Phenomenon of the Gap in Atrioventricular Conduction in the Human Heart

By Andrew L. Wit, Ph.D., Anthony N. Domoto, M.D., Melvin B. Weiss, M.D., and Charles Steiner, M.D.

ABSTRACT

The phenomenon of the "gap in atrioventricular conduction" was studied in eight human subjects, using a catheter technique for recording electrical activity of the His bundle. Premature atrial stimuli were applied throughout the basic atrial cycle, either during sinus rhythm or atrial pacing. As the coupling interval between the basic (A1) and premature (A2) atrial depolarizations was decreased, a point was reached where A2 was no longer conducted to the ventricles. The region of conduction block was localized distal to the His bundle. The interval between basic and premature His bundle depolarizations at which block occurred provided a value for the effective refractory period of the His-Purkinje system. If A2 was then made to occur earlier in the basic cycle, a point was reached where conduction of the premature response to the ventricles resumed. When this occurred, conduction delay of A2 in the atrioventricular node had increased sufficiently to allow for recovery of excitability of the His-Purkinje system (the interval between successive His bundle depolarizations was greater than the effective refractory period of the His-Purkinje system). The gap phenomenon could be abolished by decreasing the basic cycle length or by beta-receptor blockade, both of which prevented conduction block of A2 in the His-Purkinje system.

ADDITIONAL KEY WORDS: bundle of His, functional refractory period, effective refractory period, premature stimuli, conduction block, normal A-V conduction, left bundle-branch block, short P-R interval, beta-receptor blockade, atropine.

During experiments designed to elucidate the conduction properties of the atrioventricular (A-V) conduction system in both the canine (1) and human hearts (2, 3), an interesting and yet unexplained phenomenon has been occasionally noted. Premature atrial responses evoked progressively earlier in the atrial cycle show prolonged A-V conduction time. A point is reached when the evoked atrial response is no longer conducted to the ventricles and the effective refractory period of the A-V conduction system is seemingly reached. If the prematurity of the atrial extra systole is increased still further, however, conduction to the ventricles resumes. Thus, graphically relating the A-V conduction time of premature atrial depolarizations to their relative prematurity, a gap is encountered (3). This gap has been presumed to result from dual A-V nodal conduction pathways (2). In this laboratory, studies designed to determine the functional characteristics of the A-V conduction system in man using localized electrograms recorded from the bundle of His enabled a mechanism for this physiological phenomenon to be delineated.

Methods

The functional properties of the A-V conduction system were studied in 45 patients during cardiac catheterization. Thirty of the patients had normal A-V conduction systems as judged by electrocardiographic criteria (normal P-R interval of .12 to .20 second on the standard ECG, normal
ventricular depolarization) (4). Six patients had complete left bundle-branch block with normal P-R intervals, four had short P-R intervals (.1 to .12 second) and normal ventricular depolarization without cardiac arrhythmias, and five had long P-R intervals (> .20 second) and normal ventricular depolarization. All subjects were advised of the nature of the study and a signed consent was obtained.

RECORDING TECHNIQUES AND INSTRUMENTATION
Cardiac catheterization was performed in the nonsedated, postabsorptive state. A His-bundle electrogram was recorded by a tripolar electrode catheter using techniques previously described in detail (5). The recording instrumentation has also been described (5, 6).

The right atrium was paced through a bipolar electrode catheter, positioned high against the lateral wall, at a constant cycle length. Stimuli consisted of square-wave pulses, 1 to 2 msec in duration and approximately twice diastolic threshold. A square-wave test pulse of 2-msec duration and 4 to 5X diastolic threshold was introduced through the same catheter after every tenth basic drive stimulus, and was applied at any desired interval after the basic drive. Stimuli were provided by a series of Tektronix 160 waveform and pulse generators. An R-wave coupled pulse generator (Medtronic model 5867) was also used to prematurely stimulate the right atrium during normal sinus rhythm through the components of the A-V conduction system was determined by analysis of the His-bundle electrogram as previously described (6).

RESULTS
A gap in A-V conduction was found in 7 of the 45 patients during atrial premature stimulation. We have used the term gap to indicate the period, encompassed by two sets of atrial coupling intervals, during which A-V conduction of most or all premature impulses are blocked. Occasionally during this period some premature impulses may be conducted to the ventricles. Three of these patients had normal A-V conduction times, two had short P-R intervals, and two had complete left bundle-branch block. In addition, a gap in A-V conduction was found in one patient with first degree heart block (P-R interval of .26 second) after the administration of .2 mg/kg of atropine. Clinical and electrocardiographic data for this group are summarized in Table 1. No results from routine diagnostic procedures, including clinical history, physical examina-

### Table 1

<table>
<thead>
<tr>
<th>Patients</th>
<th>Clinical diagnosis</th>
<th>Drugs during study</th>
<th>SCL</th>
<th>P-R Intervals</th>
<th>QRS duration</th>
<th>BCL</th>
<th>ERP</th>
<th>VSCS</th>
<th>Repolarization</th>
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<tr>
<td>B.W.</td>
<td>NHD</td>
<td>None</td>
<td>980</td>
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<td>73</td>
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<td>1010</td>
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<td>89</td>
<td>900(S)</td>
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<td>475</td>
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<td>I.M.</td>
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<tr>
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<td>350</td>
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<td>400</td>
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<tr>
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<td>845</td>
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<td>130</td>
<td>845(S)</td>
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<td>410</td>
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<td>290</td>
<td>60</td>
<td>695</td>
<td>275</td>
<td>270</td>
<td>395</td>
</tr>
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</table>

All values expressed in milliseconds.

Abbreviations: NHD = no heart disease; ASHD = arteriosclerotic heart disease; LBBB = complete left bundle-branch block; HB = heart block; SCL = sinus cycle length; BCL = basic cycle length at which gap was found; S = sinus rhythm; AVN = A-V node; FRP = functional refractory period; VSCS = ventricular specialized conduction system; ERP = effective refractory period.
Gap in A-V conduction in a subject with a normal P-R interval. Premature atrial impulses were introduced throughout basic drive cycle length of 900 msec. Abscissa = $A_1 - A_2$ intervals, $V_1-V_2$ intervals (circles) and $H_1-H_2$ intervals (Xs) on ordinate. Conduction delay of premature atrial impulses occurred only in the A-V node at $A_1 - A_2$ intervals of 650 to 525 msec, as indicated by deviation of the descending limb of the curve from the line of no A-V conduction delay ($V_1-V_2$ and $H_1-H_2$ intervals were identical). At an $A_1 - A_2$ interval of 525 msec, conduction delay of $A_2$ also began to occur in the ventricular specialized conduction system (VSCS), as indicated by the differences in the $V_1-V_2$ and $H_1-H_2$ intervals. An aberrant QRS complex on the ECC is indicated by the solid circles. At $A_1 - A_2$ intervals of 480 to 440 msec, $A_2$ was not conducted to the ventricles and the gap in A-V conduction occurred (diagonal lines). During the gap, $A_2$ was still conducted to the bundle of His as indicated by the Xs. The gap occurred at $H_1-H_2$ intervals of less than 513 msec which is the effective refractory period of the VSCS (stippled area). At the end of the gap, $H_1-H_2$ intervals increased to values greater than 513 msec, and conduction to the ventricles resumed.

The relationship of the intervals between the basic and premature ventricular depolarization ($V_1-V_2$ intervals) to the intervals between basic and premature atrial depolarizations ($A_1-A_2$ intervals) was determined for each of the subjects exhibiting a gap. In addition, the relationship of the intervals between the basic and premature His-bundle depolarizations ($H_1-H_2$ intervals) to the $A_1-A_2$ intervals was also determined. The terms functional and effective refractory periods are used to indicate specific points on these A-V conduction curves. The functional refractory period of the A-V conduction system occurs at the minimum attainable interval between two successive ventricular responses, both propagated from the atrium (minimum $V_1-V_2$ interval on the A-V conduction curve) (1, 3, 7.9). Similarly, the functional refractory period of the A-V node is the minimum attainable interval between two successive His-bundle responses both propagated from the atrium.
Gap in A-V conduction in a subject with a normal P-R interval. Premature atrial stimuli were introduced during a sinus cycle length of 880 msec. Top trace in each panel = lead II ECG; second trace = lead V2 ECG; bottom trace = His bundle electrogram (HBE); A1 = atrial electrogram of sinus origin; H1 = His bundle deflection; V1 = ventricular electrogram; S = premature stimulus artifact; A2 = premature atrial depolarization; H2 = premature His bundle depolarization; V2 = premature ventricular depolarization; HJ interval = 100 msec; H1-V1 interval = 80 msec. A: At an A2-H2 interval of 450 msec before the onset of the gap, A-V conduction of A2 was delayed in the A-V node (A2-H2 = 136 msec). H1-H2 interval was 480 msec, greater than the effective refractory period of the VSCS (475 msec). B: Beginning of the gap occurred at an A2-H2 interval of 390 msec. Conduction block of A2 occurred distal to the His bundle. A2-H2 = 140 msec. H1-A2 interval was 445 msec, less than the effective refractory period of the A-V node. H1-H2 interval was 430 msec.
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(minimum H1-H2 interval). The entire area between the stimulating and recording electrodes, including the proximal His bundle, are factors in the consideration of this refractory period. The effective refractory period of the A-V conduction system begins with the longest A1-A2 interval at which A2 fails to propagate to the ventricles. The effective refractory period of the A-V node is the longest A1-A0 interval at which A2 fails to propagate to the His bundle. The effective refractory period of the ventricular specialized conduction system (VSCS) occurs at the H1-H2 interval at which conduction of H2 is blocked in the His-Purkinje system (10). The H1-H2 interval is the interval between the basic and premature stimulus depolarizing the His bundle and takes into account delay of the premature impulse in the A-V node (1).

Figure 1 demonstrates an A-V conduction curve in a patient with a gap in A-V conduction. As the premature atrial impulse (A2) was induced progressively earlier in the atrial cycle, an A1-A2 interval was reached where its A-V conduction was delayed in relation to the conduction time of the basic atrial impulse (A1). This conduction delay of A2 was confined to the A-V node. As the A1-A2 interval was further decreased, a point was reached in six of the eight studies where A-V conduction delay of the premature atrial impulse also began to occur in the VSCS. In two studies conduction delay of A2 did not occur in the VSCS before the gap. Further reduction of the atrial coupling interval resulted in A-V conduction block of A2 and the inception of the gap. In all studies the premature atrial impulse was blocked after it traversed the A-V node and depolarized the His bundle (Figs. 2B, C and 3B). The H1-H2 interval at which conduction of the premature impulse is blocked within the VSCS indicates the effective refractory period of this conducting system. As A1-A2 was decreased still further, conduction time of A2 through the A-V node became longer as indicated by the decreasing slope of the H1-H2 curve. However, throughout this period of A-V conduction block (the gap), the H1-H2 interval remained less than the effective refractory period of the VSCS, and the block occurred distal to the His bundle. When A2 occurred sufficiently premature, its conduction through the A-V node was delayed enough to permit recovery of the VSCS, and A2 was again conducted to the ventricles. At this point, the H1-H2 intervals increased to values greater than the effective refractory period of the VSCS and the gap in A-V conduction ended. This sequence of events is demonstrated in Figures 1 to 5. Conduction block of the premature atrial impulse in the A-V node occurred at still shorter A1-A2 intervals (effective refractory period of the A-V node). The atrial coupling intervals during which the gap occurred in these studies were readily reproducible upon repeated determinations at a constant basic cycle length.

In two studies, occasional premature impulses were conducted to the ventricles during the gap period (Fig. 4A). This occurred when the premature impulse was unexpectedly delayed in the A-V node, resulting in an Hi-H2 interval which was greater than the effective refractory period of the VSCS. The A1-A0 intervals at which these conducted impulses occurred varied on repeated exploration of the gap period.

In one subject with a long P-R interval (.26 msec), a gap in A-V conduction occurred only after the administration of .2 mg/kg of atropine (Fig. 5). Before atropine, conduction...
Gap in A-V conduction in a subject with a long P-R interval (.26 sec) after atropine administration. Premature atrial stimuli introduced during basic drive cycle length of 665 msec.

S1 = basic drive stimulus artifact; S2 = premature stimulus artifact. Abbreviations same as in Figure 2. Solid arrows indicate atrial electrogram, open arrows indicate premature stimulus artifact. A: At an A2-H2 interval of 355 msec, before onset of the gap, conduction of A2 was delayed in A-V node (A2-H2 = 220 msec); H2-H2 interval was 400 msec, greater than the effective refractory period of VSCS (395 msec). B: A-V conduction block of A2 distal to His bundle during the gap. A1-A2 = 245 msec; A2-H2 = 220 msec; H2-H2 = 390 msec (less than effective refractory period of VSCS). C: Resumption of A-V conduction at end of gap (A2-H2 = 310 msec). A2-H2 increased to 280 msec; as a result the H2-H2 interval was 420 msec (greater than effective refractory period of VSCS).

Table 1 summarizes the values for the refractory periods of the A-V conduction system (A-V node and VSCS) for the group demonstrating the gap in A-V conduction. In all cases in which the gap was found, the functional refractory period of the A-V node (minimum Hi-Hi interval) was less than the effective refractory period of the VSCS. This allowed premature atrial stimuli to traverse the A-V node rapidly enough to arrive in the Hiss-Purkinje system while it was effectively refractory, resulting in conduction block distal to the common bundle. In all cases, the H1-H2
Effect of beta-receptor blocking drug on the gap in A-V conduction in a subject with a short P-R interval (.11 second). Premature atrial stimuli were introduced throughout the basic drive cycle length of 700 msec.

A: Control. Gap in A-V conduction at A1-A2 intervals of 390 to 343 msec. H1-H2 intervals were less than 400 msec during the gap, effective refractory period of VCS (stippled area). Functional refractory period of A-V node = 360 msec. Occasional A-V conduction occurred during the gap period when A2 was unexplainably delayed in A-V node.

B: A-V conduction curve after 10 mg H56/28 (Aptine). Conduction of premature atrial impulses through A-V node were prolonged so that the functional refractory period of A-V node increased to 480 msec. H1-H2 did not decrease to the effective refractory period of the VSCS. As a result, a gap did not occur. Symbols and abbreviations same as in Figures 1 and 2.

In the group which did not demonstrate the gap phenomenon, 34 of the 37 patients had A-V nodal functional refractory periods which were greater than the effective refractory period of the VSCS. This is indicated by the fact that at the minimum H1-H2 intervals, conduction block did not occur in the His-Purkinje system. Actual values for the effective refractory periods of the VSCS in these instances could not be obtained. Three subjects in this group demonstrated conduction block of premature atrial impulses in the VCS (the functional refractory period of the A-V node was less than the effective refractory period of the VSCS). However, A2 never became sufficiently delayed in the A-V node at shorter A1-A2 intervals to permit resumption of conduction to the ventricles.

EFFECT OF BETA-RECEPTOR BLOCKADE ON THE GAP IN A-V CONDUCTION

In a single patient with a short P-R interval (.11 second) the administration of 10 mg of the beta-receptor blocking agent H56/28 (Aptine) resulted in the abolishment of the gap in the A-V conduction curve (Fig. 4). The effect of the beta-receptor blockade was not studied on any other subject with the gap phenomenon. The atrium was driven at a constant cycle length of 700 msec throughout this study. Before beta-receptor blockade, the gap in A-V conduction occurred when the H1-H2 intervals were less than 400 msec (Fig. 4A). After beta-receptor blockade, the P-R interval was prolonged to .13 second. A-V
Effect of decreased basic cycle length on the gap in A-V conduction in a subject with a short P-R interval (.11 second) (not the same subject as in Fig. 4). A: A-V conduction curve determined at a basic drive cycle length of 645 msec. Gap in A-V conduction (diagonal lines) occurred when $H_1-H_2$ intervals decreased below 348 msec (effective refractory period of VSCS). Functional refractory period of A-V node = 325 msec. B: A-V conduction curve determined at a basic drive cycle length of 500 msec. Even though the minimum $H_1-H_2$ interval decreased to 300 msec, conduction block in VSCS (and the gap) did not occur, indicating that the effective refractory period of the VSCS had decreased to less than this value. Symbols and abbreviations same as in Figures 1 and 2.

TABLE 2

<table>
<thead>
<tr>
<th>Patient</th>
<th>Basic cycle length</th>
<th>AVN ERP</th>
<th>VCS ERP</th>
</tr>
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<tr>
<td>C.G.</td>
<td>1000</td>
<td>420</td>
<td>340</td>
</tr>
<tr>
<td>J.M.</td>
<td>845 (S)</td>
<td>420</td>
<td>395</td>
</tr>
<tr>
<td>C.M.</td>
<td>500</td>
<td>420</td>
<td>390</td>
</tr>
</tbody>
</table>

Abbreviations same as Table 1. All values expressed in milliseconds.

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Discussion

Conduction delay and block of premature atrial impulses in the VSCS has been demonstrated in both the canine (1, 12-14) and human hearts (6, 15, 16). In particular, Moe et al. have extensively investigated this phenomenon in the dog (1). Although His-bundle activity was not recorded during their experiments in which a gap in A-V conduction was demonstrated, their results suggest that the conduction block was occurring distal to the A-V node. The gaps were associated with patterns of A-V conduction demonstrated to result from right bundle-branch block. Physiological interventions which prevented premature atrial impulses from entering the VSCS while it was refractory abolished the gaps (1). In the case reported by Goldreyer and Bigger, a gap in A-V conduction was noted after quinidine administration and was associated with marked ventricular aberration, suggesting conduction delay in the VSCS (3). Again, His-bundle activity was not recorded and the site of conduction block during the gap was not documented.

The gap in A-V conduction phenomenon has been attributed to the existence of dual A-V nodal conduction pathways (2). We found a gap in A-V conduction in eight subjects during the recording of His-bundle activity. In no instance was the failure of A-V conduction during the gap due to the effective refractory period of the A-V node itself. Instead, the gap occurred when the functional refractory period of the A-V node was less than the effective refractory period of the VSCS. Premature atrial impulses were able to traverse the A-V node rapidly enough to arrive at the VSCS while it was effectively refractory, preventing conduction to the ventricles. As A2 occurred more prematurely, its transit time through the A-V node was increasingly delayed. Eventually it was slowed to such an extent that most likely repolarization of the VSCS was more complete and thus recovery of excitability of the His-Purkinje system permitted resumption of conduction to the ventricles. In one study (Fig. 4), when the beta-receptor blocking agent Aiptine was given, conduction of the premature impulse through the node was slowed, preventing it from arriving in the distal VSCS before excitability had recovered. On the other hand, after atropine, conduction through the A-V node was speeded, allowing block in the VSCS (Fig. 3).

The site of the conduction block of premature impulses in the VSCS has been investigated both in vitro and in vivo. Microelectrode studies on in vitro preparations of the isolated distal A-V conduction system indicate that premature impulses are blocked in the peripheral Purkinje system, at the point of maximum duration of the refractory period in these preparations (17). However, in the intact canine heart Moe et al. concluded that conduction block occurs in the proximal bundle branches (1). This variance in results may reflect the different experimental approaches used. We have not localized the precise region of the VSCS in which conduction block occurred in our studies. However, right bundle-branch block patterns on the body surface ECG often occurred during conduction delay in the VSCS just before the gap.

The gap in A-V conduction was abolished by decreasing the basic drive cycle length in our studies. Moe et al. have demonstrated in the intact canine heart that as the basic cycle length is decreased, the functional refractory period of the A-V node and the effective refractory period of the VSCS are similarly decreased (1, 8). The effect on the VSCS was much more pronounced than the effect on the A-V node (1). Also the disparity in refractoriness between the right bundle-branch and His bundle was reduced or abolished (1). This decrease in the total refractory period of the VSCS can be explained by the decrease in duration of action potential and effective refractory period of Purkinje fibers with increased driving frequency (10, 17, 18). In our studies, even though the functional refractory period of the A-V node decreased slightly in two instances, the effective refractory period of the VSCS decreased to a much greater extent (until it was less than the A-V nodal functional refractory period). Prema-
ture atrial impulses no longer arrived at the distal VSCS while it was effectively refractory, and as a result conduction block no longer occurred.

The frequency with which a gap in A-V conduction may be demonstrated is low due to the conduction characteristics required. Only a small percent of subjects with normal A-V conduction systems show block of premature atrial impulses in the VSCS (6, 15, 16). A-V conduction block usually occurs in the A-V node. In addition, when conduction block does occur in the VSCS, A-V nodal conduction delay of earlier premature atrial impulses is not always of sufficient magnitude to allow for recovery of the His-Purkinje system and the resumption of A-V conduction. In subjects with short P-R intervals, control A-H times are significantly shorter than normal. These patients were in normal sinus rhythm and no cardiac arrhythmias were noted (19). Premature atrial impulses traversed the A-V node rapidly late in the cardiac cycle, although early premature impulses were delayed quite markedly. Thus, late premature impulses reached the VSCS while it was effectively refractory but early ones did not. In subjects with left bundle-branch block, conduction block of premature impulses in the VSCS can occur more readily. A similar conclusion was reached by Menendez et al. (1). This may be due to the disease process in the VSCS, as well as to the longer refractory period of the right bundle-branch which is the only remaining effective conduction pathway (1, 4, 17).

Although we have observed a gap in A-V conduction only when conduction block of premature atrial impulses occurs in the VSCS, the present study does not eliminate the possibility of gap phenomenon due to conduction block in the A-V node or to dual A-V nodal pathways.

References


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