Electrophysiologic Studies in Patients with Persistent Atrial Tachycardia

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SUMMARY
Clinical and electrophysiologic studies in two patients with chronic persistent atrial tachycardia unresponsive to drug or electroconversion therapy are reported. In both, exercise increased the atrial rate and decreased the atrioventricular nodal conduction time. The opposite effect occurred after β-adrenergic blockade. Single electrically-induced atrial depolarizations (A2) at progressively premature times resulted in a linear increase in the return cycle (A2A3) until plateau levels were achieved but failed to produce sinus rhythm. Abrupt cessation of continuous atrial pacing at rates up to 600 beats/min in one patient and up to 300 beats/min in the other resulted in a pause that was similar to the plateau levels of A2A3 achieved during atrial scanning with single impulses. Our findings suggest that an ectopic atrial focus is responsible for this arrhythmia. The electrophysiologic properties of the ectopic pacemaker appear to be similar to the sinoatrial node in some respects but to differ in terms of spontaneous rate and in relative immunity from the effects of overdrive pacing.

Additional Indexing Words:
Chronic atrial tachycardia, Cardiac arrhythmias, His bundle recordings, Atrial pacing

CHRONIC ATRIAL TACHYCARDIA is a rare cardiac arrhythmia with two basic types of clinical presentation.1 In one type, the atrial tachycardia frequently alternates with short periods of sinus rhythm for a period of months to years.1, 2 The second type is even more rare and consists of chronic persistent atrial tachycardia that seldom (if ever) gives way to a sinus origin.3 Our search of the literature has uncovered only 20 reports of patients with the persistent type of chronic atrial tachycardia.3–12 Furthermore, the mechanism of this arrhythmia is unknown and there are no reports of any electrophysiologic studies in these patients. Goldreyer et al.13 studied three patients with episodic bouts of atrial tachycardia by both atrial overdrive pacing and induced coupled atrial premature beats and summarized the evidence supporting an ectopic atrial focus as the mechanism of the arrhythmia. Using similar techniques, we studied two patients with chronic persistent atrial tachycardia who underwent atrial pacing for both therapeutic reasons14, 15 and for better definition of the mechanism of this rhythm disorder.

Materials and Methods
Two patients with chronic atrial tachycardia were studied. All medications were discontinued 72 hours before catheter recordings of His bundle electrograms16 were obtained. In brief, a multipolar electrode catheter was inserted into the right femoral vein and positioned across the tricuspid valve. In one patient an additional bipolar electrode catheter was inserted into the left femoral vein and positioned against the lateral wall of the right atrium to allow for atrial stimulation, while in the other patient the low right atrial catheter was repositioned against the lateral wall of the right atrium for pacing. Simultaneous recordings of the His bundle deflection right atrial electrogram and X, Y, and inverse Z leads of the Frank orthogonal lead system were obtained. The atrium was stimulated with cathodal rectangular pulses, 2 msec in duration and three times diastolic threshold. His bundle electrograms were recorded before and after both mild hand exercise in the supine position and 10 mg of propranolol (hydrochloride) (Inderal), administered intravenously at a rate of 1 mg every 2–3 min. Single successively premature (10–15 msec) atrial depolarizations were introduced after every sixth to seventh spontaneous atrial beat by means of a specially designed research pacemaker (Medtronic No. 1348), which allows for electrical stimulation with one or more electrical pulses at varying intervals following atrial depolarization. In one patient (Case No. 1) two to nine bursts of electrical impulses (110 msec apart) were introduced at varying intervals after spon-
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taneous atrial depolarization. In addition, recordings were obtained during and after graded increases in the paced atrial rate.

Case No. 1
A 33-year-old white man was first admitted to the San Francisco Veterans Administration Hospital on May 11, 1970, for evaluation of persistent tachycardia. The patient had no prior history of acute rheumatic fever but admitted to excessive ethanol intake. He was first told of a rapid heart rate in 1964 at the time of discharge from military service. Approximately one and one-half years later clinical signs and symptoms of hyperthyroidism developed, which were poorly controlled by medical management. In January, 1968, subtotal thyroidectomy resulted in relief of symptoms but tachycardia persisted; all electrocardiograms showed atrial tachycardia (atrial rate 150–150 beats/min) with varying degrees of atrioventricular (A-V) block. The patient had no signs or symptoms of heart failure and chest films showed no abnormalities. Attempts to achieve sinus rhythm with full doses of digitalis, quinidine, propranolol, and direct current countershock were unsuccessful. Digitalis and methimazole (Tapazole) therapy was instituted to control heart rate.

Physical examination at the time of evaluation (September 1972) revealed persistent tachycardia and a grade II/VI basal systolic ejection murmur. There were no clinical signs or symptoms of hyperthyroidism. Complete thyroid function studies, including serum triiodothyronine, triiodothyronine and thyroxine clearances and production rates, and thyrotropin release hormone stimulation tests, revealed no abnormalities. Serial chest films showed borderline enlargement of the cardiac silhouette, but the patient only complained of episodic palpitations. On February 7, 1973, His bundle electrograms were recorded before and after mild hand exercise and administration of propranolol. Control tracings (fig. 1A) showed atrial tachycardia (150 beats/min) with 2:1 A-V block and a short H-Q interval (normal 35–55 msec). After hand exercise (fig. 1B), the atrial rate increased slightly and was associated with lesser degrees of A-V block and increased ventricular rate (91–105 beats/min). Five minutes after exercise, atrial and ventricular rates reverted to control levels and propranolol was administered. Following infusion, the atrial rate decreased from 150 to 135 beats/min and the conduction time through the A-V node increased slightly (fig. 1C).

Figure 1

In this and in all subsequent figures, time lines are 1 sec apart; the paper speed is 100 mm/sec; R-R represents the interval between ventricular complexes; and all numbers are expressed in milliseconds. X, Y, and inverse Z leads of the Frank orthogonal lead system are recorded simultaneously with the His bundle electrogram (HBE), which was recorded from the distal electrode pair, and the right atrial electrogram (RAE) recorded from a more proximal electrode pair of the same catheter. A) Control tracing shows atrial tachycardia with atrial (A) rate of 150 beats/min and 2:1 A-V block with block proximal to the His bundle deflection (H). The short H-Q interval suggests the possibility that the right bundle branch potential was recorded rather than the His. Atrial pacing did not allow for differentiation of the two. B) Mild supine arm exercise resulted in atrial tachycardia with varying A-V block (Wenckebach conduction). The A-H interval for conducted beats is shown just below the HBE tracing. C) After intravenous infusion of 10 mg of propranolol, the ventricular rate slowed to 67 beats/min and the A-V nodal conduction time was prolonged.

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Figure 2

Spontaneous atrial rate (A, A,) is interrupted by a single electrically-induced premature atrial depolarization (A,) (arrow denotes stimulus artifact) 450 msec after a spontaneous atrial depolarization (A,) and resulted in a return cycle (A,A,) that was identical to the spontaneous cycle length (A,A,). B) A premature impulse (A,) occurring 370 msec after A, resulted in prolongation of the return cycle (A,A,). (His bundle deflections were retouched for clarity.)
Figure 3
Plot of $A_2A_3$ (abscissa) and $A_3A_2$ (ordinate) for both patients ($\bullet$ = Case No. 1, o = Case No. 2). Progressively premature, induced atrial premature beats ($A_1A_2$) resulted initially in a linear prolongation of $A_2A_3$ until plateau levels were achieved. Slanted and horizontal lines were drawn to approximate point aggregates. Vertical lines delineate the atrial effective refractory periods for each patient.

Figure 4
Representative illustrations of the effects of graded increases in the paced ($S_i$) atrial rate on the ventricular response and the effects of abrupt termination of pacing on the atrial pacemaker recovery time (APRT). A) At a paced atrial rate of 146 beats/min the ventricular rate was 71 beats/min. B) Increasing the paced atrial rate to 200 beats/min resulted in increasing degrees of A-V block proximal to the His bundle and a decrease in the ventricular rate (56-79 beats/min). C) Further increases in the atrial rate to 600 beats/min produced a ventricular response of 45-67 beats/min. For each paced rate, abrupt cessation of pacing resulted in atrial pacemaker recovery times that were similar to the plateau levels of $A_2A_3$ (See fig. 3) and the atrial cycle length following the pause was identical to the spontaneous cycle length.

Single successively premature atrial depolarizations resulted initially in a stepwise increase in the interval between atrial premature beat and the next spontaneous atrial depolarization (return cycle or $A_3A_2$) until plateau levels of 550-590 msec were reached (figs. 2 and 3). Graded increases in the atrial rate from 140 to 600 beats/min resulted in slowing of the ventricular response (fig. 4). Abrupt cessation of atrial pacing resulted in a pause before the appearance of the next spontaneous atrial depolarization (atrial pacemaker recovery time, APRT). The APRT for each paced rate was in the same range as the plateau return cycles achieved when the spontaneous atrial cycle was scanned with single successively premature impulses. Similarly, trains of impulses (110 msec apart) initiated at varying intervals following spontaneous atrial depolarization failed to induce either sinus rhythm or atrial fibrillation and were always associated with an APRT in the 560-590 msec range (fig. 5).

The patient’s ventricular rate is currently maintained at 75 beats/min with 0.5 mg digoxin/day. The patient remains asymptomatic except for occasional palpitations usually.
precipitated by exertion. Propranolol was recommended to control these symptoms.

Case No. 2

A 36-year-old white man was admitted to San Francisco General Hospital in 1962 because of palpitations and shortness of breath. He had no history of acute rheumatic fever, but admitted to intravenous self-administration of amphetamines, barbiturates, and heroin. He had been aware of a rapid heart rate since 12 years of age but was asymptomatic until 1962 when he noted dyspnea on exertion.

Physical examination revealed a heart rate of 150 beats/min and a loud apical holosystolic murmur. A chest film showed cardiomegaly and pulmonary congestion. Signs and symptoms of heart failure disappeared after digitalis and diuretic therapy but atrial tachycardia persisted. Over the ensuing years attempts to control the arrhythmia with digitalis, procaine amide, quinidine, propranolol, reserpine, and guanethidine were unsuccessful. Three attempts at direct current cardioversion were also unsuccessful. The patient was admitted to this hospital on 16 occasions for treatment of complications of drug abuse and/or congestive heart failure and the electrocardiograms showed atrial tachycardia in each instance except on two occasions when continuous electrocardiographic monitoring revealed brief episodes of sinus rhythm.

Following successful treatment of enterococcal endocarditis in August 1971, the signs and symptoms of congestive heart failure became refractory to medical therapy and cardiac catheterization documented the presence of left ventricular decompensation and moderate mitral regurgitation. On January 17, 1972, atrial overdrive pacing was instituted in an attempt to control this rhythm disorder. Intravenous administration of propranolol resulted in slight slowing of the atrial rate and prolongation of A-V nodal conduction (fig. 6). Graded increases in atrial rate resulted in a decreased ventricular response; cessation of atrial pacing resulted in a pause (ranging from 510 to 540 msec) before resumption of spontaneous atrial activity (fig. 6). Atrial pacing at a rate of 300 beats/min produced transient atrial fibrillation with an associated slower ventricular response (fig. 6).

A repeat study (July 8, 1973) showed further prolongation of infranodal conduction time delay compared with the previous study (fig. 7) that was probably due to interim progression of his cardiac disease. Mild hand exercise produced a slight increase in atrial rate and decreased A-V nodal conduction time (fig. 7). Successively premature atrial depolarizations resulted in gradual lengthening of the return cycle (A2A3) (fig. 8) until plateau values of 490-520 msec were attained (fig. 3). Graded increases in the atrial driving rate (150-400 beats/min) produced slowing of the ventricular response but the interval between the last paced beat and the next spontaneous atrial depolarization (APRT) was similar (500-560 msec) to the “plateau” values achieved when the atrial cycle was scanned with single successively premature impulses (fig. 3). Atrial fibrillation associated with slow ventricular response was noted following cessation of atrial pacing at a rate of 400 beats/min. Atrial fibrillation proved to be transient and the patient reverted to his usual atrial tachycardia 36 hours later. Mitral valve replacement with a prosthetic valve was performed and a Medtronic pediatric electrode wire was inserted into the anterior wall of the right atrium and buried in the subcutaneous tissues of the chest wall. Postoperatively, the patient improved symptomatically but atrial tachycardia persisted. Since atrial overdrive pacing at rates of 300-400 beats/min regularly produced atrial fibrillation (and a slower ventricular response), future plans include insertion of a permanent radiofrequency pacemaker battery capable of rapid atrial stimulation.

Discussion

The clinical differentiation between chronic repetitive and persistent atrial tachycardia appears to be important in terms of prognosis. The chronic repetitive arrhythmia is nearly always benign but may on occasion be associated with organic heart disease while persistent atrial tachycardia is frequently associated with cardiac enlargement and/or congestive heart failure. In addition, two instances of cerebrovascular accidents have been reported in children with this arrhythmia. Slight cardiac enlargement was observed in Case No. 1 and signs and symptoms of left ventricular failure in Case No. 2. In both instances, the tachycardia may have aggravated underlying cardiac disease (possibly alcoholic and/or thyrotoxic myocardopathy in Case No. 1 and mitral valve disease in Case No. 2). It would appear unlikely, however, that underlying cardiac disease was responsible for these persistent arrhythmias. In Case No. 1, for example, the arrhythmia clearly antedated any stigmata of heart disease and subsequent cardiac catheterization studies showed normal resting dynamics. In both patients the atrial tachycardia was resistant to drug therapy and in
only three previously reported cases was sinus rhythm maintained by drug therapy (Inderal in one, digoxin in another, and digoxin plus reserpine in a third). In previous reports quinidine and procaaineamide were found to be generally ineffective while digitalis and propranolol generally resulted in increasing degrees of A-V block. The two cases described in this report represent the only reported instances in which either external direct current countershock or atrial pacing was used in an effort to control this arrhythmia. In addition, Case No. 2 is unique in that organic mitral regurgitation (clearly antedating bacterial endocarditis) was associated with this arrhythmia. Associated cardiac malformations have not been reported in patients with chronic persistent atrial tachycardia.

The findings in the present report have important implications with regard to the mechanism of the arrhythmia in our patients. The inability to induce sinus rhythm either by direct current countershock or by scanning the spontaneous atrial cycle with single or multiple electrically-induced atrial depolarizations implies that the mechanism of the arrhythmia was due to increased automaticity of an ectopic atrial pacemaker rather than to sinus node, or A-V junctional re-entry. Clearly, if the arrhythmia were re-entrant in origin, direct current countershock and/or scanning the atrial cycle by induced atrial premature depolarization should have either abolished the arrhythmia or produced transient changes in the atrial cycle length, findings which were never seen in either patient. Likewise, our studies demonstrate that this pacemaker was different from a classic atrial parasystolic focus in that induced premature atrial depolarizations regularly gained entrance into the atrial ectopic pacemaker and produced a lengthening of the A3A5. Entrance block into the ec-
topic pacemaker was never seen in either of the patients. Finally, a rapidly discharging but otherwise normal sinus node pacemaker would appear to be an unlikely mechanism, since the responses to changes in autonomic tone (exercise and β-adrenergic blockade) were minimal and Case No. 2 showed deeply negative P waves in leads II, III, and aV F.

Several additional electrophysiologic properties of this pacemaker bear comment. The pacemaker displayed properties similar to those of the sinus node in that successively premature atrial depolarizations produced stepwise increments in the return cycle up until approximately 80–85% of the spontaneous atrial cycle; thereafter, successively premature depolarizations resulted in plateau lengthening of the return cycle (fig. 5). This phenomenon has been well described in subjects with normal sinoatrial node function as well as in patients with the "sick sinus syndrome."27, 28

The atrial pacemaker function in our two patients, however, differed significantly from the sinoatrial node pacemaker in its response to overdrive atrial pacing. In both patients abrupt cessation of atrial overdrive pacing resulted in a range of "pacemaker recovery times" that was similar to the plateau levels achieved by singly induced atrial depolarizations. This finding was independent of the paced atrial rate and is clearly different from the previous studies of postpacing sinoatrial node recovery time in both animals and man.29-31 In animals, the duration of postpacing sinoatrial node depression is linearly related to the preceding paced rate. In man, however, increases in the paced atrial rate tends to lengthen the sinus node postpacing recovery time up to atrial rates of approximately 130 beats/min, but further increases in rate are associated with shortening of the sinoatrial node recovery time.31 For any paced rate, however, the duration of the recovery time is significantly longer than the maximal return cycle achieved by singly induced atrial depolarization.27, 31

The unusual response to atrial overdrive pacing...
found in our patients cannot be explained by complete entrance block into the atrial focus since this situation would have produced variable recovery times. More likely, each atrial depolarization penetrated and depolarized the atrial focus, and the "recovery times" after singly induced atrial premature beats or sustained atrial pacing represent conduction time into and out of the ectopic pacemaker plus the spontaneous discharge rate of the pacemaker.\textsuperscript{28} In addition, abrupt cessation of overdrive atrial pacing frequently produces lengthening of several atrial cycle lengths until control rates are achieved.\textsuperscript{31} In our patients control atrial rates were always achieved immediately following the first spontaneous atrial depolarization after cessation of pacing.

Finally, the findings are very much reminiscent of a demand type pacemaker with hysteresis.\textsuperscript{28} A single or series of depolarizations is "sensed" (or depolarizes the atrial pacemaker), and after a brief pause, the control pacemaker rate returns. The anatomic or pathophysiologic basis for this type of pacemaker response remains speculative.

In treatment of patients with chronic persistent atrial tachycardia the clinician is often tempted to use excessive doses of antiarrhythmic agents and/or repeated attempts at electroconversion in order to produce sinus rhythm. Our current experience and review of the literature suggest alternative approaches. The therapeutic end point for these patients should be control of the ventricular rate rather than maintenance of a sinus mechanism. Drug therapy appears to be ineffective in the maintenance of a sinus mechanism, and similarly direct current countershock is ineffective in arrhythmia control, presumably because the more rapid ectopic pacemaker usurps sinus node function after countershock. If drug therapy is ineffective (or associated with toxicity) in producing control of the ventricular rate, then chronic overdrive atrial pacing should be considered. The latter technique may produce slowing of the ventricular response (presumably due to concealed conduction into the junctional area) or may result in atrial fibrillation, a rhythm which is usually more responsive in terms of rate control to drug therapy.

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References


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