Refractory Periods of the Accessory Pathway in the Wolff-Parkinson-White Syndrome

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SUMMARY
Antegrade (AERPAP) and retrograde (RERPAP) effective refractory periods of the accessory pathway were measured at multiple cycle lengths in 47 patients with the Wolff-Parkinson-White syndrome. In 20 patients the effect of changing cycle length on AERPAP could be determined. In 12 patients AERPAP decreased by 10-45 msec, in six it increased by 10-35 msec, and in two it was unchanged. In 13 of 15 patients in whom the effect of decreasing cycle length on RERPAP could be assessed, RERPAP decreased by 10-60 msec. In eight patients, the shortest AERPAP correlated well (r = 0.83) with the shortest R-R interval of consecutive pre-excited beats in atrial fibrillation. However, predominantly normal conduction was observed in six of 28 patients with atrial fibrillation, probably because of concealment in the bypass. Therefore, induction of atrial fibrillation during electrophysiological evaluation may provide additional information. The RERPAP at the cycle length of the arrhythmia was shorter than the cycle length of reciprocating tachycardia in all but one of 21 patients. At the same or comparable cycle lengths, AERPAP was usually greater than RERPAP.

THE USE OF TECHNIQUES for intracardiac stimulation and recording has advanced our understanding of the electrophysiological mechanisms which underlie the Wolff-Parkinson-White syndrome. These mechanisms have been discussed in recent reviews.1-7 It has been established that in the classic reciprocating tachycardia associated with the syndrome, circus movement is maintained by retrograde conduction over the accessory pathway (AP) with antegrade conduction over the His-Purkinje system. In a minority of cases, conduction may proceed over the circuit in the reverse direction. In atrial flutter or fibrillation the AP usually sustains antegrade conduction for most or all propagated beats and the resulting ventricular rate is determined by the properties of conduction and refractoriness of the AP. These properties of the AP during antegrade and retrograde conduction have been studied and compared in relatively few patients.6-8-14 The purpose of the present study was to examine the antegrade (AERPAP) and retrograde (RERPAP) effective refractory periods of the AP in a large group of patients with Wolff-Parkinson-White syndrome. The effect of alterations of basic cycle length upon AERPAP and RERPAP was determined and an attempt was made to relate refractory periods measured during regular cardiac pacing to the ventricular rate observed during atrial fibrillation and reciprocating tachycardia.

Materials and Methods
Forty-seven consecutive patients (34 M/13 F) with Wolff-Parkinson-White syndrome were studied. Their ages ranged from nine to 71 years. All patients presented with recurrent tachyarrhythmias, some of which were life-threatening. Most were referred as potential candidates for surgical division of the AP. Subsequent electrophysiological evaluation suggested that 18 patients had APs between the left atrium and ventricle, 12 had APs between the right atrium and ventricle, and in 18 the AP was thought to connect septal structures. In three of the patients, there was unidirectional antegrade block in the AP, and electrocardiographic and electrophysiological evidence of ventricular pre-excitation was not apparent. However, the AP sustained retrograde conduction in reciprocating tachycardia. Two patients had dual APs. In one, both APs were left-sided. The other patient had a right lateral and a left lateral AP. Surgery was performed in 23 of these 47 patients, confirming the suspected location of the AP. A full discussion of these patients has been presented with an account of the total experience of this institution.15

The nature of the procedure was fully explained to all patients and informed consent was obtained. In all except two patients, antiarrhythmic therapy was discontinued 48 hours prior to the time of study. Two patients were main-
tained on oral procainamide to control their extremely rapid ventricular rate in atrial fibrillation.

The patients were studied in the postabsorptive state. Diazepam, 5 mg i.v., was administered when sedation was necessary. Four catheters were used for intracardiac recording and stimulation. A 6F tripoal catheter was introduced percutaneously from the right femoral vein and positioned across the tricuspid valve for recording the His bundle electrogram. A 6F quadrupolar or hexapolar catheter was introduced from a left antecubital vein to the coronary sinus for recording left atrial and posterobasal left ventricular electrograms. Recording and stimulation of the right atrium and right ventricle was by separate 6F quadrupolar catheters introduced from the right antecubital fossa and right femoral vein, respectively. Heparin, 100 units/kg body weight, i.v., was administered after introduction of these catheters.

Intracavitary electrograms were obtained by filtering out frequencies below 50 Hz and above 1 kHz. Simultaneous recordings of surface electrocardiographic leads and intracavitary electrograms were recorded on magnetic tape at a speed of 3½ inches/sec. The tapes were played back on a Mingograph 808 S channel ink jet recorder at paper speeds of 100 mm/sec or 200 mm/sec. The faster speed was used for the measurement of cycle lengths during atrial fibrillation and reciprocating tachycardia.

A programmable digital stimulator* utilizing photoelectric isolation delivered impulses of 2 msec duration at approximately twice diastolic threshold. Programmed atrial or ventricular premature beats (A₂ or V₂) were delivered after every eighth spontaneous or paced beat (A₁ or V₁). Reciprocating tachycardia was initiated by this method in all except six patients. The site of earliest retrograde atrial activation during tachycardia was used to help localize the AP. Refractory periods were measured at several basic cycle lengths (A₁A₁ or V₁V₁) in most patients using stimulating and recording sites close to the location of the AP.12 The AERPAP was defined as the longest A₁A₂ interval near the AP which failed to conduct with pre-excitation. The RERPAP was defined as the longest V₁V₂ interval near the AP which failed to conduct over it. The observations used to detect retrograde conduction over the AP have been described elsewhere.12 16

Atrial fibrillation occurred spontaneously or was induced by right atrial pacing at a cycle length of 150–200 msec in 28 of the 47 patients. For the correlation between AERPAP and the shortest ventricular cycle length observed in atrial fibrillation, the shortest interval between two successive pre-excited beats was measured.

Results

Effect of cycle length on AERPAP. Thirty-nine patients had AERPAP estimated (table 1). Its exact measurement was possible at all cycle lengths studied in only 21 of these patients. In four of the 18 patients in whom precise determination was limited by the effective refractory period (ERP) of the atrium at some or all cycle lengths, the site of atrial stimulation was important. In these four, atrial ERP was reached prior to AERPAP at some sites, but not others.16 The

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<td><strong>Details of Antegrade Refractory Period Determinations</strong></td>
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<td><strong>Total number of patients</strong></td>
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<td><strong>Unidirectional antegrade block in AP</strong></td>
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<td><strong>Ventricular pre-excitation but AERPAP was not determined</strong></td>
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<td><strong>AERPAP determined at one cycle length only</strong></td>
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<td><strong>AERPAP determined at multiple cycle lengths</strong></td>
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<td><strong>AERPAP &gt; ERP of atrium at all cycle lengths</strong></td>
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Abbreviations: AP = accessory pathway; AERPAP = antegrade effective refractory period of the accessory pathway; ERP = effective refractory period.

shortest AERPAP of the 39 patients (limited in some cases by ERP of the atrium) is shown in figure 1. Ten patients had AERPAP ≤ 220 msec.

Thirty-five of the 39 patients had AERPAP determined at more than one cycle length. In 20 patients the effect of cycle length on refractoriness could be ascertained. In 12 of these patients, AERPAP decreased by 10–45 msec, in six patients it increased by 10–35 msec, and in two patients it was unchanged as basic cycle length decreased (fig. 2).

Relationship between AERPAP and ventricular rate in atrial fibrillation. Atrial fibrillation occurred spontaneously or was intentionally induced in 28 patients (table 2). The AERPAP was long (440 msec, 490 msec, and 540 msec) in three, and relatively short (270 msec) in only one of the six patients with either no ventricular pre-excitation or no consecutive pre-excited beats during the arrhythmia. In the other two cases with normal conduction during atrial fibrillation, the AERPAP could not be measured because of the

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*Designed by Michael Feezor, Ph.D., and built by Phil Talbert, Duke University.
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Figure 2

Plot of AERPAP against cycle length for 20 patients. At some cycle lengths, AERPAP was ≤ atrial ERP. See figure 1 for abbreviations.

predominance of normally conducted beats during the determinations. Therefore, AERPAP was probably long in these two patients also. For the eight patients in whom the AERPAP could be measured exactly, there was a significant correlation between the shortest ventricular cycle length of two consecutive pre-excited beats in atrial fibrillation and the shortest AERPAP observed at any cycle length ($r = 0.83$) (fig. 3). When the additional ten patients in whom AERPAP could not be measured exactly because of a longer atrial ERP were included, the correlation between AERPAP and the shortest ventricular cycle length of two consecutive pre-excited beats was considerably weakened ($r = 0.31$).

Retrograde Properties of Accessory Pathway

Effect of cycle length on RERPAP. Retrograde refractory periods were determined in 36 patients (table 3). The effect of alterations of basic cycle length on RERPAP could be assessed in 15 of these 36. Thirteen patients showed a decrease in RERPAP of 10-60 msec with decreasing cycle length, one showed no change, and one patient showed an increase of 15 msec (fig. 4).

Relationship between RERPAP and cycle length of reciprocating tachycardia. As shown in table 4, 21 of the 36 patients in whom retrograde refractory periods were measured had a RERPAP greater than the ventricular ERP and conducted retrogradely over their bypass during circus movement tachycardia (a patient the location of whose AP supported antegradely conducted during reciprocating tachycardia was excluded from this present correlation between RERPAP and tachycardia cycle length). In the 21 patients, the cycle length of the tachycardia correlated weakly ($r = 0.44$) with RERPAP determined at the closest basic cycle length to that of the arrhythmia (fig. 5). However, this cycle length at which refractoriness was determined averaged 107 msec greater than the cycle length of the tachycardia. The correlation coefficient was 0.55 when a further 10 patients in whom RERPAP was less than or equal to ventricular ERP were considered (fig. 5). The reason for this strengthening of the correlation is not completely apparent (see Discussion). The RERPAP was greater than the cycle length of reciprocating tachycardia in only one of these 31 patients.

Comparison of Antegrade and Retrograde Refractoriness

In 13 patients in whom neither AERPAP nor RERPAP were limited by atrial or ventricular ERP, antegrade and retrograde refractoriness could be compared at the same cycle length on 12 occasions and at

Table 2

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<th>Observations Relating to Atrial Fibrillation</th>
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<td>Patients in whom arrhythmia was observed or induced</td>
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<td>No consecutive pre-excited beats</td>
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<td>AERPAP not measured</td>
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<td>AERPAP &gt; ERP of atrium at all cycle lengths</td>
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Abbreviations: See table 1.

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similar cycle length (within 50–100 msec) on six occasions (fig. 6). The AERPAP and RERPAP were the same in six determinations, AERPAP was longer (range 10–215 msec) in ten determinations and shorter (by 10 msec and 50 msec) than RERPAP in two determinations. There was no significant correlation between AERPAP and RERPAP.

In another ten patients in whom AERPAP was measured exactly, but RERPAP was limited by ventricular refractoriness, the AERPAP was at least 10 msec longer than the RERPAP determined at the same cycle length in 15 of 16 determinations. In all 11 estimations of RERPAP in another five patients in whom RERPAP was measured exactly but AERPAP was limited by atrial refractoriness, RERPAP at the same cycle length was at least 10 msec longer. Therefore, AERPAP was more often longer (22 occasions) than the same (11 occasions) or shorter (12 occasions) than RERPAP. This tendency for RERPAP to be shorter than AERPAP was not explained by intramyocardial delay within the ventricle, as V1V2 intervals from electrograms close to known locations of the AP showed no prolongation with increased prematurity over the range of intervals studied.

Discussion

Change in refractory periods with changing basic cycle length is a characteristic phenomenon of cardiac muscle.17, 18 There is histological evidence that at least some bypass tracts in the Wolff-Parkinson-White syndrome consist of muscle fibers coursing between the atrium and ventricle.19-23 It is therefore not surprising that refractoriness of the AP should also be cycle length dependent.14, 24

In this study, AERPAP typically decreased as cycle length shortened. The definite lengthening of AERPAP with shorter cycle lengths in one patient was confirmed in separate studies on successive days. This patient also exhibited unidirectional retrograde block in the AP and reciprocating tachycardia could not be induced. The AP in this patient may have differed morphologically from the other APs.25 The maximum decrease in AERPAP in any patient in this series over the cycle lengths studied was only 45 msec, which agrees closely with the findings of Wellens and...
Durrer. However, not all patients were studied over the same or a wide range of cycle lengths and changes may have been more marked had AERPAP been determined over a wider span of cycle lengths.

The cycle length dependence of AERPAP can have practical implications during electrophysiological evaluation of patients with Wolff-Parkinson-White syndrome. The cycle length dependence of AERP of the atrium and of the AP may differ. It is therefore not rare (8/35 patients) for the AERPAP to be limited by atrial ERP at long cycle lengths but not at shorter cycle lengths. As it may be difficult to initiate reciprocating tachycardia when the AERPAP is not reached before the atrial ERP, premature atrial beats may initiate tachycardia (by blocking in the AP) at some but not all cycle lengths.

Little attention has been paid to the cycle length dependence of RERPAP. This study showed that RERPAP, in fact, depends to a greater degree than AERPAP upon cycle length. The almost uniform response is a shortening in RERPAP as cycle length decreases.

The finding that AERPAP is frequently longer than RERPAP at a comparable cycle length agrees with a previous report. Measurement of refractory periods by the extrastimulus technique depends on whether or not premature stimuli are conducted across the AP. De la Fuente et al. used an isthmus of canine atrial muscle as a model for the Wolff-Parkinson-White syndrome. They predicted that antegrade conduction might fail more easily than retrograde conduction because of impedance mismatch at the point of insertion of the AP into the ventricular muscle. Conduction and refractoriness cannot be equated, but these experimental findings may offer a possible explanation for the difference between AERPAP and RERPAP as measured in the catheterization laboratory.

Some conclusions of clinical importance can be drawn about refractoriness of the AP. In 17 of 39 patients (44%), AERPAP was so short as to be limited by atrial ERP at least at some cycle lengths. Therefore, in at least ten patients (25%) the shortest AERPAP, whether or not limited by atrial ERP, was 220 msec or less. Only a few short AERPAP have been previously reported. However, this relatively high incidence of short AERPAP in our group may not be representative of the frequency in the general population of patients with Wolff-Parkinson-White syndrome. This is because our patients were usually sufficiently symptomatic to be referred for consideration of surgery.

It has been suggested from previous studies that AERPAP can be useful in predicting the maximum ventricular rate that can be anticipated following the onset of atrial fibrillation. Theoretically, this might be expected with respect to the ventricular cycle length of pre-excited but not normally conducted beats. The present study confirmed the correlation, shown by Wellens and Durrer, between AERPAP and the most rapid ventricular response. This present study highlights a further finding of the relatively high frequency (6/28 patients or 21.5%) of conduction solely over the normal pathway during atrial fibrillation in patients who show ventricular pre-excitation during sinus rhythm. This discrepancy is most probably due to concealed conduction, which has been well described in AP. The AERPAP was usually long in these patients, and at faster rates without pre-excited ventricular beats, propagation over the normal conduction pathway was probably followed by retrograde penetration of the AP, thus tending to perpetuate normal conduction. In this situation, the ventricular rate during atrial fibrillation is limited by antegrade refractoriness of the atrioventricular node rather than of the AP. It has not been fully determined whether concealment is a consistent phenomenon. Our present experience suggests that, at least in some patients, it is not constant. Continuous electrocardiographic monitoring of one patient showed that although atrial fibrillation was associated with a normal ventricular conduction pattern during almost all of a 24 hour period, runs of rapid pre-excited beats occasionally occurred. Concealment may occur during atrial fibrillation, but not be evident when there is a slower atrial mechanism, as in atrial flutter (fig. 7).

For circus movement tachycardia to utilize the AP for retrograde conduction, it would appear necessary that the RERPAP (at the cycle length of the arrhythmia) be less than the cycle length of the tachycardia. In most of our patients, RERPAP was determined at cycle lengths greater than this. Since RERPAP is cycle length dependent, this would lead to a spuriously high estimate of the RERPAP which would obtain during tachycardia. Despite this, there was only one patient in whom the RERPAP was not less than the cycle length of spontaneous reciprocating tachycardia. It is not completely apparent to us why RERPAP should correlate with the cycle length of the arrhythmia. The cycle length should depend upon antegrade conduction time over the normal conduction system, intraventricular conduction time to the point of entrance into the AP, retrograde conduction time over the AP and intra-atrial conduction time from the point at which the impulse leaves the AP to its entry into the A-V node. Some correlation between the cycle length of the tachycardia and RERPAP would be expected if the AP is always that part of the circuit whose refractoriness limits full speed conduction. However, this has not been proven.
Based on our current experience, we feel that both AERPAP and RERPAP should be estimated at a number of cycle lengths, if possible including a shorter cycle length approximating that of reciprocating tachycardia. The AERPAP provides an index of the ventricular rate which can be anticipated during atrial fibrillation, and RERPAP allows a prediction of the maximum rate of reciprocating tachycardia which could occur (but not necessarily the actual rate). Therefore, both AERPAP and RERPAP may have potential prognostic importance and they can be used to assess the potential value of various pharmacological agents. However, we feel that because of the relatively frequent occurrence of concealed conduction in the AP, the additional step of inducing atrial fibrillation in the laboratory may provide additional information. This allows a more precise assessment of the vulnerability to a very rapid ventricular response with conduction over the AP, and a more accurate estimate of the value of antiarrhythmic therapy in controlling such a potentially lethal consequence of atrial fibrillation in the syndrome. Although synchronized cardioversion has been necessary in some cases to terminate the arrhythmia, the elective induction of atrial fibrillation has not been associated with any complications in our patients.

Addendum

Since the preparation of this manuscript, we have translated the thesis of Dr. Robert Frank, Paris, France, which was kindly sent to us. Dr. Frank’s findings corroborate a number of those in our series of patients (Apport des investigations endocavitaires et des cartographies epicardiques dans l’étude des syndromes de préexcitation ventriculaire. Editions Medicales et Universitaires, Paris, 1974).

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