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Functional Characteristics of Human Macro-Reentry: A Study of "Pre-Excited" Circuits by Extrastimulus Method

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The effect of improved conduction in areas of delay was tested during macro-reentry within the His-Purkinje system, in an attempt to separate the role of conduction delay from that of prematurity of the extrastimulus as the key determinant of reentry. Using the right ventricular extrastimulus technique (S_1S_2 method), both the critical His-Purkinje system delays and the zone of S_1S_2 intervals causing His-Purkinje system reentry were determined. Then, using a previously described technique of atrioventricular (AV) sequential pacing during the basic drive, the potential site of His-Purkinje system conduction delay was (anterogradely) excited earlier (pre-excitation), as compared with the control S_1S_2 method. This produced a decrease in retrograde His-Purkinje system delay (S_2H_2), as compared with the same S_1S_2 interval during the control method. Changing the degree of pre-excitation at each S_1S_2 interval allowed for determination of the critical (or shortest) S_2H_2 delay necessary for His-Purkinje system reentry at each coupling interval. Of importance was the observation that the critical delay was not specific for each case but varied with the prematurity of S_2. For example, the critical S_2H_2 delay required for reentry was actually less at shorter S_1S_2 intervals as compared with longer S_1S_2 intervals (from 206 ± 25 to 187 ± 20 ms, $p < 0.01$).

These data suggest that manifestation of reentry is a complex interplay between degree of prematurity and conduction delay. The so-called critical conduction delay can be readily modified by altering the site of block, which in turn may be dependent on prematurity of the extrastimulus.

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Since the introduction of programmed stimulation in 1967 (1,2), the method of premature stimulation has been widely used in the study of human reentrant circuits (3–9). This method, however, has changed little since its utility was emphasized by Schmitt and Erlanger (in 1928) (10) for the study of potential reentrant circuits. Thus, not unexpectedly, their observation, that a premature beat (S_2) may conduct slowly or block, or both, in the functionally different components of a reentrant circuit, has been consistently duplicated in various human reentrant arrhythmias (1–7). However, using conventional methods of premature stimulation, the association of progressively greater conduction delay with greater prematurity of S_2 has precluded separation of the role of conduction delay from that of prematurity of S_2 during the zone of reentry.

We have previously reported (11,12) a method in which atrioventricular (AV) sequential pacing of the human retrograde pathway facilitated conduction of a premature ventricular beat. The decrease in conduction delay was considered to result from the pre-excitation of the retrograde pathway by the paced atrial impulse (11). In the present study we hypothesized that pre-excitation of a potential macro-reentrant circuit would, by mitigating conduction delay associated with prematurity, permit the separation of their individual roles in the human reentrant phenomenon.

A pacing protocol was developed whereby the potential of S_2 to reenter, with varying degrees of conduction delay at a given coupling interval in the zone of reentry, could be systematically analyzed. The model of reentry in the His-Purkinje system was thought to be particularly suited to evaluate the effect of electrical pre-excitation. A unique advantage of the His-Purkinje system reentrant circuit is the ability to selectively pre-excite areas of delayed conduction without affecting the site of block. The results and clinical implications of such electrical (as opposed to pharmaco-

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logic) perturbation of a known reentrant circuit in the human His-Purkinje system form the basis of this report.

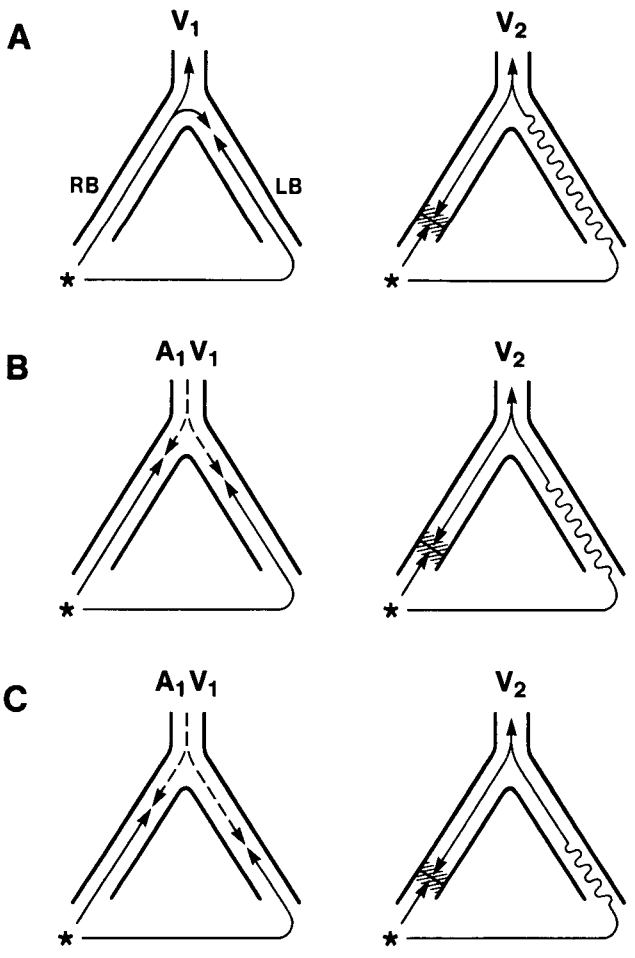
Methods

Study patients. Twelve consecutive patients who manifested a clearly defined and reproducible zone of macro-reentry in the His-Purkinje system, or so-called bundle branch reentry, were included in this study. Patients who manifested erratic His-Purkinje system behavior, that is, unexplained lengthening or shortening of conduction times during programmed stimulation, were excluded, as were the patients in whom the zone of reentry terminated before the effective refractory period of the ventricular muscle. Thus, only those patients in whom the zone of His-Purkinje system reentry behaved in a predictable manner (13–16) were considered ideal for this study. All patients had sinus rhythm, with narrow (≤0.12 second) QRS complexes. Eight patients had coronary artery disease, two had cardiomyopathy and two had no underlying heart disease.

Electrophysiologic study. Right heart catheterization was performed in the nonsedated, postabsorptive state. The nature of the procedure was explained and informed and signed consent was obtained. Three to four quadripolar 6F catheters were introduced percutaneously through peripheral veins and were fluoroscopically positioned in the high right atrium, AV junction and right ventricular apex for local bipolar recordings (filtered at 30 to 500 Hz) and electrical stimulation. Recordings from the His bundle, and in addition from the right bundle in three of the patients, were obtained. In addition to the bipolar electrograms, three surface electrocardiographic leads (I, II and V_1) and time lines were displayed simultaneously on a multichannel oscilloscope (Electronics for Medicine VR-16) and recorded on magnetic tape (Honeywell model 5600 C) for subsequent retrieval on photographic paper at 100 mm/s. Intracardiac stimulation was performed with a Bloom DTU 101 digital stimulator capable of delivering premature stimuli after a basic drive of AV sequential pacing, with adjustable AV intervals.

Pacing protocol (Fig. 1). Initial retrograde conduction studies were done according to previously described pacing methods (13). In general, after a basic ventricular drive (V_1V_1) (range 550 to 700 ms) the diastolic interval was scanned with V_2 at progressively shorter V_1V_2 intervals until the S_2 encountered ventricular muscle refractoriness (control study, Fig. 1A). After the zone of reentry in the His-Purkinje system had been defined with the control method just described, the pacing protocol was repeated, substituting for the basic ventricular drive (V_1–V_1) an AV sequential drive A_1V_1–A_1V_1 (Fig. 1B) at the same cycle length (AV sequential method). The AV interval was programmed to cause collision of the paced atrial and ventricular impulses in the His-Purkinje system so as to pre-excite the macro-reentrant circuit (see Definition of Terms) (11). After the basic drive A_1V_1–A_1V_1, V_2 was introduced at progressively shorter coupling intervals, identical to those during the control method, and the zone of His-Purkinje system reentry was again determined. The pacing protocol was repeated with longer AV intervals (by 10 to 20 ms), programmed to analyze the effect of greater pre-excitation of the His-Purkinje

Figure 1. Diagrammatic representation of the pacing protocol. **A,** Conduction of the paced ventricular impulse (**asterisk**) retrogradely through the right bundle branch (RB) and left bundle branch (LB) during the basic drive (V_1). A premature beat (V_2) (**right**) is shown to block distally in the right bundle branch (**hatched area**), manifest slow conduction in the left bundle branch and conduct in the anterograde direction in the right bundle branch. **B,** Pre-excitation of the macro-circuit during the basic atrioventricular sequential (A_1V_1–A_1V_1) drive. The paced atrial impulse depolarizes an area of the left bundle branch and a (comparatively smaller) area of the right bundle branch. The **interrupted arrow** depicts earlier depolarization of areas of the potential circuit by the atrial impulse, as compared with V_1 during the control method. Conduction of the premature beat (V_2) through the pre-excited circuit is shown (**right**) and includes a schematic representation of improved (faster) conduction through the left bundle branch. **C,** Greater pre-excitation results from programming a longer AV interval. The differential pre-excitation of the left bundle branch versus the right bundle branch and its effect on reentry within the His-Purkinje system is discussed in the text.



system (Fig. 1C) until the zone of His-Purkinje system reentry was abolished.

For the purpose of data analysis, the V_1V_2 interval was measured from the respective stimulation artifacts, that is, S_1S_2; therefore the terms S_1S_2 and V_1V_2 are used interchangeably in the text unless specified otherwise.

Definition of Terms

Atrial pacing and determination of AV intervals. The AH interval was measured from the stimulus artifact of the low atrial electrogram to the onset of the His bundle deflection and was used to program the AV interval during the AV sequential method. Generally, the retrograde His-Purkinje system conduction times are 20 to 40 ms greater than anterograde conduction time at the same cycle length (13). Thus, during AV sequential drive the programming of the AV interval 10 to 50 ms less than the AH interval permitted collision of the atrial and ventricular impulses in the His-Purkinje system (below the His bundle). This was confirmed by ensuring that the AH interval during the AV sequential drive was identical to the AH interval during atrial pacing, thereby permitting the conclusion that the His bundle was depolarized anterogradely from the atrial impulse of the AV sequential drive (11).

Electrical pre-excitation. The term pre-excitation is used in the conventional physiologic sense, as introduced by Ohnell (17). It denotes depolarization of tissue by an additional excitatory spread in advance of that during normal conduction or, as is the case in this study, the control method (Fig. 1). The word electrical is used here to stress the programmed nature of the earlier excitation and to indicate that pre-excitation is being used in a context different from the clinical pre-excitation syndromes. Thus the electrical pre-excitation of the His-Purkinje system reentrant circuit resulted from the atrial impulse during the AV sequential method. The use of progressively longer (by 10 to 20 ms) AV intervals resulted in greater portions of the His-Purkinje system depolarized by the atrial impulse and thus greater pre-excitation of the macro-reentrant circuit (Fig. 1).

Retrograde studies and determination of conduction times during His-Purkinje system reentry. During premature stimulation, retrograde H_2 and RB_2 (right bundle branch) potentials emerged from the V_2 electrograms and were identified by their configuration and physiologic behavior. The S_2H_2 (and S_2RB_2) intervals were measured from the ventricular stimulus artifact to the respective deflections, during both control and AV sequential method. During His-Purkinje system reentry, the S_2H_2 interval was taken to denote conduction time through the ventricular muscle-left bundle axis (13–15), irrespective of the occurrence of ventricular muscle latency (that is, V_1V_2 interval greater than S_1S_2 interval). This was based on the assumption that, whereas surface inscription of V_2 was delayed, localized slow conduction in the ventricular muscle (a component of the His-Purkinje system reentrant circuit) was occurring. The greatest latency was noted at S_1S_2 intervals 10 to 20 ms longer than the effective refractory period of ventricular muscle. As such, these S_1S_2 intervals were selected for analyzing the effect of slow muscle conduction on reentry.

The H_2V_3 interval, measured from the onset of H_2 to the earliest recorded ventricular activity during V_3, was considered to reflect conduction time through the right bundle-ventricular muscle axis of the reentrant circuit.

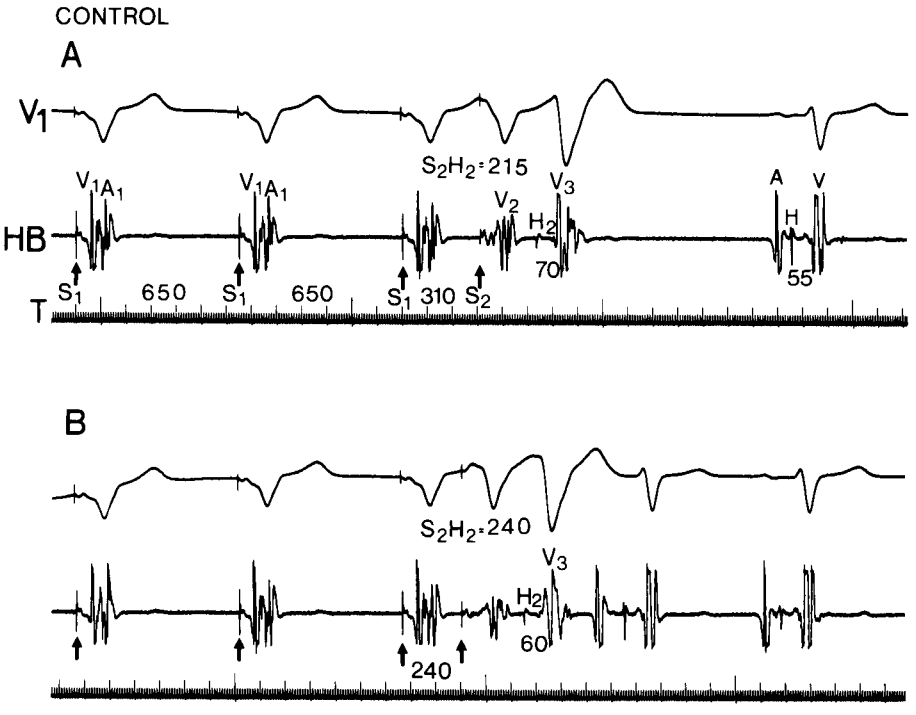


Figure 2. Case 8. The outer and inner limits of the zone of reentry during the control method. Surface electrocardiographic leads V_1, intracardiac His bundle recording (HB) and time lines (T) are shown in the same sequence here and in Figures 3 and 4. **A,** After a basic ventricular drive (S_1 to S_1) at a cycle length of 650 ms, a premature beat (S_2) at an S_1S_2 interval of 310 ms results in S_2H_2 delay of 215 ms, which is sufficient for reentry within the His-Purkinje system (V_3). The appropriate atrial, His bundle and ventricular electrograms are labeled. The H_2V_3 interval (70 ms) is also depicted. **B,** Inner limit of the zone of reentry (S_1S_2 = 240 ms).

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The zone of His-Purkinje system reentry was defined as the range of S_1S_2 intervals where S_2 produced the V_3 phenomenon. The outer and inner limits of the zone of His-Purkinje system reentry were the longest and the shortest S_1S_2 intervals that resulted in V_3.

Effective refractory period of ventricular muscle was the longest S_1S_2 interval in which S_2 did not evoke a ventricular response.

Results

Effect of pre-excitation on the zone of His-Purkinje system reentry. During the control method, the S_1S_2 intervals demonstrating His-Purkinje system reentry (that is, zone of reentry) ranged from 293 ± 18 to 240 ± 24 ms, with a mean zone of 53 ± 23 ms in the 12 patients. With the AV sequential method a decrease in the zone of reentry was observed, because the reentry was first noted at a shorter S_1S_2 interval and no change was noted in the relative or effective refractory period of the ventricular myocardium. The decrease in zone of reentry was least with the shortest AV interval used. There was, in general, a progressively greater decrease in zone of reentry with longer AV intervals (that is, greater pre-excitation of the His-Purkinje system). In all 12 patients the longest programmed AV interval totally prevented reentry at all S_1S_2 intervals.

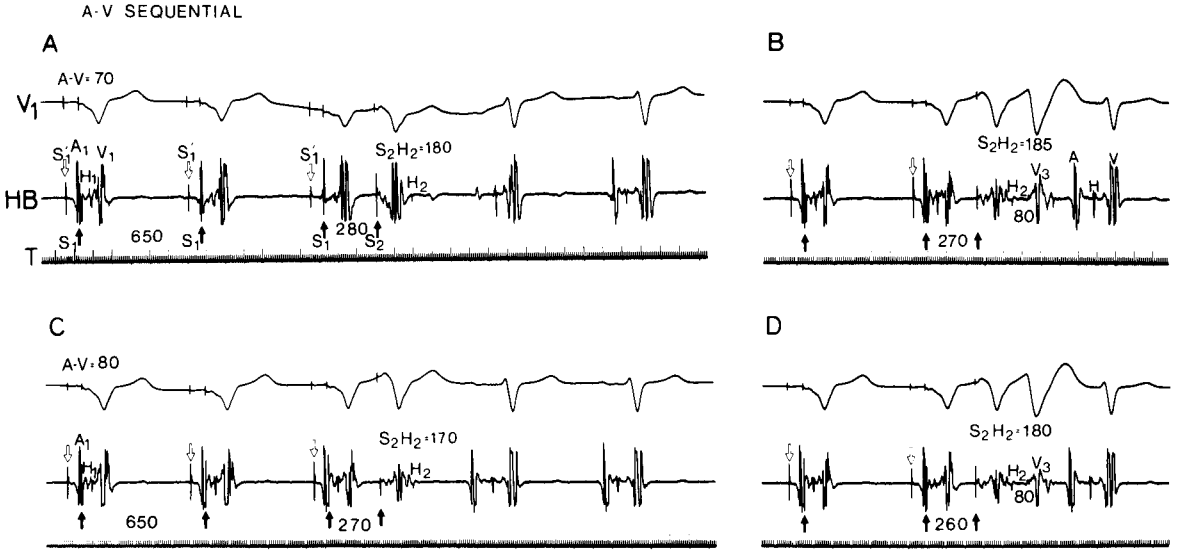
This pattern is illustrated in Figures 2 to 4 from Patient 8. His-Purkinje system reentry was demonstrated at all S_1S_2 intervals from 310 to 240 ms (Fig. 2). With the AV sequential method, at an AV interval of 70 ms (Fig. 3A and B), the zone of reentry is significantly decreased because reentry now starts at an S_1S_2 interval of 270 ms. Further increase in AV intervals causes a greater decrease in the zone of reentry (Fig. 3C and D, Fig. 4A and B) until reentry is abolished at all S_1S_2 intervals with a programmed AV interval of 100 ms (Fig. 4C).

Figure 5 shows a family of curves from the same patient and also illustrates the effect of progressively greater pre-excitation (that is, increasing AV intervals) on the entire zone of reentry. This figure is discussed in greater detail later.

Relation between retrograde conduction delay (S_2H_2) and His-Purkinje system reentry. In Figure 5, the uppermost curve typifies the relation during the control method. At an S_1S_2 interval of 310 ms, the shortest or critical S_2H_2 delay necessary for reentry is achieved. As has been observed for His-Purkinje system reentry in particular (14,15) and reentrant circuits in general (6,7), greater prematurity of S_2 resulted in longer S_2H_2 delays during the zone of reentry. This pattern was maintained until ventricular refractoriness was encountered.

Pre-excitation of the His-Purkinje system (more specifically the left bundle branch) resulted in a shorter S_2H_2 interval at an identical S_1S_2 interval (Fig. 5). A comparison

Figure 3. Case 8. Effect of "pre-excitation" on the zone of reentry. **A,** AV sequential method (AV interval = 70 ms) in the same patient. S_1' to S_1' basic drive with corresponding atrial, His bundle and ventricular electrograms are labeled (see text under Definitions). The cycle length of AV sequential drive (650 ms) is same as in Figure 2. A premature beat (S_2) delivered well within the zone of reentry (280 ms) (as demonstrated during the control method) fails to result in reentry. **B,** Outer limit of the zone of reentry which, at the programmed AV interval of 70 ms, now starts at an S_1S_2 interval of 270 ms. Note that the S_2H_2 delay (185 ms), which results in reentry, is 30 ms less than the shortest S_2H_2 interval, causing His-Purkinje system reentry during the control method (Fig. 2A). **C** and **D** demonstrate that programming a longer AV interval (of 80 ms) results in further abbreviation of the zone of reentry. Bundle branch reentry occurs with shorter S_2H_2 delays at shorter S_1S_2 intervals as compared with critical S_2H_2 delay required at longer S_1S_2 intervals (Fig. 2A).



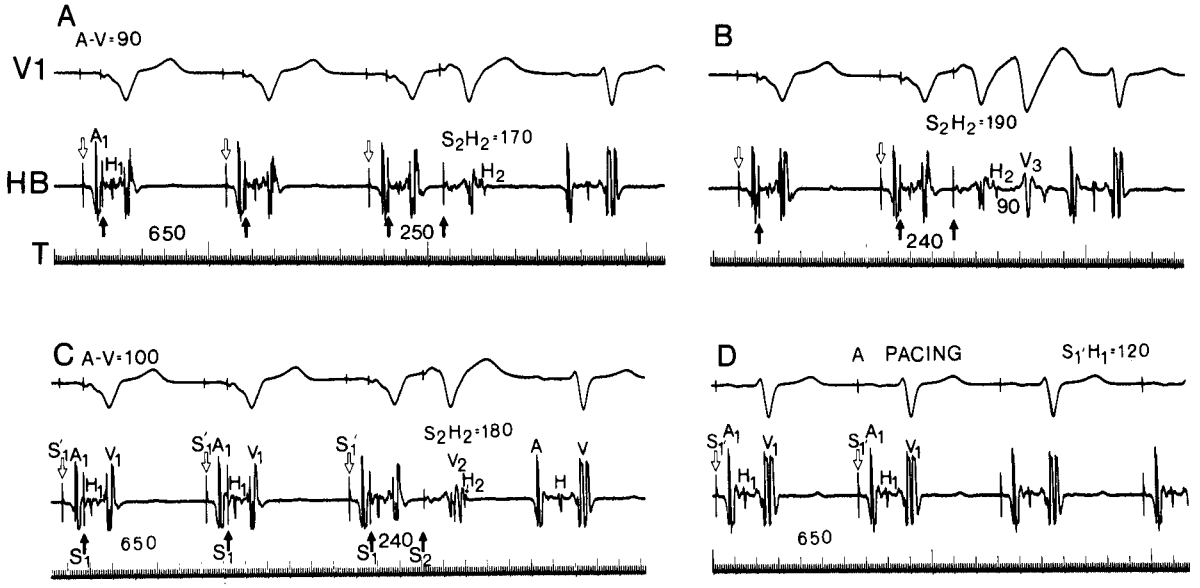


Figure 4. Case 8. Effect of increasing the degree of pre-excitation on reentry. **A** and **B** show that increasing the programmed AV interval to 90 ms further shortens the zone of reentry, now manifesting only at an S_1S_2 interval of 240 ms. **C** shows the AV interval (100 ms) at which reentry could not be elicited at all S_1S_2 intervals in the entire zone of reentry. **D** shows the S_1' to H_1 interval (120 ms) during atrial pacing at a cycle length of 650 ms. Although not labeled, the S_1' to H_1 interval during AV sequential pacing (in Fig. 3 and 4) is identical to that in this panel. This confirms that the His bundle is depolarized anterogradely from paced atrial impulse and collision of the atrial and ventricular impulses takes place in the His-Purkinje system.

of S_2H_2 intervals during the control method can be made with S_2H_2 delays associated with various degrees of pre-excitation of the left bundle branch during the basic drive. It is apparent from Figure 5 that progressive abbreviation of the zone of reentry is clearly associated with progressive shortening of the retrograde conduction times within the left bundle branch.

Relation between critical His-Purkinje system delay and prematurity of S_2. It was consistently noted that as the S_1S_2 interval decreased, the shortest or critical S_2H_2 delay required for His-Purkinje system reentry also changed. This important relation can be more clearly appreciated from Figure 5. For example, at an S_1S_2 interval of 310 ms, the shortest S_2H_2 delay causing reentry (during the control method) is 215 ms. However, at a closer coupling interval of 260 ms, the critical S_2H_2 delay is 180 ms. Similarly, an S_2H_2 delay of 190 ms fails to result in macro-reentry at an S_1S_2 interval of 320 ms, but is of sufficient magnitude for His-Purkinje system reentry at shorter S_1S_2 intervals of 260, 250 and 240 ms (AV intervals of 70, 80 and 90 ms, respectively).

Table 1 compares the so-called critical or shortest S_2H_2 delay causing His-Purkinje system reentry during the control method with the shortest S_2H_2 delay causing reentry during the AV sequential method at S_1S_2 intervals without stimulus to muscle response latency. In 10 of the 12 patients, reentry could be demonstrated at S_2H_2 delays less than the shortest S_2H_2 delays causing His-Purkinje system reentry during the control method ($p < 0.01$). In all instances the decrease in so-called critical delay was observed at shorter S_1S_2 intervals ($p < 0.001$). Note the increase in the H_2V_3 interval associated with shorter S_2H_2 intervals in some patients.

Effect of conduction delay in the ventricular muscle. This was analyzed separately. It was noted that at S_1S_2 intervals showing stimulus to ventricular muscle response latency (240 ms in Fig. 5) the critical delay was again increased (to 190 ms). In addition, such conduction delay in the ventricular muscle was also associated with prolongation of the H_2V_3 interval. In Figure 5, for example, the H_2V_3 interval associated with an S_2H_2 delay of 190 ms is longer at the S_1S_2 interval of 240 ms (with latency) as compared with the longer S_1S_2 intervals of 250 and 260 ms with identical S_2H_2 delay. Additionally, the effect of muscle latency on the H_2V_3 intervals is most prominent at the shortest S_2H_2 delays achieved at S_1S_2 intervals of 240 ms.

Table 2 compares the shortest S_2H_2 intervals obtained at S_1S_2 intervals showing stimulus to muscle response latency with similar or shorter S_2H_2 intervals without latency. The shortest S_2H_2 delays associated with muscle latency were achieved with the longest AV intervals (Fig. 5). Similarly, comparable S_2H_2 intervals at S_1S_2 intervals without latency were found either during the control method or with a shorter AV interval (less pre-excited left bundle branch). Table 2 shows that at similar S_2H_2 intervals, the effect of ventricular muscle latency was manifest as either prolongation or failure of conduction in the His-right bundle-ven-

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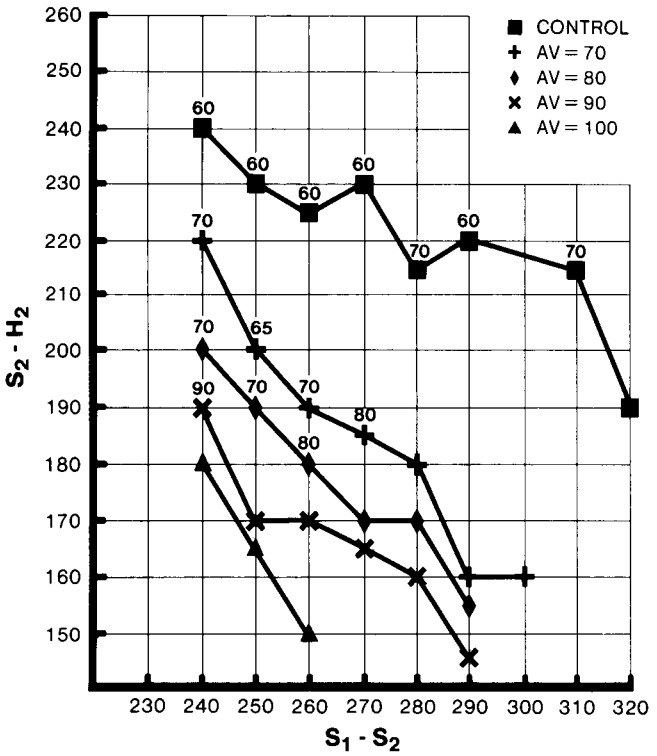

Figure 5. Case 8. Relation between prematurity and critical conduction delays. A family of curves is depicted where conduction delays (S_2H_2) are plotted against coupled intervals (S_1 to S_2) during both the control method and the AV sequential method at various programmed AV intervals (from 70 to 100 ms). The superscripts on each curve denote the H_2V_3 interval and indicate the S_1S_2 interval (**abscissa**) and S_2H_2 delay (**ordinate**) that result in reentry within the His-Purkinje system. This figure is discussed in detail in the text; however, some points are of note. 1) Reentry may occur with less than the critical S_2H_2 delay (recorded during the control method), albeit at a shorter S_1S_2 interval; and 2) the H_2V_3 intervals at an S_1S_2 interval of 240 ms are greater than the H_2V_3 intervals at identical S_2H_2 delays obtained at longer S_1S_2 intervals (for example, compare H_2V_3 intervals at the S_2H_2 delay of 190 ms when the latter is obtained at S_1S_2 intervals of 240, 250 and 260 ms).

tricular muscle axis, that is, either a longer H_2V_3 interval or absence of His-Purkinje system reentry, respectively, in all but one patient (Case 10).

Discussion

In the classic study of Schmitt and Erlanger (10), it was demonstrated that a potential reentrant circuit, quiescent when activated at a slow rate, would manifest reentry when stimulated by a premature beat. Electrocardiographic observations (18), microelectrode studies on the AV node (19–21) and isolated tissues (22–24) and, later, pioneering human studies (1–9) have, over the ensuing decades, testified to the tremendous impact of their observation on the study of reentrant circuits. It is widely recognized now that onset of a reentrant process requires an initial block of an impulse in some pathway and slow conduction along another. For a given circuit, the initial pathway of block provides the return route for the impulse if conduction delay along the slow pathway is of sufficient (or critical) magnitude to allow recovery of excitability.

Physiologic and methodologic considerations. None of the clinical studies, however, have been able to separate the role of prematurity from that of the observed conduction delay during manifest reentry. In this study we postulated that a method of pre-exciting circuits not only may permit such an analysis but also may have potential clinical applications, because it may provide a way to reduce or abolish conduction delay associated with premature beats.

The selection of reentry in the His-Purkinje system as a model for studying the effect of pre-excitation was based on physiologic as well as methodologic considerations.

1) The site of unidirectional block (that is, in the distal right bundle) has been well documented in several previous human and canine studies (15,25). The response of the pathway of slow conduction (left bundle) (16) during the zone of reentry is consistent with well known features of reentrant circuits and is easily demonstrated with the method of ventricular premature stimulation (14,15).

2) The use of a right ventricular pacing site permitted relatively greater pre-excitation (by the atrial impulse) of the left bundle (area of conduction delay) as opposed to the right bundle (site of unidirectional block) (Fig. 1). Thus, increasing the degree of pre-excitation would involve first the areas of conduction delay and later the site of retrograde block.

It should be realized that in a study of circuits involving the AV node or accessory pathway, a pre-exciting impulse will most likely have unimpeded access to both the slow pathway and the site of block, thus not permitting a separate analysis of the effect on functionally different components of a reentrant circuit.

Effect of pre-excitation of a macro-circuit on the potential for reentry by a premature beat. The improvement in the left bundle branch conduction delay by the AV sequential drive probably causes the premature impulse to arrive at the site of block (that is, right bundle branch) when it is still refractory to conduction (Fig. 1 to 4). This observation reemphasizes the importance of left bundle branch conduction delay in bundle branch reentry, as our data clearly show for the first time that a premature impulse fails to complete a reentrant loop even when delivered well within the zone of reentry. The failure of reentry to occur at all S_1S_2 intervals may be explained by the inability of S_2 to achieve the necessary conduction delay, or the long programmed AV interval may pre-excite and thus abolish conduction block along the right bundle branch (10,26), causing the premature beat to conduct up both bundle branches. The latter mechanism was thought to be operative when the

Table 1. Critical Delays for His-Purkinje System Reentry

	Control Method			AV Sequential Method		
Case	S_1S_2	S_2H_2	H_2V_3	S_1S_2	S_2H_2	H_2V_3
1	270	165	55	250	155	55
2	320	230	50	290	195	70
3	300	240	50	260	180	90
4	300	185	70	290	165	90
5	260	200	55	250	190	65
6	290	215	50	260	190	50
7	310	240	70	300	210	75
8	310	215	70	260	180	80
9	280	220	80	260	215	80
10	290	190	120	260	160	115
11	310	175	75	300	195	70
12	280	200	100	260	210	75
Mean (± SD)	293 ± 18	206 ± 25	70 ± 22	270 ± 19	187 ± 20	76 ± 17
p Value*				<0.001	<0.01	NS

*Comparing AV sequential method with control method. All values are in milliseconds.

emergence of the retrograde His bundle deflection (H_2) was no longer observed during the entire range of S_1S_2 intervals (16).

Critical delays during zone of reentry: relation to prematurity of S_2. A comparison of the methods of premature stimulation and constant cycle length pacing have led to inferences stressing that a specific (referred to in this report as critical) conduction delay, and not the prematurity or coupling interval, is the essential determinant of reentry (4). However, with the conventional method of premature stimulation, the shortest, that is, the critical, conduction delay required for reentry is known only for the longest S_1S_2 interval in the zone of reentry. The critical delay for a shorter S_1S_2 interval within the zone of reentry is impossible to ascertain because conduction time in the slow pathway continually increases with greater prematurity.

However, progressively increasing the degree of preexcitation at a given coupling interval results in progressively shorter S_2H_2 delays at the same S_1S_2 interval (see the several S_2H_2 intervals obtained at a given S_1S_2 interval in Fig. 5). Analyzing the data in this manner permits determination of the shortest S_2H_2 delay that results in reentry for a given S_1S_2 interval. It was observed that critical conduction delay was in fact related to prematurity because the returning impulse caused reentry with less (than so-called critical) delay at shorter S_1S_2 intervals. However, at S_1S_2 intervals demonstrating stimulus to muscle response latency, there was reversal of the trend of declining critical delays

Table 2. Effect of Muscle Latency on His-Purkinje System Reentry

	With Muscle Latency				Without Muscle Latency			
Case	AV Int	S_1S_2	S_2H_2	H_2V_3	AV Int	S_1S_2	S_2H_2	H_2V_3
1	120	200	200	—	C	240	200	45
2	240	260	210	80	200	300	210	75
3	140	250	245	60	C	300	240	50
4	180	230	210	65	140	280	210	50
5	90	230	200	—	C	260	200	55
6	120	210	230	—	C	270	190	50
7	70	280	260	—	C	300	250	70
8	90	240	190	90	70	260	190	70
9	140	250	215	90	100	280	215	80
10	120	250	170	105	C	270	170	130
11	120	260	195	—	100	300	195	70
12	100	250	205	—	C	260	205	80
Mean ± SD		243 ± 22*	211 ± 24†			277 ± 20*	206 ± 22†	

*$p < 0.001$; †p = NS. AV Int = AV interval; C = control.

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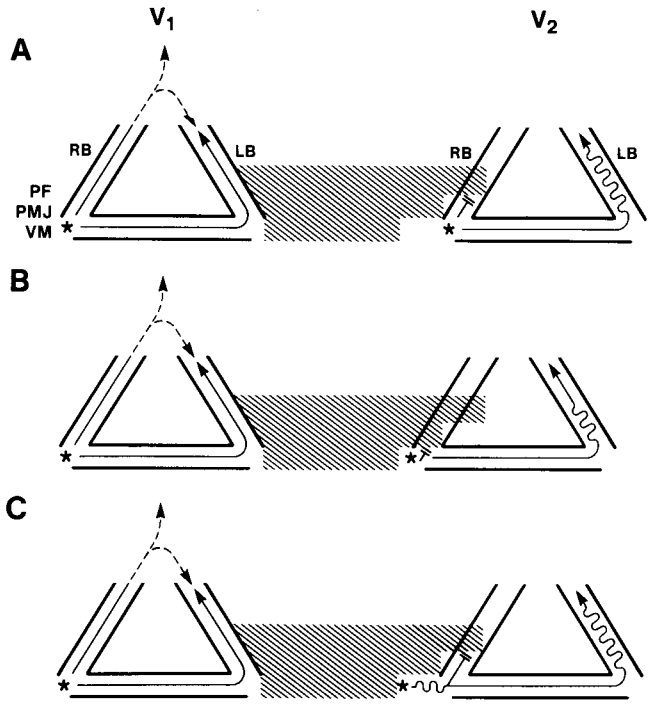

Figure 6. Postulated mechanism for variation in critical conduction delay with change in prematurity. Conduction through right and left bundle branches (RB and LB), the distal Purkinje fiber (PF), Purkinje-muscle junction (PMJ) and ventricular muscle (VM) is depicted. The hypothesis for migration of block is based on the postulation that the effective refractory period (**hatched areas**) is longest for the Purkinje fiber and decreases progressively, being shorter for Purkinje-muscle junction and shortest for ventricular muscle. **A** shows that at a longer V_1V_2 interval the site of block is at the distal Purkinje fiber. The critical conduction delay required for His-Purkinje system reentry is schematically depicted in the left bundle branch (**right**). At a shorter V_1V_2 interval (**B**) the site of block moves distally; this results in less delay being required for reentry. A schematic representation of this decrease in conduction delay is depicted in the left bundle branch. Demonstration of the decrease in critical delay, however, requires pre-excitation of the left bundle branch, which is not shown in this figure for the sake of simplicity. **C**, V_2 is delivered within the relative refractory period of the muscle. The resulting conduction delay (ventricular muscle latency) prolongs the effective input into the right bundle branch, causing the site of block to migrate proximally. This again results in an increase in the critical delay required for His-Purkinje system reentry.

with shorter S_1S_2 intervals. This was sometimes manifested as prolongation of the H_2V_3 interval or occasionally actual block in the right bundle-ventricular muscle axis at short S_2H_2 delays which had previously conducted at longer S_1S_2 intervals. These observations also provide evidence that slow conduction in the ventricular muscle affects the functional characteristics of the reentrant circuit, belying its role as a passive component of the reentrant circuit.

Changing site of block: a postulated mechanism for variation in critical delay during zone of reentry. Even in experimental studies the response of the site of block to varying coupling intervals has not been the object of intense investigation. Mendez and Moe (19) noted attenuation of the action potentials recorded from the beta pathway (site of block) in the AV node at closer atrial coupling intervals. Thus the mechanism for the decrease in critical delay required for reentry at shorter S_1S_2 intervals may only be speculated on. Both human (15) and animal (25) studies have indicated that the site of retrograde block during bundle branch reentry is quite distal. Studies in dog models using multiple recordings (25) have concluded that the site of block of S_2 is at or distal to the "gates" observed by Myerburg et al. (27). If the effective refractory periods in humans do indeed decrease progressively from the distal Purkinje fibers ("gates") to transitional cells and ventricular muscle (27) (Fig. 6), then it may be possible to explain how a shorter S_1S_2 interval can result in the site of block migrating distally in the human Purkinje fiber-Purkinje muscle junction-ventricular muscle axis (Fig. 6B). The distal migration of block and the potential shortening of refractory periods in the region of block with shorter S_1S_2 intervals (28) may explain why reentry can occur with less left bundle branch delay at a closer coupling interval.

The distal migration of the site of block cannot be explained by pre-excitation of the site of block caused by the AV sequential method for several reasons: 1) the distal site of block, in all probability, prevents it from being pre-excited during basic drive with the shorter AV intervals (Fig. 1); 2) pre-exciting the site of block may abolish conduction block (11,26), preventing reentry altogether; and 3) improvement of conduction in the area of block should result in proximal and not distal migration of the site of block, in turn requiring a greater S_2H_2 delay to cause reentry.

At S_1S_2 intervals showing stimulus to muscle response latency, the slower muscle to muscle conduction may effectively delay the input into the right bundle and shift the level of block proximally (Fig. 6C). This would require greater delay in the left bundle branch for His-Purkinje system reentry. It may be argued that proximal migration of block secondary to pre-excitation by the longer programmed AV intervals cannot be entirely ruled out. Although this may be true, it is believed that pre-excitation of the very distal site of block in the right bundle branch would result in a narrow QRS complex with almost imperceptible fusion from the right ventricular apical pacing site. Such AV sequential drives were rarely associated with retrograde H_2 deflections, presumably because of abolition of conduction block (11,26).

Clinical and experimental significance. This study clearly demonstrates that electrical pre-excitation of a human macro-reentrant circuit can prevent the reentrant process initiated by a premature beat. Pre-excitation of potential sites of conduction block or areas of delay has not been systematically studied in clinical tachycardias; however, prevention of AV node reentry with simultaneous AV pacing

(29) can ostensibly represent examples of the paced ventricular impulse pre-exciting and improving conduction in the reentrant circuit. It may be speculated that if areas of conduction delay or block can be accurately identified in ventricular muscle (30), electrical pre-excitation of these areas, in advance of depolarizing the rest of the ventricular muscle, may prevent or modify initiation of ventricular tachycardia.

Apart from prevention of reentry, use of pre-excitation may be a valuable tool in the study of reentrant circuits, especially when questions arise whether reentry is related to observable delay in (what appears to be) the slow component or to the degree of prematurity. For example, the controversy about whether bundle branch reentry is a local muscle phenomenon (31) is clearly mitigated by the direct relation between the decrease in the zone of reentry and improvement in His-Purkinje system conduction.

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