New application of direct sinus node recordings in man: assessment of sinus node recovery time

JOSEPH ANTHONY C. GOMES, M.D., ROBERT I. HARIMAN, M.D., AND IMTIAZ A. CHOWDRY, M.D.

ABSTRACT Sinus node recovery time (SNRT) is frequently used to assess sinus node function in patients with suspected sick sinus syndrome (SSS). Although SNRT is assumed to reflect sinus node automaticity, this assumption remains unproven. The purpose of this study was (1) to test the hypothesis that SNRT in patients with and without SSS reflects sinus node automaticity, and (2) to assess the role of sinoatrial conduction time in the measurement of SNRT. A total of 16 patients (mean ± SD age 63 ± 9 years), seven of which had SSS, form the basis of this report. An electrogram of the sinus node was obtained for each of the 16 patients, and overdrive pacing was performed in each at cycle lengths of 1000 to 300 msec. SNRT was measured (1) on the sinus node electrogram (direct method, measuring SNRTd) as the interval from the last pacing stimulus artifact to the onset of the upstroke of first postpacing sinus beat and (2) on the high right atrial electrogram (indirect method, measuring SNRTi). Results were as follows: (1) The longest SNRTd was significantly shorter than the longest SNRTi (989 ± 304 vs 1309 ± 356 msec, p < .001). (2) For the first postpacing sinus beat there was a significant prolongation of sinoatrial conduction time as compared with that for sinus beats before pacing (319 ± 152 vs 99 ± 35 msec, p < .001). Sinoatrial conduction time normalized within 3.6 ± 0.96 postpacing sinus beats. (3) At the pacing cycle length that resulted in the longest recovery time, sinus node depression was seen in 56% of patients, sinus node acceleration was noted in 26%, and no appreciable change in sinus node automaticity was observed in 19%. (4) Sinoatrial conduction time for the sinus beat before pacing and that for the first postpacing beat was longer in patients with SSS when compared with in patients without SSS. (5) In patients with SSS the abnormal SNRTi, when corrected for the degree of prolongation of sinoatrial conduction time for the first postpacing beat, became normal in five of six patients. We conclude that (1) SNRTi reflects both sinus node automaticity and sinoatrial conduction time, whereas SNRTd reflects sinus node automaticity, (2) overdrive atrial pacing results in marked prolongation of sinoatrial conduction time for the first postpacing beat, which is longer in patients with SSS when compared with in those without SSS, and (3) in patients with SSS the inference of abnormal sinus node automaticity on the basis of a prolonged corrected SNRTi is usually incorrect.

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THE PHENOMENON of postpacing depression of cardiac pacemakers1–7 has been used to evaluate sinus node function in man.8–17 Clinical studies have focused on the response of the human sinus node to atrial pacing at rates above the sinus rate. The method has been used to determine the time required for a sinus beat to resume activity after abrupt cessation of atrial pacing. This sinus node recovery time (SNRT) has been used in the evaluation of sinus node function in patients with sick sinus syndrome (SSS).8–17 Although SNRT is assumed to reflect sinus node automaticity in man, the contribution of sinoatrial conduction in the measurement of SNRT remains undefined.

The purpose of this study was (1) to test the hypothesis that SNRT in patients with and without SSS reflects sinus node automaticity and (2) to assess the role of sinoatrial conduction in the measurement of SNRT.

Materials and methods

A total of 22 male patients were studied after the nature of the procedure was explained to them and after they gave signed informed consent. Sixteen patients who satisfied the following criteria were included in the study: (1) Each had stable, reproducible sinus node electrograms free of baseline drift during sinus rhythm and after overdrive pacing. (2) In each the sinus node electrograms were clearly separable from the T and U wave deflections during both during sinus rhythm and after atrial overdrive pacing. The 16 patients ranged in age from 38 to 78 years (mean age, 63 ± 9 years). Nine of the 16 patients had no evidence of SSS, whereas seven of 16 had symptomatic SSS.

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All patients were studied in the electrophysiology laboratory while they were in the postabsorptive, nonsedated state. Two quadripolar catheters (USCI No. 6) with interelectrode distances of 10 mm were introduced percutaneously through the femoral vein of each patient while under local anesthesia; catheters were positioned in the high right atrium in the region of the sinus node. One catheter was used for recording sinus node electrograms,18–21 and the other for atrial pacing. The distal poles of catheter No. 1 were used for recording sinus node electrograms by a technique previously described in our laboratory.21 The proximal poles of the catheter were utilized for recording intra-atrial electrograms at filter frequencies of 30 to 500 Hz. Two or more electrocardiographic leads, sinus node electrograms at filter frequencies of 0.1 to 50 Hz and intracardiac electrograms at filter frequencies of 30 to 500 Hz, and time lines generated at 40,200 and 1000 msec were displayed on a multichannel oscilloscope (VR-12, Electronics and Medicine) and recorded on thermal paper at paper speeds of 50 to 100 and 150 mm/sec. Atrial stimulation was performed at a cycle length 100 msec below sinus cycle length for 1 min. In addition atrial pacing was performed for 8 beats in six patients. Atrial stimulation studies were performed with a programmable stimulator using stimuli at twice diastolic threshold and 2 second duration. Pacing was abruptly stopped and SNRT was assessed. Sinus node recovery time was assessed at multiple cycle lengths in decrements of 100 msec up to cycle lengths of 300 msec. Analysis of postpacing pause was done for at least 5 postpacing beats and only if the upstroke slope of the sinus node electrogram was clearly identifiable after overdrive atrial stimulation.

Definition of terms. Direct sinoatrial conduction time was measured from the onset of the upstroke slope to the onset of atrial deflection (figure 1) for the sinus beat before pacing, for the first postpacing sinus beat, and for 4 more postpacing sinus beats.

Indirect SNRT (SNRTi) was measured from the stimulus artifact to the onset of the atrial deflection (figure 1). Direct SNRT22 (SNRTd) was measured from the onset of the stimulus artifact to the onset of the upstroke slope on the sinus node electrogram. Corrected SNRTi was measured as the difference between the basic sinus cycle length minus the SNRTi. All measurements were tested for interobserver variability, which was within 10 msec. Also, the average difference among all measurement pairs was not significant.

Statistical analysis was performed by Student’s t test for paired and unpaired data. All values represent the mean ± SD.

Results

Stable and reproducible sinus node electrograms were recorded in all 16 patients during sinus rhythm. These sinus node electrograms usually showed two negatively directed deflections of low frequency and amplitude occurring after the deflections of the T and U waves but before the P wave on the surface electrocardiogram and intra-atrial recordings. The negative deflections that correspond to the diastolic and upstroke slopes of the sinus node were displayed so that they gave positive deflections. SNRT (direct and indirect) and sinoatrial conduction time for the first postpacing beat were assessed only for pacing cycle lengths wherein the upstroke slope of the sinus node on the sinus node electrogram was clearly evident. Reproducibility was tested by repeating the pacing protocol for any given pacing cycle length two or more times.

SNRT and sinoatrial conduction time. Table 1 lists the clinical and electrophysiologic data of the 16 patients and table 2 the mean values at pacing cycle lengths that resulted in the longest SNRT. The mean cycle length at which the SNRTi was obtained was 524 ± 204 msec (range 300 to 900 msec). The mean SNRTd was 989 ± 304 msec (range 740 to 1680 msec) and was significantly (p < .001) shorter than the mean SNRTi, which was 1309 ± 356 msec (range 820 to 2000 msec). This difference between SNRTd and SNRTi was primarily related to a significant prolongation of sinoatrial conduction time for the first postpacing beat when compared with sinoatrial conduction time of the sinus beats before pacing (99 ± 35 vs 319 ± 52, p < .001). The sinoatrial conduction time normalized within 3.6 ± 0.96 beats after overdrive atrial pacing. Figure 2 is a representative example from a patient without SSS. During sinus rhythm, before pacing, the sinoatrial conduction time was normal (80 msec), but after overdrive pacing at a cycle length of 400 msec, the SNRTi was 1100 msec and the SNRTd 870 msec. The difference was related to prolongation of sinoatrial conduction time to 230 msec for the first postpacing sinus beat. Figure 3 is a representative example from a patient with SSS. Sinoatrial conduction time was abnormally

FIGURE 1. The measurement of SNRT and sinoatrial conduction time. From top to bottom are the electrocardiogram (ECG), sinus node electrogram (SNE), and atrial electrogram (AT). Sinoatrial conduction time (SACT) for sinus beats before and after pacing was measured from the onset of the upstroke slope to the onset of the atrial deflection (A). After overdrive pacing, the SNRTd was measured from the stimulus artifact (Ss) to the onset of the upstroke slope on the SNE. The SNRTi was measured from the onset of the stimulus artifact (Ss) to the atrial deflection (A).

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TABLE 1
Clinical features and electrophysiologic data

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<th>Patient No.</th>
<th>Age (yr)</th>
<th>Diagnosis</th>
<th>SACT for SB (msec)</th>
<th>PCL (sec)</th>
<th>SNRTd (msec)</th>
<th>SNRTi (msec)</th>
<th>Corrected SNRTi (msec)</th>
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SACT = sinoatrial conduction time; VT = supraventricular tachycardia; SSS = supraventricular tachycardia; VPBs = ventricular premature beats; VT = atrial fibrillation; SB = sinus beats; PCL = pacing cycle length; PPB = postpacing beat; + = acceleration; − = depression; 0 = no change.

TABLE 2
Mean electrophysiologic data (pacing cycle length = 524 ± 204 msec)

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<tr>
<th>Parameter</th>
<th>Mean</th>
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<td>SACT for sinus beats before pacing (msec)</td>
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</tr>
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<td>SACT for first PPB (msec)</td>
<td>319 ± 152</td>
<td>&lt;.001</td>
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<td>Normalization of SACT (beats)</td>
<td>3.6 ± 0.96</td>
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<tr>
<td>SNRTd (msec)</td>
<td>989 ± 304</td>
<td>—</td>
</tr>
<tr>
<td>SNRTi (msec)</td>
<td>1309 ± 36</td>
<td>&lt;.001</td>
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SACT = sinoatrial conduction time; PPB = postpacing beat.

In six patients in whom pacing was performed for 8 beats and for 1 min at similar cycle lengths, it was possible to compare sinoatrial conduction time for the first postpacing beat for the two pacing periods. These studies showed that sinoatrial conduction time was longer with pacing for 1 min than with that for 8 beats (figure 5). Pacing for 8 beats at a cycle length of 400 msec resulted in a sinoatrial conduction time for the first postpacing beat of 240 msec, which normalized within the third postpacing beat (figure 5, A). Pacing for 1 min at a cycle length of 400 msec resulted in a sinoatrial conduction time of 410 msec, which normalized by the fourth postpacing beat. Note that both SNRTi and SNRTd were longer with pacing for 1 min than with that for 8 beats.

![FIGURE 2. SNRT in a patient without SSS. From top to bottom are the electrocardiographic leads 1, 2, and V1, the sinus node electrogram (SNE), and the atrial electrogram (AT). A. Sinus beats before pacing. Note that the sinoatrial conduction time for the sinus beats before pacing is 80 msec. B. After overdrive pacing at a cycle length of 400 msec, the SNRTi is 1100 msec and the SNRTd 870 msec. Note the prolongation of conduction time (230 msec) for the first postpacing beat as compared with that for sinus beats.](http://circ.ahajournals.org/doi/abs/10.1161/01.CIR.70.4.665?ijkey=ef02a6ae4b02e15f07f961ef78f34b9d&keytype=free)
FIGURE 3. SNRT in a patient with SSS. As in figures 1 and 2, from top to bottom are ECG leads 1. 2, V1, SNE, and AT. Left. A sinus beat before pacing. Note that the sinoatrial conduction time is abnormally prolonged (160 msec). Right. After overdrive pacing at a cycle length of 900 msec, the SNRTi is 1460 msec and the SNRTd 840 msec. Note the marked prolongation of conduction time (620 msec) for the first postpacing beat; for the second postpacing beat it shortens to 200 msec.

Effect of pacing cycle length on SNRT and sinoatrial conduction time. The effect of pacing cycle length on SNRTd, SNRTi, and sinoatrial conduction time for the first postpacing beat is shown in figures 6 and 7. Figure 6 is an example from a patient without SSS in whom sinoatrial conduction time for the sinus beats before pacing was 80 msec. After overdrive pacing, there was a progressive increase in sinoatrial conduction time as the cycle length was decreased, with the longest conduction time observed after pacing at a cycle length of 300 msec. The longest SNRTi was also noted after pacing at a cycle length of 300 msec. In contrast, SNRTd progressively decreased as the cycle length was decreased up to a pacing cycle length of 500 msec. There was a minimal increase in SNRTd (+ 20 msec) at pacing cycle lengths of 400 and 300 msec when compared with the pacing cycle length of 500 msec.

FIGURE 4. Secondary pause in a patient with SSS. From top to bottom are leads 1, 2, and V1, high right atrial electrogram (HRA), sinus node electrogram (SNE), and His bundle electrogram (HBE). After atrial pacing at a cycle length of 800 msec, a secondary pause of 1500 msec is noted. Note that the SNE (arrow) precedes the atrial electrogram by 760 msec. This probably reflects complete sinoatrial block followed by an atrial escape. Note that sinoatrial conduction time normalized by the fourth postpacing beat.

FIGURE 5. Changes in SNRT and conduction time for two different pacing periods. In both panels, from top to bottom, are the L1, L2, and V1 electrocardiogram leads, sinus node electrogram (SNE), and atrial (AT) electrogram. A. Pacing at 400 msec for 8 beats results in an SNRTd of 620 msec and SNRTi of 860 msec. Sinoatrial conduction time for the first postpacing beat is 240 msec and normalizes by the third postpacing beat. B. Pacing at 400 msec for 1 min results in an SNRTi of 1050 msec and an SNRTd of 640 msec. Note that the sinoatrial conduction time for the first postpacing beat is 410 msec and gradually normalizes within the fourth postpacing beat. For further explanation see text.

Note that in contrast to SNRTi, the longest SNRTd occurred after pacing at a cycle length of 700 msec. A somewhat different response to a change in pacing cycle length in a patient with SSS is shown in figure 7. The sinoatrial conduction time for sinus beats before pacing was 120 msec, but at 800 msec conduction time for the first postpacing sinus beat increased to 160 msec. At pacing cycle lengths of 500 and 400 msec, sinoatrial conduction time for the first postpacing sinus beat decreased (140 and 130 msec, respectively) as compared with that at the pacing cycle length of 700 msec; however, the conduction time for the first postpacing sinus beat was still longer than that for sinus beats before pacing. This small decrease in sinoatrial conduction time may be the result of varying degrees of retrograde sinoatrial block at pacing cycle lengths of 500 and 400 msec. The longest sinoatrial conduction time for the first postpacing beat occurred after pacing at a cycle length of 340 msec rather than at longer pacing cycle lengths. Both SNRTd and SNRTi decreased as the pacing cycle length was decreased,
6. Effect of pacing cycle length on SNRT and sinoatrial conduction time (SACT) in a patient without SSS. On the abscissa is plotted the pacing cycle length (CL) and on the ordinate the SACT (solid square), SNRTi (solid triangle), and SNRTd (solid circle). Note that as the pacing CLs decrease, there is progressive prolongation of SACT, a decrease in SNRTd, and an increase in SNRTi. For further explanation see text.

but at a pacing cycle length of 340 msec, both SNRTd and SNRTi increased. Note that the SNRTi and SNRTd curves are parallel to each other; the lower SNRTd curve is accounted for by changes in sinoatrial conduction time after pacing.

Changes in sinus node automaticity after overdrive pacing. The assessment of SNRT on the sinus node electrogram enabled us to determine whether there was sinus node depression or acceleration after overdrive pacing. At the pacing cycle lengths that resulted in the longest recovery times, sinus node depression was observed in nine of 16 patients (56%), sinus node acceleration was noted in four of 16 (25%), and no appreciable change in sinus node automaticity was observed in three of 16 (19%) (table 1). Whereas sinus node depression was observed in four of nine patients (44%) without SSS, it was noted in five of seven patients (71%) with SSS. However, in the majority of patients in whom this parameter could be assessed at multiple cycle lengths, changes in automaticity were dependent on cycle length. Figure 6 is an example from a patient without SSS in whom the basic cycle length was 800 msec before pacing. Sinus node depression (± 100 msec) was observed after pacing at a cycle length of 700 msec, whereas sinus node acceleration (−20 to −40 msec) was seen after pacing at 500, 400, and 300 msec. Figure 7 is a tracing from a patient with SSS in whom the basic cycle length was 1000 msec. Sinus node depression (± 80 to + 680 msec) was observed after pacing at cycle lengths of 700, 400, and 300 msec, whereas there was no change in sinus node automaticity after pacing at a cycle length of 500 msec.

Postpacing change in sinus pacemaker site. In five pa-
tients, two with and three without SSS, there was a change in pacemaker site after pacing at one or more cycle lengths. A change in sinus pacemaker site was suggested by the following observations: (1) loss of primary negativity,\textsuperscript{25} (2) change in atrial activation sequence, and/or (3) change in P wave morphology. A representative example of this phenomenon is shown in figure 8. During sinus rhythm, the sinoatrial conduction time was 90 msec and the atrial deflection on the sinus node electrogram was sloping upward. After atrial pacing there was acceleration of sinus node automaticity, with prolongation of sinoatrial conduction time to 200 msec, and the atrial deflection on the sinus node electrogram was sloping downward, corresponding to loss of primary negativity. Changes in P wave morphology were the most evident for the second and third postpacing beats. For the fourth postpacing beat, the sinus cycle length, sinoatrial conduction time, and atrial activation on the sinus node electrogram normalized.

Changes in sinoatrial conduction and recovery time in patients with SSS. Table 3 shows the mean values for sinoatrial conduction time for sinus beats before pacing and for the first postpacing beat and SNRT\textsubscript{d} and SNRT\textsubscript{i} in patients with and without SSS. The conduction time for sinus beats in patients with SSS was longer than that for sinus beats in patients without SSS (134 ± 16 vs 72 ± 16 msec, p < .001) and that for the first postpacing beat was also longer in patients with SSS when compared with those without SSS (411 ± 139 vs 248 ± 125 msec, p < .05), although there was an overlap of values among patients with and without SSS. The SNRT\textsubscript{d} and SNRT\textsubscript{i} were also longer in patients with SSS when compared with those without SSS. Since five t tests were done, the significance for each test was taken as .05/5: < .01 (Bonferroni’s adjustment).\textsuperscript{26} 27 Therefore, except for those for sinoatrial conduction time for the first postpacing beat, the differences determined for all comparisons were highly significant. The corrected SNRT\textsubscript{i} was abnormal (>450 msec) in six of seven patients with SSS; however, the abnormal corrected SNRT\textsubscript{i} was accounted for by the prolongation of sinoatrial conduction time in five of the six patients.

Discussion

Until recently, recordings of the sinus node were not possible in man. Sinus node function was assessed indirectly by measuring SNRT\textsuperscript{i} and sinoatrial conduction time.\textsuperscript{28} 30 Conventionally SNRT is measured from the last paced beat to the atrial electrogram in the region of the high right atrium. SNRT thus obtained was taken as a measure of sinus node automaticity. This hypothesis is based on the following assumptions: (1) The intra-atrial electrogram in the region of the high right atrium reflects sinus nodal events. (2) Sinoatrial conduction time for the first postpacing beat is not significantly altered by atrial overdrive pacing of the high atrium. The ability to record sinus node electrograms in the intact human heart by a previously described technique\textsuperscript{21} enabled us to assess direct sinus node and atrial events after overdrive atrial pacing.

The effects of overdrive atrial pacing on sinus node automaticity and conduction. The findings of this study suggest the following: (1) SNRT\textsubscript{i} reflects both sinus node automaticity and sinoatrial conduction. (2) SNRT\textsubscript{d} reflects sinus node automaticity. (3) SNRT\textsubscript{i} is significantly longer than SNRT\textsubscript{d} and the difference is accounted for by a significant prolongation of sinoatrial conduction time for the first postpacing sinus beat. (4) Overdrive atrial pacing results in significant prolongation of sinoatrial conduction time when compared with sinoatrial conduction time for sinus beats before pacing. Prolongation of sinoatrial conduction time was usually but not always dependent on pacing cycle length — the shorter the pacing cycle length the longer the sinoatrial conduction time. (5) Overdrive atrial pacing can result in sinus node depression or acceleration or no appreciable change in sinus node automaticity when assessed on the sinus node electrogram, whereas in all 16 patients it resulted in sinus node depression when assessed on the intra-atrial electrogram.

\textbf{FIGURE 8.} Postpacing change in sinus pacemaker site. From top to bottom are electrocardiogram leads 1, 2, and V\textsubscript{1}, atrial electrogram (AT), and sinus node electrogram (SNE). \textit{Left.} A sinus beat before pacing. The sinoatrial conduction time is 90 msec. \textit{Right.} After overdrive atrial pacing there is prolongation of sinoatrial conduction time in association with acceleration of sinus node automaticity and change in sinus pacemaker site, as suggested by a loss of primary negativity of the atrial deflection on the SNE. Alteration in P wave morphology is clearly evident for postpacing beats 2 and 3. For the fourth postpacing beat, the sinus cycle length, conduction, and atrial activation on the SNE normalizes. For further explanation see text.
TABLE 3

Mean sinoatrial conduction time and recovery time in patients with and those without SSS

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<td>72 ± 16</td>
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</table>

Abbreviations as in table 2.

The findings in this study of a significant prolongation of sinoatrial conduction time after atrial pacing has not been previously reported in man. Stimulation-induced discharge of acetylcholine and an excess of extracellular potassium might explain this observation.\(^3\)\(^-\)\(^7\) We have previously demonstrated that vagal massage can result in slowing of sinus rate and marked lengthening of sinoatrial conduction time in man.\(^21\) It is unclear from this study whether the postpacing prolongation of conduction time or the occurrence of sinoatrial block in the intact human heart occurs in the sinus nodal cells or in the perinodal zone. Clarification of this issue will have to await detailed microelectrode studies of the animal sinus node and atrial tissue. However, microelectrode studies of the sinus node of the cat after overdrive stimulation by Lu et al.\(^7\) have revealed that there is (1) local response of subnormal frequency, (2) action potential originating in the original pacemaker cell that fails to propagate to its subsidiary cells, (3) augmentation of block after rapid driving, and (4) decrementing propagation in the sinoatrial nodal cells. These observations caused them to postulate that postdrive depression might result in part from failure of conduction of activity from pacemaker cells as well as suppression of activity within the pacemakers. Prolongation of sinoatrial conduction time could have occurred in the perinodal zone since sinoatrial junctional tissue with distinctive action potential characteristics have been demonstrated in rabbit atrial preparations and have been shown to be a potential site of conduction delay.\(^31\)

Previous studies in the intact canine heart have shown that there is a linear increase in SNRT with an increment in atrial pacing rate.\(^32\) However, in the intact human heart, rapid declines in recovery times have been reported by some observers.\(^8\) Others, however, have reported that recovery times are independent of pacing rate in normal subjects, whereas in patients with sinus bradycardia and an abnormal recovery time, recovery time is directly dependent on the rate and duration of pacing.\(^9\) Nonetheless, the pacing rate at which the longest SNRT is reached varies from subject to subject. The results of this study reveal that at the pacing cycle length that resulted in the longest recovery times, assessment of recovery time on the sinus node electrogram (i.e., SNRTd) showed sinus node depression in 56% of patients, sinus node acceleration in 25%, and no appreciable change in sinus node automaticity in 19%. Lange\(^1\) demonstrated that a drive of somewhat less than 15% above the extrinsic rate generally provoked a compensatory acceleration of the sinoatrial pacemaker that resulted in a temporary resetting of pacemaker discharge at a temporarily higher level. Herbell et al.\(^33\) recently demonstrated acceleration of the sinus pacemaker after slow-rate pacing at intervals slightly shorter than the spontaneous sinus cycle. They demonstrated that slow-rate atrial pacing failed to capture the pacemaker center but shortened action potential duration because of electrotonic interaction between the atrium and the sinus node. Acceleration of sinus automaticity in the intact human heart after overdrive suppression may be related to enhanced sympathetic tone, shifts in pacemaker sites, or, as suggested by Herbell et al.,\(^33\) to electrotonic interaction between atrium and sinus node that results in a shortened action potential. Whereas the former two explanations may be true at rapid heart rates, the latter may be true at slow heart rates.

**Postpacing change in pacemaker site.** In this study postpacing changes in pacemaker site were demonstrated in five patients after atrial pacing at one or more cycle lengths. Postpacing change in pacemaker site was demonstrated by the observation of a loss of primary negativity and a change in P wave morphology. The shift in pacemaker site returned to its original site within 4 to 10 beats. Although shifts in sinus pacemaker sites have been previously reported in animal preparations, this is the first time that such shifts have been directly demonstrated in man after overdrive pacing. Meck and Eyster\(^34\) were the first to demonstrate a reversible shift of the pacemaker by simultaneous measurements of electrical events from several sites and
Lewis et al.\textsuperscript{25} came to a similar conclusion by measuring conduction times. West\textsuperscript{13} was the first to demonstrate pacemaker shift at a cellular level by applying acetylcholine. Other investigators\textsuperscript{35–37} have induced pacemaker shifts in animal preparations by vagal stimulation, sympathetic stimulation, increasing extracellular concentration of potassium, inducing temperature changes, and reducing extracellular calcium. However, the observation of Lu et al.\textsuperscript{7} on the isolated cat preparation of the sinus node have relevant applications to our study in humans; they usually observed shifts in pacemaker site in their preparation after overdrive pacing. In their microelectrode studies, cells other than those from which recordings were made tended to initiate the first drive propagated response. Although in this human study we noted shifts in sinus pacemaker site in only five patients, these shifts may be more common than observed after overdrive pacing. Limitations in the number of recordings at multiple atrial sites in close proximity to the sinus node makes this possibility difficult to assess.

\textbf{Postpacing changes in sinus node conduction and automaticity in patients with SSS.} Sinoatrial conduction time for sinus beats before pacing was significantly longer in patients with SSS when compared with patients without SSS. This observation is in accordance with our previous findings and those of others.\textsuperscript{20} Of considerable importance are the following observations: (1) Sinoatrial conduction time for the first postpacing beat was longer in patients with SSS when compared with patients without SSS. (2) The abnormal corrected SNRTi (>450 msec), when corrected for the degree of conduction time prolongation for the first postpacing beat, became normal (i.e., <450 msec) in five of six patients. (3) Whereas postpacing depression of sinus node automaticity was seen in 44% of patients without SSS, it was seen in 71% of patients with SSS. (4) SNRTd was significantly longer in patients with SSS when compared with patients without SSS, although two of seven patients with SSS did not show sinus node depression after overdrive pacing. These findings suggest the following: (1) Prolongation of sinoatrial conduction time for the first postpacing beat is a physiologic phenomenon, but the degree of prolongation seems to be greater in patients with SSS. Studies in a larger number of patients are needed to further clarify this issue. (2) The inference of abnormal sinus node automaticity on the basis of corrected SNRTi in patients with SSS is incorrect since in the majority of patients with SSS abnormal SNRTi was the result of a marked prolongation of sinoatrial conduction time for the first postpacing beat. It seems reasonable to postulate that the long pauses seen in patients with the tachycardia-bradycardia syndrome are probably related to abnormalities in sinoatrial conduction. (3) Depression of sinus node automaticity after overdrive pacing seems to be more common in patients with than in those without SSS. (4) Although SNRTd was significantly longer in patients with SSS, further studies in a larger number of patients are needed to better qualify what constitutes an abnormal SNRTd.

Recently Asseman et al.\textsuperscript{39, 40} studied eight patients, each with a corrected SNRT of greater than 1500 msec, and recorded sinus node electrograms during postpacing atrial pauses. They noted that the pauses in these patients were the result of high-degree sinoatrial block. Of interest was their observation that these sinus node electrograms exhibiting sinoatrial block had cycle lengths similar to the basic cycle length, thus challenging the view that postpacing pauses are due to overdrive suppression of the sinus node. However, the possibility exists that in these patients there was no penetration of the sinus pacemaker as a result of retrograde sinoatrial block during pacing.\textsuperscript{41} Basal sinoatrial conduction time during sinus rhythm on the sinus node electrogram was not assessed in these patients. In addition, these investigators did not study the effect of overdrive pacing at different cycle lengths in normal subjects and patients with SSS in whom the corrected SNRT was less than 1500 msec. Furthermore, they did not establish that the presumed sinus activity during the long pauses actually drove the atrium during sinus rhythm or after overdrive pacing when sinoatrial conduction resumed. In this systematic study we entertained the possibility of sinoatrial block in only one of our patients who demonstrated a secondary pause; however, it should be noted that none of our patients had a corrected SNRTi of greater than 1500 msec. Nonetheless, as shown in this study and as inferred from the results of Asseman et al., prolongation of SNRTi in patients with SSS seems to result from a marked lengthening of sinoatrial conduction time after overdrive pacing and/or sinoatrial block.

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