Sinus Node Re-entry
A Mechanism for Supraventricular Tachycardia

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SUMMARY
Data in 20 patients with normal sinus rhythm who, following induced premature atrial beats (PABs), manifested re-entry in the region of the sinus node are presented. PABs at coupling intervals ranging between 230-335 msec were followed by sinus node re-entry (SNR). Several criteria were applied to diagnose SNR: the temporal sequence of atrial excitation, the intra-atrial conduction time, the shape and polarity of the P waves, and manifestation of re-entry independent of atrioventricular (A-V) nodal delays. In 18 patients SNR lasting for one to several beats was observed. In the remaining two patients sustained SNR was manifested as supraventricular tachycardia (SVT), with cycle lengths ranging between 320-500 msec, which persisted for several minutes prior to its termination by properly timed atrial stimuli. In one of the latter two patients sustained SNR and SVT were produced only after atropine administration. Sinus node re-entry could be elicited at will in a specific echo zone with a duration ranging between 10-170 msec. In some cases SNR was also observed during and on cessation of regular atrial pacing. The latter observation provides a possible explanation for the unexpected sinus node acceleration seen sometimes on termination of atrial pacing. It is demonstrated that SNR for a single beat may fallaciously simulate sinus node entrance block. Simultaneous occurrence of re-entry at multiple sites, i.e., the sinus node and the A-V node, with resultant fusion P waves is also demonstrated. This study provides another mechanism for the genesis of regular and irregular SVT. The analysis and localization of the re-entry circuit may prove to be of clinical and therapeutic significance in selected patients.

Additional Indexing Words:
Sinus node acceleration  Chaotic atrial rhythm  Sinus node entrance block
Fusion P waves  Atrial echoes

Paroxysmal Supraventricular Tachycardias (SVT) may be explained on the basis of either 1) a single automatic ectopic focus firing rapidly or 2) due to self-sustained re-entry circuits. In the last decade, evidence has mounted in favor of re-entry as the most likely mechanism of SVT. Several experimental studies, along with electrophysiological studies in man, have indicated that the atrioventricular (A-V) node is the site of re-entry during episodes of SVT. Although the role of "re-entry" as one mechanism of SVT may not be denied, it is possible that the A-V node is not the exclusive site for re-entry responsible for SVT.

The necessary conditions for re-entry include 1) unidirectional block of an impulse; 2) slow conduction; and 3) full recovery of excitability by the time the impulse returns to its point of origin. If these basic prerequisites for re-entry are met, then re-entry should be possible in any tissue. Recent experimental studies in isolated tissue and thoracotomized dogs and a few reports in man have suggested that the sinus node is a possible site for re-entry.

The purpose of this report is to present the author's observations in 20 patients in whom sinus node re-entry (SNR) could be initiated by atrial stimulation. SVT was observed in two patients and unsustained SNR lasting for one to several beats was seen in the remaining 18 patients.

Materials and Methods
The 20 patients in this study ranged in age from 49 to 85 years with a mean age of 65 years. The electrocardiographic findings, along with clinical data and the cardiac medications, are given in Table 1. In six of the 20 patients supraventricular arrhythmias had been observed in previous electrocardiograms. Paroxysmal atrial fibrillation or flutter was seen in five and atrial tachycardia was observed in one patient.

All patients were studied in the postabsorptive state and were premedicated with 100 mg of pentobarbital (Nembutal) administered intramuscularly 30 min prior to the study. Informed consent was obtained in every patient. A size 5F bipolar pacing electrode catheter (with ring elec-
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trodes 1 mm wide and 1 cm apart) was introduced percutaneously via a femoral vein and placed in the His bundle (BH) region. Another similar bipolar catheter or quadripolar catheter was introduced via an arm vein and a pair of electrodes was positioned in the high right atrium (HRA) in the region of the sinus node for recording and/or stimulation purposes.

Bipolar electrograms were recorded from the HRA and BH regions simultaneous with three standard ECG leads (leads I, aVF, V1). Bipolar electrograms were displayed at frequency settings of 40-500 Hz. All recordings were made at paper speeds of 100 mm/sec. The blood pressure was monitored throughout either with an arterial needle or by blood pressure cuff. His bundle recordings were obtained and validated as described previously.19,20 Sinus node recovery time (SRT) was measured during atrial pacing (AP)21. Premature atrial beats (PABs) were induced by stimuli 2 msec in duration and twice the diastolic threshold. The high right atrial electrogram (from the region of the sinus node) triggered the sweep of an oscilloscope which, in turn, activated the stimulator. Stimulation was delivered through a specially designed electronic circuit which permits stimulation and recordings through the same set of electrodes, thus obviating a need for an extra set of electrodes or catheter. The PABs were induced after every 12th sinus cycle. The entire atrial cycle was scanned by the placement of progressively more premature beats at 10-20 msec decrements until the atrial effective refractory period was measured. The PABs were usually induced from HRA. In five patients the site of stimulation in the right atrium was changed to evaluate its effect on the generation of "sinus node re-entry" and no difference was observed. In view of the latter and similar observations reported by Pauley et al., the site of stimulation was not changed in the other 15 patients.18 In three patients the sequence of PABs was repeated after intravenous administration of atropine (2 mg).

The following events were measured in milliseconds during each study:
1) A1-A2 = Duration of the spontaneous atrial (A) cycles during sinus rhythm prior to the introduction of a PAB, i.e., the dominant cycle.
2) A1-P1 = This was measured from the atrial electrogram of the last sinus beat to the pacing impulse (P1).
3) P1-A1 = This was measured from the pacing impulse (P1) to the first post-extra systolic atrial electrogram.
4) A2-A3 = The curtailed cycle. Interval between the preceding sinus atrial electrogram (A1) and the premature atrial electrogram (A2).
5) A3-A4 = The atrial return cycle. The interval from the premature atrial electrogram (A2) to the first post-extra systolic atrial electrogram (A3).
6) Second and third post-extra systolic atrial beats were also measured.

Results

Criteria for Sinus Node Re-entry

The following criteria were utilized to diagnose the sinus node re-entry and an example is shown in figure 1.

1) The sequence of atrial activation in the re-entrant beats was similar to that of the control sinus beats, i.e., from HRA in the region of the sinus node to the low right atrium (RA) in the area of the A-V junction. In addition, the intra-atrial conduction time from high right atrium to low right atrium was almost identical to that of sinus beats (panel A).
2) The polarity and the shape of the re-entrant P waves was almost identical in all the three ECG leads (LI, aVF, V1), representing the three planes, to that of the control sinus P waves (Panel A).
3) The re-entry phenomenon was observed at specific coupling intervals (A1-A2) within a specific portion of the sinus cycle and outside the effective refractory period of the atrium. Under stable basal conditions, sinus node re-entry was reproducible at will.
4) A further increase in prematurity of the PABs resulted in the abolition of re-entry and the return cycle lengthened. The latter was longer than the dominant cycle and almost equal to the return cycle seen on either side of the zone of re-entry (fig. 2). This indicates that the capacity of the premature impulse to enter into and pass out of the sinus node was intact in the re-entry zone and that the shortened return cycles were not due to sino-atrial entrance block.
5) Re-entry was reproducible despite a change of site in right atrial stimulation.
6) The sustained sinus node re-entry, manifested as SVT, could be terminated by properly timed atrial stimulation.
7) Manifestation of sinus node re-entry was independent of A-V nodal delays.
8) If the above criteria are met, SNR may be present when a return cycle is shorter than the dominant cycle, irrespective of the sum of the curtailed cycle (CC) and RC.

It should be pointed out that the above criteria and our data suggest that the re-entrant beat originates from the high right atrium in the region of the sinus node. The limitations of the recording techniques in man do not permit a precise localization of the re-entrant circuit in the sinus node region, i.e., determination of whether the re-entrant pathway involved the sinus node per se or the adjacent fibers or the approaches of the intra-atrial tracts to the sinus node. However, the findings in these cases suggest that the sinus node is the most likely site for re-entry. Other possibilities such as local atrial re-entry and atrial vulnerability have been excluded by changing the site of RA stimulation and because of the occurrence of re-entry outside the effective refractory period of the atrium respectively.

On the basis of the above criteria 20 patients in this
### Table 1

**Clinical and Electrophysiological Data in Patients with Sinus Node Re-entry**

<table>
<thead>
<tr>
<th>Case no.</th>
<th>Age &amp; sex</th>
<th>Average sinus cycle (A—A)</th>
<th>SNR Return cycle (A—A)</th>
<th>Subsequent cycles</th>
<th>Pause on cessation of SNR</th>
<th>Atrial eff. ref. period (A—PI)</th>
<th>Conduction abnormalities</th>
<th>Atrial arrhythmias</th>
<th>Symptoms</th>
<th>Cardiac diagnosis</th>
<th>Daily drugs</th>
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<tr>
<td>1</td>
<td>60 M</td>
<td>970</td>
<td>240—260</td>
<td>2</td>
<td>470—750</td>
<td>790</td>
<td>1005</td>
<td>220</td>
<td>LAD</td>
<td>—</td>
<td>Ch. Lung Disease</td>
</tr>
<tr>
<td>2</td>
<td>56 M</td>
<td>900</td>
<td>340—420</td>
<td>1</td>
<td>710—610</td>
<td>1000</td>
<td>290</td>
<td>At. Fib. PABs</td>
<td>Dizziness</td>
<td>Syncope</td>
<td>Old M.I.</td>
</tr>
<tr>
<td>3</td>
<td>63 M</td>
<td>800</td>
<td>280—450</td>
<td>1</td>
<td>520—400</td>
<td>800</td>
<td>240</td>
<td>LAD</td>
<td>Angina</td>
<td>Old M.I.</td>
<td>Digoxin 0.25 mg</td>
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<tr>
<td>4</td>
<td>69 M</td>
<td>1170</td>
<td>270—260</td>
<td>6</td>
<td>260—365</td>
<td>270</td>
<td>1340</td>
<td>205</td>
<td>LAD</td>
<td>Dizziness</td>
<td>Old M.I.</td>
</tr>
<tr>
<td>5</td>
<td>76 F</td>
<td>800</td>
<td>240—290</td>
<td>1</td>
<td>370</td>
<td>1065</td>
<td>220</td>
<td>RAD</td>
<td>Palpitations</td>
<td>Old M.I.</td>
<td>Pronestyl 1 g</td>
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<tr>
<td>6</td>
<td>75 M</td>
<td>910</td>
<td>300—310</td>
<td>5</td>
<td>435—675</td>
<td>650</td>
<td>1125</td>
<td>250</td>
<td>At. Fib.</td>
<td>Syncope</td>
<td>Old M.I.</td>
</tr>
<tr>
<td>7</td>
<td>60 M</td>
<td>1200</td>
<td>260—310</td>
<td>3</td>
<td>770—835</td>
<td>420</td>
<td>1470</td>
<td>250</td>
<td>Syncope</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>8</td>
<td>78 M</td>
<td>1980</td>
<td>360—380</td>
<td>2</td>
<td>490</td>
<td>460</td>
<td>2050</td>
<td>320</td>
<td>LAD</td>
<td>Dizziness</td>
<td>—</td>
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<tr>
<td>9</td>
<td>49 F</td>
<td>705</td>
<td>270—290</td>
<td>1</td>
<td>520</td>
<td>850</td>
<td>220</td>
<td>At. Fib. PABs</td>
<td>RHD</td>
<td>Mit. Ins.</td>
<td>—</td>
</tr>
<tr>
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<td>65 M</td>
<td>1300</td>
<td>300—320</td>
<td>2</td>
<td>380—1150</td>
<td>1300</td>
<td>270</td>
<td>Angina</td>
<td>Old M.I.</td>
<td>Diabetes</td>
<td>—</td>
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<tr>
<td>11</td>
<td>75 M</td>
<td>700</td>
<td>295—365</td>
<td>1</td>
<td>400—500</td>
<td>1000</td>
<td>250</td>
<td>LAD PABs</td>
<td>Dizziness</td>
<td>—</td>
<td>Digoxin 0.125 mg</td>
</tr>
<tr>
<td>12</td>
<td>85 M</td>
<td>770</td>
<td>300—270</td>
<td>1—2</td>
<td>315—270</td>
<td>470</td>
<td>920</td>
<td>245</td>
<td>RBBB</td>
<td>Syncope</td>
<td>—</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>270—265</td>
<td></td>
<td></td>
<td>590</td>
<td>8VT</td>
<td>+ LAD</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>13</td>
<td>60 F</td>
<td>850</td>
<td>230—370</td>
<td>1</td>
<td>475—600</td>
<td>1200</td>
<td>200</td>
<td>LBBB</td>
<td>Dizziness</td>
<td>—</td>
<td>—</td>
</tr>
</tbody>
</table>
The phenomenon of "sinus node" re-entry either unsustained, i.e., single to a few beats, or sustained. The latter was manifested as supraventricular tachycardia (SVT).

In this study the following additional observations were made:

1) During scanning of the atrial cycle with PABs the return cycle (A2-A1) was unexpectedly shortened due to sinus node re-entry and was most commonly shorter than and rarely equal to the dominant cycle (A1-A1). In addition, the sum total of the curtailed cycle and the return cycle (A1-A1 + A2-A3) was either shorter or longer than the dominant sinus cycle (A1-A1). For example, figure 1, panel A, shows that the dominant cycle (905 msec) is longer than the sum of the curtailed cycle and return cycle (355 + 435 = 790 msec) whereas in figure 2, panel B, the sum of the curtailed and the return cycle (270 + 660 = 930 msec) is longer than the dominant cycle (700–790 msec).

2) In case of re-entry for more than one beat the subsequent post-extra systolic beats (second, third, ...) also showed a shorter cycle length than the control sinus cycle or the DC (fig. 1, panel A).

3) The re-entrant circuit in the sinus node region and the cycle length of the last re-entrant beat(s) determine the duration of the pause on spontaneous termination of re-entry and preceding the return to control sinus rhythm. The latter pause was usually longer (fig. 1, panel B) and occasionally equal to the dominant or control sinus cycle. Its mechanism may be explained as follows: On cessation of re-entry the last re-entrant beat, because of its cycle length being shorter than the dominant cycle, produces premature depolarization of the sinus node, giving an effect similar to that of a PAB on the sinus node. For example, in figure 1 the induced PAB in Panel A is followed by five sinus node re-entrant P waves (with a cycle length shorter than the dominant cycle). The last re-entrant P is shown in panel B (first P wave) and, due to cessation of SNR, is followed by an interval of 1125 msec (longer than the dominant cycle which is 905 to 930 msec). The latter is similar to the longest return cycle (1130 msec) seen following a PAB in this patient. A long pause on cessation of sinus echoes is indicative of sinus node penetration and its resetting. The long pause suggests the extension of the echo pathway into the sinus node if the other criteria for SNR are met.

4) Coupling Intervals and Zone of Re-entry. During induced PABs atrial echoes with sustained or unsustained SNR were observed at specific coupling (A1-A2) intervals (range 230–535 msec) (fig. 2). For example, in Case 20 induced PABs at coupling intervals (A1-A2) ≥ 350 msec failed to manifest re-entry (fig. 2).
Sinus node re-entry (SNR). Simultaneous recordings of bipolar electrograms (BE) from high right atrium (RA) and the A-V junction (BH) with three standard ECG leads (L-I, Vf, V1). An induced (PI) premature atrial beat (PAB) is followed by a shortened return cycle (A1-A2 = 435 msec). The time (from high RA to the A-V junction) and the shape of the post-extra systolic P wave (*) is almost identical to that of the sinus P waves. The conjoined cycle (A1-A2 + A2-A3 = 355 + 435 = 790 msec) is shorter than the dominant cycle (A1-A2 = 905 msec). This is due to sinus node re-entry (SNR) which shortens the cycle length of the subsequent apparent "sinus" P waves (650, 675, 835, 750 msec) until spontaneous cessation of re-entry occurs and is indicated by a long pause of 1125 msec (panel B, between first and second P waves). A = bipolar atrial electrogram. BH = bipolar His bundle electrogram. Time lines in this and subsequent figures are at 1 sec intervals.

3, panel A). However, as the coupling interval was shortened to 335 msec, sinus node re-entry for three consecutive beats was observed (panel B). A further progressive shortening of the coupling interval resulted in an initial decrease in the number of re-entry beats (panel C), and eventual failure to elicit re-entry despite atrial depolarization by the PABs. The zone of SNR was thus delineated and was found to be constant in a given patient. However, the zone of re-entry varied from patient to patient, ranging from 10 to 170 msec in width. The lower limits of SNR zone (or the shortest coupling interval at which re-entry could be elicited) usually preceded the atrial effective refractory period (at double the diastolic threshold) by ≥ 40 msec (table 1).

5. Number of Re-entry Beats. In 18 of the 20 patients unsustained SNR for one to five consecutive beats was observed during control conditions. SNR for a single beat only was exhibited in 11 of the 18 patients. The atrial cycle length of the sinus node re-entry beats ranged between 260 to 840 msec and usually progressively lengthened prior to spontaneous cessation of SNR.

6) Effect of Atropine. Intravenous atropine was administered in three patients. This resulted in abolition of SNR in two patients. However, one patient (Case 20) who initially exhibited unsustained re-entry (fig. 3) developed sustained SNR after atropine, manifested as supraventricular tachycardia (SVT) (fig. 4). The latter could be induced at specific coupling intervals ranging between 310 to 270 msec, whereas PABs outside this specific zone either completely failed to elicit re-entry or showed SNR only for a single beat. The sustained SNR was reproducible at will within the specific zone. The resultant SVT, after persisting for periods of 2 to 5 minutes, was terminated by properly timed atrial stimulation. Terminations of bouts of SVT due to SNR were followed by the spontaneous sinus escape beats at intervals (695 msec) almost identical to the sinus node recovery time.

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Specific zone for sinus node re-entry. Panel A) An induced PAB at a coupling interval of 425 msec is followed by a return cycle (940 msec) longer than the dominant cycle (760 msec). Panel B) A PAB with a greater prematurity (coupling interval = 270 msec) is followed by SNR for a single beat. The return cycle is shorter (660 msec) than the dominant cycle and the subsequent cycle (890 msec) is longer than the dominant cycle. Panel C) A further shortening of the coupling interval (250 msec) exhibits a return cycle longer than the dominant cycle and equal to that seen in panel A. These findings exclude sinus node entrance block as a possible mechanism for a shortened return cycle in panel B. Abbreviations: SNR = sinus node re-entry.

7) SVT Due to Sustained SNR. In two of the 20 patients SVT was manifested due to sustained SNR. In one (Case 20) of these patients the phenomenon of SNR was seen only after atropine administration (discussed above in detail). The resultant SNR and SVT initially showed fluctuations in the length of atrial cycles (ranging from 320 to 500 msec) for periods of 15 to 30 seconds before stabilizing at a fixed cycle length. However, sometimes these fluctuations in atrial cycle length persisted for the periods of observation up to 5 minutes. In the other patient (Case 12) sustained SNR was manifested with PABs during control basal conditions and the resultant SVT stabilized to a fixed cycle length (500 msec) within 2 seconds.
Showing that SNR is manifested only when PABs are induced during a specific portion of sinus cycle or zone of re-entry. Panel A) A PAB at coupling interval (A-PI) of 375 msec is followed by a return cycle (PI-A = 990 msec) longer than the dominant cycle (A-A = 625-640 msec). Panel B) A properly timed PAB (A-PI = 335 msec) is followed by three consecutive sinus node re-entrant beats (*). Panel C) A slightly more premature PAB (A-PI = 310 msec) but still within the zone of re-entry elicits only a single sinus node re-entrant A wave. A further increase in prematurity failed to elicit re-entry.

The control dominant cycle (panel A). The latter P wave is most probably the result of SNR and is almost similar in shape to the control sinus P waves with identical sequence of atrial activation (high right atrium to low right atrium) and intra-atrial conduction times. In this instance, similar to properly timed PABs, the very last paced atrial impulse is probably responsible for elicitation of SNR. In figure 6, panel C, the subsequent P waves, as well as the first spontaneous P, are in all probability the result of persistence of the sinus node re-entrant circuit; this is suggested because of an acceleration in sinus rate for

(figure 5). The SVT could be terminated by a single PAB.

8) Atrial Pacing and SNR. In several patients during regular atrial pacing unsustained sinus node re-entry for one to two consecutive beats was observed (fig. 6, panel B). The SNR was not sustained probably because of interruption of the re-entrant circuit by continuous atrial stimuli. In some cases sinus node re-entrant beats were also manifested immediately following cessation of atrial pacing. Figure 6 (panel C) shows that the last paced P wave (atrial pacing at a cycle length of 400 msec) is followed by a spontaneous P wave at an interval of 620 msec, which is shorter than
several beats before returning to control levels (fig. 6, panel A). It may be argued that the acceleration in sinus rate on cessation of atrial pacing is due to enhanced sympathetic activity. This possibility is unlikely because a) similar shortening of “sinus” cycles was observed following a single PAB (fig. 7, panel B), and b) sinus echoes (cycle length = 400–440 msec) were observed even during atrial pacing at 120 beats/min. Two seconds later cessation of atrial pacing exhibited a normal sinus node recovery time (SRT) (1150 msec) and a return to control sinus cycle length (910 msec) without any acceleration (fig. 6, panel B). In this case although SNR is the most likely mechanism, other possibilities cannot be definitely excluded.

9) Simulation of Interpolated Beats. Occasionally, an induced PAB, when followed by a single sinus node re-entrant beat, may fallaciously appear to be interpolated. For example, in a patient the PABs at coupling intervals (A-P1) of 350 and 310 msec were followed by short return cycles (fig. 7, panel A). The sum total of curtailed and return atrial cycles (930 msec) was almost identical to the dominant cycle (935 to 955 msec) and hence was compatible with the diagnosis of interpolated beats. However, in figure 7, panel A, a slight shortening of the subsequent sinus cycle to 810 msec makes one suspicious of that interpretation. Further studies did reveal that sinus node re-entry was the underlying mechanism and this became obvious as the PABs with additional shortening of the coupling intervals were induced; not only the sum total of the curtailed cycle and the return cycle exceeded the dominant cycle but also SNR persisted for more than one beat (fig. 7, panel B). The latter simulated an apparent acceleration of the sinus node by the PABs. The less premature PAB in figure 7 (panel A) was not interpolated but appeared so, due to occurrence of a single sinus node re-entrant beat at a fortuitously appropriate interval.

10) SNR Independent of A-V Nodal Delays. During the early portions of the sinus cycle more than one conducting tissue — sinus node, the atrium, and/or the A-V node — may be partially or completely refractory. The early PABs which usually result in re-entry
in the sinus node region arrive at the A-V node concurrent with the relative or absolute refractory period of the A-V node. Although unrelated to SNR, the A-V nodal (A-H) conduction time coincidently lengthens during these early PABs. For example, the absence of any role by A-V nodal delays in generation of SNR was demonstrated in Case 20. Initially the PABs with A-H time ranging between 150–175 msec (or even up to 320 msec) failed to elicit SNR (fig. 3, panel A). However, following atropine administration, the PABs with similar A-H intervals (145–160 msec) repeatedly resulted in SNR (fig. 4).

11) Multiple Sites of Re-entry. During the early portion of the sinus cycle a stage for re-entry may be set in several regions, either singly or simultaneously, as more than one of the conducting tissues may become refractory concomitantly. Such a phenomenon was exhibited by Case 20. In this patient, figure 3 (panels B and C) exhibits sinus node re-entrant beats with sequence of activation from high to low RA. However, occasionally atrial echoes due to A-V nodal re-entry were also manifested. In figure 8 (panel A) a blocked PAB at a coupling interval (A-PI) of 310 msec is followed by an A-V nodal re-entrant beat. In the latter beat the P wave is inverted in lead aVF and the sequence of atrial activation is from low to high right atrium. Panel B of the same figure is of additional interest where a PAB (A-PI = 325 msec) is followed by a re-entrant P wave with an intermediate shape and simultaneous activation of high and low right atrium. In all probability this is due to two simultaneous but independent sites of re-entry, i.e., the sinus node and the A-V node, with a resultant fusion P wave. It is to be pointed out that the possibility of a third site (besides the S-A node and the A-V node) for re-entry although unlikely cannot be completely excluded in this patient.

None of the 20 patients developed atrial fibrillation, atrial flutter, or any other complications during or following the stimulation studies.

Discussion

This study demonstrates that properly timed PABs or atrial pacing may result in single or multiple, unsustained or sustained, atrial echoes due to re-entry in the region of the sinus node. The data obtained in this study, despite the lack of precise localization of the re-entrant circuit within the region of the sinus node, demonstrate initiation of a sustained supraventricular tachycardia due to SNR, a phenomenon hitherto not
demonstrated. There is little clinical information available on sinus node re-entry in man. However, SNR has been well documented by several experimental studies in isolated tissue or intact animals. These findings of SNR in man are in agreement with the latter and the supporting criteria have already been discussed in detail above under Results.

Various prerequisites essential for the development of sinus node re-entry have been previously demonstrated by several investigators. For example;  
1) Slow propagation within the sinus node has been shown in experimental studies. In addition, these studies have demonstrated that with a PAB the conduction velocity may be reduced strikingly during impulse transmission in the sino-atrial tissue, sinus node, or the atrium.  
2) Similarly, it has also been demonstrated that the
effective refractory period of the sinus node may exceed that of the surrounding atrial tissue.14, 31, 29, 30

3) Another recent study has indicated that re-entry may even result in the absence of any anatomical obstacle.27 A functional obstacle transiently may be manifested due to a PAB as a result of slowing of conduction and aberrant atrial excitation as compared to that of the regular beats, and thus, can set the stage for the development of re-entry.

Following a PAB the shortening of return cycle may be the result of several other mechanisms besides the SNR. The following possibilities can be entertained and may be excluded as follows:

a) The return cycle may be shortened when a PAB is interpolated due to sinus node entrance block. In the latter case, the conjoined cycle (A1-A2 + A2-A3) is equal to the dominant cycle. However, during SNR for a single beat, the conjoined cycle (curtailed cycle plus return cycle) is usually not identical to the dominant cycle and only rarely may be equal. In addition, a further increase in the prematurity of the PABs (outside the zone of re-entry) is usually followed by a return cycle longer than the dominant cycle (fig. 2).

b) Re-entry at other sites, especially A-V nodal, may be excluded by the sequence of atrial activation. Independent re-entry within the atrium alone, though possible, is less likely: 1) in the absence of any demonstrable intra-atrial conduction delays; 2) with a sequence of atrial activation identical to that of the sinus beats despite atrial stimulation at sites other than the high RA.16, 27 Figure 7 (panel B) shows re-entry with earliest activation in high right atrium despite stimulation in mid right atrium.

c) Repetitive firing due to stimulation during the atrial "vulnerable period" may be excluded as the phenomenon of SNR occurred during a specific zone of sinus cycle outside atrial effective refractory period.31, 32 Its disappearance with an increase in prematurity of the PABs is additional evidence against atrial vulnerability as a cause for a shortened return

Figure 7

Sinus node re-entry for a single beat following a PAB may simulate an interpolated beat. Panel A) A PAB (A-PI = 350 msec) is followed by a shortened return cycle and the conjoined cycle (930 msec) is almost identical to the dominant cycle (935 msec). This is compatible with an interpolated PAB. Panel B) A PAB with increased prematurity (A-PI = 280 msec) is followed by a return cycle shorter than the dominant cycle but with a longer conjoined cycle (1050 msec) and indicates sinus node penetration. This suggests that the less premature atrial beat in panel A was probably not truly interpolated but appeared so due to SNR for a single beat only. A shortening of subsequent cycles suggests persistence of SNR. In this case the site of stimulation was the mid right atrium (MRA). HRA = high right atrium.
cycle (fig. 2). Furthermore, during atrial vulnerability the cycle is extremely short: less than 200 msec or 20–30% of sinus cycle.

d) Enhancement of automaticity following a PAB as suggested by Lewis has been excluded by a recent study using microelectrode recording techniques. Furthermore, the following observations are additional evidence against acceleration of automaticity: 1) a specific narrow zone for re-entry; 2) spontaneous cessation of accelerated beats, a pause greater than the dominant cycle (fig. 1); 3) demonstration of a sustained SVT and initial oscillations in cycle length; 4) a gradual increase in cycle length during the initial phase of re-entry and prior to its spontaneous cessation or stabilization at a fixed cycle length.

e) It may be argued that a PAB may discharge only a portion of the S-A node and the adjacent non-discharged fibers may be influenced electrotonically and result in premature discharge of the protected sinus node fibers. A shortening of a single return cycle may be explained in this manner, however, this hypothesis fails to support multiple accelerated sinus beats and especially sustained SVT due to SNR.

Studies by Klein et al. utilizing early PABs in isolated rabbit atrial tissue have demonstrated shortening of the sinus node return cycle which these authors classified into types I and II. In type II responses, the conjoined atrial cycle was always longer than the dominant cycle. The atrial return cycle, although shortened by early PABs, was usually longer than the dominant cycle (figs. 2 and 4, ref. 22) and occasionally shorter than the dominant cycle by no more than 50 msec. In all of the present cases the atrial return cycle was markedly shorter than the dominant cycle and in some cases even the conjoined cycle was less than the dominant cycle (fig. 1). Accordingly, the present data are not similar to type II and especially SNR for multiple beats or sustained SVT cannot be explained by the type II responses. Furthermore, in the present study the PABs which manifested SNR occurred early in the dominant cycle and the shortening of return cycle was much more precipitous. The latter response was similar to the type I responses and SNR documented by Klein et al. during microelectrode recordings. The role of vagal tone in initiation and termination

Figure 8

Shows fusion P waves due to simultaneous occurrence of re-entry at two independent sites (the same patient who showed SNR in figure 3). Panel A) A PAB (A-P1 = 310 msec) is followed by an atrial echo probably due to A-V nodal re-entry as the sequence of atrial activation is reversed (from low right atrium to high right atrium) and the P wave is inverted in ECG lead aVr. Panel B) Another PAB (A-P1 = 325 msec) is followed by an atrial echo with a P wave the shape of which is somewhere between that of the A-V nodal echo (panel A) and the spontaneous sinus or sinus node re-entrant P wave (seen in figs. 3 and 4). In addition, the atrial activation occurs simultaneously in the high and low right atrium.
of SNR is controversial.\textsuperscript{15, 16} Pauley and associates observed that vagal stimulation abolished SNR.\textsuperscript{16} On the contrary, others have indicated that SNR may be manifested by vagal stimulation.\textsuperscript{13, 15} The observations of both groups are correct. Han et al. have suggested that the degree of vagal tone is critical, as appropriate levels may facilitate induction or abolition of SNR.\textsuperscript{14} The latter viewpoint is supported by our findings. With administration of atropine SNR was abolished in two of our patients and facilitated in the third (figs. 3 and 4). This is obvious in view of the following varied effects of vagal stimulation, e.g.: a) sinus node refractory period is lengthened; b) during SNR, the return cycle or echo circuit time is lengthened; c) atrial refractory period is abbreviated.\textsuperscript{15}

The above considerations suggest that a properly timed PAB under proper settings may initiate a re-entry circuit involving the sinus node and the atrium. Accordingly, a PAB arrives at the sinus node region during the relative refractory period of the node, fails to engage one margin of the node, enters at another site and travels slowly through the relatively refractory sinus node tissue, and by the time it emerges, the atrium has recovered. Our data also suggest that SVTs, with fluctuating atrial cycle lengths, may be the result of sino-atrial reciprocation with a variable re-entrant circuit which may be interrupted by properly timed atrial stimulus(i). In some cases chaotic atrial rhythms or atrial dissociations may be explained on the basis of this mechanism.

It is suggested that the site(s) of re-entry circuit may vary at different times and with changes in prematurity of the PABs or variations in sympathetic or parasympathetic tone. Therefore, the localization of re-entrant circuit and differentiation between SNR and A-V nodal re-entry may not be possible on the basis of standard ECG or stimulation studies alone but also requires analysis of the sequence of atrial activation during SVT also. The latter view is further reinforced by the demonstration of simultaneous occurrence of re-entry at multiple sites in the same patient (fig. 8). It is to be pointed out that a mere demonstration of A-H prolongation is not a sufficient evidence to indicate A-V node as the site of re-entry as concomitant A-V nodal delays may be fortuitously observed even when re-entry is occurring elsewhere.\textsuperscript{11} The PABs which result in SVT due to SNR simultaneously arrive at the A-V node during its relative refractory period and thus are transmitted to the ventricles with an increased A-V nodal delay. The zone of SNR and the relative refractory periods of the A-V node usually overlap.

Previous workers have reported the observation of paradoxical acceleration in the sinus rate following overdrive suppression by atrial pacing or following a PAB with sinus node entrance block.\textsuperscript{30, 34} It has been suggested that the increase in rate is neurogenically mediated.\textsuperscript{30} Although it is probable but highly unlikely that the centrally mediated neurogenic increase not only occurred rarely but was limited only to a single or a few beats, the most likely explanation for this phenomenon lies in local mechanisms. Present data suggest that these unexpected accelerations of sinus rate, in all probability, are the result of sinus node re-entry (figs. 6 and 7). Our previous observations that on cessation of atrial pacing the maximum sinus node recovery time or depression was seen not in the first but in the second or third spontaneous sinus cycles may also be explained on this basis.\textsuperscript{31}

This study indicates that in some patients following a PAB sinus node re-entry for a single beat may simulate sinus node entrance block (fig. 7, panel A). Accordingly, it is suggested that an alternate explanation for some of the apparent examples of sinus node entrance block published previously by others may alternately be explained on the basis of sinus node re-entry.\textsuperscript{30} A study by Goldreyer et al. probably shows such an example (ref. 30, fig. 6, panel B). In the latter figures the conjoined cycle (430 + 440 = 870 msec), although identical to the dominant cycle, is followed by a shortened second post-extra systolic sinus cycle (750 msec). In addition, there is a definite shortening of intra-atrial conduction time (high to low right atrium) and a change in the shape of the post-extra systolic sinus P waves. The changes pointed out above are suggestive of SNR and should not have occurred with sinus node entrance block. Similarly, another illustration (ref. 30, fig. 3, panel D) in the same study is suggestive of SNR due to a shortening of the conjoined cycle to 93% as compared to the dominant cycle.

Isolated cases of interpolation of PABs or atrial parasystole have been reported by others.\textsuperscript{35, 36} In these cases the conjoined cycle (P-P'-P) containing the "interpolated" beats were longer than the dominant cycle by 80–340 msec (ref. 35) and 170 to 240 msec (ref. 36). The increase in conjoined cycle was speculated to be secondary to a delay in sino-atrial conduction of the post-extra systolic sinus beat due to the concealed atrio-sinus conduction of the PAB which failed to completely penetrate the sinus node and was interpolated. We offer an alternate and more plausible explanation to explain the records in their studies. It is suggested that the latter ECGs are not compatible with interpolation but are probably examples of SNR for the following reasons: a) systematic stimulation studies in man in this laboratory and by others have indicated that during the interpolated PABs the conjoined cycle is identical to the dominant cycle. The post-extra-systolic sinus P appears on time
and indicates the absence of any increase in sino-atrial conduction time. This is further supported by a recent experimental study with microelectrode recordings. The lengthening of the P-P₁-P intervals, especially of the large magnitude (up to 340 msec) seen in the reports by Langendorf et al. and Fleischmann, has not been seen in any systematic study; b) some of their records show a slight variation in the shape of the post extra-systolic wave and c) the PABs with increased prematurity (or shorter P-P₁-P intervals), were followed by a longer re-entry cycle, greater than the dominant cycle, and indicate complete penetration and depolarization of the sinus node. The above discussion suggests that in the latter reports the PABs were not truly interpolated and the post-extra-systolic P was in all probability the result of SNR and not due to spontaneous sinus node discharge.

This study provides another mechanism for the genesis of regular or irregular supraventricular tachycardias. The analysis and localization of the re-entry circuit may be of clinical and therapeutic significance especially in patients 1) with SVT being considered for ventricular demand pacemaker for termination of the bouts of SVT by retrograde penetration of the A-V node; 2) with Wolff-Parkinson-White syndrome and SVT under consideration for surgical ablation of the normal or the anomalous pathway.

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