Cardiac Conduction in Patients with Symptomatic Sinus Node Disease


SUMMARY
Cardiac conduction was investigated at the time of pacemaker insertion in 15 patients with symptomatic sinus node disease. Techniques included recording of His bundle potentials, atrial pacing at various heart rates, and atropine administration. Atrioventricular (AV) conduction was impaired in eight patients who manifested one or more of the following: P-R prolongation, P-H prolongation, and development of second degree AV block with atrial pacing at heart rates below 130 beats/min. Five patients had intraventricular conduction defects diagnosed electrocardiographically; none of these had H-Q prolongation. One of these five, with left bundle-branch block, subsequently developed complete heart block and had a calcific lesion involving the His bundle. Depression of cardiac automaticity was noted in four patients, with asymptomatic periods greater than 2 sec after sudden cessation of atrial pacing at rates of 100–160 beats/min. Responses to 1 mg of intravenous atropine were varied, but no patient developed sinus rates greater than 90 beats/min, suggesting the presence of primary sinus node dysfunction.

In conclusion, abnormalities of conduction and automaticity in specialized tissue in addition to the sinus node are common in patients with symptomatic sinus node disease. These abnormalities should be recognized when present, so that the ideal site for permanent pacing may be chosen.

Additional Indexing Words:
AV block  Atrial pacing  Ventricular pacing  Sick sinus node
Automaticity  Adams-Stokes syndrome

VENTRICULAR pacing has been commonly utilized in the management of bradyarrhythmias occurring in patients with symptomatic sinus node disease.1-4 Recently, atrial pacing has also been recommended in this disorder so that the hemodynamic benefits of synchronous atrial contraction may be preserved.5-8 However, the success of atrial pacing depends in part upon normal conduction distal to the pacing site.

We have studied cardiac conduction at the time of pacemaker insertion in 15 patients with symptomatic sinus node disease. Techniques utilized have included atrial pacing, ventricular pacing, His bundle recording, and atropine administration. A high incidence of atrioventricular (AV) conduction defects have been found, as well as occasional defects in intraventricular conduction. The results suggest that great care should be taken in choosing the site of pacing in patients with sinus node disease.

Methods
Patient Selection
Fifteen patients were studied, all of whom had...
<table>
<thead>
<tr>
<th>Patient</th>
<th>Age (yr)</th>
<th>Sex</th>
<th>Drugs</th>
<th>Arrhythmias prior to pacing</th>
<th>Heart rate (beats/min)</th>
<th>P-R (sec)</th>
<th>QRS (sec)</th>
<th>Other</th>
<th>Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 J.G.</td>
<td>59</td>
<td>M</td>
<td>—</td>
<td>SB</td>
<td>38–60</td>
<td>0.16</td>
<td>0.06</td>
<td>—</td>
<td>Dizziness, syncope</td>
</tr>
<tr>
<td>2 H.D.</td>
<td>74</td>
<td>F</td>
<td>—</td>
<td>SW, S Ar, JR, S Bl</td>
<td>10–40</td>
<td>0.20</td>
<td>0.10</td>
<td>Inc LBBB</td>
<td>Dizziness, syncope</td>
</tr>
<tr>
<td>3 M.M.</td>
<td>62</td>
<td>F</td>
<td>—</td>
<td>CSR, SB, PAF</td>
<td>40–60</td>
<td>0.14</td>
<td>0.08</td>
<td>—</td>
<td>Dizziness, syncope, seizures</td>
</tr>
<tr>
<td>4 J.E.</td>
<td>60</td>
<td>M</td>
<td>—</td>
<td>SB</td>
<td>38–50</td>
<td>0.20</td>
<td>0.08</td>
<td>—</td>
<td>Dizziness</td>
</tr>
<tr>
<td>5 R.C.</td>
<td>69</td>
<td>M</td>
<td>—</td>
<td>S Ar, JR, NSR</td>
<td>32–120</td>
<td>0.16</td>
<td>0.14</td>
<td>Comp LBBB</td>
<td>Syncope</td>
</tr>
<tr>
<td>6 C.P.</td>
<td>64</td>
<td>M</td>
<td>—</td>
<td>SB, S Bl</td>
<td>32–62</td>
<td>0.16</td>
<td>0.08</td>
<td>—</td>
<td>Weakness, dizziness</td>
</tr>
<tr>
<td>7 M.L.</td>
<td>73</td>
<td>F</td>
<td>—</td>
<td>SB, PAT, S Ar</td>
<td>45–160</td>
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<td>0.08</td>
<td>LAD</td>
<td>Weakness, syncope</td>
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<tr>
<td>8 E.J.</td>
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<td>M</td>
<td>—</td>
<td>CSR, SB</td>
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<td>0.09</td>
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</tr>
<tr>
<td>9 L.B.</td>
<td>57</td>
<td>F</td>
<td>—</td>
<td>SB, S Ar, PAF</td>
<td>40–58</td>
<td>0.22</td>
<td>0.08</td>
<td>LAD</td>
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<td>F</td>
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<td>SB, S Ar, JR</td>
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<td>0.08</td>
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<tr>
<td>11 S.T.</td>
<td>69</td>
<td>F</td>
<td>Aldomet (250 mg q.i.d.)</td>
<td>SB, S Ar, JR</td>
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<td>—</td>
<td>Dizziness, dyspnea, fatigue</td>
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<td>12 Jo.W.</td>
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<td>F</td>
<td>Digoxin (0.25 mg q.d.)</td>
<td>SB, S Ar, NSR, JR, 2°</td>
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<td>0.08</td>
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<td>13 Je.W.</td>
<td>58</td>
<td>F</td>
<td>Digoxin (0.25 mg q.d.)</td>
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<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
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<tr>
<td>14 J.A.</td>
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<tr>
<td>15 J.H.</td>
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<td>M</td>
<td>Digoxin (0.25 mg q.d.)</td>
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<td>30–40</td>
<td>0.18</td>
<td>0.08</td>
<td>—</td>
<td>Syncope</td>
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</tbody>
</table>

Abbreviations: SB = sinus bradycardia; SW = sinus Wenckebach; S Ar = sinus arrest; JR = AV junctional rhythm; CSR = coronary sinus rhythm; NSR = normal sinus rhythm; S Bl = sinus block; PAF = paroxysmal atrial fibrillation; PAT = paroxysmal atrial tachycardia; AVB = AV block; LBBB = left bundle-branch block; Inc = incomplete; Comp = complete; LAD = left axis deviation.
sinus node dysfunction with bradyarrhythmias necessitating temporary and/or permanent pacemaker implantation. The clinical and electrocardiographic features of the group are summarized in table 1. Ages ranged from 57 to 74 years. Serious symptoms of slow heart rates were present in all patients and included syncope, dizziness, mental confusion, and manifestations of congestive heart failure. Arrhythmias noted included sinus bradycardia, sinoatrial (SA) block, and sinus arrest.9 AV junctional and ectopic atrial escape rhythms occurred frequently. Four patients had episodes of paroxysmal supraventricular arrhythmias (three with atrial fibrillation and one with atrial tachycardias). P-R intervals were borderline in two (0.20 sec) and prolonged in three. One of the latter also had spontaneous episodes of Wenckebach type of second degree AV block.

Drugs were implicated as aggravating factors in the bradyarrhythmias of five patients (table 1). All of these patients returned to normal sinus rhythm within 2 weeks, but heart rates remained below 75 beats/min. Of the 10 patients with arrhythmias unrelated to drugs, five underwent permanent pacemaker insertion. Two patients were treated with long-term atropine, one of whom had refused permanent pacemaker. Two patients died with temporary pacemakers in place, one during an episode of asystole and the other, of congestive failure and pneumonia. In one patient, the bradyarrhythmias were self-limited, and the patient has been followed in clinic without pacemaker or medication.

Electrophysiologic Studies

Studies were undertaken at the time of temporary transvenous pacemaker insertion. His bundle electrograms could be recorded in 14 patients by use of previously described techniques with tripolar catheters percutaneously passed from the right femoral vein.10, 11 A bipolar pacing catheter was also passed via an external jugular vein and positioned along the lateral wall of the right atrium for atrial pacing and at the right ventricular apex for ventricular pacing. The latter catheter was left in place after the procedure for temporary pacing. Pacing at various rates was accomplished with a battery powered R-wave coupled pulse generator (Medtronic 5837, Minneapolis, Minnesota). Simultaneous electrocardiogram and His bundle electrograms were recorded at paper speeds of 100 and 200 mm/sec on a multichannel oscilloscopic photographic recorder (Electronics for Medicine DR 16, White Plains, New York).

The following intervals were measured in msec:

(1) P-H interval = The interval between the P wave and the His bundle potential. An interval approximating intra-atrial and AV nodal conduction times (normal, 80–140 msec).12
(2) H-Q interval = The interval between the His bundle spike and the initial deflection of the QRS complex. An interval approximating conduction time from the His bundle to the onset of ventricular activation (normal, 35–55 msec).12

The above intervals were measured in the unpaced state and with atrial pacing. The initial pacing rate was slightly above the patient's control rate. The patient was then paced at increasing atrial rates (in steps of 10 beats/min) until 1:1 AV conduction was lost and second degree AV block was noted. The normal response to atrial pacing at increasing rates is the development of Wenckebach periods at a heart rate of 130 beats/min or higher. The development of second degree AV block below a heart rate of 130 beats/min suggests impaired AV conduction.13, 14

An estimate of cardiac automaticity was obtained by pacing at the heart rate producing second degree block for 1 min (100–160 beats/min) and then turning off the pacemaker and measuring the period of asystole. The procedure was done in 10 patients. If asystole persisted for 5 sec without escape mechanism, the pacemaker was immediately turned on.

Atropine (1 mg intravenously) was administered to 11 patients at the termination of the procedure, and the effect on heart rate and intervals was noted.

Results

Atrioventricular Conduction (Table 2)

The rhythms noted at the time of study included sinus bradycardia (figs. 1A and 2, top), sinus arrest with AV junctional escape, and atrial fibrillation. P-H intervals could be measured in 12 of the 14 patients in whom His bundle electrograms were recorded. P-H intervals could not be measured in two patients who had atrial fibrillation at the time of study. The P-H interval was normal in eight patients (fig. 1A) and prolonged in four (patients 2, 4, 8, and 14) (fig. 2, top).

AV conduction was further characterized by noting the response to atrial pacing (figs. 1B, 1C, and 2, middle). As expected, all patients developed second degree AV block with

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### Table 2

*Results of Electrophysiologic Studies*

<table>
<thead>
<tr>
<th>Patient</th>
<th>HR and rhythms during study (beats/min)</th>
<th>P-H (msec)</th>
<th>H-Q (msec)</th>
<th>Lowest pacing rate producing Wenckebach periods (beats/min)</th>
<th>Response to overdrive (see of asystole)</th>
<th>Response to atropine</th>
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<tr>
<td></td>
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<td>HR (beats/min)</td>
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<tr>
<td>1</td>
<td>55 (SB)</td>
<td>124</td>
<td>49</td>
<td>160</td>
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<tr>
<td>2</td>
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<td>240*</td>
<td>40</td>
<td>110</td>
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<td>30</td>
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<tr>
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<td>42 (SB)</td>
<td>110</td>
<td>42</td>
<td>160</td>
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<tr>
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<td>100</td>
<td>1.4</td>
<td>75</td>
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<td>5</td>
<td>95 (NSR), 30 (S Ar, JR)</td>
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<td>150</td>
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<td>—</td>
</tr>
<tr>
<td>6</td>
<td>52 (SB)</td>
<td>126</td>
<td>44</td>
<td>140</td>
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<td>110</td>
<td>47</td>
<td>140</td>
<td>1.5</td>
<td>66 (JR)</td>
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<tr>
<td>8</td>
<td>54 (SB), 40 (JR)</td>
<td>200</td>
<td>35</td>
<td>100</td>
<td>—</td>
<td>70 (NSR)</td>
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<td>9</td>
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<td>55</td>
<td>—</td>
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<tr>
<td>10</td>
<td>44 (SB), 30 (JR)</td>
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<td>115</td>
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<td>62 (JR)</td>
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<td>11</td>
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<td>50</td>
<td>150</td>
<td>5</td>
<td>64 (NSR)</td>
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<tr>
<td>12</td>
<td>50 (AF)</td>
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<td>40</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>13</td>
<td>48 (SB, JR)</td>
<td>130</td>
<td>48</td>
<td>140</td>
<td>4</td>
<td>—</td>
</tr>
<tr>
<td>14</td>
<td>47 (SB)</td>
<td>146</td>
<td>50</td>
<td>100</td>
<td>1.8</td>
<td>—</td>
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<tr>
<td>15</td>
<td>40 (SB)</td>
<td>—</td>
<td>—</td>
<td>70</td>
<td>—</td>
<td>—</td>
</tr>
</tbody>
</table>

Abbreviations: HR = heart rate; AF = atrial fibrillation; others = see table 1.

*At paced heart rate of 60 beats/min.
and 12 had atrial fibrillation during the procedure, with consistently slow ventricular responses with high grade AV block occurring proximal to the His bundle. Patient 12 also had spontaneous Wenckebach periods prior to pacemaker insertion.

Patient 11, who had both normal intervals and atrial pacing studies, showed evidence of a retrograde conduction defect with ventricular pacing at heart rates of 80–100 beats/min. This patient developed retrograde Wenckebach periods with ventricular echoes at critical R-P interval (fig. 3).15

In summary, eight of 15 patients (53%) showed some evidence of impaired AV conduction. The incidence of abnormalities was 60% in the drug-related group and 50% in the drug-unrelated group. One additional patient manifested impaired VA conduction.

Intraventricular Conduction

Five patients had intraventricular conduction defects—three with abnormal left axis deviation, one with incomplete and one with complete left bundle-branch block (table 1). H-Q intervals were normal in all patients (table 2), and no patient was noted to develop block distal to the bundle of His with atrial pacing. Thus, electrocardiographic and electrophysiologic findings suggested absence of significant bilateral bundle-branch disease.

Patient 5, with left bundle-branch block, developed complete heart block 1 week following electrophysiologic study, necessitating change from atrial to ventricular pacing. The patient subsequently died with asystole. Serial section of the conduction system revealed a major calcific lesion involving the penetrating portion of the His bundle. A detailed report of this patient is presently in preparation.

Automaticity (Table 2)

An estimate of cardiac automaticity was obtained by noting the response to atrial overdrive. Four patients had asystole greater than 2 sec after cessation of atrial pacing (fig. 4). In two of these, the total asystolic episode was not measured because of the necessity of turning on the pacemaker at 5 sec. In all
patients, the first escape beat following the asystolic pause was supraventricular, either sinus, AV junctional, or ectopic atrial. One of these four patients had a history of syncope.

In summary, four of 10 patients (40%) had evidence of depression of automaticity in atrial, AV junctional, and ventricular pacemakers.

Atropine

Heart rates before and after administration of atropine are listed in table 2. Of 11 patients receiving atropine, eight were considered to be responsive to the drug, with 25–125% increase in heart rate (fig. 2, bottom). Three patients had increases in sinus rate of less than 20% with this drug. One responder and one nonresponder showed a sluggish sinus node response in that increase in the rate of junctional pacemaker preceded the increase in sinus rate (fig. 5).

Although increases in heart rate were frequent following administration of atropine, no patient developed a sinus rate greater than 90 beats/min. Significant response to atropine was frequent in both the drug-unrelated group (five of seven patients, 71%) and the drug-related group (three of four patients, 75%). All patients receiving atropine developed facilitation of AV conduction with shortening of P-R and P-H intervals in response to atropine administration (fig. 2, bottom).

Figure 2

Recording from patient 4 showing impaired AV conduction and response to atropine administration.

(Top) Sinus bradycardia at 45 beats/min with prolonged P-H interval of 160 msec. (Middle) Atrial pacing at rate of 100 beats/min resulting in second degree AV block. A 3:2 Wenckebach period is shown. The first P-H interval is 200 msec, the second is 250 msec. The third P wave is blocked proximal to H. (Bottom) Response to atropine administration with increase in sinus rate to 75 beats/min and shortening of the P-H interval to 120 msec.
is more a ventricular bundle from patient 11. Record 92 beats/min. Bach the starts atropine responders into increase in sinus node function. The last ventricular paced record occurred after a His bundle spike and a narrow QRS (R), representing a ventricular echo. The last ventricular paced beat starts the same cycle over again.

Discussion
In the present study, patients with symptomatic sinus node disease showed abnormal SA node function as measured by subnormal response to atropine administration, a generalized decrease of cardiac automaticity in both the SA node and secondary cardiac pacemakers, and a significant incidence of AV and intraventricular conduction defects.

The response to atropine administration in normal populations is an average increase in heart rate of 37-39 beats/min, with almost all patients developing heart rates greater than 100 beats/min.16, 17 Junctional rhythms have occurred after atropine administration, but are not the usual response.18 We were able to divide our patients with sinus node disease into atropine responders (with 25% or greater increase in sinus rate) and atropine nonresponders (with less than 25% increase).

However, utilizing the fastest heart rate reached with atropine, the response in all of the patients was subnormal in that no patient developed a sinus rate above 90 beats/min. In two patients, the sinus node response to atropine was "sluggish" in that junctional foci accelerated prior to the increase in sinus rate. Thus, in these two patients, the SA node response to atropine was both subnormal and delayed in onset.

With atropine, we have demonstrated impaired functional responsiveness of the SA node in patients with symptomatic sinus node disease. This suggests that primary SA node dysfunction is present in these patients. Normal or enhanced vagal tone may additionally potentiate the development of serious bradyarrhythmias.

There was also evidence of generalized depression of cardiac automaticity in patients with sinus node disease. The normal response to cessation of rapid pacing is the development of overdrive depression, with a variable asystolic period and transient bradycardia.19, 20 Experience in our laboratory suggests that cessation of atrial pacing at heart rates of 100-160 beats/min in patients without conduction disease does not produce asystolic periods lasting more than 1.4 sec. The patients with sinus node disease frequently showed an exaggeration of this normal response. Four out of 10 patients developed asystolic periods greater than 2.0 sec in duration, and in two of these, the asystole was prolonged enough to necessitate turning the pacemaker on. Diminished cardiac automaticity in these patients

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The response to atropine administration in normal populations is an average increase in heart rate of 37-39 beats/min, with almost all patients developing heart rates greater than 100 beats/min.16, 17 Junctional rhythms have occurred after atropine administration, but are not the usual response.18 We were able to divide our patients with sinus node disease into atropine responders (with 25% or greater increase in sinus rate) and atropine nonresponders (with less than 25% increase).

However, utilizing the fastest heart rate reached with atropine, the response in all of the patients was subnormal in that no patient developed a sinus rate above 90 beats/min. In two patients, the sinus node response to atropine was "sluggish" in that junctional foci accelerated prior to the increase in sinus rate. Thus, in these two patients, the SA node response to atropine was both subnormal and delayed in onset.

With atropine, we have demonstrated impaired functional responsiveness of the SA node in patients with symptomatic sinus node disease. This suggests that primary SA node dysfunction is present in these patients. Normal or enhanced vagal tone may additionally potentiate the development of serious bradyarrhythmias.

There was also evidence of generalized depression of cardiac automaticity in patients with sinus node disease. The normal response to cessation of rapid pacing is the development of overdrive depression, with a variable asystolic period and transient bradycardia.19, 20 Experience in our laboratory suggests that cessation of atrial pacing at heart rates of 100-160 beats/min in patients without conduction disease does not produce asystolic periods lasting more than 1.4 sec. The patients with sinus node disease frequently showed an exaggeration of this normal response. Four out of 10 patients developed asystolic periods greater than 2.0 sec in duration, and in two of these, the asystole was prolonged enough to necessitate turning the pacemaker on. Diminished cardiac automaticity in these patients
Intraventricular conduction defects were less common, occurring in only five patients. H-Q intervals were normal in all of these patients. One patient with left bundle-branch block developed failure of atrial pacing 1 week after electrophysiologic study, and serial histologic sections of the conduction system in this patient revealed a major lesion of the proximal His bundle. Thus, with one exception, intraventricular conduction defects in patients with symptomatic sinus node disease did not appear to be serious.

**Clinical Implications**

It is demonstrated in the present study that patients with symptomatic sinus node disease have multiple functional abnormalities of the conduction system. Diminished automaticity can complicate therapy in that failure of either atrial or ventricular pacing could be accompanied by prolonged periods of asystole. It would seem reasonable in patients with sinus node disease, particularly in those in whom diminished automaticity was demonstrated, to choose a pacing site in which most reliable chronic pacing could be achieved.

The presence of AV and intraventricular conduction defects in these patients represents a potential contraindication to atrial pacing. A minor defect, in which 1:1 conduction is present at heart rates below 100 beats/min, has the potential for worsening later in the patient's illness. Many patients with sinus node disease are elderly and susceptible to ischemic heart disease, which could further compromise conduction. Some of the patients may need digitalis or antiarrhythmic agents, both of which could also further compromise conduction. Thus, despite initial successful atrial pacing, bradyarrhythmias could recur secondary to the development of AV block. Further observations are indicated in patients with symptomatic sinus node disease, to see if these potential hazards will become real.

Before choosing a pacing site in patients with symptomatic sinus node disease, we would recommend the following evaluation:

1. Examination of the electrocardiogram for the presence of any conduction disturbance.

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*SYMPOMATIC SINUS NODE DISEASE*

In addition to depressed automaticity, the present electrophysiologic studies suggested that abnormalities in conduction were frequent in patients with symptomatic sinus node disease. AV conduction defects occurred in eight of the 15 patients studied, manifest by one or more of the following abnormalities: P-R prolongation, spontaneous second degree AV block, high grade AV block during atrial fibrillation, prolonged P-H interval, and the development of second degree AV block with atrial pacing at relatively low heart rates (below 130 beats/min). One additional patient manifested a VA conduction defect with development of a retrograde Wenckebach period with reciprocal beating with ventricular pacing at low heart rates. All the above conduction abnormalities occurred proximal to the His bundle, most likely in the AV node. Previous electrocardiographic observation also suggested a high incidence of abnormal AV conduction in patients with sinus node disease.21-26

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*Figure 5*

“Sluggish” sinus node response to atropine in patient 7. (A) Three minutes after atropine administration, the patient developed a functional escape rhythm at 67 beats/min. There is a nonconducted P wave just in front of the last complex as the sinus rate slowly increases. (B) One minute later, the sinus rate has increased to 72 beats/min and is now the predominant rhythm.

appeared to involve the sinus node and all subsidiary pacemakers. Depressed automaticity could certainly contribute to development of symptoms in patients with sinus node disease.

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(2) A study of atrial pacing at various heart rates at the time of pacemaker implantation in order to demonstrate the heart rate at which second degree block develops. If block occurs at a low heart rate, atrial pacing may be contraindicated.

(3) Measurement of the duration of overdrive depression with rapid atrial pacing.

Although recording of His bundle electrograms in these patients provides a more thorough evaluation of conduction, an estimation of conduction by the techniques listed above should be adequate to help choose the best potential pacing site.

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References


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