in conjunction with the Heart Rhythm Society was published in 2018 [13]. It is recognized that there will be cases that cannot be categorized based on these guidelines. Nevertheless, these guidelines have wide endorsement.

All guideline recommendations are subdivided into three classes to reflect the magnitude of treatment effect (Table 1.1). A class I indication pertains to a condition in which the procedure or intervention confers definite benefits. A class III indication is one where the intervention is not helpful and potentially harmful, and hence not recommended.

Additionally, the evidence supporting recommendations is ranked by the following criteria for level of evidence.

- *Level A*: Data derived from multiple randomized controlled trials (RCTs) involving a large number

Table 1.1 Classes of guideline recommendations

Class I	Conditions for which there is evidence and/or general agreement that a pacemaker implantation 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 pacemaker implantation
Class IIa	Weight of evidence/opinion in favor of efficacy
Class IIb	Usefulness/efficacy less well established by evidence/opinion
Class III	Conditions for which there is evidence and/or general agreement that a pacemaker is not useful/effective and in some cases may be harmful

of patients; meta-analysis of high-quality RCTs; one or more RCTs corroborated by high-quality registry studies.

- *Level B-R* (randomized): Moderate-quality evidence from one or more RCTs or from meta-analyses of moderate-quality RCTs.
- *Level B-NR* (non-randomized): Moderate-quality evidence from one or more non-randomized studies, observational studies or registry studies; meta-analyses of such studies.
- *Level C-LD* (limited data): Randomized or non-randomized observational or registry studies with limitations of design or execution; meta-analyses of such studies; physiological or mechanistic studies in human subjects.
- *Level C-EO* (expert opinion): Consensus based on clinical experience.

Some class I indications will necessarily lack support from level A evidence due to early non-randomized studies documenting clear benefits such that randomized trials become unethical.

Sinus node dysfunction

Disorders of the sinus node can be divided into those primarily due to intrinsic pathology of the node and surrounding atrium, or extrinsic factors such as autonomic stimulation or drug effects (Figure 1.1). The terms sinus node disease (SND), sick sinus syndrome, and SA disease are often used interchangeably. All refer to a broad range of abnormalities in the sinus node and atrial impulse formation and propagation (Table 1.2). They include persistent sinus bradycardia and/or chronotropic incompetence without identified cause, intermittent or persistent sinus arrest, and SA exit block. Frequently, atrial arrhythmias and sinus nodal dysfunction coexist and cause symptomatic sinus pauses at cessation of an atrial arrhythmia (Figure 1.4). The term tachy–brady syndrome is applied because of the frequent need for bradycardia support with pacing to allow antiarrhythmic therapy for the tachycardia.

Pathology intrinsic to the sinus node is quite common, and its incidence increases with advancing age. Several patterns have been identified: a diffuse or localized atriopathy has been suggested. Electrophysiological studies have shown structural remodeling, particularly along the long axis of the crista terminalis, and associated with a more caudal migration of the atrial pacemaker activity [8]. Progressive downregulation of the I_{CaL} channel and loss of connexin-43 expression are features in the guinea pig model [14]. In humans, such atriopathy is also associated with atrial arrhythmias, particularly atrial fibrillation that develops in 50% of patients with SND. Atrial arrhythmias further aggravate SND, and catheter ablation of fibrillation and flutter has been shown to reverse some of the adverse electrical remodeling of the sinus node [15]. Atrophic or hypoplastic sinus node has been described in association with congenital anomalies. A familial form of SND is also recognized. Finally, idiopathic SND without any detectable morphological abnormality can occur and may be related to abnormal neural innervation.

In patients with sinus node dysfunction, the correlation of symptoms with bradyarrhythmias is *critically* important. This is because there is a great deal of disagreement about the absolute heart rate or length of pause required before pacing is indicated. If the symptoms of SND are dramatic (e.g. syncope, recurrent dizzy spells, seizures, or severe heart failure), then the diagnosis may be relatively easy. However, symptoms are often non-specific (e.g. easy fatigability, depression, listlessness, early signs of dementia) and may be easily misinterpreted in the elderly. Electrophysiological studies have a low sensitivity for detection of SND and

Table 1.2 Manifestations of sinus node dysfunction and their diagnosis

Sinus bradycardia	Sinus rates persistently <50 bpm and associated with symptoms. Prolonged sinus node recovery time (following atrial pacing) is helpful in diagnosing sinus node disease but has low sensitivity
Chronotropic incompetence	Inadequate sinus rate response to exercise, defined as failure to achieve 80% of expected heart rate during exercise. Diagnosis made with exercise test or ambulatory ECG monitoring
Sinoatrial (SA) block	Sinus beats are "dropped" in a regular pattern (e.g. 2 : 1 SA block, 3 : 2 SA Wenckebach, etc.) due to blocking of impulses in the perinodal area between the sinus node and atrial muscle (by disease, medications, etc.). Diagnosis is by ECG or ambulatory monitoring
Sinus pause >3.0 s	Failure of impulse formation in the sinus node due to pathology, medications, etc. The diagnosis is made electrocardiographically by an absence of sinus P waves that occurs without any discernible pattern
Tachy–brady syndrome	The diagnosis is made electrocardiographically by alternating periods of bradycardia and tachycardia. It may be due to (i) overdrive suppression of sinus node by atrial fibrillation, flutter or tachycardia with sinus pauses that occur at the termination of tachycardia; (ii) periods of paroxysmal atrial arrhythmia with rapid rates superimposed on underlying sinus bradycardia; or (iii) persistent atrial fibrillation with periods of fast and slow AV conduction. Note that the tachy–brady syndrome associated with persistent atrial fibrillation is related to disease in the AV node and not sinus node

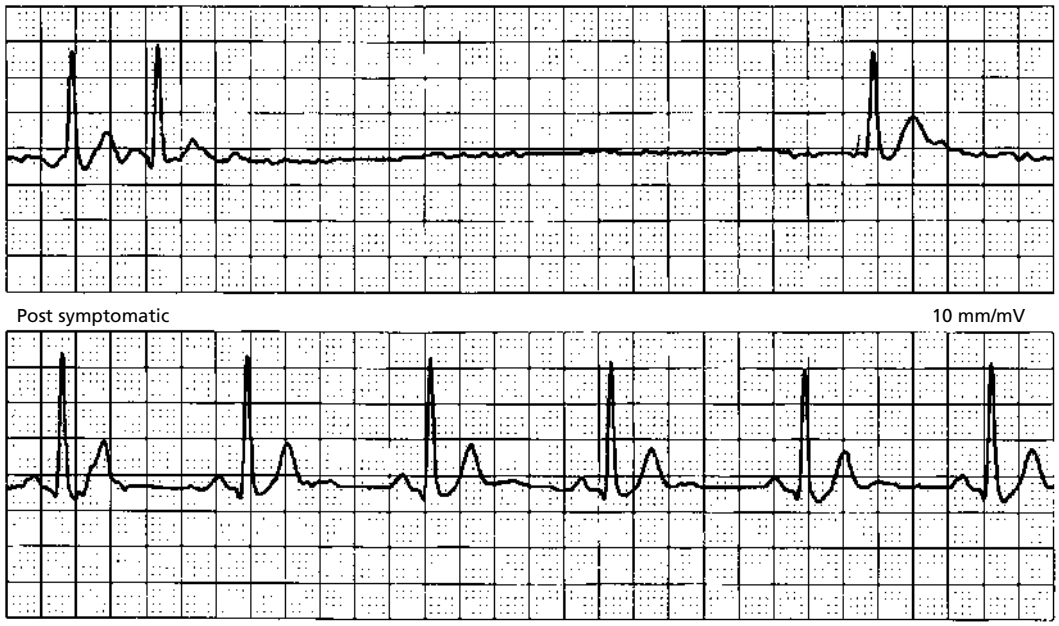

Figure 1.4 Tachy–brady syndrome due to sinus arrest at termination of atrial fibrillation. Patient-triggered event recording during presyncope in a 56-year-old male with paroxysmal atrial fibrillation shows an asystolic pause in excess of 4 s at termination of fibrillation. The sinus offset pause is intercepted by a junctional escape beat before resumption of normal sinus rhythm.

ambulatory monitoring with symptom correlation has the best diagnostic yield.

Essential drugs used for coexisting conditions can accentuate SND (Figure 1.5). If cessation of a drug is anticipated to cause deterioration of the primary condition, permanent pacing may be needed to allow continuation of medical therapy in some patients. Chronotropic incompetence is an underdiagnosed condition where patients fail to augment their heart rate with exercise, with marked

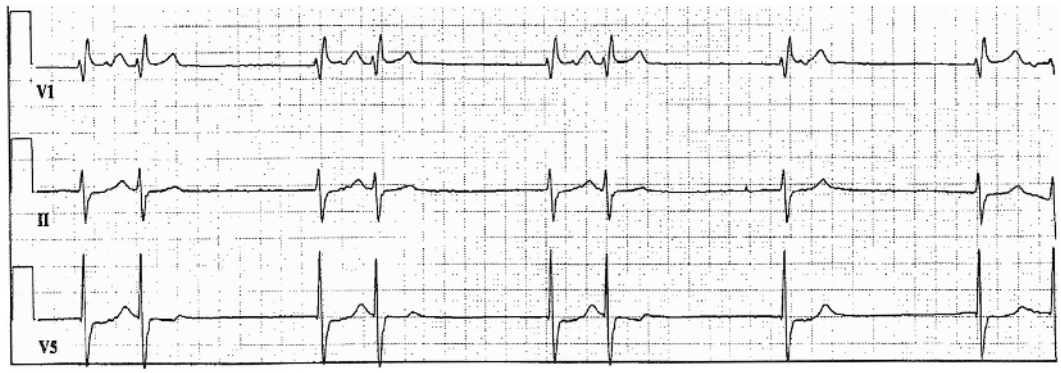

Figure 1.5 A 69-year-old male had been started on atenolol 75 mg/day for treatment of hypertension approximately 2 weeks earlier. He was seen in the emergency room complaining of feeling weak and lightheaded. The ECG shows a slow junctional escape rhythm followed by a sinus beat in a pattern termed "escape–capture bigeminy." Discontinuation of atenolol resulted in return of normal sinus rhythm within 36 hours. Patients with sinus node dysfunction may be dependent on sympathetic stimulation, and beta-blockers, even in low doses, may result in profound bradycardia.

exercise intolerance in some patients. Although no specific parameter has been established as a diagnostic standard, the most commonly used definition for chronotropic incompetence is the inability to achieve 80% of expected heart rate reserve for age; expected heart rate reserve is defined as the difference between age-predicted maximal heart rate (220 – age) and the resting heart rate.

Patients with SND may have associated disease in the AV node and His–Purkinje conduction system. However, the rate of lone SND progressing to AV block is low. The mean annual incidence of complete AV block developing in patients implanted with AAI pacemakers for SND is 0.4–1.7% [16,17]. The natural history of untreated SND is highly variable. Syncope resulting from sinus arrest tends to be recurrent and may result in falls and significant orthopedic injuries, especially in the elderly. The incidence of sudden death is low and SND very rarely affects survival regardless of whether or not it is treated with a pacemaker.

Indications for permanent pacing in sinus node dysfunction

Class I indications

1 Sinus node dysfunction with symptoms directly attributable to SND. (Level of evidence: C-LD)

2 Sinus node dysfunction as a result of essential long-term drug therapy of a type and dose for which there are no acceptable alternatives. (Level of evidence: C-EO)

Class IIa indications

1 Tachy–brady syndrome and symptoms attributable to bradycardia. (Level of evidence C-EO)

2 Symptomatic chronotropic incompetence. (Level of evidence: C-EO)

Class III (permanent pacing not indicated)

1 Permanent pacing is not indicated in asymptomatic patients with SND. (Level of evidence: C)

Acquired atrioventricular block

In the majority, sclerodegenerative changes account for progressive conduction system disease. However, in a significant proportion, AV block is secondary to other causes that are potentially reversible or associated with progressive heart disease with added risk of ventricular arrhythmias such that an implantable cardioverter–defibrillator (ICD) should be considered as a means of providing pacing therapy. In a recent review of unexplained heart block in patients under 55 years of age, cardiac sarcoidosis or giant cell myocarditis accounted for 25% of cases and these patients had a high incidence of sudden death, ventricular tachycardia (VT), or need for cardiac transplantation [18]. In younger patients presenting with advanced conduction system disease, further evaluation with cardiac magnetic resonance (CMR) imaging or positron emission tomography (PET) is useful for detection of

pathology that merits the use of an ICD as opposed to provision of cardiac pacing alone.

Based on electrocardiography (ECG) characteristics, AV block is classified as first, second, and third degree. Anatomically, block can occur at various levels in the AV conduction system: above the His bundle (supra-His), within the His bundle (intra-His), and below the His bundle (infra-His). First-degree AV block is defined as abnormal prolongation of the PR interval to greater than 200 ms and is commonly due to delay in the AV node irrespective of QRS width. Type I second-degree heart block refers to progressive PR prolongation before a non-conducted beat and a shorter PR interval after the first blocked beat. This is the classical Wenckebach type AV block usually seen in conjunction with narrow QRS complexes, implying a more proximal level of block, usually in the AV node (Figure 1.6). Type II second-degree heart block is characterized by fixed PR intervals before and after blocked beats, and is usually associated with a wider QRS complex, indicating distal levels of block in the conduction system. Type II second-degree AV block is usually below the level of the AV node (within or below the His bundle); symptoms and progression to complete AV block are common. AV conduction in a 2 : 1 pattern can be due to proximal or distal block, although the width of the QRS can help differentiate these based on the above principle. Advanced second-degree block or "high-grade" AV block refers to two or more non-conducted sinus P waves, but with resumption of conducted beats suggesting preservation of some AV conduction (Figure 1.7). In the setting of atrial fibrillation or flutter, a prolonged pause (e.g. >5 s) is often due to advanced second-degree AV block. Third-degree AV block is defined as the absence of AV conduction. In the case of atrial fibrillation, complete AV block often manifests as a regularized slow ventricular rate (Figure 1.8).

The site of AV block will to a great extent determine the adequacy and reliability of the underlying escape rhythm (Figures 1.9 and 1.10). While ECG characteristics are helpful in defining levels of block, they are not always reliable and occasionally an electrophysiological study is required. Type I second-degree block, for example, can occasionally be infranodal, even with a narrow QRS, and may warrant the consideration of pacing [19]. Certain clinical maneuvers may be helpful in determining the level of block. Increased AV conduction with exercise and atropine generally indicate block at the AV nodal level, while maneuvers that slow the atrial rate, such as carotid massage, improve His–Purkinje conduction by allowing for recovery from refractoriness (Table 1.3).

There is considerable variation in the symptomatic manifestation of AV block, ranging from an asymptomatic status to syncope and sudden death. First-degree AV block and asymptomatic type I second-degree AV block are in general benign and not an indication for cardiac pacing. However,

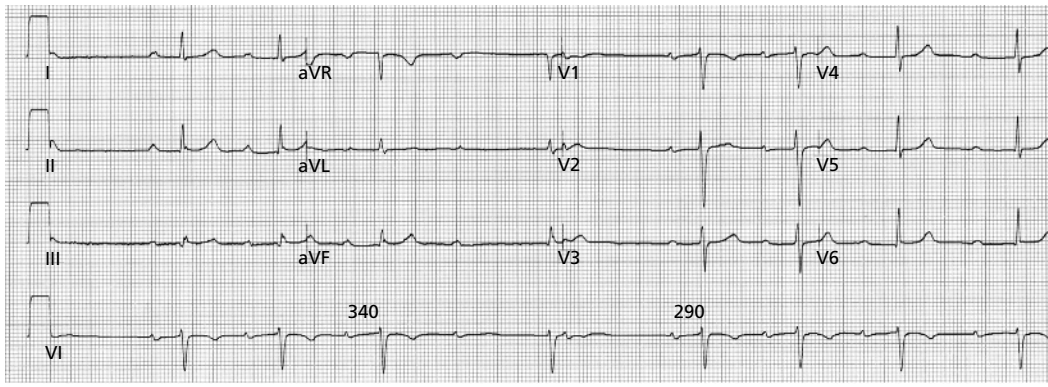

Figure 1.6 Type I second-degree AV block associated with Lyme disease. This 32-year-old male presented with complaints of palpitation due to heart beat irregularity. He had features of Lyme disease several weeks previously. There is progressive PR prolongation before the fourth P wave fails to conduct. The fourth QRS complex is a junctional escape beat. The sixth P wave that conducts has a shorter PR interval (290 ms) compared to the last conducted beat before block occurred (340 ms).

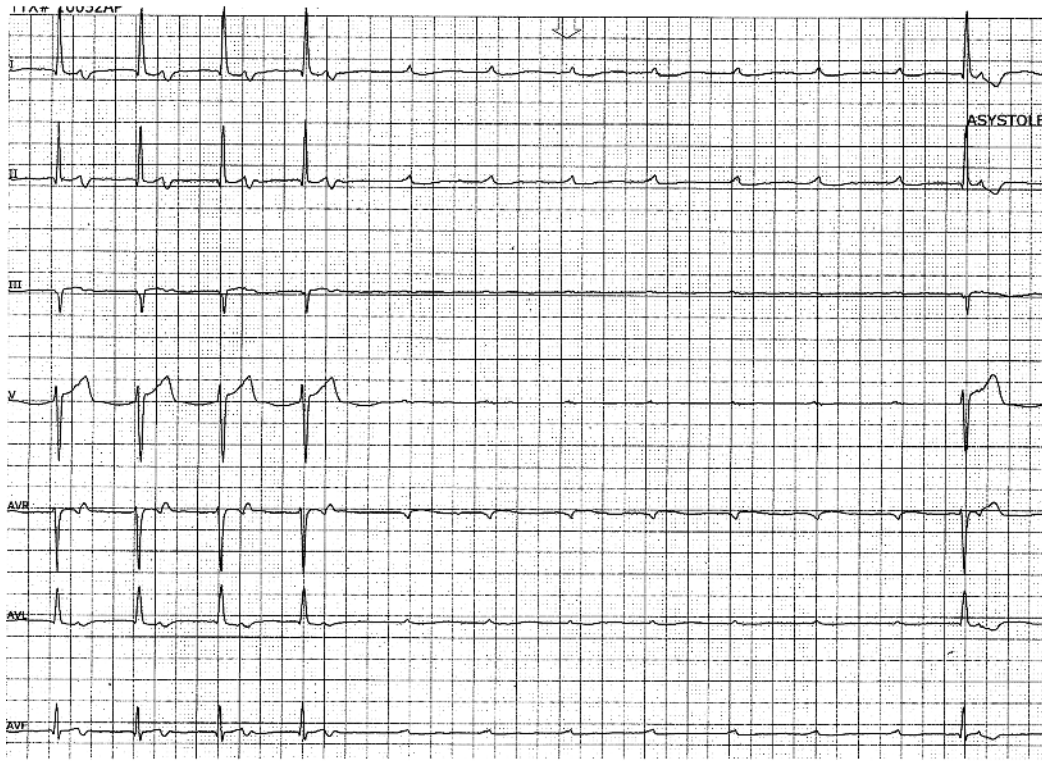

Figure 1.7 High-grade AV block. This 60-year-old female with hypertension and coronary artery disease presented with syncope. Baseline ECG showed marked first-degree AV block and voltage changes of left ventricular hypertrophy. Telemetry recorded abrupt interruption of AV conduction with multiple non-conducted P waves with spontaneous recovery. Her β-adrenergic blockers were continued as essential treatment for coronary artery disease and a permanent pacemaker was implanted.

rarely, first-degree block with marked PR prolongation can potentially cause atrial systole to occur in close proximity to the preceding ventricular systole and give rise to symptoms similar to those of a pacemaker syndrome [20]. Prolongation of the PR interval is particularly important in patients with left ventricular (LV) dysfunction as marked PR prolongation in excess of 250–300 ms can lead to impaired LV filling, increased pulmonary capillary wedge pressure, and decreased cardiac output [21]. Similar consequences can ensue in patients with type I second-degree AV block even in the absence of bradycardia-related symptoms.

Type II second-degree AV block is important as it has a high rate of progression to third-degree AV block. It usually reflects diffuse conduction system disease and often warrants permanent pacing even in the absence of symptoms. Third-degree AV block with a wide QRS escape rhythm often presents with fatigue, dyspnea, presyncope or frank unheralded syncope. Rarely, ventricular fibrillation and torsades de pointes VT can result from marked bradycardia and prolonged pauses. Permanent cardiac pacing should be strongly considered even if the escape rate is greater than 40 bpm, because it is not necessarily the escape rate that determines a safe and reliable heart rhythm but the site of origin of the escape rhythm. Infra-His escape rhythms are more likely associated with prolonged asystole, syncope, and death (Figure 1.10).

AV block, usually with 2 : 1 AV conduction, can be provoked by exercise (Figure 1.11). Patients typically complain of exertional dyspnea and dizziness. The abnormality is often reproducible by exercise testing. Once ischemia is excluded as a cause, permanent pacing is remarkably effective for symptom relief. Without pacing, these patients have a poor prognosis because the site of conduction block is below the AV nodal level [22].

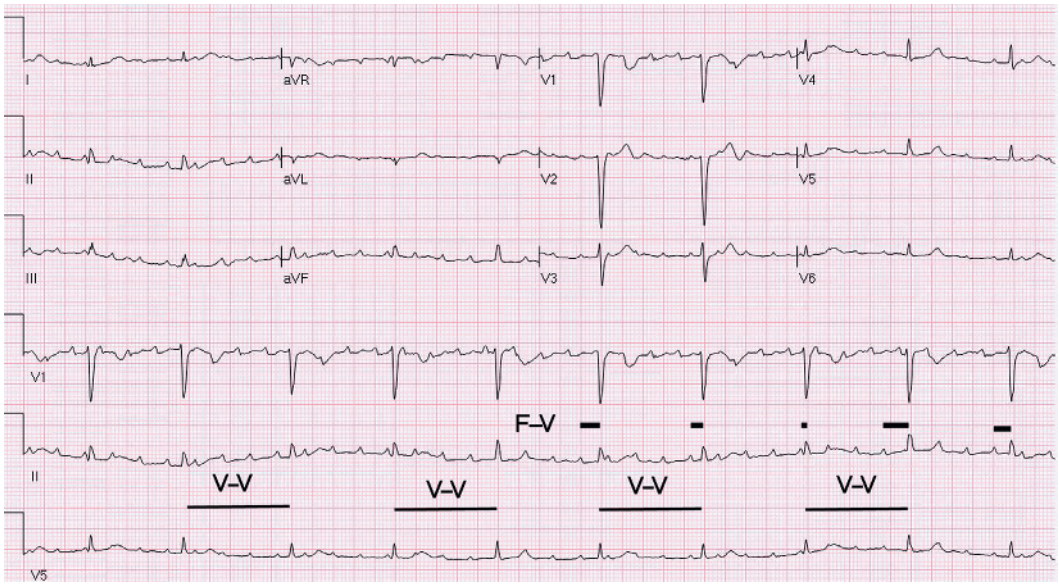

Figure 1.8 Third-degree AV block and junctional escape during atrial flutter. Identification of complete AV block during atrial flutter or atrial tachycardia may be challenging as high-level conduction block has to be considered as well. In this tracing the second QRS is likely conducted but the rest of the recording shows a regular atrial rhythm dissociated from a regular ventricular rhythm. Note that F wave to QRS duration (F–V) is variable while the ventricular rate (V–V) is stable, ruling out AV conduction. Source: courtesy of Karoly Kaszala, MD.

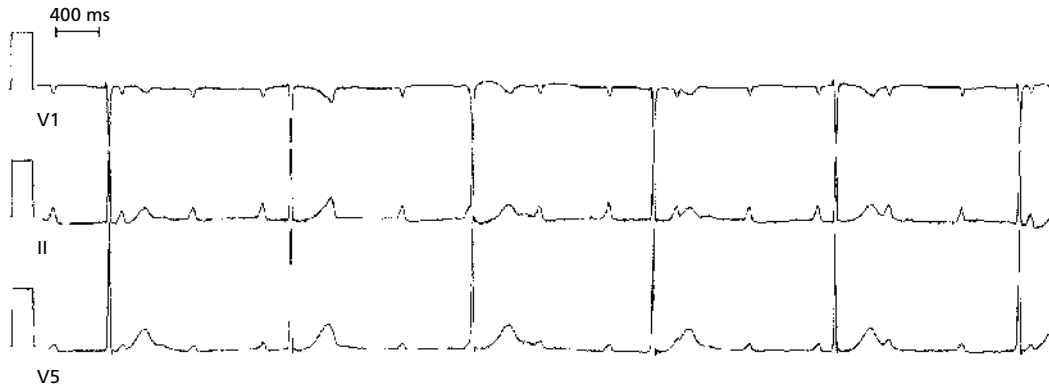

Figure 1.9 Complete heart block with narrow QRS escape rhythm. This 70-year-old male presented with fatigue. Rhythm strips reveal complete AV block and a slow junctional escape rhythm with narrow QRS complexes. A permanent dual-chamber pacemaker completely relieved his symptoms.

In general, the presence of symptoms documented to be due to AV block is an indication for permanent pacing regardless of the site of the block (e.g. above as well as below the His bundle). However, it is important to recognize potentially reversible causes of AV block despite their presentation with symptoms. Important examples include acute myocarditis (particularly that associated with Lyme carditis), AV block related to drug toxicity, transient vagotonia, and hypoxic events. Many of these conditions tend to resolve with disease-specific treatment and although temporary pacing may be required, permanent pacing is seldom necessary. One exception is drug-related AV block that may not always resolve completely on cessation of the medication and may need permanent pacing (see discussion of temporary pacing indications in subsequent sections).

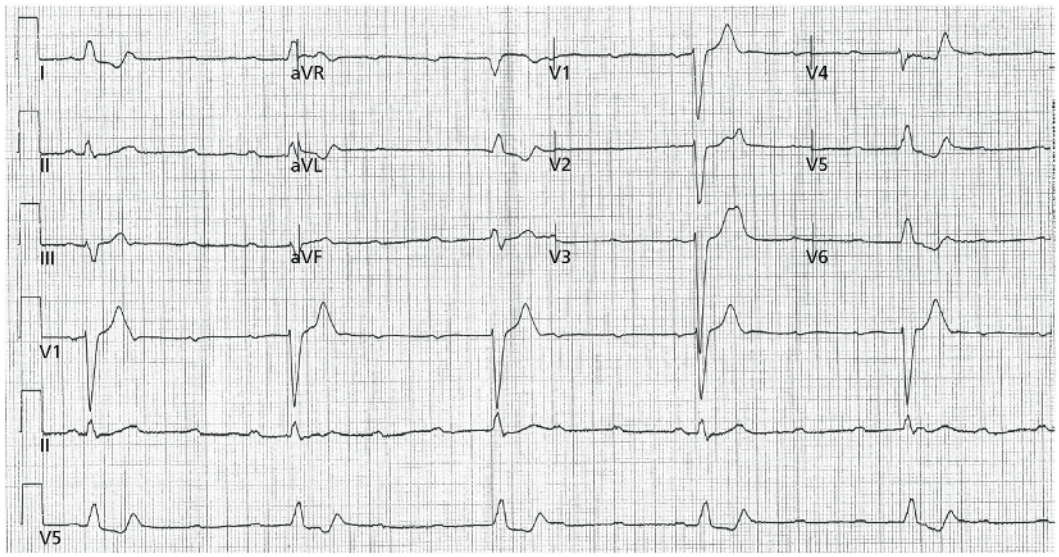

Figure 1.10 Complete AV block with wide QRS escape rhythm. This 77-year-old male presented with syncope without warning and sustained facial injuries. The slow ventricular escape rhythm at 30 bpm likely originates from the right bundle branch. Intermittent asystole due to unstable escape rhythm was the most likely cause of syncope.

Table 1.3 Responses to maneuvers to identify level of block in patients with 2 : 1 atrioventricular (AV) block

	Block above AV node	*Block below AV node*
Exercise	+	± or –
Atropine	+	± or –
Carotid sinus massage	–	+ or ±
Isoproterenol	+	– or ±

+, improved AV conduction; –, worsened AV conduction.

The indications for permanent pacing for heart block due to increased vagal tone (reflex syncope), acute myocardial infarction (MI), and congenital AV block are discussed separately.

Indications for permanent pacing in acquired AV block

Class I indications

1 In acquired second-degree Mobitz type II AV block, high-grade AV block or complete AV block not attributable to reversible or physiological causes, permanent pacing is recommended regardless of symptoms. (Level of evidence: B-NR)

2 Patients with neuromuscular disease, such as muscular dystrophy or Kearns–Sayre syndrome, who have second- or third-degree AV block or His–ventricular (HV) interval ≥70 ms should be considered for permanent pacing with a defibrillator regardless of symptoms.[1] (Level of evidence: B-NR)

3 Permanent atrial fibrillation with symptomatic bradycardia. (Level of evidence: C-LD)

4 Symptomatic AV block during clinically indicated guideline-directed medical therapy for which there is no reasonable alternative. (Level of evidence: C-LD)

Class IIa indications

1 Second-degree Mobitz type II AV block, high-grade AV block or complete heart block in patients with inflammatory or infiltrative cardiomyopathies (e.g. sarcoidosis): permanent pacing with additional defibrillator is reasonable.[1] (Level of evidence: B-NR)

2 PR interval >240 ms and left bundle branch block (LBBB) in patients with lamin A/C gene mutations, including limb girdle and Emery–Dreifuss muscular dystrophies: permanent pacing with defibrillation capability should be considered. (Level of evidence: B-NR)

[1] Defibrillator implants are for patients with an expected meaningful survival of more than 1 year.

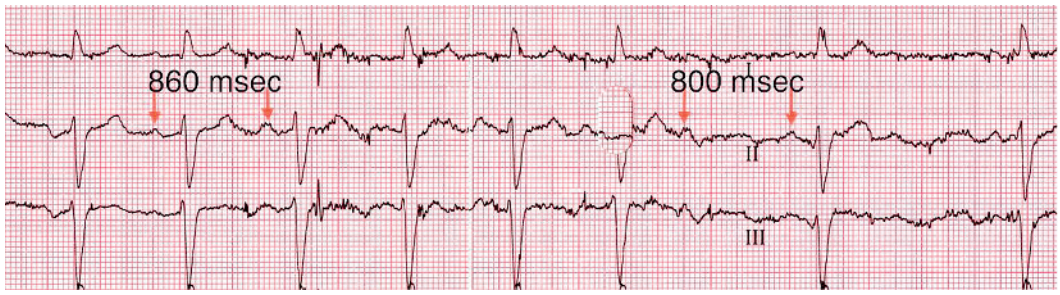

Figure 1.11 Exercise-induced AV block. This 68-year-old male presented with exertional dyspnea. His baseline ECG showed sinus rhythm with first-degree AV block and left anterior hemiblock. With gentle leg elevation exercise in the examination room while connected to the ECG, 2 : 1 AV block developed as the PP intervals shortened from 860 to 800 ms. This finding is typical of block below the AV node. Permanent dual-chamber cardiac pacing relieved his symptoms.

3 Permanent pacing is reasonable in patients with marked first-degree or second-degree Mobitz type I AV block if symptoms can be attributed to the AV block. (Level of evidence: C-LD)

Class IIb indications

1 In patients with neuromuscular diseases, such as myotonic dystrophy type 1, with PR >240 ms, QRS duration >120 ms or fascicular block, permanent pacing with defibrillation is reasonable.

Conduction system disease in the presence of 1 : 1 AV conduction

Conduction disease may involve the bundle branches or the individual fascicles of the left bundle. In bifascicular block, the ECG shows evidence of conduction delay or block in both bundles such as complete right bundle branch block (RBBB) with anterior or posterior hemiblock or complete LBBB alone. The term "alternating bundle branch block" (or bilateral bundle branch block) refers to evidence for impaired conduction in the right bundle and both fascicles of the left bundle on successive ECGs. In strict terms, evidence for disease in all three fascicles should justify the term "trifascicular block." However, the term trifascicular block has also been loosely applied to bifascicular block with first-degree AV block where the block may actually be due to a combination of AV nodal and infra-His conduction disease (Figure 1.12).

The prevalence of bundle branch block increases with age (approximately 1% in middle age, rising to 17% at age 80) [23]. LBBB is less common but its presence is associated with a higher incidence of structural heart disease. In bifascicular block, the risk of progression to advanced heart block is related to the presence of symptoms. Syncope is the sole predictor. In the absence of syncope, the annual incidence is 0.6–0.8%, whereas syncopal patients have a 5–11% annual risk of progression to AV block [24,25]. The finding of an HV interval of greater than 100 ms or the demonstration of intra- or infra-His block during incremental atrial pacing at a rate of less than 150 bpm is highly predictive for the development of high-grade AV block (Figure 1.13), but their prevalence is low and hence sensitivity is low [26,27]. Care has to be exercised during atrial pacing so as not to misinterpret the physiological AV block that is often seen with long–short intervals. The majority of patients with bifascicular block who undergo electrophysiological studies will have normal or mildly prolonged HV intervals. However, in patients with bundle branch block and a normal electrophysiological study, implantable loop monitors have shown that recurrent syncope is often due to a bradyarrhythmia, most commonly sudden-onset paroxysmal AV block [28]. The current guidelines recommend permanent pacing for syncope, bundle branch block, and HV interval >70 ms.

Because chronic bifascicular block is associated with other forms of heart disease, pacing alone, although successful for symptom relief, has not been shown to improve mortality. Echocardiography is indicated for assessment of LV function. In the presence of ventricular dysfunction, VT is an alternative mechanism for syncope and sudden death. Programmed stimulation of the ventricle may demonstrate inducibility for ventricular arrhythmia, necessitating consideration of an ICD.

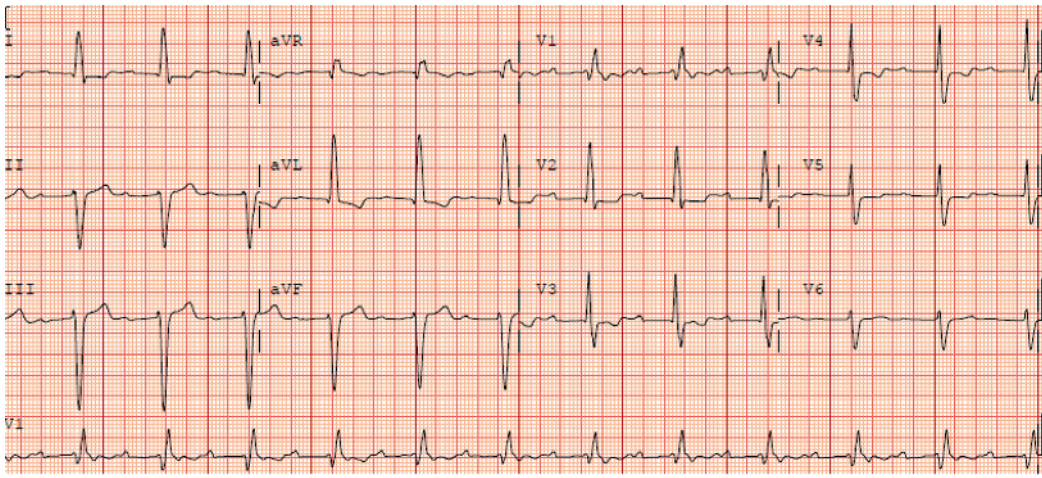

Figure 1.12 Bifascicular block due to right bundle branch block and left anterior hemiblock (note that left anterior fascicular block is diagnosed by left-axis deviation, qR in aVL, R peak time in aVL >45 ms, and rS pattern in leads II, III and aVF). There is PR prolongation to 320 ms. First-degree AV block in such patients is not always predictive of HV interval. When PR interval >300 ms, AH prolongation is present in more than 90% of patients. HV prolongation is present in 50% of patients but not predictive of progression to complete heart block, Thus, in the absence of symptoms, there is no indication for invasive study or cardiac pacing.

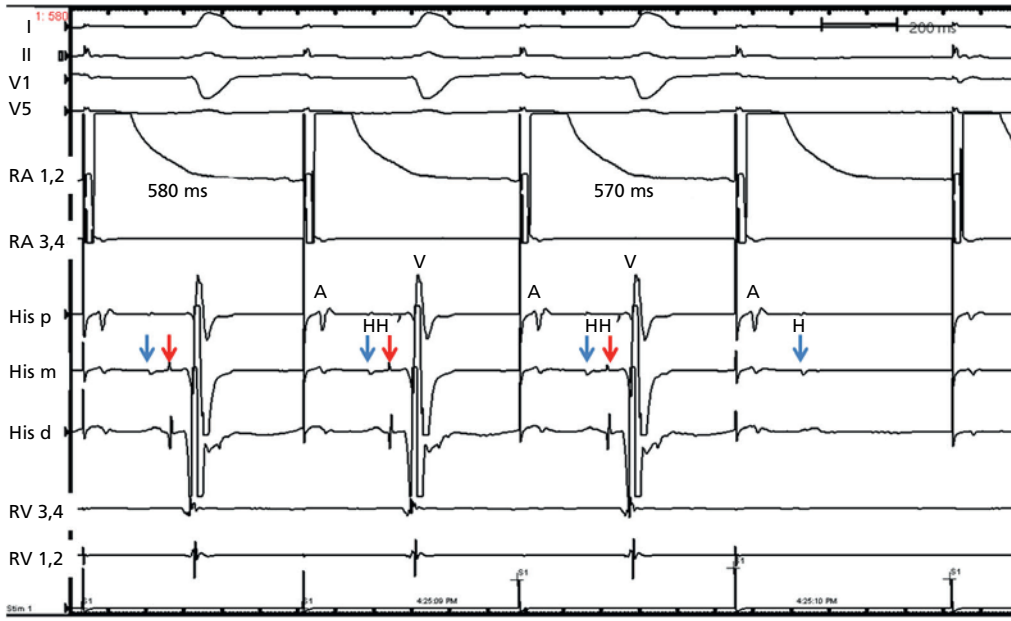

Figure 1.13 Intra- and infra-His AV block induced with atrial pacing. A 68-year-old male was admitted complaining of recurrent dizziness and syncope. His baseline 12-lead ECG showed a PR interval of 0.25 s and a left bundle branch block QRS morphology. The His bundle is split and denoted by H and H′ (blue and red arrows). With decremental atrial pacing, intra-His block (blue arrow) is demonstrated at a cycle length of 570 ms (105 bpm). These findings are indicative of severe diffuse conduction system disease. A permanent dual-chamber pacemaker was implanted, and the patient's symptoms resolved. From top to bottom: I, II, V1 and V5 are standard ECG leads; intracardiac recording from the right atrial appendage (RA 1, 2 and RA 3, 4); and His bundle (His-p, His-m, and His-d are proximal, mid and distal His recordings respectively). A, atrial depolarization; H, proximal His bundle depolarization; H′, distal His bundle depolarization; V, ventricular depolarization.

Indications for pacing in conduction system disease with 1 : 1 AV conduction

Class I indications

1 Patients with syncope and bundle branch block who are found to have an HV interval ≥70 ms at electrophysiological study. (Level of evidence: C-LD)

2 Patients with alternating bundle branch block. (Level of evidence: C-LD)

Class III (not indicated)

1 Bifascicular block with or without first-degree AV block and no symptoms.

Reflex syncope

Reflex syncope includes a group of conditions that are neurally mediated and result in a common cardiovascular response of vasodilation and/or bradycardia. Cerebral hypoperfusion results in loss of consciousness. Any one of the two components of the reflex may predominate. The cardioinhibitory response with predominant bradycardia results from increased parasympathetic tone and is characterized by sinus slowing, sinus arrest (Figure 1.14), prolongation of the PR interval and, less commonly, AV block that occurs alone or in combination. The vasodepressor response is secondary to a reduction in sympathetic activity and marked by loss of vascular tone and hypotension. This effect is independent of heart rate changes.

The two most common types of reflex syncope are neurocardiogenic (vasovagal) and carotid sinus hypersensitivity syndrome. The other types are generally referred to as situational syncope because they are generally associated with a particular stimulus (Table 1.4). Several forms are recognized based on the triggering mechanism, although the triggers may vary considerably in and between individual patients. Classical vasovagal syncope is most common in young patients and occurs as isolated episodes. Generally, patients experience a distinct prodrome of dizziness, nausea, diaphoresis, and visual changes, followed by loss of consciousness. Recovery is gradual but occurs within minutes and it is unusual to experience post-ictal states. However, one-third of patients (commonly older adults) may have minimal or no prodromal symptoms and syncope can be sudden with bodily injuries. When vasovagal syncopal spells begin at an older age, they may be an expression of a pathological process heralding early autonomic failure.

Reflex syncope becomes important when frequent syncope alters quality of life, occurs with a very short prodrome exposing patients to risk of trauma, or occurs during high-risk activity such as driving, flying, or heavy machine operation. Nonpharmacological therapy, such as avoidance measures, physical counter-pressure maneuvers, and tilt training, are useful initial interventions for control of vasovagal syncope [30]. Pharmacological interventions such as fludrocortisone and midodrine predominantly address the vasodepressor component and may occasionally be effective for individual patients, but randomized trials have not proven clear benefit from any particular drug. Although beta-blockers can lessen the degree of mechanoreceptor activation in neurocardiogenic syncope, randomized trials have not shown benefit [31]. In carotid sinus syncope, beta-blockers may, in fact, worsen symptoms.

The role of cardiac pacing in vasovagal syncope has been evaluated in multiple clinical trials with varying results. Meta-analysis of these studies suggested a 17% non-significant reduction in syncope in double-blind studies when both the paced and unpaced groups received pacemaker implants (thereby eliminating a placebo effect). More recent trials using implantable loop recorders (ILRs) to document asystole during vasovagal syncope have been more favorable to permanent cardiac pacing for symptom relief. The ISSUE 3 study randomized patients aged 40 years or older, with three or more syncope episodes and documentation of syncope with greater than 3-s asystole or 6-s asystole without syncope, to pacing-activated or -inactivated modes after implantation. The study showed a significant reduction in recurrent syncope at 2 years, from 57% in the pacing-inactivated group to 25% in the paced group [32]. However, it should be noted that 511 patients with highly symptomatic vasovagal syncope underwent implantation of an ILR in order to identify 89 (17%) patients with important asystole.

In the presence of predominantly cardioinhibitory responses, cardiac pacing tends to be effective for attenuation of symptoms and is a reasonable consideration in older patients. Dual-chamber pacing is generally preferred as VVI pacing can potentially worsen symptoms. Pacemakers that

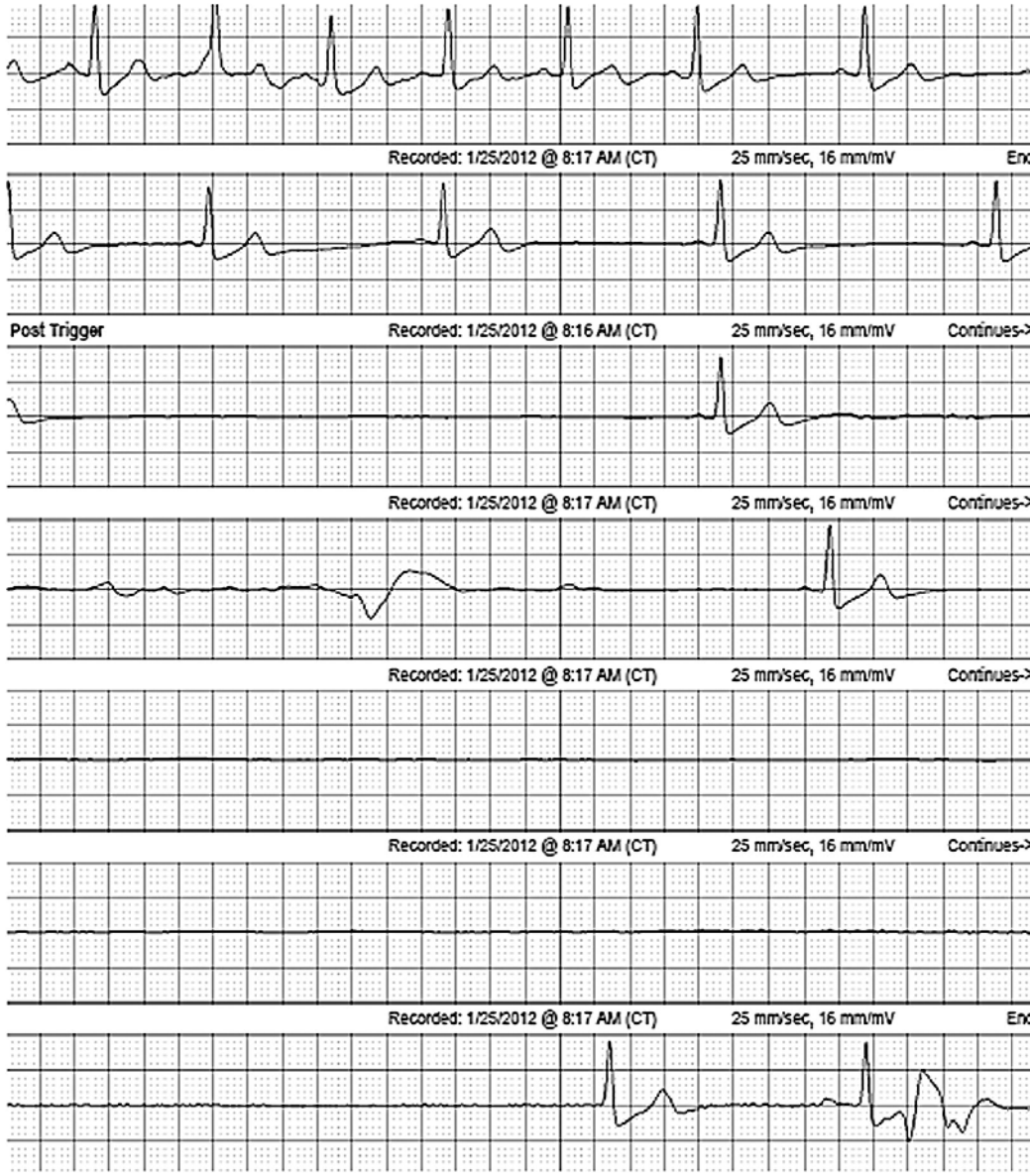

Figure 1.14 Marked cardioinhibitory response to neurally mediated syncope. This 45-year-old female presented with syncope preceded by nausea while wearing an event monitor. There was gradual sinus slowing with prolonged sinus arrest resulting in syncope. Intense vagal stimulation can suppress junctional escape rhythms.

offer closed-loop stimulation, a form of rate-adaptive pacing in response to myocardial contraction dynamics derived from right ventricular (RV) impedance changes, has shown benefit over conventional dual-chamber pacing [33]. Because the cardioinhibitory and vasodepressor components can variably manifest in the same patient during different episodes, patients should be warned of the possibility of recurrence relating to hypotension. In younger patients, however, simple measures should be exhausted before considering commitment to lifelong pacemaker therapy. In the ISSUE 3 study, pacemaker implantation was associated with complications in 6%. Longer-term complications of pacemaker generator changes and lead malfunction are more pertinent to younger patients.

Table 1.4 Types of neurally mediated syncope

Vasovagal	Mediated by emotional stress, such as fear, pain, sight of blood, instrumentation Mediated by orthostatic stress
Carotid sinus syncope	Mediated by pressure to the carotid sinus area, e.g. shaving, turning of the head, tight neck collar
Situational	Cough, sneeze Gastrointestinal stimulation: swallow, defecation, visceral pain Micturition syncope Post exercise Postprandial
Other	Triggered by increased intrathoracic pressure, e.g. laughing, playing brass instruments, weightlifting
Atypical forms	No identified precipitant Adenosine-sensitive syncope

Source: adapted from Shen *et al*. [29].

One variant of neurally mediated syncope is the hypersensitive carotid sinus syndrome. A mildly abnormal response to vigorous carotid sinus massage may occur in up to 25% of patients, especially if coexisting vascular disease is present. Some patients with an abnormal response to carotid sinus massage may have no symptoms suggestive of carotid sinus syncope. On the other hand, the typical history of syncope such as blurred vision and lightheadedness or confusion in the standing or sitting position, especially during movement of the head or neck, should suggest the diagnosis. Classical triggers of carotid sinus syncope are head turning, tight neckwear, shaving, and neck hyperextension. Syncopal episodes are generally reproducible in a given patient. Because of the predominantly bradycardic (cardioinhibitory) response to carotid hypersensitivity, permanent pacing has a high success rate for alleviating symptoms (Figure 1.15).

Paroxysmal AV block

A distinct form of paroxysmal AV block associated with syncope has been described in patients with no structural heart disease or evidence for conduction disturbance on ECG [34]. Patients present with abrupt syncope associated with abrupt onset of high-grade AV block and prolonged asystole, with recovery of normal AV conduction soon afterward. The classical sinus slowing prior to onset of AV block that is typical of vagally mediated AV block is usually absent. Electrophysiological studies show normal His–Purkinje conduction and tilt table testing is usually negative. Patients have an adenosine profile opposite to that of vasovagal syncope and characterized by low plasma adenosine levels, low expression of adenosine A_{2A} receptors, and high induction rate for transient AV block with exogenous adenosine. Cardiac pacing in these patients prevents recurrence of syncope. The entity may be similar to the one termed "low adenosine syncope" that tends to respond to theophylline and cardiac pacing [35]. Further studies are needed to define this syndrome more clearly.

Indications for pacing in neurally mediated syncope and hypersensitive carotid sinus syndrome (2018 European Society of Cardiology guidelines)

Class IIa indications

1 In patients aged >40 years, permanent pacing should be considered to reduce syncopal recurrence with documented symptomatic asystolic pauses >3.0 s or asymptomatic pauses >6 s due to sinus arrest, AV block, or the combination of both. (Level of evidence: B-R)

2 Pacing should be considered for reducing syncope recurrence in patients with cardioinhibitory carotid sinus syndrome who are aged >40 years with recurrent frequent unpredictable syncope. (Level of evidence: B)

Class IIb indications

1 Cardiac pacing may be considered for reducing syncope recurrence in patients with tilt-induced asystolic response who are aged >40 years with recurrent frequent unpredictable syncope. (Level of evidence: B)

2 Cardiac pacing may be considered for reducing syncope recurrence in patients with clinical features of adenosine-sensitive syncope. (Level of evidence: B)

Class III (not indicated)

1 Pacing is not indicated in the absence of cardioinhibitory response.

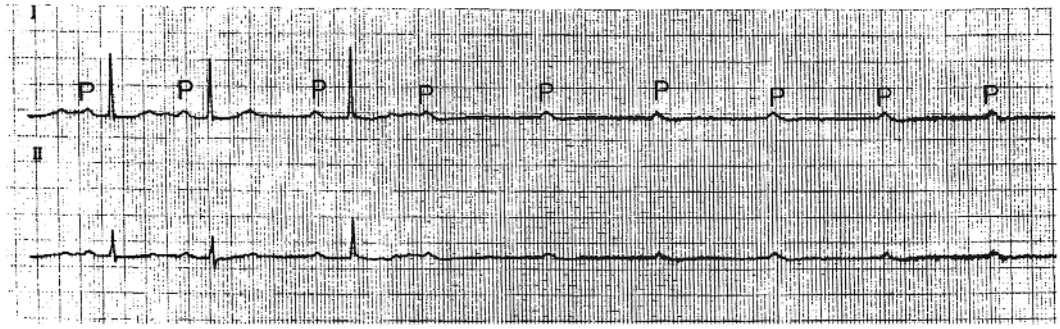

Figure 1.15 Response to gentle carotid massage in carotid hypersensitivity syndrome. A 69-year-old male complained of near-syncope, which typically occurred while shaving or turning his neck. Carotid sinus massage was performed shortly before the second QRS complex. Note that the sinus rate slows prior to the third QRS complex, followed by complete heart block with ventricular asystole.

Spinal cord injury

Based on the level and severity of spinal cord injury, bradycardia may accompany the acute phase of recovery due to a marked reduction in sympathetic tone. Cervical cord injuries are most likely to cause sinus arrest and asystole in the initial 2–4 weeks and may require temporary pacing if atropine and sympathetic stimulation are ineffective. The bradyarrhythmia is the result of unopposed parasympathetic stimulation. Hence, the use of theophylline as an adenosine receptor blocker can be effective and its use is supported by small case series [36]. Permanent pacing is best reserved for intractable cases as recurrent infections and bacteremia are common in these patients, increasing the risk of lead-related endocarditis in the longer term.

Ictal bradycardia

Rarely (<0.5%), profound bradycardia due to sinus arrest or AV block at the nodal level can complicate seizures, mostly temporal lobe epilepsy. Prolonged ictal asystole (>6.0 s) is more common with left temporal lobe epilepsy than right, and can worsen and extend the duration of syncope associated with such seizures. Pacing has been shown to reduce syncopal events and is a consideration if antiepileptic measures such as drugs and surgery fail to control epilepsy. In the 2018 guidelines for bradycardia, permanent pacing is considered a class IIa indication based on limited data [37,38].

Specific conditions associated with cardiac conduction disease

Chronic neuromuscular disorders

A number of neuromuscular disorders are associated with cardiomyopathy and a high incidence of sudden death. In general, the direct consequence of the neuromuscular defects, such as respiratory failure, limits lifespan. However, in some of these conditions, cardiac disease may be responsible for greater morbidity and mortality. Most often, bradyarrhythmias in neuromuscular disorders are due to direct involvement of the specialized AV conduction system. The relatively small numbers of patients involved and the absence of randomized placebo-controlled clinical trials make it difficult to provide definitive guidelines for pacemaker implantation. Since mortality and the incidence of sudden cardiac death are high in this group of disorders, and because conduction system disease tends to be unpredictable, the development of second- or third-degree AV block, even in the absence of symptoms, is considered a class I indication for permanent pacing. In addition, suggestive symptoms such as syncope should be promptly and aggressively investigated. Some authorities recommend yearly ECGs and 24-hour ambulatory recordings for patients with one of these disorders to facilitate early recognition of AV block. It should also be realized, however, that life-threatening ventricular arrhythmias are also fairly common in this population, especially when LV function is impaired or complicated by

hypertrophic cardiomyopathy (HCM), so use of a permanent pacemaker will not necessarily prevent sudden cardiac death.

The neuromuscular disorders most frequently associated with symptomatic conduction system disease are as follows.

Myotonic muscular dystrophy

The type 1 form (Steinert disease) is the most common adult form of neuromuscular disease and is inherited as an autosomal dominant disorder that usually becomes clinically manifest in the third decade. One-third of deaths are sudden and related to heart block or ventricular tachyarrhythmias [39,40]. Permanent pacemakers are warranted for second- or third-degree AV block, even in the absence of symptoms. A recent large non-randomized study of type 1 myotonic dystrophy patients compared an invasive electrophysiological evaluation when PR interval exceeded 200 ms and/or QRS was prolonged in excess of 100 ms with a non-invasive clinical approach. The invasive group, which underwent pacemaker implantation based on the finding of an HV interval greater than 70 ms, had a significant reduction in sudden death [41].

Duchenne muscular dystrophy

This progressive X-linked disease usually becomes clinically apparent in the mid-teens and is fatal by the end of the third decade. The ECG typically shows prominent R waves in V1 with deep narrow Q waves in the lateral precordial leads. Although cardiac involvement is almost universal, the incidence of arrhythmias is variable, with many patients dying from heart failure. In the absence of definitive data, it seems prudent to recommend permanent pacemaker implantation in patients who develop second-degree or higher degrees of AV block, especially in the setting of a wide QRS complex.

Becker muscular dystrophy

This is an X-linked condition closely related to Duchenne muscular dystrophy. It has similar electrocardiographic abnormalities, but progresses more slowly. The severity of cardiac involvement does not parallel the severity of neuromuscular disease. Although there is less experience with this disorder, the indications for permanent pacing are similar to those for patients with Duchenne muscular dystrophy.

Emery–Dreifuss muscular dystrophy

This is a slowly progressive X-linked muscular dystrophy with a high incidence of conduction system disease and arrhythmias. Sudden cardiac death due to bradyarrhythmias has been well documented, and permanent pacemakers are often necessary.

Limb girdle muscular dystrophy

This is a heterogeneous group of disorders that usually begin with weakness in the upper legs and pelvic musculature. Cardiac involvement is variable, although there is a familial form with a high incidence of conduction system disease. Patients with a family history of heart block or sudden death should be considered for permanent pacing relatively early in the course of their disease.

Kearns–Sayre syndrome

This is a multisystem mitochondrial disorder characterized by progressive external ophthalmoplegia, pigmentary retinal degeneration, and AV block. Involvement of the distal conduction system is the rule and high-degree AV block is common. Although definitive data are lacking, it seems prudent to implant a permanent pacemaker prophylactically when marked first-degree AV block becomes manifest.

Infiltrative and inflammatory disorders

The infiltrative cardiomyopathies are characterized by deposition of abnormal substances that commonly lead to stiffening of the ventricular myocardium, causing diastolic dysfunction. Many of these diseases increase wall thickness, and may present with small ventricular volume and occasional LV outflow tract (LVOT) obstruction so as to mimic HCM. Some may have minimal structural abnormalities by echocardiography but involve the conduction system early such that initial presentation may be with heart block or ventricular arrhythmias. Infiltrative and inflammatory cardiomyopathies particularly prone to manifest cardiac conduction disease include sarcoidosis, giant cell myocarditis, amyloidosis, Wegener granulomatosis, metabolic diseases such as hemochromatosis, primary oxaluria, and hematological malignancies

and cardiac tumors. Some metabolic diseases such as Fabry disease and the glycogen storage diseases (e.g. Danon disease) demonstrate frequent cardiac involvement. AV block, although rare, is well recognized in these conditions. In South American countries, Chagas disease is a common cause of bradyarrhythmias requiring cardiac pacing.

The prognosis of many of these disorders is usually more closely related to the underlying disease, although the actual cause of death may be cardiac. For example, malignancies involving the heart, especially "solid" tumors, tend to have a uniformly poor prognosis. Nonetheless, infiltrative disorders may directly affect the conduction system and cause life-threatening bradyarrhythmias and tachyarrhythmias. In these situations, permanent pacemakers or defibrillators can be life-saving.

Sarcoidosis

This is a relatively common disorder of unknown etiology and is characterized by formation of noncaseating granulomas in various organs, including the myocardium. After an early stage of granulomatous inflammation, sarcoidosis may resolve completely or progress with end-organ fibrosis. Cardiac involvement is common in autopsy studies but infrequently recognized clinically, and is a common cause of death. Approximately 5% of patients will have cardiac-predominant disease without evidence for other organ involvement [42]. Granulomas typically involve the basal septum and posterior wall, resulting in conduction system disease, localized LV aneurysms, and VT. Definitive diagnosis requires demonstration of cardiac granulomas, but patchy myocardial involvement reduces yield from cardiac biopsy to a low 25–30%. Imaging with fluorodeoxyglucose (^{18}F-FDG) and PET or CMR can identify inflammation and has better diagnostic accuracy compared with older techniques [43].

Although conduction abnormalities are the most common cardiac presentation, the risk of sudden death from ventricular arrhythmias is high in the presence of significant cardiac involvement. Hence, once a diagnosis of cardiac sarcoidosis is established, it is common to consider an ICD [44]. Treatment with corticosteroids has been shown in retrospective studies to stabilize LV function, but has no significant impact on conduction disease or ventricular arrhythmias [45].

Amyloidosis

The amyloidoses are a group of multisystem diseases characterized by deposition of the extracellular proteinaceous material amyloid. These deposits occur as a result of misfolding of a precursor protein [46]. The most common clinical amyloidoses that involve the heart are those due to deposition of light chains (AL amyloid), and a hepatically expressed protein, transthyretin (TTR). A form of wild-type TTR infiltration is seen in men aged older than 70 years and is termed senile amyloidosis. Cardiac involvement is the most common cause of death in amyloidosis and manifests as marked wall thickening due to infiltration in all anatomical distributions, including the atria, ventricles, and perivascular space. Because the infiltration is extracellular, despite the appearance of increased wall thickness on echocardiography, the voltage on surface ECG will be low and is a clue to the diagnosis. Perivascular fibrosis can affect the specialized conduction system, causing SND, intraventricular conduction defects, or AV block. Conduction system disease is common to all forms of cardiac amyloidosis but patients with senile cardiac amyloidosis most commonly progress to heart block. Permanent pacing is helpful in alleviating symptoms, but has not been demonstrated to provide a survival benefit [47,48].

Collagen vascular diseases

Several systemic inflammatory diseases can involve the heart and vascular structures, resulting in pericarditis, myocarditis, and vasculitis, including coronary artery disease. Arrhythmias are not common, but fibrosis of the conduction system has been reported to cause AV block, particularly in Wegener granulomatosis and polymyositis. An acute inflammatory AV block that reverses with treatment has been reported with Wegener granulomatosis. Congenital heart block associated with the transmission of anti-SSA/Ro antibodies from the mother occurs in systemic lupus erythematosus and to a lesser extent in primary Sjögren syndrome (see section Pacing for children and adolescents) [49].

Chagas disease

This chronic inflammatory disease, caused by the protozoan *Trypanosoma cruzi*, is largely restricted to endemic areas in Central and South America.

The acute phase of the infection usually goes unrecognized and is rarely life-threatening. Approximately 20% of patients will develop chronic Chagas disease several (10–20) years after the initial infection. Conduction system disease precedes other manifestations, such as localized cardiac aneurysms, thromboembolism, and a diffuse cardiomyopathy with marked cardiomegaly. Sinus bradycardia, atrial fibrillation, AV block, and ventricular arrhythmias are common. Even the early phases of conduction abnormalities, such as RBBB and fascicular block, are associated with an increased risk of sudden death [50].

Genetic cardiomyopathies

Familial or genetic cardiomyopathies account for 20–30% of disease originally diagnosed as idiopathic dilated cardiomyopathy. The work-up of these cardiomyopathies shares common management strategies. Once the proband is recognized, evaluation of family members can identify clinically silent cardiomyopathy and allow for early interventions. Genetic testing can be helpful in some diseases, especially if the pathogenic mutation is identified [51].

Dilated cardiomyopathy

Cardiomyopathies resulting from mutations in the gene coding for the nuclear envelope protein lamin A and C (*LMNA*) and mutations in the *SCN5A* gene are particularly associated with conduction system disease and ventricular arrhythmias [51]. Mutations in *LMNA* associated with cardiomyopathy are highly penetrant, with most carriers demonstrating some evidence of cardiac involvement by 65 years of age. Initial manifestations may be first-degree AV block with gradual progression to complete heart block. Associated atrial arrhythmias are common. Cardiomyopathy usually follows the development of conduction system disease by several years and risk of ventricular arrhythmias is highest when significant systolic dysfunction is present [51]. The diagnostic possibility of an inherited cardiomyopathy has two implications for the relatively young patient presenting with complete heart block: (i) a cardiac evaluation is warranted prior to permanent pacemaker implantation and (ii) periodic assessment of LV function is essential after cardiac pacing for early detection of LV dysfunction. Indications for pacing in dilated cardiomyopathy are discussed in the section Pacing for systolic heart failure.

Hypertrophic cardiomyopathy

This is a common disease entity caused by autosomal dominant mutations in genes encoding protein components of the sarcomere and its constituent myofilament elements. It is characterized by excessive myocardial hypertrophy without cavity dilatation, but varying degrees of phenotypic expression exist. The disease may manifest with LVOT obstruction, diastolic dysfunction, mitral regurgitation, myocardial ischemia, arrhythmias including atrial fibrillation, and sudden death. The distinction between the obstructive and non-obstructive varieties is important because management strategies are largely dependent on symptoms of obstruction. LVOT obstruction is well recognized to be dynamic. Although initially attributed to systolic contraction of the hypertrophied basal ventricle encroaching on the outflow tract, recent studies emphasize the importance of drag forces on an abnormally positioned mitral apparatus that push the leaflets into the outflow tract during systole [52].

In HCM with significant LVOT obstruction, atrial synchronized RV apical pacing results in decrease in outflow gradient and symptomatic improvement in a subset of patients. The exact mechanism of improvement is unclear, but may be related to paradoxical septal movement during systole, although alternate or additional mechanisms such as ventricular dilatation and chronic remodeling may play a part.

Initial enthusiasm for dual-chamber pacing in obstructive HCM was tempered by randomized trials that eliminated a placebo effect. In three randomized crossover trials of continuous DDD pacing compared with AAI pacing, the overall reduction in outflow tract gradient with DDD pacing was modest (20–40%), with substantial variation among individual patients, and symptomatic improvement was no different from that in AAI-paced patients [52]. Acute hemodynamic studies and echocardiographic LV morphology do not predict long-term benefit from dual-chamber pacing. One subgroup that appears to derive most benefit is patients over the age of 65 years [53]. When

pacing is performed to relieve outflow tract obstruction in HCM, it is important to optimize AV delay to allow ventricular preexcitation, but not to compromise ventricular filling with too short a delay. In addition, rate-adaptive AV delay is necessary to maintain ventricular preexcitation during exercise. The position of the ventricular lead should be such that it provides distal apical capture.

Permanent pacing is currently not considered an early mode of intervention for symptomatic obstructive HCM. Surgical myomectomy or alcohol septal ablation has been shown to provide more reliable and consistent clinical improvement. Pacing is therefore considered only for patients who are not candidates for these interventions or for those with preexisting dual-chamber pacing devices. Approximately 10–20% of patients will develop persistent complete heart block following alcohol septal ablation and will require permanent cardiac pacing. The risk of ventricular arrhythmias following septal ablation ranges in various reports from 2 to 5% per year. The choice of pacemaker versus ICD should be based on current guideline recommendations [52].

Indications for permanent pacing for HCM (adapted from ACC/AHA guidelines published in 2011 [53] and ESC guidelines in 2014 [54])

Class I indications

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

Class IIa indications

1 In patients with HCM who have had a dual-chamber device implanted for non-HCM indications, it is reasonable to consider a trial of dual-chamber AV pacing from the RV apex for the relief of symptoms attributable to LVOT obstruction. (Level of evidence: B)

Class IIb indications

1 AV sequential pacing may be considered in medically refractory symptomatic patients with obstructive HCM in sinus rhythm, with resting or revocable gradient >50 mmHg and who are not candidates for septal reduction therapy. (Level of evidence: C)

Pacing for systolic heart failure

Early studies suggested that dual-chamber pacing, especially with a short AV delay, improved hemodynamics by optimizing ventricular filling or reducing diastolic mitral regurgitation. However, randomized studies failed to confirm these beneficial effects. In contrast, there is considerable evidence that the use of biventricular pacing, by providing cardiac resynchronization therapy (CRT), reduces heart failure symptoms and lowers heart failure mortality with or without an ICD [55]. CRT has been well studied in randomized trials involving over 6000 patients and has demonstrated favorable structural remodeling with improved LV function and reduced mitral regurgitation in 70% of patients. Recent trials of less symptomatic patients (NYHA class I and II) show a reduction in composite end points of heart failure hospitalization and death, but mortality reduction is limited to class II patients [56,57]. All but one trial of CRT involved the use of an ICD as opposed to a CRT pacemaker. Consequently, it is common practice to incorporate defibrillator therapy when CRT pacing is indicated. However, CRT pacing alone has a significant impact on improving quality of life and functional status, and is a reasonable choice in older patients when prolongation of life is not the primary consideration. In addition, for patients who demonstrate a cardiomyopathy as a result of dyssynchrony induced by RV pacing, addition of a LV pacing lead to provide biventricular pacing alone may result in adequate reversal of cardiomyopathy and avoid the need for an ICD.

CRT device implantation is more difficult than placement of a non-CRT pacemaker or ICD and complication rates are greater, usually related to the additional manipulations required for the lead and its delivery systems. Lead dislodgement requiring revision is particularly more common [58]. Appropriate patient selection for this therapy is therefore crucial for ensuring benefit. In post-hoc subgroup analyses of clinical trials, factors associated with the most benefit from CRT include nonischemic dilated cardiomyopathy, the presence of LBBB, and QRS duration of 150 ms or longer [59]. The recent 2012 focused update guideline of the ACC, AHA and Heart Rhythm Society (HRS) limits the class I indication for CRT to patients with

LBBB and QRS duration of 150 ms or longer [55]. Between 2011 and 2016, several national societies published guidelines for CRT in heart failure creating some inconsistencies, especially with respect to QRS duration and non-LBBB QRS. For example, earlier recommendations suggested QRS duration greater than 120 ms as an indication for CRT. The ECHO CRT study, published in 2013, showed increased cardiovascular mortality with CRT in patients with QRS duration less than 130 ms [60]. Hence, more recent guidelines have set the cutoff at 130 msec below which CRT is not a recommendation.

The role of biventricular pacing in atrial fibrillation is less well established. As the purpose of pacing is to correct LV dyssynchrony, adequate heart rate control in atrial fibrillation is essential to allow for consistent biventricular pacing. Often this requires AV nodal ablation [61].

Indications for pacing in heart failure and impaired LV systolic function (based on the 2013 ACC/AHA guideline [62] and the 2016 ESC Heart Failure Society guideline [63])

Class I indications

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

2 CRT pacing in patients with an LV ejection fraction (LVEF) of 35% or less, sinus rhythm, LBBB, and QRS duration of 150 ms or longer, and heart failure with reduced ejection fraction on guideline-directed medical therapy (GDMT). (Level of evidence: A for NYHA III/IV and B for NYHA class II)

Note that the ESC Heart Failure Society guideline extends the class I indication to patients with the above characteristics and LBBB with QRS >130 ms. (Level of evidence: B)

3 CRT rather than RV pacing is recommended for patients with heart failure and reduced ejection fraction regardless of NYHA class for patient with an indication for ventricular pacing in order to reduce morbidity (Level of evidence: A)

Class IIa indications

1 CRT pacing can be useful in patients with an LVEF of 35% or less, sinus rhythm, LBBB with a QRS duration of 130–149 ms, and NYHA class II, III or ambulatory IV symptoms on GDMT. (Level of evidence: B). Note that this is a class I indication according to ESC Heart Failure Society 2016 guideline.

2 CRT can be useful in patients with an LVEF of 35% or less, sinus rhythm, non-LBBB pattern with a QRS duration of 150 ms or longer, and heart failure with reduced ejection fraction on GDMT. (Level of evidence: B)

3 CRT can be useful in patients with atrial fibrillation and an LVEF of 35% or less on GDMT if:

a the patient requires ventricular pacing or otherwise meets CRT criteria; and

b AV nodal ablation or pharmacological rate control will allow near 100% ventricular pacing with CRT. (Level of evidence: B)

4 CRT can be useful in patients on GDMT who have an LVEF of 35% or less and are undergoing device placement or replacement with anticipated requirement for significant (>40%) ventricular pacing. (Level of evidence: B)

Class IIb indications

1 CRT may be considered for patients who have an LVEF of 35% or less, sinus rhythm, non-LBBB pattern with a QRS duration 130–149 ms, and NYHA class III/ambulatory class IV symptoms on GDMT. (Level of evidence: B)

Class III (not indicated)

1 CRT pacing is not recommended for patients with a QRS duration <130 ms. (Level of evidence: A)

Pacing to prevent or terminate tachycardias

Pacing techniques may terminate arrhythmias that depend on a reentrant mechanism. For supraventricular tachycardias (SVTs) and atrial arrhythmias, antiarrhythmic drugs or catheter-based ablation is often effective in preventing recurrence and hence, in contemporary practice, the use of cardiac pacing is limited to patients who have associated bradyarrhythmias. Rarely, a patient who fails one or is unsuitable for drugs or ablation may benefit from antitachycardia pacing if reliable and repetitive termination of the arrhythmia can be demonstrated without proarrhythmic effects (Figure 1.16). Such devices for pacing without defibrillation capability

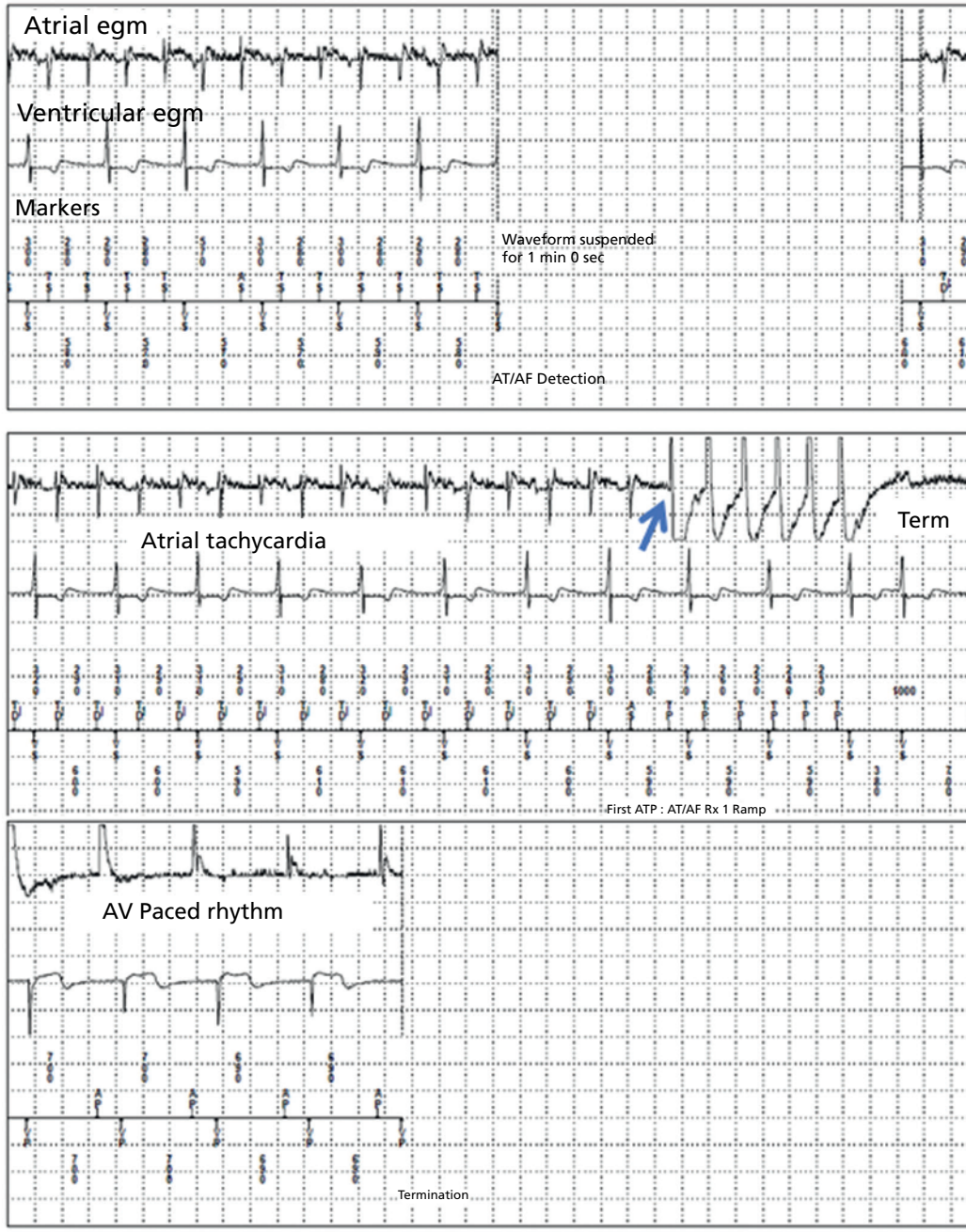

Figure 1.16 Atrial overdrive pacing to terminate atrial tachycardia. This 75-year-old female with pulmonary hypertension and recurrent atrial tachycardia had a dual-chamber pacemaker for tachy–brady syndrome. Her atrial arrhythmia was reproducibly terminated with atrial overdrive pacing. (*Top to bottom*) Atrial bipolar electrograms, ventricular electrograms, and marker channels. At baseline, an atrial tachycardia at a cycle length of 250 ms (240 bpm) was present. A burst of atrial overdrive pacing was delivered (blue arrow) and resulted in termination of tachycardia (term) with resumption of AV synchronized pacing.

are limited to the atrium. Ventricular antitachycardia pacing is currently only available with ICDs.

Ventricular arrhythmias may be pause dependent and pacing prevents prolonged pauses and can prevent the arrhythmia in some patients. Typically, the onset of torsades de pointes VT in patients with a prolonged QT interval is preceded by long RR intervals (Figure 1.17). Pacing combined with β-adrenergic blockers has been shown to reduce the occurrence of sudden cardiac death in patients with the congenital long-QT syndrome [64]. In patients with long-QT syndrome at high risk for sudden death, however, such pacing is usually provided via an ICD.

Several modes of permanent pacing therapy have been tested for prevention of atrial fibrillation. However, none of the special pacing techniques, such as dual-site atrial pacing, biatrial pacing, alternative sites for atrial pacing in the region of the Bachmann bundle or low septum, or atrial overdrive pacing algorithms, has shown significant benefit [65]. In patients with SND, the use of atrial-based pacing is superior to VVI pacing in reducing atrial fibrillation and stroke. Benefit is maximal when ventricular pacing is minimized.

Indications for permanent pacing to prevent or terminate tachycardias

Class I indications

1 Permanent pacing is indicated for sustained pause-dependent VT, with or without QT prolongation. (Level of evidence: C)

Class IIa indications

1 Permanent pacing is reasonable for high-risk patients with congenital long-QT syndrome. (Level of evidence: C). Note that most of these patients will qualify for an ICD.

2 Symptomatic recurrent SVT 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)

Class IIb indications

1 Prevention of symptomatic, drug-refractory recurrent atrial fibrillation in patients with coexisting sinus node dysfunction. (Level of evidence: B)

Class III (not indicated or recommended)

1 The presence of accessory pathways with the capacity for rapid anterograde conduction whether

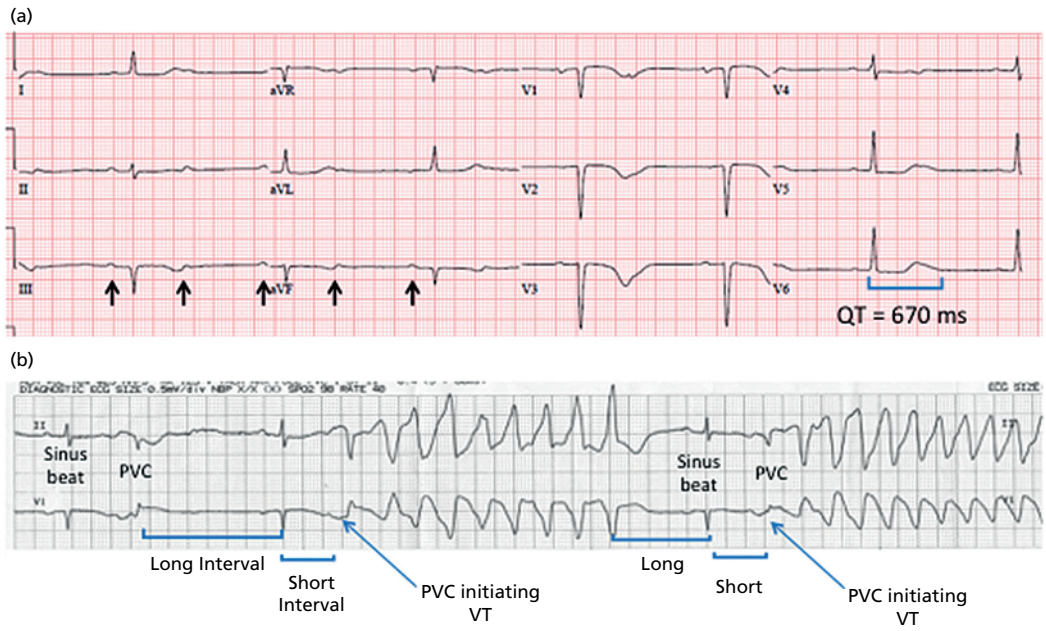

Figure 1.17 Bradycardia-related torsades de pointes ventricular tachycardia (VT). (a) Marked QT prolongation related to 2 : 1 AV block in an 80-year-old woman hospitalized with syncope and facial injuries. The black arrows denote P waves. (b) A premature ventricular contraction (PVC) that arises on the T wave causes a post-PVC pause, further lengthening QT interval. Self-limiting torsade de pointes VT is initiated by a long–short RR interval and is repeated.

or not the pathway(s) participate in the mechanism of the tachycardia.

2 Frequent or complex ventricular ectopic activity without sustained VT in the absence of the long-QT syndrome.

3 Torsades de pointes VT due to reversible causes.

Pacing for children and adolescents (including all patients with congenital heart block)

There are no randomized clinical trials of permanent pacing in pediatric patients and those with congenital heart disease. Hence, the level of evidence for most recommendations is consensus based. The general indications for pacing in children and adolescents are similar to those for adults but with several additional considerations. The diagnosis of important bradycardia in children is age dependent. Whereas a heart rate of 45 bpm would be considered normal for an adult, the same rate would indicate profound bradycardia in a newborn or infant with marked hemodynamic consequences. In addition, the abnormal cardiovascular physiology resulting from palliative surgery for congenital heart diseases can place postsurgical patients at risk for decompensation from bradycardia or loss of AV synchrony that may have been well tolerated by patients with normal physiology. Further, the risk of paradoxical embolism from thrombus on endocardial leads is a consideration in patients with significant intracardiac shunts. Finally, the technical challenges of vascular access and long-term consequences of endovascular leads in children often prompt the consideration of epicardial systems at early ages. While this may be appropriate for children weighing less than 10–15 kg, in larger children the risks of thoracotomy and the higher rate of epicardial lead failures have to be balanced against vascular occlusions from endovascular lead placement. Long-term RV pacing can lead to ventricular dysfunction and periodic assessment by echocardiography is helpful in the detection of early LV dysfunction, especially in patients with congenital heart disease and genetic cardiomyopathies.

The common indications for pacing in children, adolescents, and patients with congenital heart disease can be broadly divided into (i) sinus bradycardia, (ii) tachy–brady syndrome, and (iii) congenital or postsurgical advanced second- or third-degree AV block. SND is rare in pediatric patients but, when present, may be associated with mutations in the *SCN5A* gene [66]. Pacing is usually reserved for situations where symptoms such as syncope can be correlated with bradyarrhythmias (<40 bpm or >3-s pause). It should be recognized that apnea, seizures, and neurocardiogenic mechanisms might cause concurrent bradycardia. Correction of the primary abnormality is more effective than long-term pacing for these conditions.

The common form of tachy–brady syndrome seen in children follows surgery for congenital heart disease. Intra-atrial reentrant tachycardia with loss of sinus node function can manifest as recurrent palpitation, hemodynamic compromise, and prolonged sinus pauses at termination of the atrial tachycardia. Although permanent atrial-based pacing, including antitachycardia pacing to terminate intra-atrial reentry, is a potential treatment option, catheter-based ablation of these arrhythmias is optimal if it can be achieved successfully.

Congenital complete AV block is a rare anomaly that results from abnormal embryonic development of the AV node and is not associated with structural heart disease in 50% of cases. Patients can be broadly divided into groups that are antibody (maternal anti-SS/Ro and/or anti-SSb/La antibodies) positive and antibody negative. When anti-SSA/Ro antibodies are present in the sera of mothers with connective tissue disease, the incidence of congenital heart block in live births has been reported to be 1–2% [67]. The antibodies cross the placenta and damage the conduction system; heart block develops *in utero* and in the early neonatal stage. Less commonly, late postnatal development of heart block has been described. The antibody-negative group tends to present at a later stage and heart block is progressive.

Most children with isolated congenital complete AV block have a stable escape rhythm with a narrow complex. The indications for pacing continue to evolve. Pacing is generally indicated in symptomatic children with complete heart block or if the heart rate in the neonate is less than 55 bpm. In the asymptomatic child or adolescent with complete congenital AV block, several criteria, including average heart rate, pauses in intrinsic rate, associated structural

heart disease, QT interval, and exercise tolerance, have been suggested as indications for pacing [68,69].

Congenital heart diseases such as corrected transposition of the great arteries, ostium primum atrial septal defects, and ventricular septal defects may be associated with complete heart block. Patients who develop permanent postsurgical complete AV block have a poor prognosis without cardiac pacing. Hence, advanced AV block that persists for longer than 7–10 days postoperatively is considered a class I indication for pacing.

Indications for permanent pacing in children and adolescents (based on 2018 ACC/AHA/HRS guidelines [13])

Class I indications

1 In adults with congenital heart disease (CHD) and symptomatic SND or chronotropic incompetence, atrial-based permanent pacing is recommended. (Level of evidence: B-NR)

2 In adults with CHD and symptomatic bradycardia due to AV block, permanent pacing is recommended. (Level of evidence: B-NR)

3 In adults with congenital complete AV block with any symptomatic bradycardia, a wide QRS escape rhythm, mean daytime heart rate below 50 bpm, complex ventricular ectopy or ventricular dysfunction, permanent pacing is recommended. (Level of evidence: B-NR)

4 In adults with CHD and postoperative second-degree Mobitz-type II AV block, high-grade AV block or complete AV block that is not expected to resolve, permanent pacing is recommended. (Level of evidence: B-NR)

5 Congenital third-degree AV block in an infant with a ventricular rate of less than 55 bpm or with congenital heart disease and a ventricular rate of less than 70 bpm. (Level of evidence: C-EO)

Class IIa indications

1 In asymptomatic adults with congenital complete AV block, permanent pacing is reasonable. (Level of evidence: B-NR)

2 In adults with repaired CHD who require permanent pacing for bradycardia indications, a bradycardia device with atrial antitachycardia pacing capabilities is reasonable. (Level of evidence: B-NR)

3 In adults with CHD with preexisting sinus and/or AV conduction disease who are undergoing cardiac surgery, intraoperative placement of epicardial permanent pacing is reasonable. (Level of evidence: C-EO)

Class IIb indications

1 In adults with CHD and pacemakers, atrial-based permanent pacemakers for the prevention of atrial arrhythmias maybe considered. (Level of evidence: B-NR)

Class III (not indicated or harm)

1 In selected patients with adult CHD and venous-to-systemic intracardiac shunts, placement of endocardial leads is potentially harmful. (Level of evidence: B-NR)

Permanent pacing after the acute phase of myocardial infarction

Bradyarrhythmias and conduction defects are relatively common after acute myocardial infarction (MI). They are the result of both autonomic stimulation and ischemia or necrosis of the conduction system. In a large randomized trial of thrombolysis in acute MI, AV block occurred in approximately 7% [70]. The location of the infarction influences the type of conduction defect. AV block associated with inferior wall MI is often at the AV nodal level with narrow QRS escape rhythms, is usually transient, and has a good prognosis. Permanent pacing is rarely required. AV block in association with an anterior MI is most often due to extensive myocardial necrosis that includes the conduction tissue, tends to be infranodal with unstable wide QRS escape, and carries a high mortality, although acute revascularization strategies have improved outcomes in these patients (Figures 1.18 and 1.19). Intraventricular conduction defects (IVCDs) after acute MI occur transiently in up to 18.4% of patients and in a permanent form in 5.3% [71]. The incidence of AV block is higher in post-MI patients who develop transient AV block associated with a persisting peri-infarct IVCD other than isolated left anterior fascicular block.

Although temporary pacing is often necessary in the acute phase of infarction, the need for permanent pacing is less common and mostly dictated by the presence of IVCDs and not necessarily by the presence of symptoms. The long-term

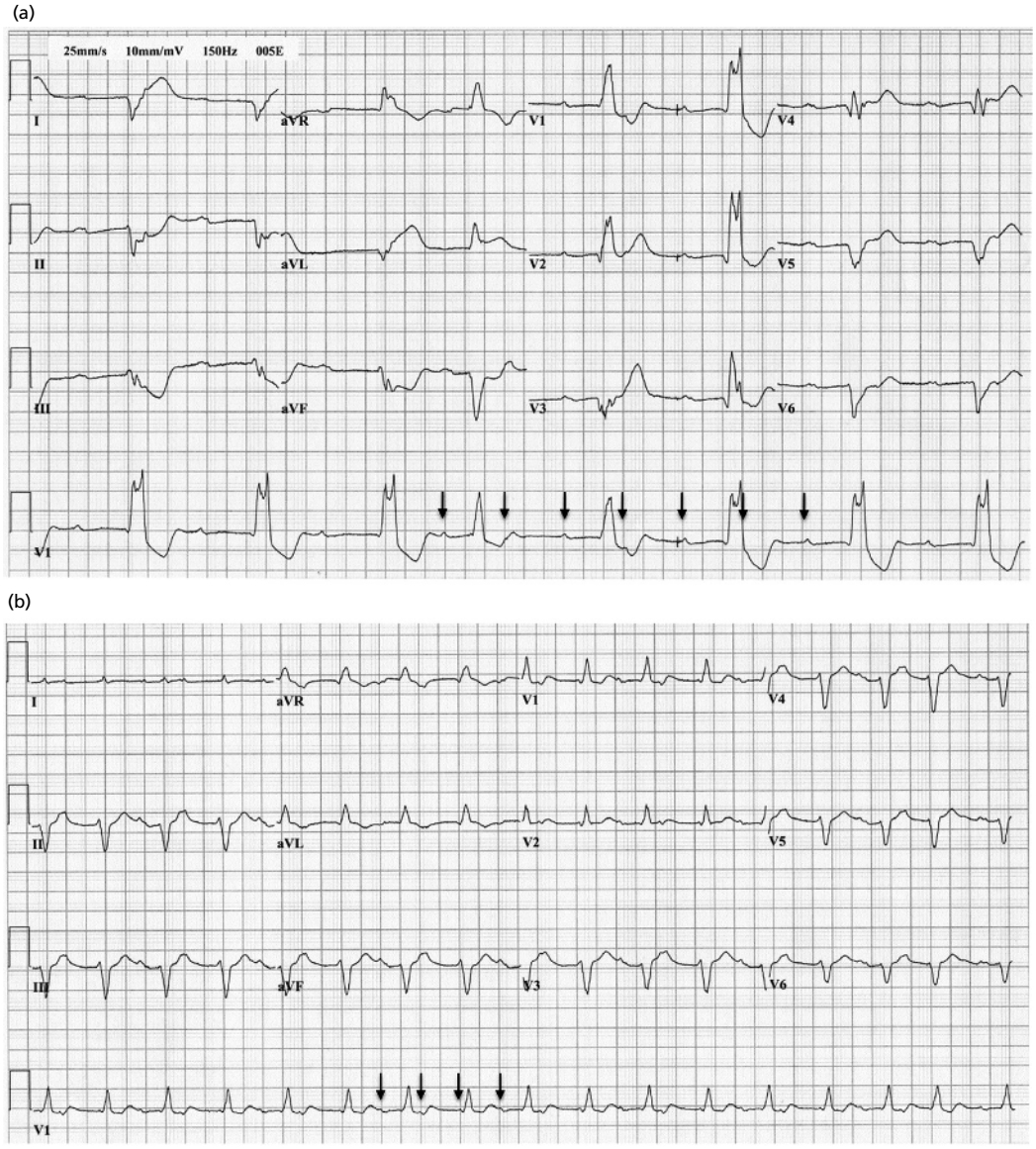

Figure 1.18 Acute anterior myocardial infarction complicated by complete AV block. This 82-year-old male presented with acute left main coronary artery occlusion in cardiogenic shock. (a) The initial ECG shows complete AV block with wide complex escape and evidence of ST-elevation myocardial infarction. The fourth and probably also the fifth complexes are conducted beats. P waves are indicated by arrows. He underwent temporary pacing, percutaneous intervention for acute revascularization, and hemodynamic support with a percutaneous left ventricular assist device. (b) ECG on the following day shows persistent complete AV block and an accelerated junctional rhythm with right bundle branch block and left anterior hemiblock. Although the conduction abnormalities are indications for pacing, the associated myocardial damage and hemodynamic compromise limit prognosis. This patient succumbed to progressive multiorgan failure.

prognosis for patients who develop AV block and an IVCD is strongly influenced by the extent of myocardial injury and hemodynamic status (Figure 1.18). The need for temporary pacing in the acute stages of infarction is not by itself an indication for permanent pacing. Patients who have an indication for permanent pacing after ST-elevation MI and severe LV dysfunction should be

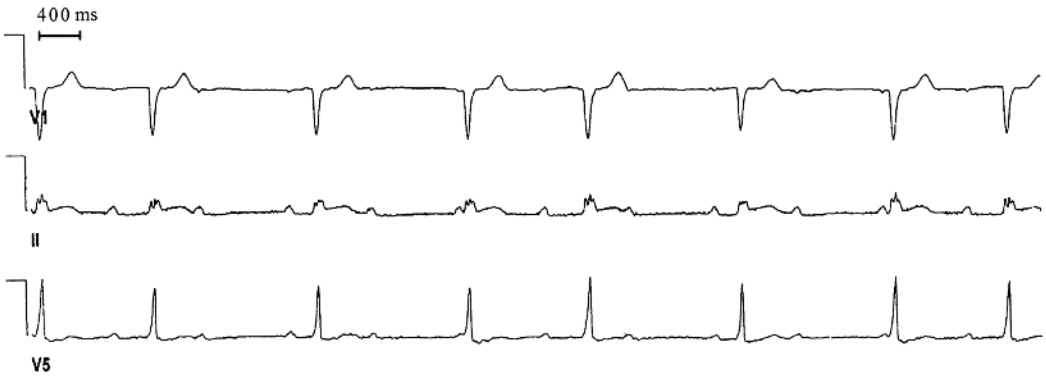

Figure 1.19 AV block associated with acute inferior myocardial infarction. Rhythm strips recorded from a 63-year-old female with an acute inferior wall myocardial infarction showing high-grade AV block with junctional escape beats. Some of the P waves are conducted with a prolonged PR interval (e.g. second QRS is captured by atrial conducted beat). The presence of junctional escape beats precludes typical Wenckebach conduction. Because the patient was asymptomatic, no therapy was administered. Normal AV conduction resumed the following morning.

evaluated for an ICD indication if recovery of ventricular function is not anticipated.

Indications for permanent pacing following acute myocardial infarction

Class I indications

1 Patients who present with sinus node dysfunction or AV block in the setting of an acute MI should undergo a waiting period before determining the need for permanent pacing. (Level of evidence: B-NR)

2 In patients presenting with an acute MI with second-degree Mobitz type II AV block, high-grade AV block, alternating bundle branch block or complete AV block (persistent or infranodal), permanent pacing is indicated after a waiting period. (Level of evidence: B-NR)

Class III (not indicated or harm)

1 In patients with an acute MI and transient AV block that resolves, permanent pacing should not be performed. (Level of evidence: B-NR)

2 In patients with an acute MI and a new bundle-branch block or isolated fascicular block in the absence of second- or third-degree AV block, permanent pacing should not be performed. (Level of evidence: B-NR)

Pacing after cardiac surgery and transcatheter aortic valve implantation

Approximately 3–5% of patients will develop persistent bradyarrhythmias after open heart surgery, with a higher incidence following repeat surgery. Sinus node dysfunction may result from right atrial cannulation for cardiopulmonary bypass, but mostly resolves within a week. The development of paroxysmal atrial arrhythmia in conjunction with SND can be particularly troublesome to treat without temporary pacing support. However, once sinus node function recovers, antiarrhythmic drugs can often be employed safely for postoperative atrial arrhythmias.

In adults, persistent AV block is most common after valvular surgery, particularly tricuspid valve replacement (12%). Risk is higher with multivalvular surgery, up to 25% for triple valve replacement [72]. In one large retrospective study, preexisting RBBB was more predictive than LBBB, but preoperative PR prolongation, repeat surgery, and age over 70 years were all predictors for the need for permanent pacing [72]. The aortic valve is closely related to the His bundle and surgical valve replacement carries a higher risk for persistent AV block. Hence, the threshold for pacing for heart block complicating aortic valve surgery is lower. Mitral valve surgery more commonly affects the AV node partly due to injury to the AV nodal artery. As the block is at the nodal level, threshold for pacing is higher. The majority of patients who develop postoperative bradyarrhythmias recover conduction and hence it is customary to wait 5–7 days before consideration of permanent pacing. If there is evidence for continued improvement in sinus node function or AV block at the nodal level, longer waiting times may be justified. Patients who ultimately undergo permanent cardiac pacing tend to have a good prognosis and only about 40% remain dependent on pacing in the longer term [73]. Septal

myomectomy or alcohol septal ablation for hypertrophic obstructive cardiomyopathy is associated with AV block requiring pacing in 10–14% of patients [74]. The risk of sudden death is estimated to be approximately 1% per year and does not warrant the routine use of defibrillators. However, in the presence of other risk factors such as marked LV thickening, family history, or syncope, a defibrillator rather than a pacemaker is indicated.

Transcatheter aortic valve replacement (TAVR) is rapidly evolving as an effective alternative to valve surgery for patients with aortic stenosis. Unlike in the surgical procedure where the valve is excised prior to replacement, the calcified valve remains *in situ* in TAVR. Transcatheter placement of a valve prosthesis and balloon dilatation within this calcified valve produce a mass effect in the region of the membranous septum and adjoining conduction system. This potential mechanism leads to persistent heart block requiring cardiac pacing in 2–20% of patients, with the more recent studies documenting a lower incidence of persistent conduction defects [75,76]. New LBBB occurs in 20–50% of patients, and high-grade AV block in approximately 10% of patients but half of these resolve before discharge [75]. QRS duration of less than 120 ms was predictive of recovery [77]. Patients with new LBBB that persists after TAVR are also at risk of late heart block after discharge. In one study, an HV interval of more than 65 ms after TAVR had an 80% sensitivity and specificity for subsequent risk for heart block [78].

Earlier studies had shown a higher propensity for AV block based on type of prosthesis used but newer valves and better positioning have reduced the incidence. However, the risk of AV block in patients who develop new LBBB and timing of pacemaker implant remain ill-defined. Current guidelines recommend that a pacemaker may be considered for persisting LBBB after TAVR (class IIb indication) [13]. As more patients undergo non-surgical aortic valve replacement, larger studies will be needed to define risk of persistent AV block.

Drug-induced bradycardia

A number of medications may produce transient bradycardia that may require temporary pacing until the effect of the drug dissipates. These drugs may cause sinus node dysfunction and/or AV block; if drugs are used in combination, their effects may become more potent and exacerbate mild or latent conduction system disease. If long-term therapy with these agents is necessary for an underlying disorder and a substitute cannot be found, permanent pacing may be required (Figure 1.5). Drug-induced AV block might not always resolve after discontinuation of the potentially offending drug. In one series, approximately half of patients who developed heart block in the context of therapy with an AV nodal blocking agent required permanent pacing for persistent or recurrent AV block [75]. Cessation of digoxin therapy has the best chance of recovery of AV nodal conduction, but β-adrenergic blocker therapy often unmasks underlying conduction disease [79,80].

Sleep-disordered breathing and bradycardia

Nocturnal bradycardia is common in the young and conditioned athletes. Sinus bradycardia, sinus arrest, and varying degrees of AV block at the nodal level are observed and, in most circumstances, is physiological and vagally mediated. No intervention is required in the asymptomatic patient [81]. The prevalence of nocturnal bradyarrhythmia is lower in middle-aged and older healthy individuals.

A higher prevalence of sleep-related bradycardia is seen in patients with sleep apnea syndrome; the bradyarrhythmia tends to correlate with hypopneic events. Sinus node dysfunction is most common (7–40%) but second- or third-degree AV block is observed in 1–13% of patients [82]. Prevalence of bradyarrhythmias correlates with severity of sleep apnea. These patients have normal rhythm during wakeful hours. Continuous positive airway pressure reduces sleep-related bradyarrhythmia by 70–80% and eliminates the need for cardiac pacing in the majority. Symptomatic bradycardia is rare during long-term follow-up.

Summary

In patients with symptomatic and potentially life-threatening bradyarrhythmias, cardiac pacing is a cost-effective intervention to relieve symptoms and prevent death. However, the possible complications and the potentially complex longer-term management of permanent pacemaker systems require that careful consideration be given to the indications before implantation.

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