Mechanism-Specific Effects of Adenosine on Atrial Tachycardia

Erica D. Engelstein, MD; Neal Lippman, MD; Kenneth M. Stein, MD; Bruce B. Lerman, MD

Background Recent reports suggest that adenosine, in addition to terminating supraventricular tachycardia involving the atrioventricular (AV) node, may have antiarrhythmic effects on atrial tachycardia. The electrophysiological effects of adenosine on supraventricular tissue include shortening of action potential duration in atrial myocytes mediated by the potassium current, I_{KATP}.1,2 Shortening of action potential duration and hyperpolarization in sinus node cells; and antiadrenergic electrophysiological effects resulting from inhibition of adenyl cyclase. We therefore hypothesized that the response of atrial tachycardia to adenosine would be mechanism specific, with termination of atrial tachycardia due to sinus node reentry or cAMP-mediated triggered activity, transient suppression of automatic atrial tachycardia, and an absence of antiarrhythmic effect on tachycardia due to intra-atrial reentry.

Adenosine’s antiarrhythmic effects on supraventricular tachycardia were originally thought to be confined to tachycardias involving the atrioventricular (AV) node such as AV nodal reentrant tachycardia and reciprocating tachycardia using an accessory AV pathway.1,2 Most other forms of atrial tachycardia are considered to be insensitive to adenosine,3,4 as are most forms of ventricular tachycardia.5,6 Although earlier studies showed that (with rare exceptions) adenosine failed to terminate atrial fibrillation,7 atrial flutter,3,8 intra-atrial reentry,4,7 and automatic atrial rhythms,9-11 the present role of adenosine in identifying the mechanism of tachycardia in patients presenting with narrow complex tachycardia is unclear because recent reports suggest that adenosine may terminate as many as 80% of these arrhythmias.12,13

The antiarrhythmic effects of adenosine relate to its site-specific cellular electrophysiological effects. Activation of the adenosine A1 receptor in the sinus node and atria, which is coupled to the guanine nucleotide-binding inhibitory protein Gi, results in activation of the outward potassium current, I_{KATP}.1,2,14 This current hyperpolarizes supraventricular cells toward the equilibrium potential of potassium (E_K ≈ −90 mV) and shortens action potential duration. In the sinus node, these effects result in sinus slowing and arrest,15-17 whereas in the atrium, the effect of hyperpolarization is minimal, and shortening of the action potential duration may precipitate atrial fibrillation. Adenosine also causes minimal (12% to 18%) inhibition of nonstimulated, basal inward calcium current (I_{Ca}) in atrial myocytes18,19 and antagonizes the electrophysiological effects of catecholamines through inhibition of adenyl cyclase. The latter effect includes antagonism of the stimulatory actions of catecholamines on I_{Ca}, the transient inward current, I_{it}; and in sinus node cells, the pacemaker current, I_{p}.2 Based on these cellular actions, we hypothesized that the effects of adenosine on atrial tachycardia are mechanism specific and that adenosine would therefore terminate atrial tachycardia due to sinus node reentry and cAMP-mediated triggered activity, would transiently suppress automatic atrial tachycardia, and would have little if any effect on non-catecholamine-dependent intra-atrial reentrant tachycardia.

Methods and Results Adenosine (mean±SD, 143±54 μg/kg IV) was administered to 27 patients (55±19 years) in atrial tachycardia whose mechanism was confirmed by electrophysiological study. Adenosine terminated sinus node reentrant tachycardia in 6 of 6 patients and terminated atrial tachycardia due to triggered activity in the 1 patient in whom it was identified. Adenosine transiently suppressed automatic atrial tachycardia in 7 of 7 patients and had no effect in 13 patients with intra-atrial reentrant tachycardia, including 8 patients with atrial flutter.

Conclusions These findings demonstrate that adenosine’s effects on atrial tachycardia are mechanism specific and can be used to differentiate between reentrant tachycardia confined to the region of the sinus node or atria and between nonreentrant atrial tachycardia due to either triggered activity or automaticity. (Circulation. 1994;89:2645-2654).

Key Words • tachycardia • sinus node • adenosine

Received February 3, 1994; revision accepted March 7, 1994.
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positioned in the coronary sinus to record left atrial activity. Bipolar intracardiac electrograms were filtered at 40 to 400 Hz and displayed simultaneously with three surface ECG leads (I, aVF, and V1) on a multichannel oscilloscope. Real-time recordings were made using a paper recorder (Astro-Med Inc) at recording speeds of 50 to 200 mm/s. Programmed stimulation was performed using a programmable stimulator with an isolated constant-current source (Bloom Associates). Stimuli were delivered as rectangular pulses of 2-millisecond duration at four times diastolic threshold. The stimulation protocol included rapid atrial and ventricular pacing and the introduction of single and double atrial extrastimuli as well as single, double, and triple ventricular extrastimuli at multiple basic drive cycle lengths. The sinus node recovery time and corrected sinus node recovery time were determined using standard techniques.20,21 Reset patterns in response to extrastimuli were determined by plotting the coupling interval of each extrastimulus delivered during tachycardia versus the corresponding return cycle.22 Resetting was defined by the presence of a noncompensatory pause after the extrastimulus was delivered.22 Blood pressure was monitored throughout the study using a noninvasive sphygmomanometer (Dinamap, Critikon). In selected patients, isoproterenol was infused to decrease the sinus cycle length by approximately 30%.

Sinus Node Reentrant Tachycardia

Sinus node reentrant tachycardia23-26 was identified by (1) an atrial tachycardia with an antegrade atrial activation sequence similar to that recorded during sinus rhythm, (2) P waves on the surface ECG during tachycardia similar to those of sinus rhythm, (3) the ability to initiate and/or terminate the tachycardia with programmed stimulation, (4) initiation of tachycardia that was independent of AV nodal or intra-atrial conduction delays, and/or (5) termination of tachycardia by vagal maneuvers and by blockade of the slow-inward calcium current with verapamil.

Atrial Flutter

Atrial flutter27,28 was identified by (1) monomorphic atrial tachycardia with a fixed rate between 240 and 350 beats per minute (with the exception of 2 patients receiving antiarrhythmic therapy who had a slower rate), (2) characteristic “saw-toothed” configuration of the atrial waves in the inferior surface ECG leads (type I flutter), (3) the ability to initiate or terminate the tachycardia with programmed stimulation (in those patients undergoing electrophysiological study), and (4) the demonstration of transient entrainment during rapid atrial pacing at multiple cycle lengths.28

Intra-atrial Reentrant Tachycardia

Intra-atrial reentrant tachycardia27 (other than atrial flutter) was identified by (1) monomorphic atrial tachycardia with a fixed rate between 120 and <240 beats per minute without antiarrhythmic drugs, (2) the ability to initiate and/or terminate the tachycardia by programmed stimulation, (3) an atrial activation sequence different from that recorded during sinus rhythm, (4) P waves on the surface ECG during tachycardia different from those during sinus rhythm, (5) the demonstration of transient entrainment during rapid atrial pacing, (6) initiation of tachycardia dependent on intra-atrial conduction delay, and/or (7) lack of effect of verapamil and vagal maneuvers on the tachycardia.

Automatic Atrial Tachycardia

Nonreentrant atrial tachycardia due to automaticity29-31 was identified by (1) atrial tachycardia with an atrial activation sequence different from that recorded during sinus rhythm, (2) P waves on the surface ECG different from those during sinus rhythm, (3) inability to initiate or terminate the tachycardia with programmed stimulation, (4) spontaneous acceleration and deceleration of the tachycardia rate, and (5) demonstration of overdrive suppression of tachycardia with rapid atrial pacing.

Triggered Activity

Atrial tachycardia presumed due to CAMP-mediated triggered activity32 was identified by (1) initiation and termination with programmed stimulation, (2) different atrial activation sequence and P-wave morphology during tachycardia as compared with sinus rhythm, (3) an inability to entrain the tachycardia at multiple pacing cycle lengths, (4) facilitation of tachycardia induction with catecholamine stimulation, and (5) sensitivity of the tachycardia to verapamil and edrophonium.

Pharmacological Testing

Pharmacological testing was performed to assess the effects of acute administration of adenosine on atrial tachycardia. Adenosine (Adenocard, Fujisawa USA) was administered as a rapid bolus injection through a central venous catheter, followed by a 10-mL bolus of normal saline flush. The dose of adenosine was titrated incrementally until atrial tachycardia was terminated and/or transient AV nodal block occurred. Verapamil, up to a maximal dose of 10 mg, was given intravenously over 60 seconds. Edrophonium was given as an injection of 1 mg over 1 minute, followed by 9 mg over the next minute. Propranolol (0.1 mg/kg) was infused at a rate of 1 mg/min. Transient suppression of tachycardia was defined as transient cessation of the arrhythmia (<20 seconds) followed by spontaneous resumption.

Statistical Analysis

Differences between groups were determined by ANOVA. Values are expressed as mean±SD for continuous variables. A value of P<.05 was considered statistically significant.

Results

Adenosine was administered to 27 patients in atrial tachycardia. The mechanism of tachycardia was determined to be sinus node reentry in 6 patients, atrial flutter in 8 patients, intra-atrial reentry in 5 patients, automatic atrial tachycardia in 7 patients, and nonreentrant atrial tachycardia due to triggered activity in 1 patient. The clinical and electrophysiological characteristics of these patients are listed in the Table. Patients with automatic atrial tachycardia were significantly younger than patients with sinus node reentry, atrial flutter, intra-atrial reentrant tachycardia, or triggered activity (34±18 versus 58±16, 62±8, 70±8, and 79 years, respectively; all P<.05). There were no significant age differences among the other group of patients. Structural heart disease was present in 3 of 6 patients with sinus node reentrant tachycardia, 6 of 8 patients with atrial flutter, 5 of 5 patients with intra-atrial reentrant tachycardia, and 2 of 7 patients with automatic atrial tachycardia.

Sinus Node Reentrant Tachycardia

Sustained sinus node reentrant tachycardia was demonstrated in 6 patients. There was no evidence of sinus node dysfunction in any patient as determined by clinical history, telemetric monitoring, or 24-hour ambulatory ECG recordings. The sinus node recovery time and corrected sinus node recovery time were normal in all patients. Sustained sinus node reentrant tachycardia was induced with programmed atrial stimulation and/or occurred spontaneously in 4 patients. In the 2 remaining patients, nonsustained sinus node reentrant tachycardia was inducible at baseline, and the tachycardia became...
## Patient Characteristics and Electrophysiological Results

<table>
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<tr>
<th>Patient</th>
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<th>Cardiac Diagnosis</th>
<th>Atrial Cycle Length, ms</th>
<th>Induced/Terminated With PS</th>
<th>Adenosine Dose, μg/kg</th>
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</table>

PS indicates programmed stimulation; AT, atrial tachycardia; CAD, coronary artery disease; MVP, mitral valve prolapse; CM, cardiomyopathy; MR, mitral regurgitation; MS, mitral stenosis; AR, aortic regurgitation; TR, tricuspid regurgitation; IHSS, idiopathic hypertrophic subaortic stenosis; AVR, status post aortic valve replacement; MVR, status post mitral valve replacement; ND, not done; CSP, carotid sinus pressure; Iso, isoproterenol; +, termination; ++, transient slowing/suppression; and –, no effect.

*Atrial flutter occurred after cardioversion of ventricular tachycardia and could not be terminated with atrial pacing.†Concurrent infusion of isoproterenol was sometimes needed to induce atrial tachycardia.

Sustained during isoproterenol infusion. In these patients, differentiation between sinus node reentrant tachycardia and sinus tachycardia was confirmed by the observation that the sinus cycle length of sinus node reentry was at least 75 milliseconds (and usually 150 to 200 milliseconds) less than the cycle length during sinus tachycardia and by the fact that sinus node reentry was terminated by programmed stimulation whereas sinus tachycardia was not. The tachycardia cycle length ranged from 300 to 510 milliseconds. No patient had
FIG 1. Surface ECGs recorded during sinus rhythm and during sinus node reentrant tachycardia (patient 4). A, Sinus rhythm. Note that a single atrial premature depolarization is present. B, Sinus node reentrant tachycardia. The P waves during tachycardia are nearly identical to those recorded during sinus rhythm.

symptoms of presyncope or syncope during tachycardia, and no adverse hemodynamic changes were associated with the arrhythmia. The tachycardia was reproducibly terminated by programmed atrial stimulation in all 6 patients.

The P-wave morphology on the surface ECG recorded during sinus rhythm and during tachycardia was identical in all 12 leads (Fig 1). The atrial activation sequence was anterograde and identical to that recorded during sinus rhythm in all cases (Fig 2). Intravenous verapamil administered to 3 patients resulted in termination of the tachycardia in all 3 patients (Fig 2A) and suppressed reinduction of the rhythm despite concurrent infusion of isoproterenol in the 2 patients in whom reinduction was attempted. Vagal simulation (either carotid sinus pressure or Valsalva) was ineffective in terminating the tachycardia in 2 of 2 patients. However, edrophonium (10 mg IV) terminated the tachycardia (1 of 1). Further confirmatory evidence of sinus node reentry included the ability to dissociate the high right atrium (4 patients), the low septal right atrium (3 patients), and the left atrium (1 patient) from the tachycardia during the introduction of single atrial extrastimuli (Fig 3). Of interest was the ability to induce tachycardia with single ventricular extrastimuli or rapid ventricular pacing during isoproterenol infusion in 2 patients. This occurred without significant retrograde conduction delay in the AV node–His-Purkinje system, thus allowing the ventricular extrastimulus to reach the region of the sinus node with sufficient prematurity to induce the tachycardia.

Adenosine (127±85 μg/kg) terminated sinus node reentrant tachycardia within 15 seconds of administration in all patients. Termination of tachycardia occurred before adenosine-induced AV nodal block was manifest (Fig 2B) and was coincident with the development of flushing and dyspnea. Adenosine-induced atrial or ventricular premature depolarizations did not occur in association with termination of the rhythm in any patient. In all patients, the tachycardia was induced and reproducible termination of the tachycardia with adenosine was confirmed.

Atrial Flutter

Atrial flutter was induced with programmed stimulation (3 patients) or occurred spontaneously during
gram, but did not affect the atrial flutter cycle length in any of the 8 patients.

Intra-atrial Reentrant Tachycardia

Five patients had intra-atrial reentrant tachycardia at a cycle length ranging from 260 to 420 milliseconds. The tachycardia was initiated and terminated with programmed stimulation in all patients. Reset curves demonstrated a flat-increasing pattern (Fig 4). Adenosine at doses sufficient to produce transient AV block (152±48 μg/kg) did not terminate atrial tachycardia and had no effect on tachycardia cycle length (Fig 5). In 1 patient, administration of adenosine converted atrial tachycardia to atrial flutter, which then terminated spontaneously after 10 seconds.

Automatic Atrial Tachycardia

Automatic atrial tachycardia was present spontaneously in 7 patients. In 3 patients, it occurred in repetitive runs of 3 to 10 beats, separated by only a few consecutive sinus beats. In 2 patients, incessant atrial tachycardia was present throughout the electrophysiological study, and in 2 patients, tachycardia occurred spontaneously at baseline and became sustained during infusion of isoproterenol. The tachycardia could not be initiated or terminated by programmed stimulation in any patient. The tachycardia cycle length ranged from 360 to 580 milliseconds and was associated with palpitations in 4 patients. In 5 patients, overdrive suppression of the atrial tachycardia was demonstrated after rapid atrial pacing. Oscillations in tachycardia cycle length consistent with acceleration and deceleration of the tachycardia were present in 5 patients. Dissociation of His bundle activation from the tachycardia was demonstrated with appropriately timed ventricular extrastimuli. The P-wave morphology of the atrial tachycardia was different than that during sinus rhythm in all 7 patients.

Adenosine (161±52 μg/kg) transiently (5 to 18 seconds) suppressed or slowed automatic atrial tachycardia in all patients (Fig 6). Suppression of the tachycardia occurred after adenosine-induced transient AV nodal block. Verapamil (10 mg) had no effect on atrial tachycardia in the 2 patients to whom it was administered.

Triggered Activity

The characteristics of atrial tachycardia in 1 patient were consistent with triggered activity. The tachycardia was initiated with atrial or ventricular pacing at cycle lengths of 300 to 400 milliseconds with and without concurrent infusion of isoproterenol. Tachycardia was terminated with single atrial premature extrastimuli and with rapid atrial pacing. The tachycardia cycle length was 430 milliseconds. Adenosine (186 μg/kg) terminated the tachycardia 6 to 7 seconds after administration, before development of transient AV nodal block (Fig 7A). Edrophonium (10 mg) also terminated the tachycardia (Fig 7B), which was then noninducible for approximately 20 minutes after drug administration. Similarly, the tachycardia terminated during administration of verapamil (10 mg; Fig 7C) and thereafter was noninducible with and without concurrent administration of isoproterenol. Based on the site of earliest atrial activation during tachycardia, the concordance of P-wave morphology during tachycardia with that ob-
Fig 3. Localization of the reentrant circuit to the high right atrium (HRA) (patient 5). Surface leads I, aVF, and V1 and intracardiac recordings from the HRA, His bundle (HBE), left atrium (recorded from the coronary sinus [CS]), and right ventricular apex (RVA) are shown. An atrial premature extrastimulus (A0) is introduced during sinus node reentrant tachycardia, resulting in dissociation of atrial activation in the HRA, low septal right atrium, and left atrium from the tachycardia. The tachycardia beat following the atrial extrastimulus was not advanced or reset. Note that although sinus node activity is dissociated from atrial activity, HBE activation appears to be unperturbed by the atrial extrastimulus. This apparent paradox is explained by a decrement in atrioventricular nodal conduction that is exactly equal to the prematureity of the atrial extrastimulus (A0).

tained during pace-mapping from that site, and the site of successful radiofrequency ablation, the site of origin of the tachycardia was determined to be the right anterior atrial wall, near the base of the right atrial appendage.

Discussion

This study demonstrates the differential effects of adenosine on atrial tachycardia. Adenosine reproducibly terminates atrial tachycardia due to either sinus node reentry or cAMP-mediated triggered activity, transiently suppresses automatic atrial tachycardia, and has no effect on intra-atrial reentrant tachycardia or atrial flutter. These findings suggest that the effects of adenosine on atrial tachycardia are mechanism specific and further delineate both the diagnostic and the therapeutic role of adenosine in patients with supraventricular tachycardia.

Sinus Node Reentrant Tachycardia

Binding of adenosine to the sinus node or atrial A1 receptor activates an outward potassium current, which can also be activated by acetylcholine (IKAChAdo). This results in hyperpolarization of the resting membrane potential to $E_K$. Because the resting membrane potential of atrial myocytes is near $E_K$, the effect of adenosine-mediated hyperpolarization in this tissue is minimal. In contrast, sinus node cells, which have a resting membrane potential near $-60$ mV, may undergo significant hyperpolarization and arrest. This differential effect of adenosine on sinus node and atrial tissue likely accounts in part for the ability of adenosine to terminate sinus node reentry but not intra-atrial reentry.

Under basal conditions, adenosine has no known direct effect on sinus node currents other than IKAChAdo. However, adenosine also antagonizes the stimulated response of the pacemaker current I and the slow inward current ICa to catecholamines through inhibition of adenyl cyclase. This antiadrenergic effect could account in part for adenosine's antiarrhythmic effects in the 2 patients in whom sinus node reentry became sustained only during catecholamine stimulation. Verapamil, which exerts its electrophysiological effects by direct blockade of ICa and does not affect intra-atrial reentry, also terminated sinus node reentrant tachycardia and prevented its reinduction.
ADENOSINE 12 mg

There is a relative paucity of data regarding the effects of adenosine on sinus node reentrant tachycardia. One previous report identified 2 patients who received adenosine during sinus node reentrant tachycardia. In 1 patient, the tachycardia slowed but did not terminate in response to adenosine (150 μg/kg), whereas in the other patient, an atrial premature depolarization occurred coincident with termination of the tachycardia. Thus, the possibility that the tachycardia was terminated by an adenosine-induced atrial extrastimulus rather than by a direct effect of adenosine on the sinus node could not be excluded. Another report identified 1 patient with sinus node reentrant tachycardia that did not terminate with 37.5 μg/kg adenosine; however, in the present study, 2 patients required adenosine doses of more than 150 μg/kg for tachycardia termination. Atrial (or ventricular) premature depolarizations did not occur coincident with termination of the tachycardia in any patient in the present study. With presently available techniques, definitive differentiation of sinus node reentry from triggered activity originating within or contiguous to the sinus node cannot reliably be made.

Intra-atrial Reentry and Atrial Flutter

Adenosine had no effect on intra-atrial reentrant tachycardia or atrial flutter but facilitated diagnosis by inducing transient AV block during tachycardia and unmasking the P-wave morphology. This is consistent with the experience of others. The lack of effect of adenosine on intra-atrial reentry is congruent with the known effects of adenosine on the wavelength of atrial excitation. Perturbations that lengthen the wavelength (refractory period multiplied by conduction velocity) are in general antiarrhythmic, whereas interventions that shorten the wavelength are arrhythmogenic. Adenosine decreases atrial refractoriness but likely has negligible effects on conduction velocity since the resting membrane potential of atrial myocytes is $\sim E_K$. As a result, adenosine shortens the atrial excitation wave (through its effects on refractoriness) and therefore facilitates induction of (rather than termination of) reentrant arrhythmias, such as intra-atrial reentry, atrial flutter, and atrial fibrillation. Similar findings have been confirmed experimentally with acetylcholine, which shortens refractoriness but has no effect on conduction velocity and thus also shortens the wavelength of atrial excitation.

There are at least three unusual circumstances in which adenosine may potentially terminate intra-atrial reentry. The first involves a reentrant circuit that includes decremental atrial tissue, an infrequent finding. We have previously shown that decremental atrial tis-
ADENOSINE 12 mg (+6 sec)

V1

HRA

HBE

\[ \text{----} = 400 \text{ msec} \]

Fig 6. Transient slowing of automatic atrial tachycardia by adenosine (patient 24). Surface ECG lead V1 and intracardiac recordings from the high right atrium (HRA) and His bundle (HBE) are shown. After administration of adenosine, the atrial tachycardia slows for approximately 5 seconds before it resumes (associated with a warm-up phenomenon).

As well as accessory pathways with decremental conduction properties (believed to be composed of partially depolarized working atrial tissue) are sensitive to adenosine. Adenosine, by hyperpolarizing these fibers to \(-E_K\), would be expected to increase conduction velocity and increase the wavelength of the atrial reentrant circuit, possibly leading to termination. The second circumstance in which adenosine may terminate intra-atrial reentry involves tachycardia that is dependent on cAMP-mediated changes in conduction and refractoriness for perpetuation. Adenosine, through its antiadrenergic effects, could in theory terminate this form of tachycardia. This is likely to be an unusual event because intra-atrial reentrant tachycardia has rarely (if ever) been definitively shown to be responsive to vagal stimulation (which, through the release of acetylcholine, has a similar mechanism of action as adenosine). Finally, it is possible that adenosine may induce an atrial premature beat that terminates the arrhythmia or, by shortening atrial refractoriness, converts intra-atrial tachycardia to atrial flutter or fibrillation, which then terminates spontaneously. In the latter case, flutter or fibrillation may not sustain because a critical number of reentering wavelets are not continuously activated after the effects of adenosine subside. This is likely the explanation for the one reported case of adenosine-mediated termination of atrial flutter. The flutter was first converted to atrial fibrillation, which then terminated spontaneously. A similar phenomenon occurred in the present study. In 1 patient, adenosine converted intra-atrial reentrant tachycardia to atrial flutter, which then terminated spontaneously. Therefore, this form of response of intra-atrial reentry or atrial flutter to adenosine is not mechanism specific and is independent of adenosine’s primary effects on these arrhythmias.

**Automatic Atrial Tachycardia**

Adenosine suppressed automatic atrial tachycardia for 3 to 18 seconds. The basis for automatic atrial tachycardia is either enhanced automaticity, which is manifest in fully polarized atrial myocytes, or abnormal automaticity, which occurs in partially depolarized atrial tissue. The patients in the present study were believed to have enhanced automaticity since 5 of 7 showed overdrive suppression and none were sensitive to verapamil. Several patients were considered to have a cAMP-dependent mechanism because they required isoproterenol to sustain the tachycardia. The effects of adenosine on automatic tachycardia may be explained in part by the actions of adenosine on \(I_{KAdo}\). Therefore, adenosine may transiently suppress automaticity by activation of \(I_{KAdo}\), thus shortening and extinguishing atrial action potentials, or through its antiadrenergic effects.

Previously reported responses of automatic atrial tachycardia to adenosine include an absence of effect, transient slowing and termination, and termination. In view of the often incessant nature of this tachycardia and the short duration of the effects of adenosine, it is unlikely that adenosine actually terminates the tachycardia. We defined transient suppression as absence of tachycardia for less than 20 seconds, followed by resumption of tachycardia at its previous rate.

**Triggered Activity**

One patient in the present study had atrial tachycardia consistent with triggered activity and delayed afterdepolarizations. This diagnosis was based on initiation of the tachycardia with rapid atrial pacing during concurrent infusion of isoproterenol and termination of tachycardia with verapamil and edrophonium as well as adenosine. The pattern of reset responses to extrastimuli introduced during tachycardia can also potentially differentiate between reentrant and triggered mechanisms, but the introduction of atrial extrastimuli terminated the tachycardia before sufficient data on reset patterns could be obtained. The tachycardia was differentiated from sinus node reentry based on a different P-wave morphology and atrial activation se-
A. ADENOSINE

B. EDROPHONIUM

C. VERAPAMIL

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= 200 msec

FIG 7. Pharmacological responses of atrial tachycardia due to cAMP-mediated triggered activity (patient 27). Surface ECG lead aVF and intracardiac recordings from the high right atrium (HRA) are shown. A, Termination of atrial tachycardia 6 seconds after administration of 6 mg adenosine IV. B, Termination of atrial tachycardia after administration of edrophonium (10 mg IV). C, Termination of the atrial tachycardia after administration of 10 mg verapamil IV. Note that there is oscillation of the tachycardia cycle length immediately before termination. The tachycardia was not inducible after the administration of verapamil.

quency during tachycardia and sinus rhythm. Although this mechanism of atrial tachycardia has not been previously identified, triggered activity has been demonstrated in experimental atrial preparations. The cellular mechanism for triggered activity is related to an increase in intracellular calcium. Activation of the adenosine A1 receptor results in inactivation of the catalytic subunit of adenyl cyclase, thus reducing intracellular cAMP levels. It is this antiadrenergic action of adenosine that accounts for termination of ventricular tachycardia due to triggered activity and likely explains termination of the tachycardia in the present study, although direct effects of adenosine on IK,Acet,Ado (and secondary decrease in ICaL) could also be contributory.

It should be recognized that the clinical diagnosis of triggered activity is at best inferential, and we cannot definitively rule out intra-atrial reentry in this case. However, because initiation of tachycardia was dependent on burst pacing and catecholamine stimulation and based on the specificity of receptor-mediated responses to adenosine and acetylcholine as well as termination of tachycardia with blockade of the slow-inward calcium current, the mechanism of tachycardia in this patient is most consistent with that of triggered activity.

Conclusions
The findings in the present study demonstrate that there is an important role for adenosine in identifying the mechanism of atrial tachycardia. In addition to its well-known effects on AV nodal reentry and AV reciprocating tachycardia, as well as its effects on ventricular tachycardia due to triggered activity, adenosine is useful as a diagnostic probe for suspected sinus node reentrant tachycardia. Furthermore, because adenosine has no effect on reentrant atrial tachycardia but instead transiently suppresses automatic atrial tachycardia and terminates atrial tachycardia presumed due to triggered activity, adenosine may be useful in differentiating
between these arrhythmias. Responsiveness of triggered atrial tachycardia to adenosine may account for some instances where adenosine has been previously thought to terminate intra-atrial reentrant tachycardia.

Addendum
Since submission of this manuscript, we have identified another patient with adenosine-sensitive atrial tachycardia. The electrophysiological findings in this 71-year-old woman were consistent with triggered activity. The tachycardia was initiated with rapid atrial pacing during concurrent infusion of isoproterenol (4 μg/min), had a P-wave morphology and atrial activation sequence that differed from sinus rhythm, and could not be entrained from multiple atrial sites. Termination of tachycardia was achieved with either rapid atrial pacing or verapamil or adenosine independent of electrophysiological effects on the atrioventricular node.

Acknowledgments
This work was supported in part by a grant from the National Institutes of Health (RO1-44747). Dr Lerman is an Established Investigator of the American Heart Association.

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Circulation. 1994;89:2645-2654
doi: 10.1161/01.CIR.89.6.2645

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