Sinoatrial Pacemaker Shift
Following Atrial Stimulation in Man

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SUMMARY Indirect evidence of a sinoatrial pacemaker shift after programmed atrial stimulation in man is presented. Following electrically induced beats, time intervals and postextrasystolic morphology of atrial electrogram and P waves were scrutinized in 30 catheterization studies. Applying premature atrial stimulation, a decrease of the interval between the last basic atrial depolarization and the stimulus-produced atrial excitation (curtailed cycle) below a critical interval was followed by a sinoatrial pacemaker shift in three cases. This electrophysiologic event consisted of a concomitant change in shape of high right atrial electrogram and an increase of atrial cycle length. Simultaneous alteration of P waves could be detected in 2/3 patients. Assuming that the pacemaker shift indicates the arrival of ectopic activation in the sinus node, capture of the sinus node by the premature beat could be distinguished from failure to capture. Thus, pacemaker shift can be used for estimating sinoatrial conduction time in addition to present methods using measurement of postextrasystolic atrial intervals. The changes described could be seen both before and after atropine administration. Tracings of a pacemaker shift after cessation of rapid atrial pacing are also presented.

In summary, we found a sinoatrial pacemaker shift underlying sinus node response to ectopic atrial activation in man, a phenomenon which contributes to our understanding of indirect assessment of sinoatrial conduction time by the premature stimulation technique.

RECOGNITION OF THE CLINICAL IMPORTANCE OF SINOATRIAL DISEASE is growing.1-2 Provocative pacing methods have been developed to evaluate sinus node function: rapid atrial stimulation was applied to measure sinus node recovery time;3-4 premature atrial depolarizations (either occurring spontaneously or stimulation-induced) were used as a means for indirect estimation of sinoatrial conduction properties.5-7 Attention was focused on the time intervals between the ectopic atrial beats and the subsequent spontaneous atrial activity. The shape of postextrasystolic atrial recording, however, has been examined only rarely.8

In this report we present electrophysiologic data from three patients. During premature atrial stimulation, a decrease of the interval between the last basic atrial depolarization and stimulus-produced atrial excitation (curtailed cycle) below a critical interval was followed by a concomitant change in shape of postextrasystolic atrial electrogram and an increase of atrial cycle length. Changes were also seen after atrial pacing.

We interpret our findings as indirect expression of a sinoatrial pacemaker shift which hitherto has been validated in animal experiments only.9 10 Furthermore, such observations serve to contribute to the present debate about measuring sinoatrial conduction time in man.
Methods

All patients gave informed, written consent for evaluation of sinus node function. They were studied in the cardiac catheterization laboratory in the nonsedated state and did not receive any cardioactive drugs unless stated otherwise. In all patients sinus rhythm was present during the study. A quadripolar electrode catheter was inserted via the right basilic vein, and the tip placed at the lateral wall of the right atrium. The caudal-distal pair of electrodes (interelectrode distance 8 mm) was always used for stimulation. From the proximal pair of electrodes lying closer to the sinus node, a high right atrial electrogram was simultaneously recorded with a standard electrocardiogram at a paper speed of 100 mm/sec. A bipolar electrode catheter was passed percutaneously by way of the right femoral vein to the right atrium to lie across the tricuspid valve for recording of a His bundle electrogram by use of a previously described technique.11 Premature atrial depolarizations were elicited after every eighth spontaneous atrial activation of sinus origin by use of a programmable stimulator. For that purpose the bipolar atrial electrogram was used as trigger signal. Electrical stimuli passed an isolation unit, were rectangular in shape, twice diastolic threshold, and 2 msec in duration. Thus, the entire atrial cycle was scanned except for the refractory period.

Applying the premature atrial stimulation technique, the following time intervals were measured:

1) the interval between the last two spontaneous atrial depolarizations preceding the stimulation impulse (a1-a2);
2) the interval between the last atrial depolarization and the stimulus-induced atrial excitation (so-called curtailed cycle, a1-a2);
3) the interval between the stimulus-induced atrial excitation and the next spontaneous atrial depolarization (so-called postextrasystolic cycle, a2-a3);
4) the interval of the subsequent spontaneous atrial cycle (so-called post-postextrasystolic cycle, a3-a4).

The postextrasystolic cycle a2-a3 is plotted in a diagram as a function of the curtailed cycle a1-a2, both values expressed as a percentage of the spontaneous atrial cycle a1-a3. For calculation of sinoatrial conduction time (SACT), the postextrasystolic cycle following the longest curtailed cycle which captured the sinus node was taken. Determination of capture was based on the lengths of a2-a3, a3-a4, and a changed configuration of a5 (see Results and Discussion). We theoretically assume that the a2-a3 interval following capture, subtracted from a1-a2, represents the sum of conduction time in a cable-like structure from the site of bipolar electrogram to the sinus node and back the same way to the recording electrodes. Half of the total sum of conduction time gives SACT, assuming that antegrade and retrograde conduction velocity is the same. The sinus node recovery time is defined as the time interval between the last paced atrial activation and the first spontaneous beat of sinus origin after cessation of rapid atrial stimulation. Sinus node recovery time was measured after stimulation with rates slightly higher than sinus rhythm. The pacing rate was then increased by steps of 10 beats/min up to a maximal rate of 160 or 170 beats/min, and corresponding sinus node recovery time was measured.

Each pacing period lasted one minute.

Results

Results of premature atrial stimulation in a 69-year-old patient are plotted in figure 1.

Before atropine (A and B), a wide scatter of sinus node responses to premature atrial stimuli is present. Mean a1-a3, length amounted to 1000 msec ± 71 (± SD), the measured intervals ranging from 870 msec to 1120 msec. Expressing the curtailed cycle and the postextrasystolic cycle as a percentage of the a1-a3 interval is valid only when we can assume that the cycles following a1-a3 would have been unchanged if the premature stimuli had not been given. This prerequisite is probably not met in figure 1A and 1B, thus precluding analysis of sinus node response. After atropine administration (fig. 1C and 1D), sinus rate is increased and stabilized: mean a1-a3 is 795 msec ± 13 (± SD). Abnormal responses to premature stimuli obtained prior to drug administration are significantly curtailed. The line drawn represents the compensatory line. A and B) No medication, a1-a3, 1000 msec ± 71 (± SD) (N = 35). C and D) Atropine, 1 mg intravenously: a1-a3, 795 msec ± 13 (± SD) (N = 62). Filled circles represent a2-a3 and a3-a4 intervals where spontaneous atrial complexes are unchanged (example in fig. 2A). Unfilled circles indicate a2-a3 and a3-a4 intervals in which a change of a5 configuration was obvious (example in fig 2B). In C, capture of the sinus node is assumed to occur at transition from a compensatory to a noncompensatory pause (at a curtailed cycle of about 87.5%); calculated SACT amounts to 50 msec. Within the noncompensatory pause a2-a3 and a3-a4 cycles are slowly but steadily increasing.

![Figure 1](http://circ.ahajournals.org/FIGURE/1)
becoming regular, which is a normal finding. Zones of compensatory and noncompensatory pauses can be clearly identified by measuring postextrasystolic cycle length. Careful inspection of the atrial electrogram revealed that occurrence of a noncompensatory \(a_2-a_3\) interval coincides with an alteration of the \(a_3\) complex (unfilled circles in fig. 1C) as well as with a lengthening of the \(a_3-a_2\) cycle (unfilled circles in fig. 1D), whereas such a pattern is not seen in the case of a compensatory pause (filled circles in fig. 1C and 1D).

Figure 2 shows a tracing taken during premature atrial stimulation. In panel A, a premature beat is elicited late in atrial diastole, followed by a compensatory pause. The subsequent atrial cycle \(a_2-a_3\) is identical to the \(a_3-a_4\) interval. Also, the configuration of atrial activation \(a_3\) and \(a_4\) is unaltered — as seen in the atrial electrogram — when compared with \(a_1\). In figure 2B the premature stimulus is applied even earlier. The pause is not compensatory. The shape of the \(a_3\) beat terminating that pause and the corresponding P wave in II and III are altered; \(a_4-a_5\) is increased. Normal morphology of P waves and atrial electrogram as seen prior to stimulation is completely re-established only after several beats in \(a_9\).

Early premature beats lead to a shortening of the \(a_2-a_3\) cycles and similar changes of P waves and atrial electrogram (see unfilled circles below the horizontal axis of fig. 1A and 1C). However, \(a_9\) is not completely interpolated since the sum of \(a_1-a_2\) and \(a_2-a_3\) is always more than \(a_1-a_2\). Quite similar observations have been reported for the intact dog heart (fig. 10 of reference 13).

Changes of atrial electrogram and P waves were also recorded after cessation of rapid atrial pacing (fig. 3). The first two atrial complexes after cessation of pacing show a changed configuration in the atrial electrogram, II, and III quite similar to that observed following single premature

**Figure 2.** Lead I, II, III, His bundle (HBE) and atrial electrogram (AE) during premature atrial stimulation after atropine, 1 mg intravenously. Same patient as in figure 1. A) After the second spontaneous atrial activation of sinus origin, a late premature beat is followed by a compensatory pause (745 msec + 840 msec = 2 times 795 msec). Five spontaneous cycles preceding \(a_2\) ranged from 785 msec to 975 msec. B) Two continuous tracings are shown. A curtailed cycle of 375 msec is followed by a noncompensatory pause (375 msec + 905 msec < 2 times 795 msec). Three cycles preceding \(a_2\) with complexes identical to \(a_3\) ranged from 759 msec to 800 msec. Alteration of activation pattern is apparent in the atrial electrogram as well as in the surface leads (the P waves corresponding to \(a_3\) and \(a_4\) being negative in III, and isoelectric in II), whereas changes are not apparent in the HBE. \(a_9\) to \(a_{10}\) represent an intermediate activation pattern with return of small positive P waves in II, but P remaining negative in III. With reappearance of an initial negative vector in AE in \(a_9\), and more clearly in \(a_{10}\), the P waves have become normal (positive in II, biphasic in III). Cycle length up to \(a_2-a_3\) is increased following one premature beat; \(a_3-a_4\) tends to become normal.
stimuli in the same patient (for comparison see fig. 2B).

A similar clear-cut change in atrial rate and postextrasystolic atrial electrogram was observed in a 71-year-old male patient with carotid sinus hypersensitivity. Plotted data of the premature atrial stimulation technique are given in figure 4. In A (left side), zones of compensatory and noncompensatory pauses can be easily identified. Unlike figure 1, however, postextrasystolic cycles at transition are slightly overcompensatory (data points falling above the theoretical line).

Figure 5 gives an example in which not only the noncompensatory responses but also the overcompensatory ones were associated with a change in $a_2$ configuration and an increase in $a_3-a_2$ interval.

All sinus node responses exhibiting the alterations shown in figure 5 are indicated by an unfilled circle in figure 4. When SACT is calculated from figure 4A by using a mean noncompensatory atrial cycle subtracted by $a_2-a_3$, a value of 65 msec is reached. However, the observation of a change in shape of postextrasystolic atrial activation as well as the
behavior of the $a_3-a_4$ cycles (see fig. 4B) indicate that the sinus node is already captured by curtailed cycles between 85 and 90% of $a_3-a_1$. If capture is arbitrarily chosen to occur with curtailed cycles of 87.5%, a SACT is calculated to be 45 msec.

After atropine administration (fig. 4C and D, right side), mean $a_3-a_4$ cycle length decreased slightly from 721 msec to 678 msec. Except for the absence of overcompensatory pauses, quite similar results are obtained after pharmacologic blockade of the vagus nerves. The length of $a_3-a_4$, $a_3-a_4$, and the change in $a_3$ configuration both point to a capture of the sinus node following a curtailed cycle close to 85%. Accordingly, a SACT of 50 msec is calculated, indicating that atropine caused a minor acceleration of sinus rate and practically no change of SACT in this patient.

Following premature beats, which had been elicited very early in atrial diastole, a mixed sinus node response occurred both before and after atropine administration (see crosses in fig. 4): configuration of $a_3$ is altered only slightly, however, $a_3$ being clearly changed; the $a_3-a_4$ intervals are abruptly prolonged, falling close to the theoretical line, and the $a_3-a_4$ cycles are increased. From such a pattern one may speculate that these premature atrial beats have been elicited during the relative refractory period of the sinoatrial junction.

Figure 6 delineates the results of premature atrial stimulation in a 27-year-old female patient with atrial septal defect. Data points roughly follow the compensatory line, thus indicating a sinus node entrance block. However, lengthening of the $a_3-a_4$ intervals and an altered shape of $a_3$, occurring about the time that curtailed cycles below 80% are recorded, contradict such an interpretation. A representative ECG tracing of this patient is shown in figure 7.

Discussion

Pacemaker Shift

In a microelectrode study on the effects of atrial overdrive on isolated mammalian sinus node cells, Lu et al. observed...
The pacemaker action shifting to a distant site. The first postdrive propagated responses originated from other pacemaker cells. Dominance by the cells from the original pacemaker site was re-established slowly.

Following single electrically induced premature beats, a change in latency between onset of activation of an impaled pacemaker fiber and the complex of a surface electrogram from crista terminalis was demonstrated by Bonke et al. in 1969. This event was paralleled by a change in the time lapse between two unipolar atrial electrograms. The conduction time after the premature beat was proved not to have changed, strongly suggesting that these changes show a shift of the pacemaker which occurred when the atrial premature beat was elicited early enough to discharge the node.

The phenomenon of altered atrial complexes following premature beats is also known in clinical electrocardiography. It has, however, usually been interpreted as aberrant atrial conduction.

In this study we present examples of a concomitant change in configuration of atrial complexes and in atrial intervals following single premature beats. Similar changes were observed after cessation of rapid atrial stimulation. We observed these phenomena in three cases out of 30 catheterization studies. In these patients, the shape of spontaneous atrial activity in high right atrial electrogram remained constant throughout the study — a condition sine qua non for our observations. Four more cases showed similar changes of postextrasystolic atrial activation pattern but are not reported in detail because of unstable electrograms (possibly due to catheter movement), or the temporary nature of these changes.

Alteration of the shape of P waves, atrial electrogram, and the increase in cycle length following single premature beats in the patients presented were reproducible throughout the study. Their appearance clearly depended on a critical prematurity of stimulation. This makes it unlikely that other influences such as an increased right atrial fiber stretch or blood pressure, a stretch-induced pacemaker shift, catheter dislocation, respiratory effects, and other artifacts are the underlying mechanisms. Alteration of atrial activity could be detected in the surface leads in two patients, with no change in the recordings of low right atrial activity in His bundle tracings. The alterations described could be elicited after atropine administration as well (fig. 4) or were seen more often after drug exposure (fig. 1) and cannot therefore be attributed to vagal stimulation, an influence which has been demonstrated to facilitate a pacemaker shift.

In 1972, aberrant atrial conduction following ectopic beats was proposed as a new electrocardiographic entity. The mechanism was assumed to be an altered atrial refractory period immediately after an ectopic impulse, thus causing some degree of concealed atrial conduction. This mechanism cannot account for the observed interval changes seen in our cases. Chung noted that aberrant atrial conduction is not often seen after interpolated atrial premature contractions. In such a case of interpolation one assumes that the sinus node pacemaker is not affected by the premature beat. The further observation that the ECG recordings at times showed atrial cycles to be changed after an ectopic beat (fig. 3 and 4 of reference 8) suggest that in some of his cases a pacemaker shift rather than isolated aberrant atrial conduction occurred following an ectopic beat.

A sinoatrial pacemaker shift remains the most likely explanation for our findings. Even with the limited recording techniques available in man, which show only gross shifts, our findings indicate that such changes can occur in man following single or multiple ectopic beats. We do not know where the pacemaker has moved. We think it reasonable, based on the animal studies of Bonke et al., to assume that a sufficient intranodal translocation of the center might have
ensued in our cases so that the activation front moved into another direction. Thus, atrial activation could be changed by an event confined entirely to the sinus node.16

Sinoatrial Conduction Time

Recently, the microelectrode technique was used in an experimental preparation to test whether sinoatrial conduction time might be derived indirectly from the length of the postextrasystolic atrial cycle after single premature beats.23 It was concluded that this method is only of limited value for derivation of sinoatrial conduction time (SACT) in man.24 If a pacemaker shift occurs after discharge of the sinus node by the ectopic wave,10 recognition of this phenomenon can be used in our patients to identify capture of the sinus node. Therefore, it serves as another way of assessing SACT. Values obtained in our patients (45 msec–60 msec) are in the lower range of normal values reported in the literature.25–28 This may be explained in light of a pacemaker shift following a premature beat: the conduction time in this case represents the time conduction takes to reach the new site of pacemaker function, and not the conduction time to the original pacemaker.

Comparison between the length of the postextrasystolic cycle and activation pattern revealed that capture and a subsequent pacemaker shift underlay the overcompensatory response in figure 4A. In plots with a sharp transition from a compensatory to a noncompensatory atrial cycle, this event closely paralleled the concomitant change in atrial cycle and shape of activation (fig. 1C, 4A and C). Thus, we used the shortest noncompensatory a2–a3 intervals before transition for indirect estimation of SACT in those patients in whom a sharp discrimination of the two zones — as in the examples given — was possible. This choice might be preferable, since, with increasing prematurity of stimulation within the noncompensatory pause, changes of both sinus node automaticity and sinoatrial conduction time have been amply demonstrated.10,29 Finally, the altered shape of atrial activation and an increase in a2–a3 cycle argue against the assumption of a sinus node entrance block in case 3 (fig. 6). We speculate that in this case a pacemaker other than the dominant one is prematurely discharged after curtailed cycles below 80% of a1–a2. The new pacemaker is then able to take over pacemaker function for one beat with a postextrasystolic interval which simulates sinus node entrance block.

The length of the a2–a3 cycle has been proposed to be useful for monitoring sinus node depression.16,26 It appears that post-postextrasystolic cycle prolongation in our cases was produced by two electrophysiologic mechanisms:

1) Shift of pacemaker dominance to a fiber with an intrinsic rate lower than that of the original pacemaker; such an event has been observed in the isolated right atrium of the rabbit with qualitatively similar, quantitatively smaller effects on a2–a3 length than now presented for man.10
2) Beat-to-beat differences in antegrade sinoatrial conduction time due to a shifting pacemaker.27

The first mechanism probably accounts for several prolonged atrial intervals following one premature beat (example in fig. 2B). However, if only a2–a3 is prolonged (and a1–a2 to a slight degree or not at all, as in fig. 6), cycle lengthening could be entirely or partially caused by the second mechanism.

Prolongation of a2–a3 similar to our cases has also been demonstrated in the intact dog heart.13 However, these authors did not describe changes in morphology of postextrasystolic P wave, atrial electrogram, or sequence of activation. In man, lengthening of a2–a3 generally to a minor degree and not associated with changes of P waves and atrial electrogram, have also been observed by us in catheter studies not reported here, as well as by others.26 An obvious question follows: does sinus node depression resulting in a2–a3 prolongation also exist without any pacemaker shift? It is our opinion that this electrophysiologic event, though possible, is not proved by the recording techniques available in man; also the use of electrodes fixed to atrial epicardial surface in animals is probably too insensitive to detect a minor, intranodal translocation of pacemaker function. Hence, the final answer to this question can only come from appropriate microelectrode studies.

Whether our observations of gross pacemaker shift after a premature beat have clinical relevance and signify pathologic fractionation of sinus node function in these patients is not clear at present. These three cases demonstrated carotid sinus hypersensitivity, sinus bradycardia with intermittent atrial fibrillation, and atrial septal defect of the secundum type. In the patient with congenital heart disease, we did not have clinical or electrocardiographic indications that sinus node function was impaired. Sinus node recovery time was well within the normal range in all patients.

In conclusion, we described a pacemaker shift underlying sinus node response to ectopic atrial activation in three patients out of 30 catheterization studies. Recognition of this phenomenon and determination of the relationship between curtailed and postextrasystolic cycle length helped to identify capture of the sinus node, and hence, to derive SACT. We believe that our findings may also contribute to the interpretation of results in other patients in whom similar data — but no recordable pacemaker shift — are obtained by the programmed atrial stimulation technique.

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Mechanisms of Spontaneous Alternation between Reciprocating Tachycardia and Atrial Flutter-Fibrillation in the Wolff-Parkinson-White Syndrome

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SUMMARY In a group of 36 consecutive patients with the Wolff-Parkinson-White (WPW) syndrome undergoing electrophysiological studies because of paroxysms of reciprocating tachycardia (RT) and/or atrial flutter-fibrillation (AF), 7 patients (19%) had repeated episodes of spontaneous alternation between RT and AF. Electrophysiological studies demonstrated left-sided anomalous pathways (AP) in all 7 patients. Atrial vulnerability, as evidenced by the occurrence of repetitive atrial responses or a paroxysm of AF following a single atrial premature stimulus, was also noted in all. Invariably, spontaneous conversion of RT to AF (7 patients) was triggered by an atrial premature depolarization which resulted in atrial asynchrony during the atrial vulnerable phase. In contrast, spontaneous conversion of AF to RT (3 of the 7 patients) required the presence or the development of antegrade unidirectional block in the AP prior to the cessation of AF.

The demonstration of atrial vulnerability in association with the phenomenon of spontaneous alternation between RT and AF provides further information pertaining to the understanding of the mechanisms of tachyarrhythmias in the WPW syndrome. It is suggested that the occurrence of this electrophysiological phenomenon may be more common than is generally appreciated, and optimal medical treatment should be directed toward controlling both RT and AF in this group of Wolff-Parkinson-White patients.

TACHYARRHYTHMIAS, predominantly supraventricular tachycardia and atrial flutter-fibrillation, are a key feature of the clinical syndrome described by Wolff, Parkinson, and White (WPW). The frequent episodes of supraventricular tachycardia are generally a form of reciprocating tachycardia utilizing both normal and anomalous atrioven-

cular (A-V) pathways. On the other hand, the occurrence of atrial flutter-fibrillation in association with this syndrome is not well understood and may, in some instances, be related to coexisting sinus nodal and intraatrial disease. 

Spontaneous conversion between reciprocating tachycardia and atrial flutter-fibrillation has also been described in patients with the WPW syndrome; however, little information is available concerning its underlying mechanisms.

In seven of the 36 consecutive patients with the WPW syndrome undergoing electrophysiological studies, spontaneous conversion between reciprocating tachycardia and atrial flutter-fibrillation was repeatedly observed. The purpose of this paper is to describe the mechanisms responsible for this unique electrophysiological phenomenon and to discuss its possible clinical implications.
Sinoatrial pacemaker shift following atrial stimulation in man.
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