Unmasking and Conversion of Gap Phenomenon in the Human Heart

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SUMMARY

Two types of gap phenomena (types I and II) have been described in human hearts and their electrophysiologic bases have been delineated. In both types of gap phenomena relatively early premature atrial impulses are blocked within some portion of the His-Purkinje system (HPS). By increasing the prematurity of the atrial depolarization, conduction to the ventricles resumes due to delay of the premature impulse with the atrioventricular node (A-VN) (type I gap) or within the proximal HPS (type II gap). Gap phenomena are not observed when the refractory period of the A-VN exceeds that of the HPS. Since atropine decreases refractoriness of the A-V node, its effect on the gap phenomena was studied in nine subjects. After administration of atropine (0.2–0.5 mg i.v.) type I gap was demonstrated in six subjects and type II gap in three subjects. When atropine shortened the functional and effective refractory period (ERP) of the A-V node, premature atrial impulses arrived at the HPS during its ERP. By a similar mechanism, type I gap was converted into type II gap in three subjects following atropine administration. Decreasing the basic atrial drive rate converted type II gap into type I (two subjects) and ultimately abolished both types of gap phenomena in all subjects. These results suggest that the gap phenomenon may be functional in nature and may be readily manifested or abolished by varying the refractoriness of the A-V node relative to that of the HPS.

Additional Indexing Words:
Atrial cycle length  Atrial refractoriness  Atrioventricular nodal refractoriness
Distal His-Purkinje system  Proximal His-Purkinje system

THE PHENOMENON OF THE GAP in atrioventricular (A-V) conduction has been described in both canine1 and human hearts.2–5, 12 In this phenomenon early atrial premature impulses fail to conduct to the ventricles, whereas conduction resumes with still earlier atrial premature impulses. Thus far, two types of gap phenomena in A-V conduction have been described in human hearts and these have been arbitrarily designated as types I and II. Common to both types of gaps is that early atrial premature impulses initially block within some part of the His-Purkinje system (HPS); resumption of conduction occurs when earlier premature beats encounter delay proximal to the site of initial block, and thereby allow sufficient time for distal recovery to occur. In type I gap the area of proximal delay occurs within the A-V node,3, 5 while in type II gap the delay occurs within the proximal portion of the His-Purkinje system (HPS).5 Demonstration of the gap phenomenon depends upon the fact that the effective refractory period (ERP) of some part of the HPS is longer than the functional refractory period (FRP) of the A-V node.

During studies designed to evaluate the effects of atropine sulphate on the functional properties of the A-V conducting system, it was noted that the drug consistently decreased refractoriness of the A-V node without affecting refractoriness of the HPS.6 When atropine decreased A-V nodal refractoriness to a smaller value than that of the His-Purkinje system, the setting for the unmasking of gap phenomena was present. The results obtained in nine subjects receiving atropine form the basis of this report.

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UNMASKING GAP PHENOMENON

Materials and Methods

Right heart catheterization was performed on nine patients in the postabsorptive, nonsedated state. The nature of the study was explained and a signed consent obtained. Bundle of His electrograms were recorded, as previously described, using a bipolar electrode catheter which was introduced percutaneously into the right femoral vein and fluoroscopically positioned in the region of the tricuspid valve. A no. 7 quadripolar catheter was introduced percutaneously into an antecubital vein and advanced to the high right atrium near its junction with the superior vena cava. The two distal electrodes were used to stimulate the atrium and the two proximal electrodes were used to record high right atrial activity. Intracardiac electrograms as well as electrocardiographic leads I, II, III, V1 and time lines generated at 10 and 100 msec were simultaneously displayed on a multichannel oscilloscope and relayed to a magnetic tape recorder. The records were subsequently reproduced at paper speed of 150 mm per second. The functional properties of the A-V conduction system were determined at one or more basic cycle length using the atrial extrastimulus method.

Electrical stimulation was accomplished using a programmed digital stimulator which delivered impulses of 1.5 msec at approximately twice diastolic threshold. The right atrium was stimulated at a predetermined basic cycle length (A1A1), and following every eighth basic drive beat a premature atrial impulse (A2) was introduced at progressively decreasing A1A2 intervals to the point of atrial refractoriness. Careful attention was paid to the grounding of all equipment. After completing the control studies, a small dose of atropine (0.2–0.5 mg) was given i.v. and the studies repeated 10–15 min after the injection.

Definition of Terms

A1, H1, V1: The atrial, His bundle, and ventricular depolarizations during the basic atrial drive.

A0, H0, V0: The atrial, His bundle, and ventricular depolarizations resulting from coupled premature atrial stimulation.

Refractory Periods

Effective refractory period (ERP) of the atrium is defined as the longest S1 S2 interval at which S2 fails to depolarize the atrium, S representing the stimulus artifact.

ERP of the A-VN is defined as the longest A1A2 interval at which A2 fails to propagate to the HPS.

Functional refractory period (FRP) of the A-VN is defined as the shortest H1H2 interval that results from any A1A2.

ERP of the HPS is defined as the longest H1H2 interval at which H2 fails to conduct to the ventricles.

Relative refractory period (RRP) of the HPS is defined as the longest H1H2 interval at which H2 conducts to the ventricles with a longer H-V time than the basic drive beat or with a QRS of aberrant configuration.

Results

Essential clinical data are given in table 1. All patients had normal P-R intervals and were not taking any medications. The results of the refractory period studies before and after atropine are presented in table 2. Atropine shortened both the effective and functional refractory periods of the A-V node at all cycle lengths tested, and thereby, allowed for the following changes to occur.

Unmasking of Type I Gap

In six subjects (nos. 1, 2, 5, 6, 7, and 8, table 2) atropine produced a type I gap, at atrial cycle lengths of 700, 550, 800, 665, 700, and 650 msec, re-

Table 1

<table>
<thead>
<tr>
<th>No.</th>
<th>Patient</th>
<th>Age</th>
<th>Sex</th>
<th>Diagnosis</th>
<th>Resting ECG</th>
<th>Sinus cycle length (msec)</th>
<th>Prior medications</th>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Before atropine 1100</td>
<td>After atropine 950</td>
<td>None</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>1</td>
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<td>57</td>
<td>M</td>
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<td>Normal</td>
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</tr>
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<td>2</td>
<td>K.N.</td>
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<td>F</td>
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<td>Right bundle branch block</td>
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<td>650</td>
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<tr>
<td>4</td>
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<td>54</td>
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<td>LGEB by voltage criteria</td>
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<td>870</td>
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<tr>
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<td>T.D.</td>
<td>61</td>
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<td>Atrial premature beats</td>
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<td>820</td>
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<tr>
<td>6</td>
<td>G.D.</td>
<td>50</td>
<td>M</td>
<td>No heart disease</td>
<td>1st degree A-V block</td>
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<td>675</td>
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<tr>
<td>7</td>
<td>D.J.</td>
<td>45</td>
<td>M</td>
<td>Ischemic heart disease</td>
<td>Normal</td>
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<td></td>
</tr>
<tr>
<td>8</td>
<td>L.R.</td>
<td>25</td>
<td>M</td>
<td>No heart disease</td>
<td>Normal</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>M.F.</td>
<td>57</td>
<td>M</td>
<td>Ischemic heart disease</td>
<td>Left axis deviation</td>
<td>1200</td>
<td>700</td>
</tr>
</tbody>
</table>

*Although it is recognized that the HPS is a trifascicular system, in the absence of multiple recording sites along individual fascicles, it is impossible to measure the ERP versus the RRP of any given fascicle. Thus, for the purposes of this study, it was elected to consider the HPS as a single functioning unit.

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Table 2

Atrial Refractory Period Data

<table>
<thead>
<tr>
<th>Subject</th>
<th>Atrial ERP</th>
<th>A-V Node ERP</th>
<th>His-Purkinje System ERP</th>
<th>Comments</th>
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<tr>
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<td>No. C.L.</td>
<td>BA AA</td>
<td>BA AA</td>
<td>BA AA</td>
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<tr>
<td>1 K.T.</td>
<td>900</td>
<td>310 320</td>
<td>—</td>
<td>480 415</td>
</tr>
<tr>
<td></td>
<td>700</td>
<td>290 300</td>
<td>350 &lt;320 515 430</td>
<td>— 430</td>
</tr>
<tr>
<td></td>
<td>600</td>
<td>280 270</td>
<td>360 &lt;320 520 455</td>
<td>— 470</td>
</tr>
<tr>
<td>2 K.M.</td>
<td>650</td>
<td>250 240</td>
<td>— 390</td>
<td>410 420</td>
</tr>
<tr>
<td></td>
<td>600</td>
<td>250 230</td>
<td>— 380</td>
<td>395 395</td>
</tr>
<tr>
<td></td>
<td>550</td>
<td>250 240</td>
<td>260 &lt;240 385 365</td>
<td>— 370</td>
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<tr>
<td></td>
<td>500</td>
<td>250 240</td>
<td>270 &lt;240 385 360</td>
<td>— 395</td>
</tr>
<tr>
<td>3 W.M.</td>
<td>700</td>
<td>260 260</td>
<td>290 &lt;260 370 350</td>
<td>375 430</td>
</tr>
<tr>
<td></td>
<td>600</td>
<td>230 230</td>
<td>310 270 365</td>
<td>— 385</td>
</tr>
<tr>
<td>4 T.A.</td>
<td>800</td>
<td>320 310</td>
<td>300 360 &lt;320 485 405</td>
<td>450 470</td>
</tr>
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<td></td>
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<td></td>
<td>600</td>
<td>290 300</td>
<td>340 &lt;300 495 395</td>
<td>395</td>
</tr>
<tr>
<td>5 T.D.</td>
<td>800</td>
<td>280 280</td>
<td>380 &lt;280 450 385</td>
<td>390 455</td>
</tr>
<tr>
<td></td>
<td>700</td>
<td>280 280</td>
<td>390 &lt;280 465 390</td>
<td>390</td>
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<tr>
<td>6 G.D.</td>
<td>665</td>
<td>240 240</td>
<td>345 270 420 375</td>
<td>395</td>
</tr>
<tr>
<td>7 D.J.</td>
<td>700</td>
<td>250 250</td>
<td>— 385 380</td>
<td>— 430</td>
</tr>
<tr>
<td></td>
<td>650</td>
<td>230 240</td>
<td>— 385 370</td>
<td>— 425</td>
</tr>
<tr>
<td>8 L.R.</td>
<td>650</td>
<td>230 220</td>
<td>— 315 370</td>
<td>— 410</td>
</tr>
<tr>
<td></td>
<td>600</td>
<td>240 230</td>
<td>260 &lt;230 400 360</td>
<td>— 390</td>
</tr>
<tr>
<td>9 M.F.</td>
<td>600</td>
<td>260 240</td>
<td>— 355 340</td>
<td>345 395</td>
</tr>
<tr>
<td></td>
<td>500</td>
<td>230 220</td>
<td>— 345 330</td>
<td>345</td>
</tr>
</tbody>
</table>

All values are in milliseconds. Abbreviations: C.L. = cycle length; BA = before atropine; AA = after atropine; ERP = effective refractory period; FRP = functional refractory period.

respectively, whereas no gap in A-V conduction was present in the control period at these same cycle lengths. Figures 1 and 2 provide representative examples of these findings. Figure 1 illustrates that in the control study progressive shortening of the A1A2 interval resulted in progressive prolongation in A-V nodal conduction (A1H2) and eventual block within the A-V node (panels A to D). The ERP of the A-V node was 350 msec (table 2). At shorter A1A2 intervals (panel D) and up to the point of atrial refractoriness, premature atrial impulses continued to be blocked within the A-V node. Thus, in the control period, the ERP of the A-V node exceeded that of the His-Purkinje system.

Panel B of figure 2 demonstrates that, following atropine, there is an enhancement of A-V nodal conduction and premature atrial impulses are blocked within the His-Purkinje system at an H1H2 interval of 425 msec. Upon further shortening of the A1A2 interval (panel C), conduction to the ventricles resumed (type I gap) because the premature atrial impulse encountered sufficient A-V nodal delay so that the resultant H1H2 interval (515 msec) now exceeded the effective refractory period of the HPS.

Unmasking of Type II Gap

In three subjects (nos. 2, 4, and 9), no gap in A-V conduction was present prior to administration of atropine at atrial cycle lengths of 650, 800, and 600 msec, respectively, whereas after drug administration type II gap occurred at these same basic cycle lengths. In patient no. 4, at an atrial cycle length of 800 msec, the FRP of the A-V node (485 msec) was longer than the effective refractory period of the HPS (table 2). Following atropine the FRP of the A-V node was decreased (405 msec) to a value less than that of the ERP of the His-Purkinje system (450 msec). The graphic demonstration of a type II gap occurring after atropine is illustrated in figure 3. Panel B demonstrates that atropine shortened the FRP of the A-V node and allowed the premature atrial impulses to reach some portion of the His-Purkinje system during its ERP. As illustrated in panels C and D, A-V conduction resumed as the A1A2 interval was decreased further. However, resumption of conduction occurred at H1H2 intervals which were less than those associated with the previously blocked atrial impulses (panel B). The mechanism postulated to explain this type of gap is that atropine enhances A-V nodal conduction,
allowing the premature impulse to enter the HPS earlier (shorter $H_1H_2$) and then be delayed in the more proximal parts of this system so that the premature atrial impulse arrived in the more distal system after it is no longer effectively refractory.

**Conversion of Type I Gap Into a Type II Gap**

In three subjects (nos. 1, 2, and 3) a type I gap was converted into a type II gap after atropine administration. Figures 4 and 5, recorded from subject no. 1, demonstrate this phenomenon.

As shown in table 2, decreasing the basic cycle length abolished the gap phenomena in all patients. In subjects 1 and 2, the effect of decreasing the basic atrial cycle length was to convert a type II gap into a type I gap before the gap phenomenon was finally abolished at the faster pacing rates.

**Discussion**

The phenomenon of gap in A-V conduction was originally described in the canine heart by Moe et al. The phenomenon was characterized by an
absence of A-V conduction (the gap) encompassed by preceding and succeeding periods in which A-V conduction consistently occurred. Durrer subsequently extended these observations to human hearts.2

Electrophysiological Basis for Type I Gap

The electrophysiological basis for type I gap was provided by the clinical studies of Wit et al.3 In these studies, during the period when no A-V conduction occurred, the nonconducted atrial impulses blocked within the HPS and were associated with H1H2 intervals which were less than or equal to the ERP of the HPS. Also, it was noted that during the period when A-V conduction resumed, premature atrial impulses encountered greater A-V nodal delay and the resultant H1H2 intervals were

Figure 3

Unmasking of type II gap (Subject no. 4). Basic atrial cycle length (A1A2) is the same in all panels. Before atropine, at an A1A2 interval of 430 msec (panel A), A2 encounters A-V nodal delay and the resulting H1H2 interval of 505 msec is greater than the ERP of the His-Purkinje system. After atropine (panel B), at the same A1A2 interval as in panel A, A2 now blocks within the His-Purkinje system at an H1H2 interval of 450 msec. As A1A2 further decreases (panel C), A2 once again conducts to the ventricles, however at a shorter H1H2 interval compared to panel B, and a longer H1V1 interval (type II gap) compared to the preceding beat. The resulting QRS complex shows that conduction occurred mainly through the distribution of the right bundle branch and anterior division of the left bundle branch (left posterior hemiblock pattern). Panel D demonstrates that A2 is able to conduct to the ventricles at the even shorter H1H2 interval of 395 msec. The longer H1V1 of 160 msec and the QRS configuration suggests further delay of the premature impulse in the distribution of the right bundle branch and anterior division of the left bundle branch. The second tracing in each panel is lead II of ECG; other tracings are as identified in legend to figure 1.

Figure 4

Conversion of type I gap in A-V conduction into type II gap (Subject no. 1). A typical type I gap during the control period. At an A1A2 interval of 445 msec, A2 blocks within the HPS (panel B). Conduction of A2 to the ventricles resumes as a result of A-V nodal delay on decreasing A1A2 intervals (panel C and D).
Figure 5
(Subject no. 1). After atropine at the same atrial cycle length as figure 4 (900 msec), A2 blocks within the distal His-Purkinje system (panel B) at an H1H2 interval of 490 msec. As shown in panel C, on increasing the prematurity of atrial depolarization, A2 conducts to the ventricles at a shorter H1H2 interval and a longer H2V2 interval compared to the preceding beat (type II gap). Atropine, by enhancing A-V nodal conduction, allowed earlier arrival of A2 at the proximal His-Purkinje system, i.e., within its relative refractory period, and thereby enabled recovery of refractoriness in distal areas. Further decreasing the A1A2 interval resulted in block of the premature atrial impulse within the proximal His-Purkinje system (panel D, H1H2: 415 msec).

greater than the ERP of the His-Purkinje system. Clinical studies by Gallagher et al.\(^5\) confirmed that, during the gap period, the site of maximum refractoriness was within the HPS and not within the ventricular muscle.

Electrophysiological Basis for Type II Gap

Subsequently, the mechanism for type II gap was described in clinical studies by Cannom et al.\(^4\) and Gallagher et al.\(^5\) In type II gap the period of no A-V conduction is also characterized by atrial impulses which are blocked within the HPS. However, during the period when A-V conduction resumes, the conducted atrial impulses are associated with H1H2 intervals which are less than prior blocked beats and almost always associated with significantly prolonged H2V2 intervals. It has been postulated that in type II gap the premature atrial impulses are initially blocked in some portion of the distal His-Purkinje system and that during the period of resumed A-V conduction, at shorter H1H2 intervals, the premature atrial impulses encounter delay in the proximal HPS which in turn permits the impulse to arrive at the previously refractory distal area after the latter has recovered. Thus, in the type II gap the proximal HPS functions as the A-V node does in a type I gap.

Ventricular Aberration in the Gap Phenomenon

In type I gap the QRS complexes during the period of resumed A-V conduction may be normal or aberrant depending upon the degree of A-V nodal delay to which the premature impulse is subjected. If the resultant H1H2 interval is greater than the relative refractory period of the HPS, then the QRS complexes will be normal. In type II gap the QRS complexes during resumed A-V conduction are almost always aberrant since proximal delay in the HPS is almost never uniformly distributed throughout the trifascicular conducting system, and some degree of asynchronous recovery of excitability and conduction results. Theoretically, normalization of QRS complexes could occur in type II gap if equal and simultaneous delay occurred along both sides of the conduction system.

Functional Nature of the Gap Phenomenon

The gap phenomenon is seen in those subjects in whom the ERP of some portion of the HPS exceeds the FRP of the A-V node. The gap phenomenon is generally not seen in those subjects in whom the ERP of either the A-V node or atrium exceeds that of the HPS. The ability of small doses of atropine to shorten both the FRP and ERP of the A-V node without directly affecting refractoriness of the HPS permitted a consistent demonstration of the gap phenomenon, and exposed its functional nature. Larger doses of atropine were not used in this study in order to avoid a significant increase in ventricular rate which, by itself, might prevent the demonstration of the gap phenomenon by significantly shortening the ERP of the HPS. In this study both types of gap were abolished at short, paced atrial
cycle lengths (usually 500 msec or less) in all subjects due to both rate related decreases in the ERP of the HPS and to increased delay of conduction within the A-V node. The latter mechanism is responsible for the abolishment of gaps following the use of sympathetic β-receptor blocking agents.3

In some subjects in whom the ERP of the HPS is greater than the FRP of the A-V node, the demonstration of the gap phenomenon is not possible because (1) atrial refractoriness occurs before a sufficient delay in the proximal region can be achieved or (2) the ERP of the A-V node is only slightly less than that of the HPS, and decreasing the A1 A2 interval causes block within the A-V node.

In no instance was the change in ERP of the atrium after atropine a significant factor in demonstrating the gap phenomenon in these subjects (table 2).

For intact human hearts the ERP of the HPS has generally been defined as the longest H1 H2 interval at which H2 fails to conduct to the ventricles.10 The existence of a type II gap (fig. 5) exemplifies the limitations of this functional definition. In type II gap the longest H1 H2 interval at which H2 fails to conduct to the ventricles defines the ERP of a distal area within the HPS, whereas it is possible for the ERP of a more proximal part of the HPS to be defined as the longest H1 H2 interval at which H2 fails to conduct to the ventricles during a period when actually A-V conduction has resumed. The latter H1 H2 interval (i.e., the ERP of the proximal HPS) is less than the former (the ERP of the distal HPS).

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References

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