A 66-year-old white woman with a greater than 20-year history of electrocardiographic evidence of the Wolff-Parkinson-White syndrome, including documented recurrent supraventricular tachycardias, was studied. Despite the disappearance of the delta wave after initiation of therapy with digoxin and quinidine sulfate, the patient continued to have frequent episodes of supraventricular tachycardia. At a time when the serum levels of digoxin and quinidine were in the therapeutic range, extensive electrophysiologic studies were performed. Supraventricular tachycardia at a rate of 160 beats per minute was initiated by induced atrial premature depolarizations. The circuit of tachycardia involved anterograde conduction through the pathway of the atrioventricular node and His bundle and retrograde conduction through the bypass tract. We concluded that elimination of the delta wave and other electrocardiographic characteristics of the Wolff-Parkinson-White syndrome cannot be relied upon to indicate successful pharmacologic prophylaxis for induction of tachyarrhythmia associated with this syndrome.

In the classical form of the Wolff-Parkinson-White syndrome, the surface electrocardiogram demonstrates a short P-R interval, a delta wave, and a widened QRS complex. The Wolff-Parkinson-White syndrome is further characterized by episodes of paroxysmal supraventricular tachycardias. The anatomic features of this syndrome, accessory pathway(s) of conduction bypassing the system of the atrioventricular node and His bundle, have been well established. Furthermore, recent clinical electrophysiologic studies have greatly increased our understanding of the pathophysiology of the various aspects of this syndrome.

The delta wave represents premature ventricular activation, ie, preexcitation. Therefore, the presence of a delta wave is an indicator for satisfactory conduction across the bypass tract and, thus, the potential for development of tachycardia. It would be conceivable that elimination of the delta wave on the surface ECG by depression of bypass conduction should serve as a biologic marker for successful therapy with antiarrhythmic drugs in patients with the Wolff-Parkinson-White syndrome. It is the purpose of this report to demonstrate the failure of this biologic assay as a clinical means to assess therapy in this syndrome.

**Case Report**

A 66-year-old white woman with a greater than 20-year history of electrocardiographic evidence of the Wolff-Parkinson-White syndrome, palpitations, and documented recurrent supraventricular tachycardias was studied. Several years prior to this admission, the patient had been placed on therapy with digoxin (0.25 mg daily) in an attempt to control increasingly frequent episodes of tachycardia. Despite failure of the drug to control either the frequency or the rate of the supraventricular tachycardia, the patient was maintained on this medication until the time of the present admission. The ECG was essentially unchanged over the past decade. There was no history of angina, syncope, or other central nervous system symptoms.

Upon admission, the blood pressure was 130/60 mm Hg, and the pulse rate was 80 beats per minute and regular. The findings from the remainder of the physical examination were unremarkable. The ECG (Fig 1) and vectorcardiogram had findings consistent with the Wolff-Parkinson-White syndrome and had the delta wave vector directed to the right, inferiorly and anteriorly. The serum level of digoxin was 0.7 mg/ml.

During the patient's hospitalization, repeated episodes of paroxysmal supraventricular tachycardia occurred (Fig 1). On the second day of hospitalization, the dose of digoxin was increased to 0.375 mg daily, and therapy with quinidine sulfate (200 mg orally every six hours) was added to the drug regimen. Serial ECGs demonstrated persistence of the delta wave and short P-R intervals until the seventh day of hospitalization, at which time the ECG normalized (Fig 1). On the eighth day, when the serum level of digoxin was 2 mg/ml and the end-dose serum level of quinidine sulfate was 1.5 mg/ml, a study of the His bundle was performed. This study was performed using standard techniques. Electrograms of the high right atrium, low right atrium, His bundle, and coronary sinus and standard leads 1, 2, and 3 were recorded on a photographic oscillographic recorder at a paper speed of 100 mm/sec.

**Results**

**Control Recordings of Electrograms**

Electrograms of the His bundle recorded during the control state demonstrated no delta wave, a normal time for atrial-to-His conduction (A-H interval), and, more significantly, a normal time for His-to-ventricular conduction (H-V interval), confirming that anterograde conduction through the bypass tract had been successfully blocked following the administration of quinidine.

**Atrioventricular Refractory Periods**

Rafactory periods of the atrioventricular node were evaluated using the extrastimulus technique at a pacing frequency of 1.5/sec.
rate of 90 beats per minute. By this method the relative refractory period was 452 msec, the functional refractory period was 403 msec, and the effective refractory period was 300 msec (Fig 2A). In addition, utilizing the extra-stimulus method the time for sinus-to-atrial conduction was prolonged to 224 msec, and the effective refractory period of the atrium was 270 msec. Utilizing the technique of atrial pacing, anterograde atrioventricular conduction proceeded through the pathway of the atrioventricular node and His bundle with 1:1 conduction up to an atrial rate of 150 beats per minute, with the A-H interval prolonging to 230 msec. By this technique the effective refractory period of the atrioventricular node was 390 msec.

**Ventriculoatrial Refractory Periods**

Ventricular pacing was performed at increasing rates to assess ventriculoatrial conduction. Until a ventricular rate of 150 beats per minute was achieved, 1:1 ventriculoatrial conduction via the bypass tract was present.

![Figure 1. Thirteen-lead ECG. Left hand panel of each lead shows QRS complex with normal atrioventricular conduction, and right hand panel shows QRS complex with accelerated atrioventricular conduction. Rhythm strip (V3R) at bottom shows typical episode of tachycardia.](image)

![Figure 2. A (left), Measurements of atrioventricular refractory period (AVRP) at basic pacing rate of 90 beats per minute. Note induction of supraventricular tachycardia (SVT) designated by asterisks. Horizontal axis represents coupling interval of premature atrial beats (A1A2). Vertical axis identifies responses of His bundle. B (right), Measurements of ventriculoatrial refractory period (VARP) at basic pacing rate of 90 beats per minute. Horizontal axis identifies coupling interval of premature ventricular beats (V1V2). Vertical axis shows high right atrial responses. Note that late responses all fall on line of identity. ERP, Effective refractory period; FRP, functional refractory period; and RRP, relative refractory period.](image)
Variable ventriculoatrial block occurred at higher rates of ventricular pacing. The time for ventriculoatrial conduction was 190 msec. Ventriculoatrial refractory periods were assessed utilizing the ventricular extrastimulus method. For ventriculoatrial conduction the effective refractory period was 260 msec, and the functional refractory period was 420 msec (Fig 2B).

Induction of Tachycardia

Supraventricular tachycardia at a rate of 160 beats per minute was initiated by induced atrial premature depolarizations at a coupling interval of 300 to 372 msec (Fig 3). The onset of activity in the coronary sinus before low atrial or high atrial activity during supraventricular tachycardia indicates the presence of retrograde bypass conduction from the left ventricle to the left atrium. Therefore, during supraventricular tachycardia, anterograde conduction proceeded via the pathway of the atrioventricular node and His bundle, and retrograde conduction occurred through a bypass tract, producing narrow QRS complexes on the surface ECG.

**DISCUSSION**

Prior to the administration of quinidine and the increased dosage of digoxin, the patient’s surface ECG suggested that during normal sinus rhythm, anterograde conduction proceeded, at least in part, through a bypass pathway, as evidenced by the short P–R interval, the wide QRS complexes, and the presence of a delta wave. Following the new drug regimen, surface ECGs during sinus rhythm demonstrated that anterograde conduction through the bypass tract was now blocked and proceeded entirely through the pathway of the atrioventricular node and His bundle. Despite the elimination of the electrocardiographic features of the Wolff–Parkinson–White syndrome, spontaneous episodes of paroxysmal supraventricular tachycardia continued. Also, these episodes could be easily initiated by induced premature atrial depolarizations.

Differences in the electrophysiologic properties of the normal and accessory pathways are essential to the genesis and perpetuation of reentrant tachycardias in patients with the Wolff–Parkinson–White syndrome.14–16 The differential effect of antiarrhythmic agents on the electrophysiologic properties of these two pathways is responsible for changing the electrocardiographic patterns and altering the probability of the occurrence of tachycardias.

Wellens and Durrer17 have shown that administration of digitalis acutely prolongs the refractory period of the atrioventricular node, increases the time of A–H conduction, and shortens the refractory period of the bypass pathway. As a consequence of these changes in the critical temporal relations between the velocity of conduction and the refractory periods of the different parts of the tachycardiac circuit, the tachycardiac zone was markedly narrowed in two of six patients and completely eliminated in two other patients.

In a subsequent study, Wellens and Durrer18 investigated the short-term effects of intravenous administration of quinidine gluconate on the pathway of the atrioventricular node and His bundle and on the accessory pathway. The result of their electrophysiologic studies suggest that quinidine prolongs the refractory periods of the accessory pathway to a greater extent than the refractory periods of the pathway of the atrioventricular node and His bundle in both the anterograde and retrograde directions; however, in the accessory pathway, conduction was depressed more in the retrograde than in the anterograde direction. In contrast, our patient, who was receiving long-term oral therapy, demonstrated greater depression of anterograde bypass conduction than of retrograde conduction, if it is assumed that therapy with digitalis did not differentially shorten bypass conduction in the retrograde and anterograde directions.

Previous studies have reported the disappearance of
the pattern of preexcitation following intravenous administration of procainamide, while tachycardias could still be initiated by a properly timed atrial premature depolarization. These authors proposed that a differential effect of this drug on atrioventricular and ventriculoatrial conduction over the accessory pathway might explain this finding.

In the present study, anterograde and retrograde conduction through the bypass tract were differentially influenced by the antiarrhythmic agents. Thus, while therapy with quinidine in low doses successfully blocked anterograde bypass conduction, eliminating the delta wave on the surface ECG, retrograde bypass conduction remained intact, allowing for reentrant initiation and perpetuation of the tachyarrhythmia. Unfortunately, we were not able to perform electrophysiologic studies in the drug-free state, and, therefore, we were unable to assess the net effect that the differential influence of quinidine on atrioventricular and ventriculoatrial conduction through the bypass pathway had on the tachycardiac zone; however, it seems reasonable to assume that therapy with digitalis and quinidine would allow only late atrial premature beats to be conducted in an anterograde direction through the pathway of the atrioventricular node and His bundle and through the bypass pathway, respectively. As can be assessed from the surface ECG, therapy with quinidine depressed anterograde conduction through the bypass to a greater extent than therapy with digitalis depressed conduction through the atrioventricular node. This would indicate that the frequency of tachycardias could be reduced; however, the partial delay in conduction through the depressed pathway of the atrioventricular node and His bundle probably allowed the quinidine-depressed retrograde bypass tract to recover sufficiently to permit retrograde conduction to the atrium. Thus, while the tachycardiac zone shifted to the right (to longer premature beat intervals), the width of the zone probably did not change. The net effect could potentially lead to an increase in induction of tachycardias, since late atrial premature depolarizations may appear more frequently in the clinical situation than early premature depolarizations.

We concluded the following: (1) antiarrhythmic agents can have differential effects on atrioventricular and ventriculoatrial conduction through the accessory pathway; (2) the clinical consequences of this differential effect are dependent upon the net alteration it imposes on the critical temporal relations between the velocity of conduction and the refractory periods of different parts of the tachycardiac circuit; and (3) elimination of the delta wave and other characteristics of the Wolff-Parkinson-White syndrome in the surface ECG cannot be relied upon alone to indicate successful pharmacologic prophylaxis for induction of the tachyarrhythmia associated with this syndrome; however, it is necessary to conclude with a note of caution, in that short-term and long-term studies of drugs may have significant differences in terms of the magnitude and, possibly, the direction, of electrophysiologic changes.

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