Differential electrophysiologic properties of decremental retrograde pathways in long RP' tachycardia

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ABSTRACT Long RP' supraventricular tachycardias (SVT) often demonstrate both slow and decremental conduction properties in the retrograde pathway of the reentrant circuit. The electrophysiologic properties of these pathways are poorly understood. We studied 10 patients with long RP' SVT (RP'/RR, 0.52 to 0.71); five had the unusual form of atrioventricular nodal reentry (fast-slow) and five patients had accessory AV pathways with slow, decremental retrograde conduction properties. During SVT, the effects of intravenous adenosine (37.5 to 150 g/kg), which increases potassium current (iK) in supraventricular tissue and hyperpolarizes membrane potential toward Ek (-90 mV), and the response to slow-inward channel blockade with verapamil (0.10 to 0.20 g/kg iv) were evaluated. Adenosine and verapamil have similar effects in the presence of fast-slow AV nodal reentry since both agents terminated SVT by producing block in the retrograde slow AV nodal pathway. In contrast, adenosine and verapamil had differential effects on retrograde conduction in decremental accessory pathways. Adenosine terminated all episodes of SVT in the retrograde decremental pathway, whereas verapamil had a direct effect on this tissue in only two of five patients. Decremental retrograde accessory pathways can therefore demonstrate at least two types of electrophysiologic responses. Pathways that respond only to adenosine-induced hyperpolarizing K+ current likely comprise depressed fast-Na+ channel tissue, i.e., partially depolarized (> -60 to -70 mV) atrial tissue. In contrast, decremental accessory pathways that respond to both modulation of the slow-inward calcium current and K+ conductance have pharmacologic properties similar to those of the AV node and may represent more completely depolarized atrial fibers with resting membrane potentials of -60 mV or less.


FOR DIAGNOSTIC and therapeutic purposes, reentrant supraventricular tachycardia (SVT) is often classified on the basis of the RP' interval. In the absence of sinus node or intra-atrial reentry, long RP' SVT (RP'/RR >50%) is usually due to slow conduction in the retrograde limb of the reentrant circuit. Some of these slow retrograde pathways also manifest decremental conduction properties and are thought to be located either intranodally (atrioventricular [AV] nodal tissue) or extranodally (accessory AV connection). The intranodal type or the fast-slow form of AV nodal reentry is thought to utilize the fast AV nodal pathway in the anterograde direction and the slow pathway for its retrograde limb, but this has not been shown unequivocally to occur. The electrophysiologic properties of decremental extranodal AV pathways, including posteroseptal connections associated with the permanent form of junctional reciprocating tachycardia (PJRT) and laterally located accessory AV pathways, are also not completely understood nor adequately defined. It has been postulated that these extranodal pathways may represent either an accessory AV nodal–like structure or an accessory AV pathway with decremental properties. Therapy of these tachycardias could be rationally designed if their underlying electrophysiologic properties were better defined.

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The purpose of this study was to characterize the functional properties of the decremental retrograde conduction pathways in patients with long RP' tachycardia by examining the response of the tachycardia to adenosine and verapamil. Both agents, although highly effective in terminating reentrant rhythms involving AV nodal tissue, have different mechanisms of action.14,15 Adenosine hyperpolarizes membrane potential toward E_{K} and increases K+ conductance, whereas verapamil blocks the slow-inward Ca^{2+} channel.16

Methods

Electrophysiologic study. All studies were performed in patients in the nonseated, postabsorptive state after informed consent was obtained. All antiarrhythmic agents were discontinued for at least five half-lives before the study. Four quadrupolar electrode catheters were inserted percutaneously and advanced under fluoroscopic guidance to the right atrium, coronary sinus, right ventricular apex, and AV junction for recording of the His bundle. Bipolar intracardiac recordings were filtered at 30 to 500 Hz and simultaneously displayed with three electrocardiographic leads on a multichannel oscilloscope (Electronics for Medicine, VR-16, White Plains, NY). Data were stored on magnetic tape (Honeywell model 101, Waltham, MA) and were later retrieved on photographic paper for illustrative purposes. Real-time recordings were made with an ink-jet recorder (Siemens Elema Mingograph, Iselin, NJ). Stimulation was performed with a programmable stimulator and isolated constant current source (Bloom Associates, Narberth, PA). Stimuli were delivered as rectangular pulses of 2 msec duration at four times diastolic threshold.

Our stimulation protocol has been previously reported and includes the introduction of single, double, and triple extrastimuli and rapid burst pacing from multiple atrial and ventricular sites at several paced cycle lengths and during sinus rhythm.14 In addition, during tachycardia extrastimuli were introduced from the atria and right ventricle in an attempt to define the mechanism responsible for the tachycardia.

Administration of adenosine and verapamil. During SVT, the effects of intravenous adenosine and verapamil were evaluated. Crystalline adenosine (Sigma Chemical Co., St. Louis) was dissolved in normal saline at a concentration of 5 mg/ml and was prepared under sterile conditions as previously described.17 Adenosine (which has an elimination half-life in blood of <2 sec) was injected into a central line and was flushed with 10 ml of saline. Additional incremental doses of adenosine (37.5 µg/kg) were injected until termination of the tachycardia occurred (37.5 to 150 µg/kg).

The response to slow-inward channel blockade was assessed by administering 0.10 to 0.20 mg/kg of intravenous verapamil during tachycardia over 1 to 2 min.

The procedures described in this study were performed in accordance with a protocol approved by the Human Investigations Committee of the University of Virginia.

Definitions

(1) Decremental conduction of the retrograde pathway was considered to exist if one or more of the following observations were made: (A) Prolongation of ventriculoatrial conduction during SVT with the introduction of programmed ventricular extrasystoles, (B) a progressive increase in the V_{1}-A_{2} or H_{2}-A_{2} and A_{1}-A_{2} intervals during the introduction of progressively premature ventricular extrasystoles during ventricular pacing, (C) a progressive increase in the ventriculoatrial interval with repetitive Wenckebach periodicity in response to fixed-rate ventricu-

lar pacing, and (D) a spontaneous progressive increase in the ventriculoatrial interval during tachycardia before termination in the retrograde pathway.

(2) Fast-slow AV nodal reentry was defined as AV nodal reentry with anterograde conduction occurring over the fast AV nodal pathway and retrograde conduction occurring over the slow pathway. The atria and ventricles were not necessary components of the reentrant circuit. Retrograde atrial activation occurred earliest in the septal region and ventricular extrastimuli were unable to preexcite the atria.

(3) PJRT was defined as incessant macroreentrant tachycardia involving anterograde conduction over the AV node and His-Purkinje system and retrograde conduction occurring over a posteroseptal accessory AV pathway that had slow, decremental conduction properties.8

Results

Clinical characteristics. This study included 10 patients with SVT who had a long RP' tachycardia with decremental retrograde conduction properties; two of the patients were briefly mentioned in a previous report.14 Patients ranged in age from 10 to 78 years (table 1). One patient had a persistent left superior vena cava, two had a cardiomyopathy, one had coronary artery disease, and six patients had no structural heart disease. Long RP' tachycardia was due to fast-slow AV nodal reentry in five patients, orthodromic reciprocating tachycardia involving PJRT in three patients, and left lateral accessory AV pathways in two patients. The RP'/RR during tachycardia ranged from 0.52 to 0.71.

Characteristics of tachycardia: fast-slow AV nodal reentry. Tachycardia was initiated in all patients with programmed atrial and/or ventricular extrastimuli and was terminated by programmed atrial or ventricular extrastimuli. Earliest retrograde atrial activation was observed in the low right atrial septum. Three patients showed discontinuous retrograde conduction curves (V_{1}-V_{2} vs A_{1}-A_{2} and V_{2}-A_{3}). Initiation of tachycardia with ventricular extrastimuli followed block in the retrograde fast pathway with conduction proceeding over the retrograde slow AV nodal pathway.

An extranodal retrograde pathway did not participate in the tachycardia circuit. Spontaneous (or induced) ventricular extrasystoles occurring during tachycardia dissociated ventricular activity from both atrial and His bundle activity (figure 1). It was observed that the tachycardia cycle length of 450 msec, as reflected in the atrial and His bundle deflections, remained constant while ventricular activity was asynchronous. This observation suggests that the tachycardia is not dependent on infra-Hisian tissue, i.e., bundle branches or ventricular myocardium, and therefore a macroreentrant circuit involving a retrograde nodoven-tricular tract or an extranodal accessory pathway cannot account for this tachycardia.
The His bundle was also not required for perpetuation of the tachycardia. As shown in figure 2, carotid sinus pressure induced 2:1 AV block above the level of the His bundle just before termination (figure 2, A). The tachycardia cycle length, as reflected by the atrial electrogram, remained undisturbed despite AV block. Thus, block occurred above the His bundle, indicating that the His-Purkinje system was not necessary for maintenance of the tachycardia. Figure 2, B, shows that the distal AV node was not necessary to sustain the tachycardia. Intranodal Wenckebach block occurred during tachycardia distal to the site of the AV nodal reentrant circuit. Intra-atrial reentry was eliminated as a mechanism of the arrhythmia by the ability of programmed atrial extrastimuli introduced during tachycardia to dissociate atrial activity from the His-Purkinje system, by termination of tachycardia with carotid sinus pressure (figure 2, A), and by the response to adenosine described below.

Adenosine terminated fast-slow AV nodal reentrant tachycardia in the retrograde slow pathway within 13 to 22 sec (table 1). Adenosine primarily prolonged retrograde conduction before block, while the anterograde fast pathway was relatively unaffected. One patient did not respond to adenosine (patient 3). This finding was expected since the patient was taking aminophylline for treatment of asthma and had a serum theophylline level of 19.6 \( \mu \text{g/ml} \). Aminophylline is a known competitive antagonist of adenosine and blocks the extracellular \( A_1 \)-adenosine receptor at this concentration.

Adenosine’s effects on retrograde conduction prop-

### TABLE 1

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>Age (yr)</th>
<th>Sex</th>
<th>Cardiac diagnosis</th>
<th>SVT mechanism</th>
<th>Earliest retrograde atrial activation (msec)</th>
<th>CL (msec)</th>
<th>AH (msec)</th>
<th>HV (msec)</th>
<th>VA-HBE (msec)</th>
<th>Adenosine dose (mg)</th>
<th>Response to adenosine</th>
<th>Verapamil dose (mg)</th>
<th>Response to verapamil</th>
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<tbody>
<tr>
<td>1</td>
<td>78</td>
<td>M</td>
<td>NL</td>
<td>AVNR:F/S</td>
<td>0.62</td>
<td>HB</td>
<td>385-460</td>
<td>110-135</td>
<td>50</td>
<td>225-260</td>
<td>3.2 Term. retrograde (13 sec)</td>
<td>5 Term. retrograde</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>22</td>
<td>M</td>
<td>NL</td>
<td>AVNR:F/S</td>
<td>0.71</td>
<td>HB</td>
<td>260-310</td>
<td>60-70</td>
<td>50</td>
<td>150-200</td>
<td>4.8 Term. retrograde (14 sec)</td>
<td>10 Term. retrograde</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>72</td>
<td>F</td>
<td>NL</td>
<td>AVNR:F/S</td>
<td>0.68</td>
<td>HB</td>
<td>310</td>
<td>60</td>
<td>40</td>
<td>210</td>
<td>19 No effect*</td>
<td>5 Term. retrograde</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>73</td>
<td>M</td>
<td>NL</td>
<td>AVNR:F/S</td>
<td>0.63</td>
<td>HB</td>
<td>460</td>
<td>150</td>
<td>70</td>
<td>240</td>
<td>3.6 Term. retrograde (17 sec)</td>
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<td></td>
</tr>
<tr>
<td>5</td>
<td>58</td>
<td>M</td>
<td>CAD</td>
<td>AVNR:F/S</td>
<td>0.57</td>
<td>HB</td>
<td>410</td>
<td>100</td>
<td>70</td>
<td>230</td>
<td>5.3 Term. retrograde (22 sec)</td>
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</tr>
<tr>
<td>6</td>
<td>10</td>
<td>F</td>
<td>CM</td>
<td>PJRT</td>
<td>0.66</td>
<td>OS</td>
<td>420-475</td>
<td>105-130</td>
<td>50</td>
<td>260-320</td>
<td>4.2 Term. retrograde (15 sec)</td>
<td>5 No effect</td>
<td></td>
</tr>
<tr>
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<td>19</td>
<td>M</td>
<td>CM</td>
<td>PJRT</td>
<td>0.52</td>
<td>OS</td>
<td>400-500</td>
<td>140</td>
<td>40</td>
<td>235-320</td>
<td>7.3 Term. retrograde (8 sec)</td>
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<td></td>
</tr>
<tr>
<td>8</td>
<td>12</td>
<td>F</td>
<td>NL</td>
<td>PJRT</td>
<td>0.71</td>
<td>OS</td>
<td>350-390</td>
<td>80</td>
<td>50</td>
<td>220-260</td>
<td>1.4 Term. retrograde (13 sec)</td>
<td>5 No effect</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>44</td>
<td>M</td>
<td>NL</td>
<td>AVRT</td>
<td>0.58</td>
<td>CS</td>
<td>360-380</td>
<td>150-160</td>
<td>40</td>
<td>180-190</td>
<td>4.5 Term. retrograde (16 sec)</td>
<td>15 Term. anterograde (AVN)</td>
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<tr>
<td>10</td>
<td>10</td>
<td>M</td>
<td>Persistent</td>
<td>AVRT</td>
<td>0.52</td>
<td>CS</td>
<td>250-340</td>
<td>90-140</td>
<td>40</td>
<td>120-160</td>
<td>1.5 Term. retrograde (17 sec)</td>
<td>4.5 Term. retrograde</td>
<td></td>
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</tbody>
</table>

AVN = atrioventricular node; AVNR = atrioventricular nodal reentry; AVRT = atrioventricular reciprocating tachycardia; CAD = coronary artery disease; CL = cycle length; CM = cardiomyopathy; CS = coronary sinus; F/S = fast-slow; HBE = His bundle electrogram; LSVC = left superior vena cava; ND = not done; NL = normal.

*Aminophylline level 19.6 \( \mu \text{g/ml} \).
properties could not be systematically evaluated since the drug's half-life in the central compartment is less than 2 sec.

Verapamil terminated all episodes of fast-slow AV nodal reentry within 25 to 60 sec after injection in the three patients to whom it was given. The retrograde slow pathway was always the site of termination. Verapamil increased the paced cycle length of retrograde AV nodal Wenckebach block by 50 msec compared with control (400 to 450 msec) in the one patient in whom it was examined (No. 2).

Characteristics of tachycardia: decremental retrograde accessory AV pathways

Electrophysiologic properties. Five patients with SVT had accessory AV pathways with decremental retrograde conduction properties; three had posteroseptal pathways (PJRT) and two had left lateral AV connections (table 1). The rhythm in patients with PJRT (patients 6 to 8) was incessant, showed large variation in cycle length, and was interrupted by occasional sinus beats.7,8 The tachycardia resumed after shortening of the sinus P-P interval and did not require prolongation of the PR interval. Earliest retrograde atrial activation was mapped to the os of the coronary sinus. PJRT was differentiated from the fast-slow form of AV nodal reentry by the ability of ventricular extrastimuli to preexcite the atrium during His bundle refractoriness without altering the retrograde activation sequence, thus indicating the presence of an extranodal pathway (figure 3, A). The presence of an extranodal pathway was also demonstrated by terminating the tachycardia in its retrograde pathway with a ventricular extrastimulus that failed to capture the atrium that was introduced after anterograde His bundle activation (figure 3, B). The decremental properties of the retrograde pathway were demonstrated by introducing ventricular extrastimuli during SVT and/or ventricular pacing.

Two patients had left lateral accessory pathways with decremental retrograde conduction properties. In patient 9, orthodromic reciprocating tachycardia was initiated with a programmed ventricular extrastimulus. There was eccentric retrograde atrial activation, with the earliest activity occurring in the region of the distal coronary sinus. Decremental conduction in the retrograde AV pathway was demonstrated by introducing progressively premature ventricular extrastimuli during tachycardia and showing progressive prolongation in the ventriculoatrial conduction interval as measured from the local coronary sinus electrogram. Intraventricular or intra-atrial conduction delay did not account for the increase in ventriculoatrial conduction.

The other patient (No. 10) with a left lateral decre-
FIGURE 2. A, Two-to-one AV nodal block (supra-Hisian) during fast-slow AV nodal reentry induced by carotid sinus pressure (CSP) in patient 1. The His bundle is not necessary for perpetuation of the tachycardia since the atrial rate is constant during AV nodal block. After one sequence of 2:1 AV nodal block, the tachycardia terminates in the retrograde slow pathway of the AV node. Reproducible termination with CSP indicated that the tachycardia was not due to intra-atrial reentry. Abbreviations are as in figure 1. B, AV nodal Wenckebach block during tachycardia in the same patient after a spontaneous decrease in cycle length. There is progressive prolongation of the AH interval from 110 to 265 msec during tachycardia until intranodal block occurs. The atrial cycle length during tachycardia is unaffected by AV nodal block. These figures provide evidence that the distal AV node and the His-Purkinje system are not necessary for the reentrant circuit.

mental retrograde AV pathway showed retrograde discontinuous conduction curves (dual pathways) in the extranodal tract (figure 4). Ventricular extrastimuli (coupling intervals from 400 to 280 msec) introduced at 10 msec decrements after an 8 beat ventricular drive at 500 msec resulted in progressive prolongation of ventriculoatrial conduction from 125 to 205 msec (measured from the coronary sinus electrogram). A ventricular extrastimulus introduced at a coupling interval of 270 msec resulted in a 130 msec prolongation in ventriculoatrial conduction to 335 msec, with the retrograde atrial activation sequence unchanged (mid coronary sinus activation earliest). It may be argued that this retrograde discontinuity represents conduction block in the accessory pathway and alternate conduction across the AV node or an additional accessory pathway. This is unlikely, however, since eccentric retrograde atrial activation was unchanged after the discontinuity and progressive decremental conduction in the AV pathway was observed until ventricular refractoriness was reached (230 msec).

Response to adenosine. Adenosine reproducibly terminated tachycardia in the decremental retrograde accessory pathway in all five patients (table 2; figures 5 and 6, A). Termination was usually preceded by progressive prolongation in the retrograde limb. A typical example is shown in figure 5 (patient 9). The ventriculoatrial interval progressively increased from 120 to 180 msec in response to adenosine before tachycardia broke in the accessory pathway.

Response to verapamil. Incremental retrograde accessory pathways were sensitive to verapamil in only two
of five patients (table 2). In patient 6, verapamil had no effect on conduction in the retrograde pathway during tachycardia or on the cycle length of pacing-induced Wenckebach block (490 msec). Direct effects of verapamil on the accessory pathway were demonstrated in patient 7. Verapamil caused a modest increase in pacing-induced retrograde Wenckebach block from 400 to 430 msec and transiently terminated SVT in the retrograde pathway. Termination was preceded by progressive ventriculooatrial prolongation. Verapamil did not terminate SVT in patient 8. Small spontaneous oscillations in retrograde conduction were observed during SVT and were not affected by verapamil. Verapamil had no direct effect on the retrograde pathway in patient 9 since conduction over the pathway (ventriculoatrial interval) was unaltered before termination of tachycardia. In contrast, direct effects of verapamil on the AV node were manifest in this patient by termina-

FIGURE 3. A, Preexcitation of the atrium during His bundle refractoriness in a patient with PJRT (No. 6). A premature ventricular extrastimulus introduced after the His bundle has been anterogradely depolarized preexcites the atrium by 20 msec without altering the retrograde atrial activation sequence. This indicates the presence of an extranodal pathway. Although the retrograde atrial sequence suggests early septal atrial activation, complete mapping of the coronary sinus and tricuspid valve during tachycardia indicated that atrial activity in the region of the os of the coronary sinus was the earliest site (not shown). CS_d = distal coronary sinus; CS_m = mid coronary sinus; S = stimulus artifact. Other abbreviations are as in figure 1. B, Termination of PJRT in the same patient. A premature ventricular extrastimulus introduced during His bundle refractoriness terminates tachycardia without capturing the atrium. The site of termination is the septal AV accessory pathway. Abbreviations are as in figure 1.
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FIGURE 4. A, Demonstration of retrograde discontinuous conduction in a lateral accessory AV pathway (patient 10). After an 8 beat ventricular drive at a cycle length of 500 msec, a ventricular extrastimulus is introduced at a coupling interval of 280 msec. The retrograde ventriculoatrial conduction intervals measured from the stimulus artifact from the HBE, CSm, and CSd are 265, 205, and 220 msec, respectively. Abbreviations are as in previous figures. B, A ventricular extrastimulus introduced at a coupling interval of 270 msec (10 msec less than in A) results in a marked prolongation of retrograde conduction. There is still eccentric retrograde atrial activation, with the CSm earliest; however, the conduction interval has increased from 205 (A) to 335 msec. This suggests the presence of longitudinal dissociation of the retrograde accessory AV pathway. The slight change in septal atrial activation is due to fusion from retrograde conduction across both the AV node and accessory pathway. Abbreviations are as in previous figures.

TABLE 2
Pharmacologic responses of decremental retrograde accessory pathways

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>Location of AP</th>
<th>Verapamil sensitive</th>
<th>Adenosine sensitive</th>
</tr>
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<tbody>
<tr>
<td>6</td>
<td>Posteroseptal</td>
<td>–</td>
<td>+</td>
</tr>
<tr>
<td>7</td>
<td>Posteroseptal</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>8</td>
<td>Posteroseptal</td>
<td>–</td>
<td>+</td>
</tr>
<tr>
<td>9</td>
<td>Left lateral</td>
<td>–</td>
<td>+</td>
</tr>
<tr>
<td>10</td>
<td>Left lateral</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>

AP = accessory pathway.

Verapamil caused retrograde block in the accessory pathway during tachycardia in patient 10, although oscillation in AV nodal conduction preceded termination (figure 6, B). A relatively long AH interval was followed by a relatively short AH, raising the possibility of Ashman’s phenomenon in the accessory pathway; however, the changes in AH were relatively small. Furthermore, it is likely that verapamil had a direct effect on the accessory pathway during tachycardia since it increased the retrograde refrac-
FIGURE 5. Termination of AV reciprocating tachycardia in the retrograde accessory pathway after adenosine (patient 9). Adenosine caused a progressive increase in retrograde ventriculoatrial conduction before termination.

FIGURE 6. A, Termination of tachycardia by adenosine in the retrograde limb in a patient with retrograde longitudinal dissociation in the left lateral accessory AV connection (patient 10). There is right bundle branch block aberration during tachycardia. B, Termination of tachycardia in the retrograde pathway in the same patient after verapamil (aberration is no longer present). Note slight oscillations in the AH interval before termination. See text for explanation. Abbreviations are as in previous figures.
tor period of the accessory pathway during ventricular extrastimulus testing from 230 to 300 msec.

Discussion

Evidence supporting fast-slow AV nodal reentrant tachycardia. In this study we demonstrated the existence of fast-slow AV nodal reentry and defined its anatomic requirements. Most previous reports on fast-slow AV nodal reentry have not eliminated the presence of a decremental septal accessory AV pathway because they failed to demonstrate dissociation of atrial and ventricular activity during tachycardia. Furthermore, exclusion of intra-atrial reentry has not always been definitively shown. This lack of evidence has caused some investigators to doubt the existence of fast-slow AV nodal reentry. Recently it has been shown that the ventricle could be dissociated from atrial and His bundle activity in a single patient with inverted P waves in leads II, III, and aVF and long RP' tachycardia. The authors interpreted this finding as evidence of fast-slow AV nodal reentry. A Hisian-atrial connection comprising the retrograde pathway of the circuit was not excluded in this report, however. In the present study, we were able to show that in none of our patients with fast-slow AV nodal reentrant tachycardia were the ventricles or His-Purkinje system part of the reentrant circuit (figures 1 and 2). Furthermore, in two patients we demonstrated that the distal AV node was not required for the tachycardia circuit. These data provide evidence against the presence of a macroreentrant circuit using either a septal accessory AV pathway or a Mahaim tract for retrograde conduction. Intra-atrial reentry from a low septal site was also an unlikely mechanism of tachycardia due to the method of termination of tachycardia, i.e., application of carotid sinus pressure, dissociation of atrial activity from the His-Purkinje system during tachycardia, and termination of tachycardia with adenosine, an agent that has no known effect on intra-atrial reentry. The body of evidence therefore strongly supports fast-slow AV nodal reentry as the mechanism of long RP' SVT in these patients and suggests that it should be considered an intranodal tachycardia with only part of the AV node required for the reentrant circuit.

Electrophysiologic properties of retrograde intranodal and extranodal pathways. The functional properties of retrograde intranodal and extranodal pathways that give rise to slow, decremental conduction in patients with long RP' tachycardia are incompletely understood. The effects of adenosine and verapamil, two pharmacologic agents that slow AV nodal conduction and increase refractoriness by different mechanisms of action, were studied to further define the electrophysiologic properties of these pathways.

Adenosine is an endogenously produced nucleoside whose electrophysiologic effects on supraventricular tissues result in hyperpolarization of the resting membrane potential toward the potassium equilibrium potential (E_k, -90 mV) and shortening of action potential duration by an increase in K^+ conductance. Verapamil, which blocks the slow-inward calcium current, along with adenosine, would therefore be expected to terminate fast-slow SVT since both the slow-inward calcium current and outward K^+ current have important roles in impulse propagation through the AV node.

As predicted, adenosine and verapamil had similar effects on fast-slow AV nodal reentry since both terminated tachycardia by producing conduction block in the retrograde slow pathway. Verapamil either caused progressive slowing in the retrograde pathway before termination or broke the tachycardia abruptly, whereas adenosine was always associated with prolongation of the retrograde slow pathway before termination. Verapamil and adenosine have been shown to prolong refractoriness and slow conduction in both the anterograde slow and retrograde fast pathways in the usual form of AV nodal reentry.

Adenosine and verapamil had differential effects on decremental retrograde accessory AV pathways. Adenosine terminated all episodes of tachycardia in the five patients by producing block in the retrograde pathway, whereas verapamil had a direct effect on this pathway in only two of five patients.

Histologically, retrograde accessory AV connections have been shown to consist primarily of atrial fibromuscular bundles. Decremental conduction has been attributed to the tortuous course of the accessory pathway, with concomitant changes in axial resistivity. An alternative, although not mutually exclusive, explanation is that decremental conduction in these pathways is also due to partial depolarization (depressed fast-Na^+ channels) of the anomalous atrial fascicles. This would account for adenosine's negative dromotropic effects on this tissue. This hypothesis is also consistent with our previous observations in which adenosine was found to have no effect on intra-atrial reentry or on normally conducting, nondecremental accessory pathways in which resting membrane potential is presumably near E_k.

Our findings suggest that decremental retrograde AV pathways may have heterogenous properties and consist of partially depolarized atrial fibers with de-
pressed fast-Na⁺ channels. Atrial tissue with a resting membrane potential of greater than −60 to −70 mV (i.e., depressed fast action potential) would be expected to respond to adenosine²⁶ but not to verapamil.²² The lack of response of depressed fast-Na⁺ channel tissue to slow-inward current blockade²⁴ is not unexpected when resting membrane potential is greater than −60 mV and Vmax is greater than 20 V/sec.²³

Therefore, retrograde pathways that respond only to adenosine would suggest that the hyperpolarizing K⁺ current, which decreases excitability in tissues that depend primarily on depressed fast-Na⁺ current, plays a significant role in determining the electrophysiologic properties in these tissues. Decremental conduction in these pathways, therefore, does not appear to be calcium dependent, unlike conduction in the AV node.

The observation in patients 9 and 10 that some accessory AV pathways functionally resemble AV nodal tissue since they respond to both adenosine and verapamil indicates that these particular connections are also dependent on calcium conductance. Relevant to these observations are reports of verapamil-induced conduction block in lateral accessory pathways.²⁵⁻²⁷ Another finding consistent with AV nodal-like tissue is the presence of discontinuous retrograde conduction curves (dual pathways) in the accessory pathway of patient 10. However, the electropharmacologic results from this study along with previous histologic findings²² suggest that these pathways are more appropriately classified as markedly depolarized atrial fascicles (resting membrane potential ≤ −60 mV) rather than as true AV nodal tissue.

It is important to emphasize that separation of extranodal pathways into functional subtypes on the basis of their response to adenosine and verapamil may be somewhat arbitrary since these effects may represent a continuum in identical tissue under different conditions. In addition, it is also possible that changes in autonomic tone and the electrophysiologic milieu may convert an accessory connection from verapamil insensitive to verapamil sensitive. Nevertheless, at present it seems reasonable to assume that decremental accessory AV pathways in patients with long RP' tachycardia can functionally demonstrate at least two different types of electrophysiologic properties. The adenosine-induced hyperpolarizing K⁺ current may have a primary role in determining the retrograde electrophysiologic properties in some decremental accessory AV pathways and suggests the presence of depressed fast-Na⁺ channel tissue with membrane potential greater than −60 mV (i.e., partially depolarized atrial tissue). In contrast, decremental AV pathways that respond to both modulation of the slow-inward calcium current and K⁺ conductance have functional properties similar to those of the AV node but likely comprise markedly depolarized atrial tissue. Based on these observations, development of long-acting analogs of adenosine may prove useful in the pharmacologic treatment of patients with long RP' tachycardia and retrograde decremental conduction properties.

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