Adenosine: electrophysiologic effects and therapeutic use for terminating paroxysmal supraventricular tachycardia

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ABSTRACT Adenosine was administered intravenously to 17 patients undergoing intracardiac electrophysiologic studies. At a mean dose of 179 ± 88 μg/kg (± SD), adenosine suppressed sinus node automaticity and depressed atrioventricular (AV) nodal conduction. These effects were less than 20 sec in duration and were not influenced by muscarinic blockade with atropine (0.02 to 0.03 mg/kg). Adenosine at this dose had no effect on antegrade conduction over accessory pathways in patients with Wolff-Parkinson-White syndrome. No independent hemodynamic effects were observed. In six patients, adenosine was administered intravenously during stimulation-induced paroxysmal supraventricular tachycardia. In the five patients in whom the reentry loop of their tachycardia included the AV node, adenosine at a mean dose of 83 ± 35 μg/kg (± SD) terminated their tachycardia within 20 sec after peripheral intravenous injection. The dose of adenosine required to terminate these tachycardias did not produce manifest sinus node suppression, and sinus rhythm promptly resumed in all patients. Adenosine did not terminate either supraventricular tachycardia due to intra-atrial reentry or atrial flutter, but did produce transient AV block during these arrhythmias. Our findings demonstrate that the human sinus and AV nodes are sensitive to physiologic doses of adenosine and that adenosine may be used safely and effectively to terminate acute episodes of supraventricular tachycardia that involve the AV node in the reentry pathway.

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ADENOSINE is an intermediate metabolite in many important biochemical pathways and has been shown to play a role in the regulation of a number of physiologic processes including coronary and systemic vascular tone, platelet function, and lipolysis in adipocytes.1,2 In 1929, Drury and Szent-Gyorgy3 reported that adenosine produced sinus bradycardia and atrioventricular (AV) block in several animal species and could restore sinus rhythm to canine hearts in which atrial fibrillation had been experimentally produced. Several years later, Honey et al.4 and Jezer et al.5 observed that intravenous adenosine depressed both sinus rate and AV conduction in humans, but they reported no effect on atrial arrhythmias. We have recently demonstrated in isolated guinea pig and rabbit hearts and in the heart of the anesthetized dog in situ that the AV delay produced by adenosine is localized to the AV node.6,7 Data from our laboratory and others have also suggested that adenosine released during ischemia or hypoxia may mediate the sinus bradycardia or AV nodal block seen in these conditions.7-9 These effects of adenosine in animals appear to be the result of an interaction with a specific extracellular receptor that is blocked by methylxanthines but not by atropine.10

The dose-response relationship of adenosine for its electrophysiologic and hemodynamic effects in man has not been previously characterized. In this study we sought to determine the nature and time course of the electrophysiologic effects of graded doses of intravenous adenosine in man and to assess the hemodynamic changes produced by the doses required to produce these effects. We also sought to test the hypothesis that the production of transient AV nodal block by an intravenous bolus of adenosine might permit the safe and
rapid termination of paroxysmal supraventricular tachycardias in which the AV node was part of the reentrant circuit.

Methods

Patients studied. There were 10 men and seven women in this study, with a mean age of 51.2 ± 16.5 (± SD) years. All were undergoing electrophysiologic study to help determine future antiarrhythmic therapy. The clinical characteristics of the patients studied, as well as significant findings obtained at electrophysiologic study, are detailed in tables 1 and 2. Eleven patients (group 1) did not have paroxysmal supraventricular tachycardia initiated by programmed cardiac stimulation, whereas six patients (group 2) did manifest supraventricular tachycardia in response to programmed stimulation during the study. Fifteen patients were in sinus rhythm at the time of study, whereas two patients (Nos. 6 and 7) were in chronic atrial fibrillation. One patient (No. 10) had a history of symptomatic sinus bradycardia, and one patient (No. 4) had an abnormal corrected sinus node recovery time. Baseline parameters of sinus and AV nodal function were normal for all other patients, even though one patient (No. 1) had carotid sinus hypersensitivity and one patient (No. 11) had recurrent syncope, so we suspected was due to vagally mediated bradyarrhythmias. Three patients had abnormal His-Purkinje conduction, and four manifested preexcitation when in sinus rhythm.

Drugs known to influence adenosine metabolism (e.g., diprydamole, diazepam, and phenobarbital) and all antiarrhythmic drugs were withheld for at least 48 hr before study. Digoxin was continued in patients 6 and 7 for control of ventricular rate during atrial fibrillation and in patient 3 because of congestive heart failure.

Protocol of electrophysiologic study. Electrophysiologic studies were performed with patients in the fasting nonsedated state after informed consent had been obtained from all patients. Three No. 6F quadripolar electrode catheters (USCI, Billerica, MA) with a 1 cm interelectrode distance were introduced percutaneously via the right and left femoral veins and were positioned by fluoroscopic guidance in the high right atrium, across

| TABLE 1 |

| Patients without paroxysmal supraventricular tachycardia |

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Cardiac diagnosis</th>
<th>Age (yr)</th>
<th>Sex</th>
<th>Reason for study</th>
<th>Control electrophysiologic findings</th>
<th>ADO dose for SB/AVB (µg/kg)</th>
<th>Response during programmed stimulation</th>
</tr>
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<tbody>
<tr>
<td>1 CAD</td>
<td>CAD</td>
<td>81</td>
<td>M</td>
<td>Recurrent syncope</td>
<td>NSR (1130)</td>
<td>75</td>
<td>Carotid sinus hypersensitivity</td>
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<td>2 CAD</td>
<td>CAD</td>
<td>55</td>
<td>F</td>
<td>Recurrent VT</td>
<td>NSR (790)</td>
<td>225</td>
<td>VT with ventricular stimulation, AF1, and AF with rapid atrial pacing</td>
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<tr>
<td>3 CAD</td>
<td>CAD</td>
<td>42</td>
<td>M</td>
<td>Out-of-hospital cardiac arrest (VF)</td>
<td>NSR (570)</td>
<td>450</td>
<td>Normal response to programmed stimulation</td>
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<td>4 CAD</td>
<td>CAD</td>
<td>48</td>
<td>M</td>
<td>Out-of-hospital cardiac arrest (VF)</td>
<td>NSR (920)</td>
<td>225</td>
<td>VF with programmed stimulation</td>
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<td>5 CAD</td>
<td>CAD</td>
<td>79</td>
<td>M</td>
<td>Recurrent VT</td>
<td>NSR (890)</td>
<td>225</td>
<td>VT with programmed stimulation</td>
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<tr>
<td>6 Cardiomyopathy</td>
<td>M</td>
<td>Dizzy spells, nonsustained VT</td>
<td>AF (800)</td>
<td>—</td>
<td>—</td>
<td>50</td>
<td>112.5</td>
</tr>
<tr>
<td>7 CAD</td>
<td>CAD</td>
<td>66</td>
<td>F</td>
<td>Nonsustained VT</td>
<td>AF (750)</td>
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<td>No VT with programmed stimulation</td>
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<td>8 NSHD</td>
<td>NSHD</td>
<td>30</td>
<td>M</td>
<td>Recurrent VT</td>
<td>NSR (1020)</td>
<td>262.5</td>
<td>Left lateral bypass tract, no PSVT, AF with rapid atrial pacing</td>
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<tr>
<td>9 WPW</td>
<td>WPW</td>
<td>21</td>
<td>M</td>
<td>AF</td>
<td>NSR (780)</td>
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<td>Bypass tract, no PSVT, AF with atrial pacing</td>
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<tr>
<td>10 Constrictive pericarditis</td>
<td>M</td>
<td>Recurrent AF and AFI</td>
<td>NSR (900)</td>
<td>&gt;60</td>
<td>Unable to measure</td>
<td>75</td>
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<td>11 NSHD</td>
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<td>36</td>
<td>F</td>
<td>Recurrent syncope</td>
<td>NSR (660)</td>
<td>225</td>
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ADO = adenosine; AF = atrial fibrillation; AFI = atrial flutter; AVB = atrioventricular block; CAD = coronary artery disease; CL = cycle length; CSNRT_max = maximum corrected sinus node recovery time; NSHD = no structural heart disease; NSR = normal sinus rhythm; PSVT = paroxysmal supraventricular tachycardia; SB = sinus bradycardia; VT = ventricular tachycardia; VF = ventricular fibrillation; WPW = Wolff-Parkinson-White syndrome.

*No history of symptomatic bradyarrhythmias.

*Sinus function could not be assessed due to atrial fibrillation.
TABLE 2
Patients with paroxysmal supraventricular tachycardia

<table>
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<tr>
<th>Patient No.</th>
<th>Cardiac diagnosis</th>
<th>Age (yr)</th>
<th>Sex</th>
<th>Reason for study</th>
<th>Rhythm (CL)</th>
<th>CSNRT_max</th>
<th>AH</th>
<th>HV</th>
<th>SVT mechanism (CL)</th>
<th>ADO dose for SB/AVB (μg/kg)</th>
<th>Dose required to terminate individual episodes (no. of episodes)</th>
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<tr>
<td>12</td>
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<td>67</td>
<td>F</td>
<td>Recurrent PSVT</td>
<td>NSR (765)</td>
<td>250</td>
<td>100</td>
<td>40</td>
<td>Reciprocating tachycardia (350)</td>
<td>112.5</td>
<td>37.5 μg/kg (5)</td>
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<td>75.0 μg/kg (1)</td>
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<td>NSHD</td>
<td>61</td>
<td>M</td>
<td>Recurrent PSVT</td>
<td>NSR (675)</td>
<td>230</td>
<td>105</td>
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<td>AV node reentry (445)</td>
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<td>75.0 μg/kg (5)</td>
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<td>NSR (640)</td>
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<td>120</td>
<td>10</td>
<td>Reciprocating tachycardia (250)</td>
<td>150</td>
<td>112.5 μg/kg (1)</td>
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<td></td>
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<td>150.0 μg/kg (2)</td>
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<td>RHD</td>
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<td>F</td>
<td>Recurrent PSVT</td>
<td>NSR (790)</td>
<td>400</td>
<td>110</td>
<td>50</td>
<td>AV node reentry (320)</td>
<td>187.5</td>
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<td>M</td>
<td>Recurrent AF</td>
<td>NSR (820)</td>
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<td>90</td>
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<td></td>
<td>75.0 μg/kg (2)</td>
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<tr>
<td>17</td>
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<td>M</td>
<td>Recurrent PSVT</td>
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<td>85</td>
<td>38</td>
<td></td>
<td>Intraatrial reentry (310)</td>
<td>262.5</td>
<td>112.5 μg/kg (0)</td>
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</tbody>
</table>

ADO = adenosine; AF = atrial fibrillation; AV = atrioventricular; AVB = atrioventricular block; CL = cycle length; CSNRT_max = maximum corrected sinus node recovery time; NSHD = no structural heart disease; NSR = normal sinus rhythm; PSVT = paroxysmal supraventricular tachycardia; RHD = rheumatic heart disease; SB = sinus bradycardia; WPW = Wolff-Parkinson-White syndrome.

*After atropine.

All episodes were recorded after atropine administration that was required to prevent frequent spontaneous termination of PSVT.

High grade AV block without termination of SVT.

the tricuspid valve in the region of the bundle of His, and in the right ventricular apex. In patients 9 to 16, a No. 6F quadripolar catheter was also inserted via either an antecubital or subclavian vein and was positioned within the coronary sinus. Intracardiac electrogams were filtered below 30 and above 500 Hz and were displayed simultaneously with scalar electrocardiographic leads I, II, and V1 on a multichannel oscilloscope (Electronics for Medicine, VR-16, Pleasantville, NY). Signals were stored on frequency-modulated magnetic tape (Honeywell Model 101, Waltham, MA) and were later retrieved on photographic paper at speeds of 50 to 200 mm/sec. Programmed cardiac stimulation was carried out with a programmable constant current stimulator (Medtronic 5325, Minneapolis) that delivered rectangular pulses of 2 msec duration at four times diastolic threshold.

The protocol used for atrial and ventricular stimulation has been previously described.11 The maximum corrected sinus node recovery time was measured after right atrial pacing at a minimum of three basic cycle lengths from just below the sinus cycle length down to a paced cycle length of 350 msec.12 Atrial-His (AH) and His-ventricular (HV) intervals were measured by standard techniques.13 For this study, adenosine-related sinus bradycardia was defined as a greater than 50% increase in the sinus cycle length after adenosine injection. Adenosine-related AV block was defined as one of the following: transient appearance of second- or third-degree AV block during either sinus rhythm or atrial pacing at a cycle length just below the sinus cycle length; the production of pauses greater than 2.5 sec in duration during atrial fibrillation; or a marked change in the QRS complex to one similar to that observed at the maximal point of preexcitation during premature atrial stimulation (in four patients with preexcitation).

Systemic blood pressure was continuously monitored throughout the study via an intra-arterial cannula placed in either a radial or femoral artery and connected to a Statham P23-ID pressure transducer (Gould Medical Products, Oxford, CA).

Adenosine administration. Crystalline adenosine (Sigma Chemical Co., St. Louis) was suspended in normal saline (by USP standards) to a final concentration of 10 mg/ml. The solution was prepared under sterile conditions and was assayed by high-pressure liquid chromatography.14 The adenosine solution was 95% pure with small amounts of the spontaneous breakdown products of adenosine (inosine and hypoxanthine). Inosine and hypoxanthine have previously been shown to produce no electrophysiologic effects in vitro at low concentrations.15

The protocol for adenosine administration was as follows:

1. During the patient’s intrinsic rhythm, an initial intravenous bolus of 37.5 μg/kg was injected and flushed into a peripheral vein with saline over a period of 2 to 3 sec. If no electrophysiologic change was observed, repeat injections at 2 to 3 min intervals were made with 37.5 μg/kg increments in the dose administered, until either sinus bradycardia or AV block was observed.

2. Once the dose that reproducibly resulted in sinus bradycardia or AV block was determined, the same dose was repeated.
during atrial pacing at a cycle length just under the patient's sinus cycle length, during ventricular pacing, and during AV sequential pacing. Only ventricular pacing could be performed in those patients with atrial fibrillation.

(3) In six patients, paroxysmal supraventricular tachycardia was initiated with programmed atrial or ventricular stimulation. The tachycardia was allowed to continue for at least 1 min before the effect of adenosine was assessed by rapid intravenous injection of a bolus of 37.5 μg/kg of adenosine. If no effect was observed, the dose for subsequent injections was increased in 37.5 μg/kg increments until the tachycardia was terminated or until AV block was produced. Injections were made at 2 to 3 min intervals. The effective dose was then repeated during subsequent episodes of tachycardia; when the tachycardia persisted, the next larger dose was then tested. The number of episodes thus treated ranged from one to 12 per patient with the number determined by the ability of the patient to tolerate the tachycardia comfortably.

(4) In two patients (Nos. 2 and 10), adenosine was administered in similar incremental doses during stimulation-initiated atrial flutter until an effect on AV conduction was observed.

(5) Ten patients (Nos. 1, 6, 8, and 11 through 17) received atropine (0.02 to 0.03 mg/kg) intravenously, and the effects of adenosine were reexamined as described above. Atropine was not administered to patients with angina pectoris or when its use would have interfered with the performance of the clinically indicated portions of the electrophysiologic study.

All procedures in the study were approved by and conformed to the guidelines of the Human Investigations Committee of the University of Virginia.

**Results**

**Effects on sinus node function.** Intravenous adenosine produced sinus bradycardia in all 15 patients who were initially in sinus rhythm. The mean dose that resulted in a greater than 50% increase in sinus cycle length was 190 ± 88 μg/kg (± SD). In all patients, we observed a sudden abrupt change in sinus cycle length that occurred between 10 and 20 sec after the injection of adenosine, once the effective dose was reached. As might be expected from the rapid uptake and metabolism of adenosine, this effect was quite transient and lasted less than 10 sec. A mild sinus tachycardia was usually seen immediately after the brief period of bradycardia. As shown in figure 1, sinus tachycardia was not observed when adenosine was administered during asynchronous ventricular pacing, suggesting that the sinus tachycardia was not a delayed effect of adenosine itself.

**Effects on AV conduction.** Adenosine at a mean dose of 179 ± 88 μg/kg (± SD) prolonged AV nodal conduction leading to AV nodal block in all patients. In those patients with normal sinus rhythm in which an AH interval could be measured for all conducted beats, we observed a dynamic prolongation of the AH interval before the onset of second-degree AV nodal block (figure 2). The onset (10 to 20 sec) and duration (less than 10 sec) of the AV nodal conduction delay were similar to that described above for the depression of sinus node function. The HV interval remained unchanged from baseline in all patients. In those patients

![Figure 1](http://circ.ahajournals.org/)

**FIGURE 1.** Effect of adenosine on the sinus node. The top and bottom panels represent continuous recordings of surface electrocardiographic lead II and the lateral right atrial electrogram obtained from patient 1. The tracing began 6 sec after intravenous injection of adenosine (75 μg/kg) during ventricular pacing at a cycle length of 700 msec. There was no VA conduction at this cycle length. The intervals between local atrial activity are seen to increase from 1160 msec to 5560 msec and then gradually recover to 1170 msec. LRA = lateral right atrial electrogram; S = stimulus artifact; PVC = premature ventricular contraction.
with preexcitation, the QRS complex gradually became more preexcited as the AH interval became longer than the AV conduction time over the accessory pathway. During atrial pacing at a constant cycle length, there was no change in the interval from the atrial stimulus to the onset of ventricular activation in those patients with preexcitation, despite the change in morphologic characteristics of the QRS complex (figure 3).

**Effects on supraventricular tachycardia.** Six patients in this study (Nos. 12 to 17) manifested paroxysmal supraventricular tachycardia in response to programmed cardiac stimulation (table 2). Three patients had AV reciprocating tachycardia, and two had AV nodal reentry. In these five patients, intravenous adenosine was uniformly effective in terminating the tachycardia. As shown in figure 4, adenosine produced a progressive increase in the AH interval before the tachycardia was terminated by AV block during antegrade conduction through the AV node. The mean dose required to terminate the tachycardia was 82 ± 35 μg/kg (± SD). In all patients, this dose was less than or equal to the dose required to produce bradycardia or AV block during sinus rhythm. We noted no episodes of sinus bradycardia or AV block after termination of tachycardia. Thirty-two episodes of supraventricular tachycardia were terminated in these five patients by intravenous adenosine, with every termination occurring within 20 sec after peripheral injection of the appropriate dose. In the remaining patient in this group, the tachycardia initiated by programmed stimulation met the criteria for supraventricular tachycardia due to intra-atrial reentry.\(^\text{16, 17}\) In this patient, adenosine did not terminate the tachycardia but produced transient AV block without interrupting or changing the cycle length of the reentry circuit within the atrium (figure 5).

**Hemodynamic effects.** Single intravenous doses of adenosine sufficient to produce measurable changes in electrophysiologic parameters had no effect on systemic blood pressure. This was demonstrated by injection of a dose shown earlier to produce sinus bradycardia or AV block during (1) AV pacing in those patients who initially had normal sinus rhythm, (2) ventricular pacing for those patients in atrial fibrillation, and (3) atrial

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**FIGURE 2.** Production of sinus bradycardia and second-degree AV block (2° AVB) by adenosine. The tracings were obtained from patient 11 and represent (from top to bottom) surface electrocardiographic lead II and intracardiac recordings from the right atrium (RA) and the bundle of His (HB). Adenosine 225 μg/kg was injected intravenously 4 sec before the beginning of the tracing. The sinus cycle length is seen to increase from 550 msec to 1080 msec, and there is progressive lengthening of the AH interval from 100 to 200 msec before onset of second-degree AV block.

**FIGURE 3.** Hemodynamic effects of adenosine. The tracings were obtained during electrophysiologic study in patient 9 and represent surface electrocardiographic lead II and a pressure tracing obtained from a radial artery catheter. Adenosine (187.5 μg/kg) was injected during atrial pacing at a cycle length (CL) of 200 msec. The QRS complex was seen to shift transiently from partial preexcitation to full preexcitation when AV nodal conduction was delayed and then returned to baseline. No change in blood pressure was noted. Note also that there was no change in the interval from the stimulus artifact (S) to the onset of the δ wave.
pacing for the patients with preexcitation. Typical tracings obtained when adenosine was injected during pacing are shown in figure 3. In the illustrated example, the atrial rate was constant due to atrial pacing at a fixed rate and a dose of adenosine that produced enough AV nodal delay to change the QRS complex to complete preexcitation, which did not alter systemic blood pressure.

Adenosine also did not produce hypotension when administered to patients during supraventricular tachycardia. A typical example is shown in figure 6. In all five patients in whom adenosine successfully terminated episodes of paroxysmal supraventricular tachycardia, we noted no major change in blood pressure after adenosine injection until the tachycardia was interrupted. At the point when normal sinus rhythm resumed, the blood pressure increased 21 ± 7 mm Hg over that observed during the tachycardia.

Adenosine did produce transient facial flushing in five patients, even when administered during pacing. This may represent local cutaneous vasodilation caused by adenosine, but we were unable to demonstrate any change in systemic arterial pressure that was not related to alterations of rhythm.

Other effects. The electrophysiologic effects of adenosine were not abolished by pretreatment with atropine (0.02 to 0.03 mg/kg). In all 10 patients who received atropine, the same dose of adenosine was required to produce sinus bradycardia or AV block after atropine as had been required during the control portion of the study. In the five patients with supraventricular tachycardia that responded to adenosine, the nucleoside was still able to terminate the arrhythmia after atropine. However, in two patients (Nos. 12 and 16), an increase of 37.5 μg/kg over the previously effective dose was required for termination of the arrhythmia.

Adenosine was administered to two patients during atrial flutter. The results were similar to those observed in the patient with intra-atrial reentry; adenosine had no effect on atrial cycle length, although higher-grade AV block could be produced.

Discussion

In experimental preparations, adenosine depresses automaticity of the sinus node and Purkinje fibers, hyperpolarizes the membrane and shortens the plateau phase of the action potential of atrial myocytes, and depresses AV nodal conduction. These electrophysiologic effects of adenosine are mediated by a depression of calcium-mediated slow-channel conduction, an increase in potassium conductance, and possibly, indirect antiadrenergic effects. The direct effects are due to the interaction of adenosine with a specific extracellular receptor different from the muscarinic cholinergic receptor. Our data showing that adenosine has negative chronotropic and dromotropic effects in patients undergoing electrophysiologic studies are consistent with the results obtained from studies.
FIGURE 5. Effects of adenosine on intra-atrial reentry. The tracings in both panels are labeled as in figure 4. A, A regular tachycardia in which the earliest atrial activation was recorded by the coronary sinus electrode catheter. The atrial cycle length was 310 msec and there was 1:1 AV conduction. B, Tracings begun 9 sec after injection of adenosine, 112.5 μg/kg. High-grade AV nodal block was seen to occur with no alteration in the atrial cycle length or activation sequence. The patient returned to 1:1 AV conduction 3.5 sec after the end of this tracing (not shown). Tracings are from patient 17. HRA = high right atrium; CS = coronary sinus; HB = His bundle.
of other animal species. These findings may have relevance to the management of certain clinical arrhythmias.

Adenosine may prove to be a well-tolerated and highly effective drug for treating episodes of paroxysmal supraventricular tachycardia. The nucleoside is rapidly taken up by most types of cells and is enzymatically deaminated to inactive inosine by the cellular elements of the blood, resulting in essentially total clearance from the plasma in less than 30 sec. Thus, there is no persistent drug effect after termination of tachycardia. The rapid clearance from plasma would allow the clinician to titrate the dose of adenosine individually, monitoring the response to any given dose over only 1 or 2 min, then gradually increasing the dose until the arrhythmia is stopped. Our data indicate that this approach would be safe and highly effective in that 90% of patients with recurrent paroxysmal supraventricular tachycardia in whom the AV node is part of the reentry loop. The induction of AV block in other atrial arrhythmias that do not involve the AV node should not prove dangerous for the patient because of the very transient duration of the pharmacologic effect of adenosine. Furthermore, the diagnostic use of adenosine might establish the mechanism of these arrhythmias and thus aid in their management.

The safety and efficacy of adenosine should be compared with that of other drugs available for the short-term treatment of paroxysmal supraventricular tachycardia. Although digoxin, propranolol, edrophonium, and cardioversion were formerly used to manage acute episodes, intravenous verapamil is the current drug of choice. A high percentage of patients with paroxysmal supraventricular tachycardia will convert after receiving 10 or 15 mg of intravenous verapamil, but hypotension, bradycardia, or aggravated heart failure may result from its use. The α and β half-lives for intravenous verapamil are 30 to 45 min and 3 to 4 hr, respectively, and this persistence of active drug in the circulation may complicate the management of those patients in whom side effects appear. Thus, although verapamil is highly effective and usually well-tolerated, adenosine may prove to possess a more favorable therapeutic profile once controlled comparative studies have been performed.

Adenosine shortens the atrial action potential duration, and thus could theoretically facilitate the initiation of atrial fibrillation. However, adenosine also produces membrane hyperpolarization, which should stabilize the membrane and thus oppose the potential

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**FIGURE 6.** Blood pressure during termination of supraventricular tachycardia. The tracings were obtained in patient 16 and are labeled as in figure 4. The radial artery pressure is shown in the bottom tracing. Adenosine, 75 μg/kg, produced antegrade block that terminated the tachycardia and restored sinus rhythm with varying degrees of preexcitation. Radial artery pressure, which has been constant at 118/66 during the tachycardia, increased to 140/82 when sinus rhythm was restored.
fibrillatory effect of adenosine. We did not observe initiation of atrial fibrillation by adenosine in any of our patients, but further studies will be necessary to determine whether this will occur with any significant frequency in clinical practice.

Although it is not available in the United States as a therapeutic drug, adenosine triphosphate (ATP) has been used in some parts of Europe under the trade names Striadyne (Laboratories Auclair) and ATP-Ormonotapia (Richter) for the termination of acute episodes of paroxysmal supraventricular tachycardia. Somlo, Komor and Garas, Coumel et al., Motte et al., and more recently, Greco et al. have reported a high degree of success after injection of between 10 and 70 mg of ATP in adults and after injection of 3 to 15 mg of ATP in infants and children. Our data and other recent evidence suggest that these actions of ATP are due to adenosine produced by in vivo and/or in vitro hydrolysis of ATP. In our series of adult patients, a mean dose of adenosine of only 5.3 ± 1.4 mg (+ SD) was required to terminate paroxysmal supraventricular tachycardia, a dose much smaller than the dose of ATP usually required. Ronca-Testoni and Borghini have shown that ATP is almost completely metabolized to adenosine and inosine during a single passage across the heart. Finally, we have shown in vitro that premixture of ATP with adenosine deaminase, an enzyme that converts adenosine to inosine but does not directly degrade ATP, completely abolished the effects of ATP on AV conduction and that less hydrolyzable analogs of ATP do not prolong AV nodal conduction.

Although not examined in this study, other data have suggested that adenosine released endogenously by ischemic cells mediates some of the bradyarrhythmias observed clinically during occlusion of the blood supply to the regions of the sinus and AV nodes. Our findings that the sinus and AV nodes are sensitive to physiologic doses of adenosine are consistent with this hypothesis. Since the electrophysiologic effects of adenosine may be antagonized by methylxanthines, one can speculate that management of bradyarrhythmias seen during inferior ischemia might be made more specific by the use of adenosine antagonists.

In summary, we have shown that intravenous adenosine depresses sinus node automaticity and AV nodal conduction and that it may be a useful drug for terminating some reentrant supraventricular arrhythmias. Further clinical investigation appears warranted to assess the possible future clinical role of adenosine as both a therapeutic and diagnostic drug and as a mediator of clinical bradycardias.

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