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 atroventricular 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 atroventricular (A-V) conduction has been described in both canine and human hearts. 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, while in type II gap the delay occurs within the proximal portion of the His-Purkinje system (HPS). 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. 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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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 tripolar 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 (A1A2), 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 S1S2 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>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>K.T.</td>
<td>57</td>
<td>M</td>
<td>No heart disease</td>
<td>Normal</td>
<td>1100</td>
<td>None</td>
</tr>
<tr>
<td>2</td>
<td>K.N.</td>
<td>73</td>
<td>F</td>
<td>No heart disease</td>
<td>Right bundle branch block</td>
<td>950</td>
<td>None</td>
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<tr>
<td>3</td>
<td>W.N.</td>
<td>21</td>
<td>M</td>
<td>No heart disease</td>
<td>Normal axis</td>
<td>690</td>
<td>650</td>
</tr>
<tr>
<td>4</td>
<td>T.A.</td>
<td>54</td>
<td>M</td>
<td>Hypertensive cardiovascular disease</td>
<td>LVH by voltage criteria</td>
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<td>870</td>
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<tr>
<td>5</td>
<td>T.D.</td>
<td>61</td>
<td>M</td>
<td>Ischemic heart disease</td>
<td>Atrial premature beats</td>
<td>900</td>
<td>820</td>
</tr>
<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>
<td>700</td>
<td>675</td>
</tr>
<tr>
<td>7</td>
<td>D.J.</td>
<td>45</td>
<td>M</td>
<td>Ischemic heart disease</td>
<td>Normal</td>
<td>900</td>
<td>720</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>1030</td>
<td>800</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.
Table 2

Atrial Refractory Period Data

<table>
<thead>
<tr>
<th>Subject</th>
<th>Atrium ERP</th>
<th>A-V Node ERP</th>
<th>His-Purkinje ERP</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>C.L.</td>
<td>BA AA</td>
<td>BA AA</td>
<td>BA AA</td>
</tr>
<tr>
<td>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>&lt;320 515 430</td>
<td>—</td>
</tr>
<tr>
<td></td>
<td>600</td>
<td>280 270</td>
<td>&lt;320 520 455</td>
<td>430 470</td>
</tr>
<tr>
<td>K.M.</td>
<td>650</td>
<td>250 240</td>
<td>—</td>
<td>390 375</td>
</tr>
<tr>
<td></td>
<td>600</td>
<td>250 230</td>
<td>—</td>
<td>390 370</td>
</tr>
<tr>
<td></td>
<td>550</td>
<td>250 240</td>
<td>&lt;240 380 365</td>
<td>—</td>
</tr>
<tr>
<td></td>
<td>500</td>
<td>250 240</td>
<td>&lt;240 385 360</td>
<td>—</td>
</tr>
<tr>
<td>W.M.</td>
<td>700</td>
<td>260 260</td>
<td>&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>385 385</td>
</tr>
<tr>
<td>T.A.</td>
<td>800</td>
<td>320 310</td>
<td>&lt;320 485 405</td>
<td>450 470</td>
</tr>
<tr>
<td></td>
<td>750</td>
<td>310 300</td>
<td>&lt;320 490 400</td>
<td>—</td>
</tr>
<tr>
<td></td>
<td>700</td>
<td>310 310</td>
<td>&lt;320 490 395</td>
<td>—</td>
</tr>
<tr>
<td></td>
<td>600</td>
<td>290 300</td>
<td>&lt;300 495 395</td>
<td>—</td>
</tr>
<tr>
<td>T.D.</td>
<td>800</td>
<td>280 280</td>
<td>&lt;280 450 385</td>
<td>390 455</td>
</tr>
<tr>
<td></td>
<td>700</td>
<td>280 280</td>
<td>&lt;280 465 390</td>
<td>—</td>
</tr>
<tr>
<td>G.D.</td>
<td>665</td>
<td>240 240</td>
<td>345 270 420 375</td>
<td>395 —</td>
</tr>
<tr>
<td>D.J.</td>
<td>700</td>
<td>250 250</td>
<td>—</td>
<td>385 380</td>
</tr>
<tr>
<td></td>
<td>650</td>
<td>230 240</td>
<td>—</td>
<td>385 370</td>
</tr>
<tr>
<td></td>
<td>650</td>
<td>230 220</td>
<td>—</td>
<td>415 370</td>
</tr>
<tr>
<td>L.R.</td>
<td>600</td>
<td>240 230</td>
<td>&lt;230 400 360</td>
<td>—</td>
</tr>
<tr>
<td>M.F.</td>
<td>650</td>
<td>260 240</td>
<td>—</td>
<td>355 340</td>
</tr>
<tr>
<td></td>
<td>500</td>
<td>230 220</td>
<td>—</td>
<td>345 330</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 (A2H2) 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,
Unmasking of type I gap (Subject no. 1). In all panels the basic atrial cycle length is constant at 700 msec. During the control period, as the interval between $A_1A_2$ is decreased, $A_3$ encounters progressive delay within the A-V node where it eventually blocks (panel A to D). All values are in milliseconds. Tracings from top to bottom are standard lead I, III, $V_2$, high right atrial electrogram (HRA), His bundle electrogram (HBE); and time lines (T). S denotes stimulus artifact. The same abbreviations will be used in subsequent tracings.

Figure 1

Unmasking of type I gap (Subject no. 1). Basic atrial cycle length is the same as figure 1. After administration of atropine at an $A_1A_2$ interval of 380 msec, $A_3$ blocks within the His-Purkinje system (panel B). This happens because atropine, by decreasing the FRP of the A-V node, allows arrival of the premature atrial impulse at the His-Purkinje system during its ERP ($H_1H_2$:425). As the $A_1A_2$ interval further decreases (panel C and D), $A_3$ is delayed within the A-V node long enough to produce $H_1H_2$ intervals that are now longer than the ERP of the His-Purkinje system; at this point conduction to the ventricles resumes (type I gap).

Figure 2

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.\textsuperscript{1} 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 H2H3 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 H2H3 intervals were
Gallagher et al. 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 $H_1H_2$ intervals which are less than prior blocked beats and almost always associated with significantly prolonged $H_2V_2$ 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 $H_1H_2$ 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 $H_1H_2$ 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

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**Electrophysiological Basis for Type II Gap**

Subsequently, the mechanism for type II gap was described in clinical studies by Cannom et al. and
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.  

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. The existence of a type II gap (fig. 5) exemplifies the limitations of this functional definition. In type II gap the longest H₁H₂ 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 H₁H₂ interval at which H₂ fails to conduct to the ventricles during a period when actually A-V conduction has resumed. The latter H₁H₂ 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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