

*Primary Care***THE EVALUATION AND MANAGEMENT OF BRADYCARDIA**

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BRADYCARDIA is a common finding during the clinical evaluation of both healthy patients and those who are ill. Bradycardia may be caused either by intrinsic dysfunction of or damage to the conduction system or by the response of normal tissues to extrinsic factors. In many cases, even profound bradycardia may be asymptomatic and have no immediate or long-term pathologic importance. In this article, we will briefly review the clinical presentation, pathophysiology, diagnostic evaluation, and treatment of patients with bradycardia.

CLINICAL PRESENTATION

Cardiac output is the left ventricular forward stroke volume multiplied by the heart rate. Patients with bradycardia may be asymptomatic if changes in stroke volume compensate for the decrease in heart rate. In asymptomatic persons, bradycardia may be noted as an incidental finding during a routine physical examination or identified on an electrocardiogram or rhythm strip obtained for other purposes. Bradycardia may also be found during the evaluation of patients with a variety of symptoms and signs. In cases in which symptoms suggestive of bradycardia are intermittent and specific (e.g., syncope), establishment of the correlation between symptoms and simultaneous changes in rhythm is the key to diagnosis and management. However, the patient's presenting symptoms are often nonspecific and chronic (e.g., dizziness, fatigue, weakness, or heart failure). In such cases, the relation between symptoms and bradycardia is less certain, and unless the latter is extreme, interventions designed solely to correct bradycardia may not prove to be effective.

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NORMAL ANATOMY AND PHYSIOLOGY OF THE CONDUCTION SYSTEM

The sinus node is a collection of specialized cells located in the sulcus terminalis at the junction of the superior vena cava and the right atrium that depolarize spontaneously.¹ The sinus node is supplied with blood by the sinus-node artery, which originates from the proximal right coronary artery in 65 percent of patients, the circumflex artery in 25 percent, and both in 10 percent. Normally, impulses originate in the sinus node and propagate through the right atrium to the atrioventricular node in the low septal right atrium.

The atrioventricular node receives its blood supply from the atrioventricular nodal artery, which arises from the proximal portion of the posterior descending artery. This artery arises from the right coronary artery in 80 percent of patients, the circumflex coronary artery in 10 percent, and both in the remainder. Impulses are conducted through the atrioventricular node to the bundle of His, which courses through the membranous septum, then separates into two major divisions — the right and left bundle branches.

The conduction system of the heart is heavily innervated by both the sympathetic and the parasympathetic nervous systems. Parasympathetic tone decreases sinus-node automaticity and slows atrioventricular nodal conduction. A very strong vagal stimulus, such as that seen during vomiting, can transiently depress the automaticity of the sinus node or block transmission across the atrioventricular node, even in healthy persons. Sympathetic output increases automaticity and enhances conduction.

A patient's base-line heart rate and conduction velocity are determined by the balance between the output of the parasympathetic nervous system and that of the sympathetic nervous system. The intrinsic heart rate after full autonomic blockade ranges from 85 to 105 beats per minute and is inversely related to age.² This rate is higher than the normal resting heart rate in adults, reflecting the fact that parasympathetic tone predominates under basal conditions. In addition, variation in the heart rate throughout the day has been well described, with the slowest heart rates occurring at night.^{3,4}

HEART RATE IN NORMAL SUBJECTS

There is considerable variation in the resting heart rate among the healthy, asymptomatic population. Spodick and others estimated that the "normal" range of heart rates in the afternoon was 46 to 93 beats per minute for men and 51 to 95 beats per minute for women.⁵⁻⁷ Nocturnal rates are slower, decreasing during sleep by an average of 24 beats per minute in

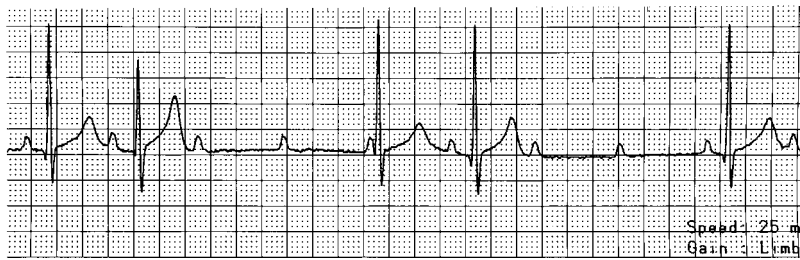


Figure 1. Asymptomatic Bradycardia in an 18-Year-Old Male Athlete.

This electrocardiographic tracing was obtained while the patient was relaxing after lunch. The tracing shows vagally mediated sinus slowing and atrioventricular block with one junctional escape beat. Similar rhythms were noted while the patient was sleeping. On the same 24-hour recording, sinus rates of more than 180 beats per minute, with a normal PR interval, were seen during exercise. No symptoms developed during long-term follow-up without therapy.

young adults and by 14 beats per minute in those over 80 years of age.^{3,8} Ambulatory electrocardiography in healthy, asymptomatic persons has shown that transient bradyarrhythmias are common during sleep.⁹⁻¹² Heart rates between 30 and 35 beats per minute, sinus pauses of 2.5 seconds or less, sinoatrial block, junctional rhythms, and first-degree and second-degree atrioventricular nodal block are common enough during sleep to be considered normal variants. Trained athletes are particularly prone to bradycardia, with heart rates below 40 beats per minute common at rest (Fig. 1).^{4,13,14} In one series, sinus pauses lasting between two and three seconds were found in 37 percent of athletes during sleep.⁴ In view of these findings, the current guidelines of the American College of Cardiology and the American Heart Association for pacemaker implantation suggest that asymptomatic episodes of sinus bradycardia (with the heart rate as low as 30 beats per minute), sinus pauses of up to three seconds, and atrioventricular nodal Wenckebach block should be considered to be within the normal range.¹⁵ Even if more pronounced bradycardia is documented, reversible causes may be responsible. For example, profound bradycardia often develops in patients with obstructive sleep apnea and hypoxia but may be eliminated if the sleep apnea is appropriately treated.^{16,17}

Patients with atrial fibrillation require special consideration, because they have greater variations in heart rate than their counterparts in sinus rhythm.^{18,19} Although symptomatic bradycardia during atrial fibrillation is common and accounts for up to 13 percent of the indications for implantation of a pacemaker, asymptomatic, prolonged ventricular pauses also occur frequently.²⁰ Pitcher et al.²¹ reviewed Holter-monitor tracings from 66 asymptomatic patients with chronic atrial fibrillation and found that two thirds of them had pauses longer than two seconds and 20 percent had pauses longer than three seconds. Therefore, they concluded that daytime pauses of up to 2.8

seconds and nighttime pauses of up to 4.0 seconds during atrial fibrillation should be considered to be within expected limits. On the basis of these data, it is wise to interpret isolated, asymptomatic pauses during atrial fibrillation conservatively.

Another feature of heart rate is its ability to increase appropriately in response to exercise. Failure to do so has been termed "chronotropic incompetence." Unfortunately, there is no universally accepted precise definition of chronotropic incompetence. Proposed definitions have included the failure to reach a heart rate that is 85 percent of the age-predicted maximum ($220 - \text{age in years}$) at peak exercise, the failure to achieve a heart rate of 100 beats per minute, or a maximal heart rate more than 2 SD below that in a control population.²²⁻²⁵

SINUS-NODE DYSFUNCTION

Sinus-node dysfunction, also referred to as "sick sinus syndrome,"^{26,27} is a common cause of bradycardia. The prevalence of sinus-node dysfunction has been estimated to be as high as 1 in 600 patients over the age of 65 years, and the syndrome accounts for approximately 50 percent of pacemaker implantations in the United States.²⁸ Sinus-node dysfunction may be due to intrinsic pathologic characteristics of the sinus node itself, or it may be due to extrinsic causes (Table 1).²⁹⁻³³ Intrinsic disease is characterized by the replacement of nodal tissue with fibrous tissue. Since the sinus node is a complex of cells in the atrial wall, permanent injury by infarction or infection is uncommon. Extrinsic causes of sinus-node dysfunction include the use of pharmacologic agents (e.g., β -adrenergic blockers, calcium-channel blockers, digoxin, some antihypertensive agents, and antiarrhythmic drugs), electrolyte imbalance, hypothermia, hypothyroidism, increased intracranial pressure, and excessive vagal tone.

Sinus-node dysfunction, either intrinsic or extrinsic, may have several electrocardiographic presentations

TABLE 1. CAUSES OF BRADYCARDIA.**Intrinsic causes**

Idiopathic degeneration (aging)
 Infarction* or ischemia
 Infiltrative diseases
 Sarcoidosis
 Amyloidosis
 Hemochromatosis
 Collagen vascular diseases
 Systemic lupus erythematosus
 Rheumatoid arthritis
 Scleroderma
 Myotonic muscular dystrophy
 Surgical trauma
 Valve replacement
 Correction of congenital heart disease
 Heart transplantation
 Familial diseases
 Infectious diseases*
 Chagas' disease
 Endocarditis

Extrinsic causes

Autonomically mediated syndromes
 Neurocardiac syncope
 Carotid-sinus hypersensitivity
 Situational disturbances
 Coughing
 Micturition
 Defecation
 Vomiting
 Drugs
 β -Adrenergic blockers
 Calcium-channel blockers
 Clonidine
 Digoxin
 Antiarrhythmic agents
 Hypothyroidism
 Hypothermia
 Neurologic disorders
 Electrolyte imbalances
 Hypokalemia
 Hyperkalemia

*This condition causes atrioventricular-conduction disturbances only.

(Fig. 2). Sinus bradycardia is due to depressed automaticity in the sinus node itself. Sinus pauses or sinus arrest may be due to failure of either impulse formation or conduction out of the nodal region to the surrounding atrium. Abnormal automaticity and conduction in the atrium predispose patients to atrial fibrillation and flutter, and the bradycardia-tachycardia syndrome is a common manifestation of sinus-node dysfunction. The combination of tachycardia and sinus bradycardia in patients with sinus-node dysfunction is particularly worrisome, since overdrive suppression of sinus automaticity may result in long pauses and syncope when tachycardia terminates. Therapy to control the ventricular rate during tachycardia by blocking atrioventricular conduction with β -adrenergic blockers, calcium-channel blockers, or digitalis may not be possible, because it may further depress the sinus node.

ATRIOVENTRICULAR-CONDUCTION DISTURBANCES

Atrioventricular conduction may be delayed in either the atrioventricular node or the bundle of His. Delays exclusively below the bifurcation of the bundle of His result in bundle-branch or fascicular blocks, but atrioventricular conduction should be maintained unless all three fascicles are simultaneously affected. As with sinus-node dysfunction, atrioventricular-conduction disturbances can be caused by both intrinsic disease and extrinsic factors (Table 1). Unlike the sinus node, however, the atrioventricular node and bundle of His provide a discrete connection between the atria and ventricles, so focal injury from infarction, infection, or catheter-related trauma is a common cause of problems. The location of atrioventricular-conduction delay can often be learned from the surface 12-lead electrocardiogram (Fig. 3).

First-degree atrioventricular block is a common electrocardiographic finding. The PR interval represents the conduction time from the sinus node through the atrium, atrioventricular node, and His-Purkinje system to the onset of ventricular depolarization. By convention, values over 0.2 second with a retained 1:1 atrioventricular relation constitute first-degree atrioventricular block. First-degree atrioventricular block does not by itself cause bradycardia, but it is often seen in conjunction with second-degree or third-degree block or sinus-node dysfunction. Some patients with marked first-degree atrioventricular block have symptoms owing to a loss of atrioventricular synchrony that resolve with pacing.

Second-degree atrioventricular block occurs when an organized atrial rhythm fails to conduct to the ventricle in a 1:1 ratio but some atrial-ventricular relation is maintained. Several patterns are seen. Mobitz type I second-degree atrioventricular block (Wenckebach block) is diagnosed when the electrocardiogram shows a stable PP interval and a progressive increase in the PR interval until a P wave fails to conduct. The PR increment usually decreases with each beat in the cycle, so that the RR intervals actually shorten. After the blocked P wave, the next PR interval returns to the initial value. Mobitz type I block is usually due to a delay in the atrioventricular node but may occur in the bundle of His in patients with advanced disease. In Mobitz type II second-degree atrioventricular block, there is a stable PP interval with no measurable prolongation of the PR interval before an abrupt conduction failure. Mobitz type II block is most often associated with disease of the His-Purkinje system. In atrioventricular block with a 2:1 conduction ratio or higher (e.g., 3:1 or 4:1), it is impossible to observe prolongation of the PR interval before the block, so a designation of type I or type II is not appropriate. In 2:1 block, a narrow QRS complex and associated periods of Wenckebach block, or simultaneous sinus slowing ("vagotonic block"), suggest that

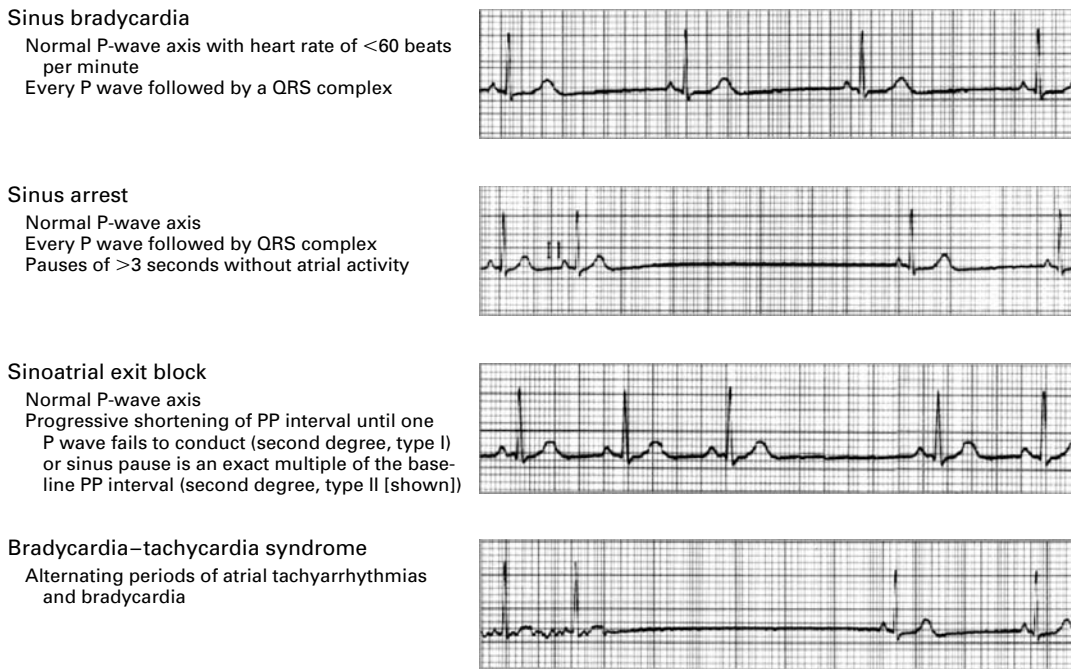


Figure 2. Electrocardiographic Findings Associated with Sinus-Node Dysfunction.

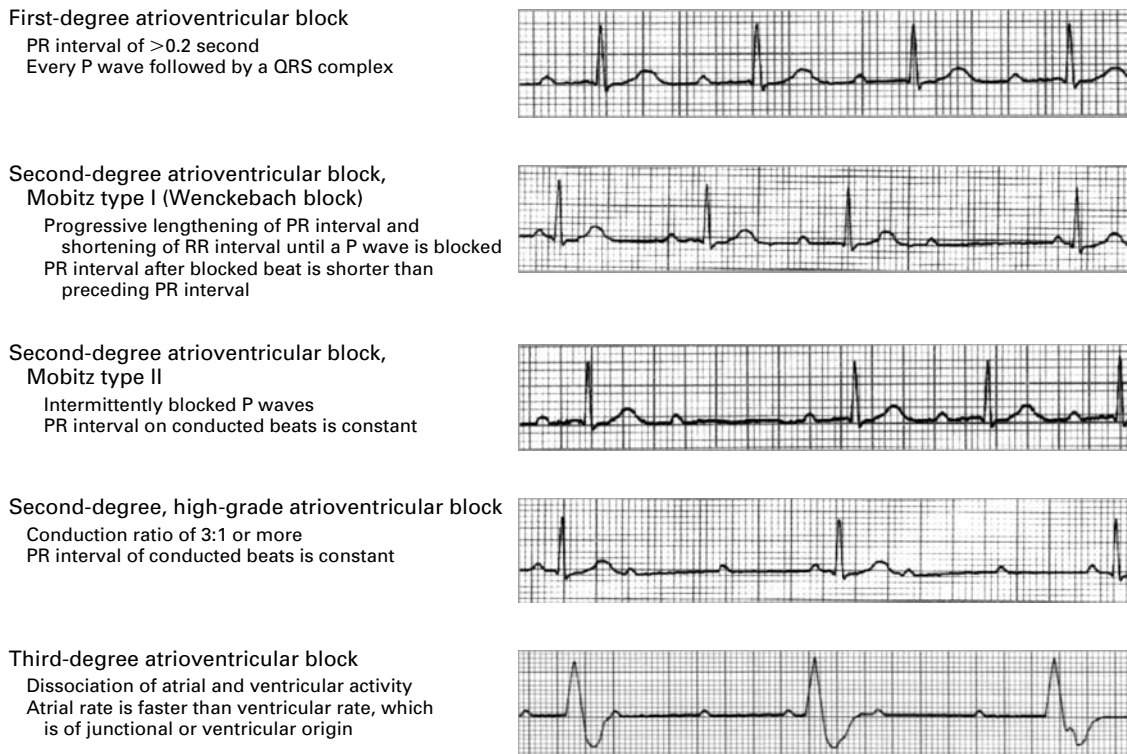


Figure 3. Electrocardiographic Findings Associated with Atrioventricular-Conduction Disturbances.

atrioventricular nodal block is present, whereas a wide QRS complex suggests the presence of infranodal block.

Third-degree atrioventricular block is often referred to as “complete heart block.” In such cases, atrial activity and ventricular activity are independent of each other. The location of the block is implied by the escape rhythm. A narrow QRS complex, typically with a rate between 40 and 60 beats per minute, implies the presence of atrioventricular nodal block. Wide QRS escape rhythms at slower rates imply that the block is located in the His–Purkinje system.

EVALUATION

In patients with confirmed or suspected bradycardia, possible intrinsic or extrinsic causes of sinus-node dysfunction or atrioventricular block should be sought in the history taking and physical examination. If bradycardia is episodic, the patient should be questioned about precipitating factors and associated symptoms or signs. Severe nocturnal bradycardia should raise a strong suspicion of obstructive sleep apnea. A careful history of the medications the patient has used is important, since many pharmacologic agents, including some used for noncardiovascular conditions, may produce bradycardia (Table 1). Laboratory studies should include tests of thyroid function.

Many patients are not specifically aware of slow heart rates, and deficits in the peripheral pulse resulting from atrial or ventricular arrhythmias may confuse patients and even trained observers. Therefore, bradycardia must be confirmed by electrocardiography. The standard 12-lead electrocardiogram will not only confirm the mechanism if the patient has bradycardia at the time, but it may also provide insights into the patient's cardiac condition. For patients with intermittent symptoms, correlation of symptoms with bradycardia is usually sought with the use of ambulatory electrocardiographic monitoring.^{34,35} A continuous 24-to-48-hour electrocardiographic recording is useful in patients with frequent or continuous symptoms. Patients with less frequent symptoms should be evaluated with intermittent electrocardiographic recorders. Both external and implantable intermittent recorders are available for this purpose.^{36,37} Chronotropic incompetence is usually diagnosed by exercise testing or ambulatory monitoring.^{22,38,39} The diagnosis of neurocardiogenic syncope, also commonly called vasovagal syncope, can usually be made on clinical grounds. If the diagnosis is uncertain, testing while the patient is lying in a head-up position on a tilt table may be used to provoke an episode of syncope and confirm changes in heart rate and blood pressure during such episodes.⁴⁰ Referral to a cardiologist is important if the primary care physician remains uncertain about the importance of any of the findings or if pacing therapy is clearly indicated.

Invasive electrophysiologic testing is rarely required

in patients with bradycardia that is confirmed by electrocardiographic monitoring, but it may be helpful if the mechanism responsible for bradycardia remains uncertain, if attempts to monitor the heart rate have been unsuccessful, or if symptoms suggest the presence of a potentially life-threatening arrhythmia.⁴¹ His-bundle electrocardiography accurately measures atrioventricular nodal and His–Purkinje conduction times and identifies the site of the block. Its ability to assess the risk of future atrioventricular block is limited, however, except at extreme HV intervals (the conduction intervals between the His bundle and the ventricular myocardium).^{15,41,42} Programmed stimulation can be used to assess refractory periods and responses to changes in atrial rate. Sinus-node function can be assessed both by measurement of the magnitude of overdrive suppression (sinus-node recovery times) and by direct and indirect measures of sinoatrial conduction.^{43,44}

MANAGEMENT

The management of bradycardia is determined by the severity of symptoms, the degree of correlation between symptoms and confirmed bradycardia, and the presence of potentially reversible causes. There are few indications for intervention in patients with bradycardia who are truly asymptomatic. The American College of Cardiology and American Heart Association guidelines for the implantation of pacemakers¹⁵ list only the following as universally accepted (class I) indications in asymptomatic patients: third-degree atrioventricular block with documented asystole lasting three or more seconds (in sinus rhythm) or escape rates below 40 beats per minute in patients while awake; third-degree atrioventricular block or second-degree atrioventricular Mobitz type II block in patients with chronic bifascicular and trifascicular block; and congenital third-degree atrioventricular block with a wide QRS escape rhythm, ventricular dysfunction, or bradycardia markedly inappropriate for age. Potential (class II) indications for pacing in asymptomatic patients include third-degree atrioventricular block with faster escape rates in patients who are awake, second-degree atrioventricular Mobitz type II block in patients without bifascicular or trifascicular block, and the incidental finding on electrophysiologic study of block below or within the bundle of His or an HV interval of 100 msec or longer. When bradycardia, even if extreme, is present only during sleep, pacing is usually not indicated.

Among symptomatic patients, the correlation between symptoms and confirmed bradycardia and the potential reversibility of causative factors are the keys to appropriate decision making. Symptoms definitely related to simultaneous, confirmed bradycardia that is caused by intrinsic sinus-node dysfunction or atrioventricular block should be treated with permanent pacing. The sinus and atrioventricular nodes are rel-

actively resistant to permanent injury by infarction or infection, and normal function should be recovered over time; therefore, sinus bradycardia or atrioventricular nodal block in these settings rarely requires permanent pacing. Permanent damage occurs more readily to the bundle of His than to the sinus and atrioventricular nodes, and even transient complete atrioventricular block in the His–Purkinje system due to infarction or infection justifies the insertion of a pacemaker. In cases in which only nonspecific symptoms, such as fatigue, dizziness, or heart failure, are present and the associated bradycardia is not extreme, pacing is rarely indicated. Among patients with recurrent unconfirmed syncope and chronic bifascicular or trifascicular block, pacing is indicated if other likely causes (e.g., ventricular tachycardia) have been ruled out.

When symptomatic bradycardia is due to extrinsic causes, clinical judgment is required. Although a change in therapy should be considered if drug-induced bradycardia is suspected, pacing may be an acceptable approach if no agent with equivalent efficacy is available. Occasionally, use of pindolol, a β -adrenergic blocker with intrinsic sympathomimetic activity, may prevent bradycardia while the patient is at rest. Pacing is also appropriate in patients with the bradycardia–tachycardia syndrome if the agents required for control of the ventricular rate during atrial arrhythmias cause bradycardia during sinus rhythm. Atrium-based pacing is preferred in patients with sinus-node dysfunction because it reduces the incidence of atrial fibrillation, pacemaker syndrome, and thromboembolism.⁴⁵ Dual-chamber pacing is needed if atrioventricular block is also present. When bradycardia occurs only in specific situations, patient education and prevention strategies should be tried first.

The role of pacing in patients with neurocardiac syncope and confirmed bradycardia is controversial. Many of these patients also have a prominent vasodepressor component to their syndrome, and standard pacing techniques may not completely relieve symptoms. New algorithms that include short periods of high-rate pacing when bradycardia is detected may be more effective.⁴⁶ Patient education and pharmacologic trials are indicated before pacing in most patients with neurocardiac syncope.

CONCLUSIONS

Bradycardia is a common clinical finding. The clinician must determine the relation between bradycardia and symptoms and differentiate between physiologic and pathologic conditions. In cases in which bradycardia is symptomatic and irreversible, pacemaker therapy is highly effective for the relief of symptoms.

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