

Short PR Interval

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A short PR interval may be associated with an otherwise normal electrocardiogram or a myriad of bizarre electrocardiographic abnormalities. Clinically, the individual may be asymptomatic or experience a variety of complex arrhythmias, which may be disabling and rarely cause sudden death. In life insurance applicants, it is important to recognize these abnormalities and to assess their risk appropriately.

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CASE SCENARIO

A 34-year-old businesswoman is applying for a large life insurance policy. She is asymptomatic at the time of her application. While attending university 14 years ago, she had two episodes of “tachycardia.” Both occurred when she had been drinking an excessive amount of coffee while cramming for final examinations. Both episodes lasted less than an hour and had disappeared by the time she arrived in the local emergency room. After her examinations that year, the university medical clinic referred her to a cardiologist in her hometown for follow-up assessment. She was told she had a benign arrhythmia and did not require medications. She has had no recurrences and has tolerated 3 pregnancies during the interim.

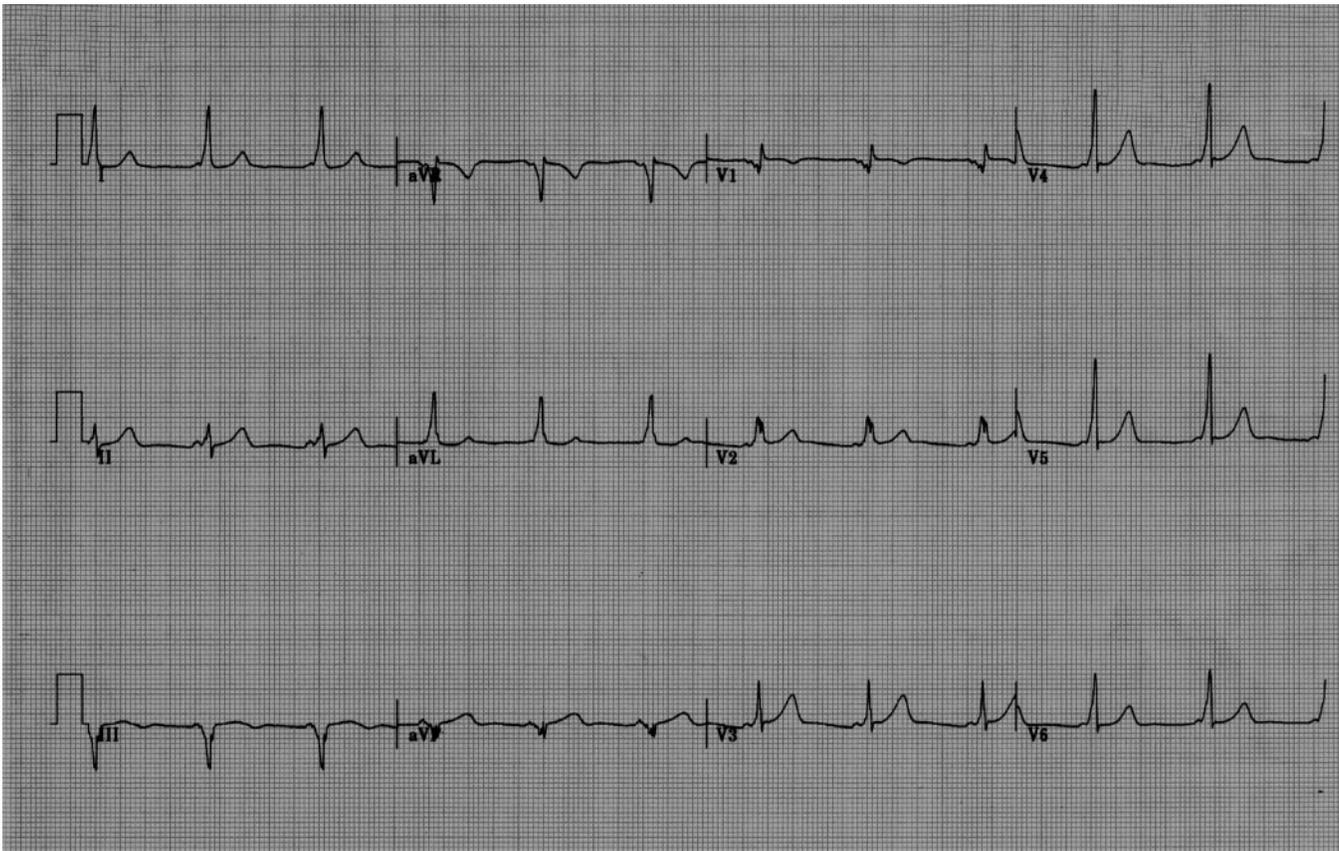
Because of this history, the underwriter assessing her application requested an attending physician’s statement (APS) from the car-

diologist and ordered an electrocardiogram (ECG). The APS disclosed that she had a normal cardiovascular examination at that time. Her investigations, which included a resting and exercise ECG, a 24-hour ambulatory ECG and an echocardiogram, were all reported as normal.

The ECG done as part of the current risk selection process for her application is contained in the Figure. What do you think? Is it normal or abnormal? The underwriter thinks she may have had a previous myocardial infarction, do you agree? How do you account for her previous normal ECG and does the change have any prognostic value?

ECG INTERPRETATION AND ANALYSIS

The prevailing rhythm is sinus in origin with an average ventricular rate of 62 beats per minute. The PR interval is very short (0.08 seconds) and in most leads, no clear-cut PR



Applicant's electrocardiogram.

segment is visible. The QRS complexes are abnormally wide and measure 0.13 seconds. In leads I, II, AVL, and V_3 - V_6 , the wide QRS complexes rise directly from the end of the P wave, eliminating the PR segment. These QRS complexes are deformed by a broad slur on the initial part of the upstroke of the R wave. The ST segment and T waves appear normal.

Although a short PR interval may be a normal variant, it also has been noted in a number of clinical conditions including: hypertrophic cardiomyopathy, Ebstein's anomaly, tricuspid valve atresia, corrected transposition of the great vessels, mitral valve prolapse, Duchenne muscular dystrophy, Pompe's disease and Fabry's disease. These conditions are usually obvious on clinical grounds. A short PR interval is also seen in a number of electrophysiological disorders including: AV junctional rhythms, ectopic atrial rhythms and preexcitation syndrome.

In AV junctional rhythms with retrograde atrial activation, the retrograde P-waves may

occur before the QRS complex with a short PR interval. In this situation, the negative P-waves in II, III and AVF point to the correct diagnosis. In isorhythmic AV dissociation, the P-waves are dissociated from the QRS complexes but frequently the P and QRS rates are similar resulting in the phenomenon of acco-chage with the P-wave marching back and forth across the QRS complex and at times creating the appearance of a sinus P-wave with a short PR interval. Ectopic atrial rhythms originating near the AV node may have a short PR interval because atrial activation is originating from near the AV node, however the P-wave morphology will be different from the sinus P.

Two subsets of the preexcitation syndrome are associated with a short PR interval. The Lown-Ganong-Levine syndrome (LGL) has a short PR interval but is associated with a normal QRS complex. In our applicant, the short PR interval, the wide QRS complexes and the broad slur on the upstroke of the R wave tak-

en together are characteristic ECG features found in individuals with the commonest form of ventricular preexcitation. The eponym for these findings is the Wolff-Parkinson-White (WPW) pattern. This will be the focus of our case discussion.

PATHOPHYSIOLOGY

The PR interval starts from the beginning of the P-wave (SA node depolarization) and includes the whole P-wave, ie, the whole of atrial depolarization. There is then a flat segment as depolarization reaches the AV node creating an electrical interlude. The AV node delays conduction of the electrical impulse long enough for the ventricles to be filled by atrial contraction before they themselves contract.

The PR interval ends as ventricular depolarization begins (the start of the QRS complex). Thus the PR interval represents the time it takes for the atria to depolarize and pass its message to the ventricles. It is measured from the beginning of the P-wave to the beginning of the QRS complex. The normal PR interval measures 0.12 to 0.20 seconds in duration.¹ However, it is important to remember that normal PR intervals are distributed on a bell-shaped curve so that 1%–2% of normal individuals will have a PR interval less than 0.12 seconds.

In the normal heart, electrical impulses originate in the sinus node located in the right atrium and spread throughout the atrial tissue, eventually arriving at the AV node. Within the AV node, physiologic slowing of the impulse occurs followed by conduction through the bundle of His, bundle branches and Purkinje system to the ventricular muscle. Preexcitation occurs when the atrial impulse activates ventricular muscle earlier than would be expected if the impulse traveled only by way of the normal specialized conduction system. This premature activation is caused by muscular connections composed of working muscular fibers that exist outside the specialized conducting system and connect the atrium and the ventricle while bypassing

AV nodal conduction delay.² These additional or alternative pathways are called accessory pathways or connections. In the WPW pattern, the accessory pathway is called the bundle of Kent.

The ECG findings in our applicant can be explained as follows. The PR interval is short because the PR segment has disappeared. The PR segment has disappeared because of rapid AV conduction through an accessory pathway bypassing the AV node. The so-called preexcited QRS complex is a fusion between early ventricular activation caused by preexcitation and later ventricular activation resulting from transmission through the AV node and the normal specialized conducting system to the ventricles. The initial part of ventricular activation is slowed, and the upstroke of the QRS is slurred because of slow muscle fiber to muscle fiber conduction; this is called a delta wave. This process is inherently slower than ventricular depolarization resulting from rapid His-Purkinje system conduction. Thus, the net effect is earlier initial excitation of the ventricles (via the accessory pathway) but slower activation of the ventricular myocardium than occurs normally. As a result, the QRS is wider than normal. The morphology of the resultant preexcited QRS complex is determined, in part, by the relative conduction velocities and refractory periods of both limbs, and by the origin of the supraventricular impulse, relative to the location of the accessory pathway. Thus, the fusion complex may show gradations of distortion, ranging from minimal to maximal preexcitation.³

Two types of QRS patterns were originally identified in patients with WPW syndrome: A and B. With type A (due to a left-sided bypass pathway), there was a tall R wave in leads V_1 – V_3 (ie, a positive or upward delta wave). Whereas with type B (due to a right-sided bypass pathway), there were QS complexes in leads V_1 – V_3 (ie, a negative or downward delta wave).³ Although it was thought that this classification might be helpful in identifying the location of the accessory pathway, subsequent electrophysiologic studies

and mapping have shown that accessory pathways may be located anywhere along the AV ring (groove) or in the septum.² The location of accessory pathways in descending order of frequency is: left free wall (50%), posteroseptal (30%), right free wall (10%) and anteroseptal (10%). Several algorithms are available to help localize the accessory pathway by analyzing the ECG.^{4,5} However, the ECG appearance of activation depends upon the extent of preexcitation and fusion. As a result, the same pathway may not always produce the identical ECG pattern. In approximately 10% of patients, multiple accessory pathways are encountered.

The WPW pattern is only one form of preexcitation. Several other patterns occur depending upon the anatomy of the accessory pathway and the direction in which the impulses are conducted. In one of these, the Lown-Ganong-Levine (LGL) syndrome, the electrophysiologic mechanism for the short PR interval is abnormal AV node function. Some of these patients have enhanced AV node conduction (EAVNC), which can be demonstrated on electrophysiologic testing. In others, preexcitation may occur via an accessory pathway arising from within the atria and inserting in the low portion of the AV node or bundle of His. The net effect is a short PR interval without a delta wave or QRS prolongation.

It should be noted that the histopathologic correlation and functional significance of accessory pathways in LGL has not been established like it has been in the WPW syndrome. Indeed, the current view of LGL is that it is of historical interest only, having been described before the advent of catheter-based electrophysiologic studies (EPS). There is no convincing evidence to suggest that LGL is a syndrome separate from other known phenomena. EPS studies have shown that the short PR interval of LGL likely represents the lower end of the spectrum of normal PR intervals, and the tachyarrhythmias are AV nodal reentrant tachycardias.^{6,7}

Although not illustrated in our applicant's ECG, the abnormal sequence of ventricular

activation often gives rise to an abnormal sequence of repolarization, resulting in ST-T wave abnormalities. The direction of the ST-T wave abnormalities is usually oriented opposite to the vectors of the delta wave and QRS complex.

Because of the altered sequence of ventricular activation in WPW syndrome, the ECG may mimic other conditions and thus is occasionally overlooked or misdiagnosed. This depends on the location of the accessory pathway and thus the configuration of the delta wave. In some cases a wide, positive QRS complex in V_1 and V_2 is noted, simulating right bundle branch block, true posterior myocardial infarction or right ventricular hypertrophy. In other cases there may be a wide, negative QRS complex in lead V_1 or V_2 , similar to that seen in left bundle branch block or left ventricular hypertrophy.

A negative delta wave as seen in our applicant's ECG in leads III and AVF may simulate a Q wave and thus give the appearance of a prior myocardial infarction.⁸ Intermittent WPW may be mistaken for frequent ventricular beats. The WPW pattern is occasionally seen on alternate beats and may suggest ventricular bigeminy.

The presence of the WPW pattern in our applicant's ECG, in itself, does not cause any clinical manifestations. It is important to distinguish between the WPW pattern (ie, ECG abnormalities in asymptomatic patients) and the WPW syndrome. The term WPW syndrome is used when patients with this pattern develop a variety of supraventricular tachyarrhythmias, which may lead to unpleasant, disabling symptoms, and in rare instances sudden death.

In the majority of cases, the accessory pathways are characterized by very rapid, non-decremental antegrade/retrograde conduction. Nondecremental means the accessory pathway itself does not have the ability to reduce the number of impulses transmitted onto the ventricles. This is in contrast to the decremental conduction in the AV node, which is only able to conduct a fixed number of impulses to the ventricles per unit of time.

Antegrade/retrograde refer to the direction which the electrical impulse travels across the accessory pathway.⁸ Occasionally, some pathways are only able to carry impulses in the retrograde direction and thus are “concealed” pathways, ie, they are “silent” with normal PR interval and QRS complex, and there is no delta wave.

The most common arrhythmia seen in WPW patients is atrioventricular reentrant or reciprocating tachycardia (AVRT). In the setting of AVRT, activation of the ventricle occurs through either the normal conduction system and/or the accessory pathway with return of the impulse to the atrium by the other pathway. There are two forms of AVRT: orthodromic and antidromic.

Orthodromic, AV reciprocating tachycardia is a reentrant tachycardia in which the atrial stimulus is conducted to the ventricle through the AV node with a return of the impulse to the atria through the accessory pathway. The ECG will show a normal QRS complex with a retrograde conducting P-wave after the completion of the QRS complex in the ST segment or early in the T wave. QRS alternans may be present in 30%–40% of patients during the tachycardia. This tachycardia represents about 90% of AVRT cases seen in the WPW syndrome.^{2,8}

In approximately 10% of AVRT patients with WPW syndrome, an antidromic (retrograde) reciprocating tachycardia occurs. In this form, the reentrant circuit conducts in the opposite direction, with antegrade conduction down the accessory pathway and return of the impulse retrograde to the atria via the His-Purkinje fibers, bundle branches and AV node. With this pathway, the QRS complexes appear wide (essentially an exaggeration of the delta wave), and the 12-lead ECG displays a very rapid, wide-complex tachycardia that is nearly indistinguishable from ventricular tachycardia.^{2,8}

Patients with WPW syndrome can have other types of tachycardia in which the accessory pathway is a “bystander,” that is uninvolved in the mechanism responsible for the tachycardia. This can occur in patients

who develop atrial fibrillation or atrial flutter where the arrhythmia begins in the atria unrelated to the accessory pathway. Propagation of the arrhythmia can therefore occur over the normal conducting system through the AV node, bundle of His and bundle branches or the accessory pathway. In patients with a normal conducting system, the ventricles are protected by the refractory period of the AV node against a very high ventricular rate during a rapid atrial rhythm.

Accessory pathways, however, lack the feature of decremental conduction mentioned above; thus, the pathway can conduct atrial beats at or above 300 beats per minute. These patients almost always have inducible AVRT as well, which can develop into atrial fibrillation. Atrial fibrillation and atrial flutter, therefore, represent a potentially serious risk if the accessory pathway has a short antegrade refractory period, which would allow for very rapid conduction over the accessory pathway. The rapid ventricular response can exceed the ability of the ventricle to function in an organized manner and can result in a fragmented, disorganized ventricular activation and hypotension and lead to ventricular fibrillation.^{9,10}

DISCUSSION

The combination of a short PR interval and slurred initial part of the QRS had been described by several authors before publication of the famous 1930 paper in which Louis Wolff, Sir John Parkinson and Paul Dudley White associated the abnormality with supraventricular tachyarrhythmias.^{11,12,13} Wolff, Parkinson and White erroneously conjectured that the wide QRS complex was caused by a type of bundle branch block. The role of an accessory pathway was first described by Wolferth and Wood in 1933.¹⁴

The prevalence of a WPW pattern on the surface ECG is 0.15% to 0.25% in the general population.^{15,16} The prevalence is increased to 0.55% among first-degree relatives of affected patients suggesting a familial component. The prevalence of WPW pattern in a survey

of 19,734 consecutive electrocardiograms obtained in insurance applicants by Metropolitan Life insurance Company was 0.20%.¹⁷ The yearly incidence of newly diagnosed cases of WPW in the general population is substantially lower, at 0.004%, 50% of whom will be asymptomatic.¹⁶

The incidence in males is slightly higher than females. The WPW pattern on the ECG may be intermittent and may even disappear over time. The intermittent and/or persistent loss of preexcitation may indicate that the accessory pathway has a relatively longer baseline refractory period, which makes it more susceptible to age-related degenerative changes and variations in autonomic tone.

The prevalence of WPW syndrome, defined as a WPW pattern on the ECG associated with arrhythmia is substantially lower than that of the WPW pattern alone. The reported incidence of preexcitation syndrome depends in large measure on the population studied and varies from 0.1 to 3 per 1000 in apparently healthy subjects, with an average of about 1.5 per 1000.¹⁸

In a review of 22,500 healthy aviation personnel, the WPW pattern was seen on an ECG in 0.25%, and only 1.8% had documented tachyarrhythmias.¹⁹ Among supraventricular arrhythmias managed in the emergency department, WPW is encountered in 2.4% of cases.²⁰

WPW syndrome is found in all age groups from fetal and neonatal periods to the elderly. A familial form of WPW has infrequently been reported and is usually inherited as an autosomal dominant. In some families the gene responsible has been identified.^{21,22} Most adults with preexcitation have normal hearts, although a variety of acquired and congenital cardiac defects have been reported including Ebstein's anomaly, mitral valve prolapse and hypertrophic cardiomyopathy. An inherited form of WPW associated with familial hypertrophic cardiomyopathy has been described.²³

The majority of patients with preexcitation syndromes remain asymptomatic throughout their lives. When symptoms do occur, they

are usually secondary to tachyarrhythmias. Approximately 80% of WPW patients with tachycardia have AVRT, 15% to 30% have atrial fibrillation, and 5% have atrial flutter.²⁴ The frequency of paroxysmal tachycardia increases with age, from 10% in patients with WPW pattern in a 20- to 39-year-old age group, to 36% in patients older than 60 years. Some children and adults can lose their tendency for the development of tachyarrhythmias as they grow older, possibly because of fibrotic or other changes in the accessory pathway.

The prognosis is excellent in patients without arrhythmias or structural heart disease. For most patients with recurrent tachycardia, the prognosis is also good. Sudden death due to ventricular fibrillation is a rare but lethal complication in patients with WPW syndrome. Natural history studies report a sudden death incidence ranging from 0% to 0.6% per year.^{16,25}

In WPW patients, the presence of a short antegrade refractory period of the accessory pathway is an obvious risk factor. Several noninvasive tests have been proposed as useful in stratifying patients for risk of sudden death. Intermittent preexcitation during sinus rhythm (which probably explains the difference in our applicant's two electrocardiograms) and abrupt loss of conduction over the accessory pathway after intravenous procainamide or ajmaline and with exercise suggest that the refractory period of the accessory pathway is long and that the patient is not at risk for a rapid ventricular rate should atrial fibrillation or flutter develop.¹⁸ These approaches are relatively specific, but not very sensitive, with a low positive predictive accuracy. Exceptions to these safeguards can occur. Hence these noninvasive tests are considered inferior to electrophysiologic testing in the assessment of sudden cardiac death risk and play little role in patient management at present.

Electrophysiologic testing allows reproduction of the patient's arrhythmia by programmed stimulation and the properties of the arrhythmia can be characterized. In addition it is possible to map the precise ana-

tomical location of the accessory pathway. This led to the development of surgical cure for WPW syndrome. In the 1980s, endocardial-catheter techniques performed with the use of radiofrequency energy emerged. These techniques have usurped the role of pathway ablation that previously belonged to surgery.²⁶

Asymptomatic patients who have only the ECG abnormality, without tachyarrhythmias, have traditionally been treated expectantly, not requiring electrophysiological evaluation or therapy. However, with the reporting of rare cases of ventricular fibrillation as the first manifestation of WPW syndrome, appropriate strategy for asymptomatic patients has become controversial.^{27,28} Some cardiac electrophysiologists have advocated for electrophysiologic testing in these patients and ablative therapy for those felt to be at high risk (ie, those with preexcited RR intervals <250 milliseconds during spontaneous or induced atrial fibrillation, multiple accessory pathways, Ebstein's anomaly, high risk professions, professions involving risk to others, athletes and those with a family history of sudden death).²⁷⁻²⁹

For symptomatic patients, prophylactic therapy is usually initiated. Long-term prophylaxis with antiarrhythmic drugs can be fraught with difficulty due to ineffectiveness of antiarrhythmic agents and the potential proarrhythmic properties of these medications. Thus chronic drug therapy is often limited to those with infrequent, non-life-threatening and well-tolerated episodes and for older, sedentary individuals with limited life expectancy.

Radiofrequency catheter ablation is the treatment of choice for patients with recurrent, multiple and hemodynamically significant tachyarrhythmias, wide QRS tachycardias (antidromic type) and with atrial fibrillation. The success rate of radiofrequency catheter ablation in experienced centers is approximately 95%. About 10% of these patients, however, will require a second procedure because of a return of accessory pathway conduction. The recurrence rate is higher

with ablation of multiple pathways or right or left free wall or septal accessory pathways. Approximately one half of recurrences occur in the first 12 hours after the procedure. Recurrent atrial fibrillation is more common than AVRT.³⁰

In conclusion, the presence of a short PR interval in an applicant's ECG may be a normal variant, or it can be related to underlying structural heart disease. By careful analysis of the other components of the ECG and appropriate use of an APS and selected tests, proper assessment of the applicant's risk can be accomplished.

REFERENCES

1. Understanding ECGs: Minding your Ps and Qs. Available at: <http://www.studentbmj.com/backissues/1001/education/374.html>.
2. Miles WM, Zipes DP. Atrioventricular reentry and variants: Mechanisms, clinical features, and management. In: Zipes DP, Jalife J, eds. *Cardiac Electrophysiology: From Cell to Bedside*. 3rd ed. Philadelphia, Pa: WB Saunders; 2000:638–655.
3. Gauer K, Curry Jr RW. *Clinical Electrocardiology*. Cambridge, Mass: Blackwell Scientific Publications; 1992:227–235.
4. Milstein S, Sharma AD, Guiraudon GM, et al. An algorithm for the electrocardiographic localization of accessory pathways in Wolff-Parkinson-White syndrome. *Pacing Clin Electrophysiol*. 1987;10:555–563.
5. Basiouny T, de Chillou C, Fareh S, et al. Accuracy and limitations of published algorithms using the 12-lead ECG to localize overt atrioventricular accessory pathways. *J Cardiovasc Electrophysiol*. 1999; 10:1340–1349.
6. Jackman WM, Prystowsky EN, Nacarelli GV, et al. Reevaluation of enhanced AV nodal conduction: evidence to suggest a continuum of normal AV nodal physiology. *Circulation*. 1983;67:441–448.
7. Josephson ME, Kastor JA. Supraventricular tachycardia in Lown-Ganong-Levine syndrome: atrionodal versus intranodal reentry. *Am J Cardiol*. 1977; 40:521–527.
8. Rosner MH, Brady WJ, Kefer MP, et al. Electrocardiography in the patient with the Wolff-Parkinson-White syndrome: diagnostic and therapeutic issues. *Am J Emerg Med*. 1999;17:705–714.
9. Klein GJ, Bashore TH, Sellers TD. Ventricular fibrillation in the Wolff-Parkinson-White syndrome. *N Engl J Med*. 1979;301:1080–1085.
10. Wellens HJJ, Durrer D. Wolf-Parkinson-White syn-

- drome and atrial fibrillation: relation between refractory period of accessory pathway and ventricular rate during atrial fibrillation. *Am J Cardiol.* 1974;34:777-782.
11. Wilson FN. A case in which the vagus influenced the form of the ventricular complex of the ECG. *Arch Intern Med.* 1915;16:1008-1027.
 12. Hamburger WW. Bundle branch block: 4 cases of intraventricular block showing some interesting and unusual clinical features. *Med Clin North Am.* 1929;13:343-362.
 13. Wolff I, Parkinson J, White PD. Bundle branch block with short PR interval in healthy young people prone to paroxysmal tachycardia. *Am Heart J.* 1930;5:685-704.
 14. Wolfarth CC, Wood FC. The mechanism of production of short PR intervals and prolonged QRS complexes in patients with presumably undamaged hearts: Hypothesis of an accessory pathway of auriculoventricular conduction (bundle of Kent). *Am Heart J.* 1933;8:297-311.
 15. Krahn AD, Manfreda J, Tate RB, et al. The natural history of electrocardiographic preexcitation in men. The Manitoba follow-up study. *Ann Intern Med.* 1992;116:456-460.
 16. Munger TM, Packer DL, Hammill SC, et al. A population study of the natural history of Wolff-Parkinson-White syndrome in Olmstead County, Minnesota, 1953 to 1989. *Circulation.* 1993;87:866-873.
 17. Ferrer MF. Electrocardiographic variations, arrhythmias, pacemakers. In: Lew EA, Gajewski J, eds. *Medical Risks: Trends in Mortality by Age and Time Elapsed.* New York, NY: Praeger; 1990:7.1-7.64.
 18. Wellens HJ, Rodriguez LM, Timmermans C, et al. The asymptomatic patient with the Wolff-Parkinson-White electrocardiogram. *PACE.* 1997;20 (Part III):2082-2086.
 19. Smith RF. The Wolff-Parkinson-White syndrome as an aviation risk. *Circulation.* 1964;29:672-679.
 20. Brady WJ, DeBehnke DJ, Wickman LL, et al. Treatment of out-of-hospital supraventricular tachycardia: adenosine versus verapamil. *Acad Emerg Med.* 1996;3:574-585.
 21. Vidaillet HJ, Presley JC, Henke E, et al. Familial occurrence of accessory atrioventricular pathways (preexcitation syndrome). *N Engl J Med.* 1987;317:65-69.
 22. Gollob MH, Green MS, Tang AS. Identification of a gene responsible for familial Wolff-Parkinson-White syndrome. *N Engl J Med.* 2001;344:1823-1831.
 23. MacRae CA, Ghaisas N, Kass S, et al. Familial hypertrophic cardiomyopathy with Wolff-Parkinson-White syndrome maps to a locus on chromosome 7q3. *J Clin Invest.* 1995;96:1216-1220.
 24. Bartlett TG, Friedman PL. Current management of Wolff-Parkinson-White syndrome. *J Card Surg.* 1993;8:503-515.
 25. Leitch JW, Klein GJ, Yee R, et al. Prognostic value of electrophysiology testing in asymptomatic patients with Wolff-Parkinson-White pattern. *Circulation.* 1990;82:1718-1723.
 26. Lerman BB, Basson CT. High-risk patients with ventricular preexcitation—a pendulum in motion. *N Engl J Med.* 2003;349:1787-1789.
 27. Todd DM, Klein GJ, Skanes AC, et al. Asymptomatic Wolff-Parkinson-White syndrome: Is it time to revisit guidelines? *J Am Coll Cardiol.* 2003;41:245-248.
 28. Pappone C, Manguso F, Santinelli R, et al. Radiofrequency ablation in children with asymptomatic Wolff-Parkinson-White syndrome. *N Eng J Med.* 2004;351:1197-1205.
 29. Steinbeck G. Should radiofrequency current ablation be performed in asymptomatic patients with Wolff-Parkinson-White syndrome? *Pacing Clin Electrophysiol.* 1993;16:649-652.
 30. Scheinman MM, Huang S. The 1998 NASPE prospective catheter ablation registry. *Pacing Clin Electrophysiol.* 2000;23:1020-1028.