Effect of sudden rate acceleration on the human His-Purkinje system: adaptation of refractoriness in a dampened oscillatory pattern

Patrick J. Tchou, M.D., Michael H. Lehmann, M.D., John Dongas, M.D., Rehan Mahmud, M.D., Stephen T. Denker, M.D., and Masood Akhtar, M.D.

ABSTRACT Although the refractoriness of the human His-Purkinje system (HPS) during constant-rate pacing appears to be closely related to the cycle length of the stimulation, the mode of adaptation of this refractoriness with sudden rate acceleration is not well understood. A systematic evaluation of this adaptation was performed in 14 patients with normal QRS durations and HV intervals referred for electrophysiologic evaluation. The relative refractory period of the HPS (HPS-RRP) was evaluated by the extrastimulus (S2) method during a constant ventricular drive (S1) having a cycle length close to sinus rhythm as possible. An accelerated train of 6 ventricular beats (S1) was then added to the constant drive and the HPS-RRP of each successive beat of this train was similarly determined. Mean S1 cycle length was 750 ± 164 msec (range 600 to 1000). Mean S2 cycle length was 475 ± 55 msec (range 400 to 600). The HPS-RRP of each successive beat of the accelerated train was significantly shorter than that during the S1 drive and behaved in a dampened oscillatory fashion alternating from a lower value on the odd-numbered beats to a higher value on the even-numbered beats. In contrast, the effective and relative refractory periods of the ventricular myocardium during the accelerated train behaved in a cumulative manner, decreasing progressively with the first 2 beats of the train before reaching a plateau value. In conclusion, the data reported here present a new and intriguing picture of the mode of adaptation of the HPS refractoriness to sudden rate acceleration. At least in the range of the cycle lengths used in this study, the refractoriness of the HPS behaves in a dampened oscillatory manner that is radically different from the behavior of the ventricular myocardial refractoriness.


THE REFRACTORINESS of the human His-Purkinje system (HPS) during constant-rate pacing appears to be closely related to the cycle length of the stimulation. The effect of an abrupt acceleration in pacing rate on the human HPS refractoriness is poorly understood. Studies by Denker et al.2-3 evaluated the effect on the HPS refractoriness of a single beat at an abbreviated cycle length that followed a constant cycle length drive. Their data suggested an “excessive” shortening of the HPS refractoriness during sudden shortening of the cycle length when compared with a similar constant cycle length drive. However, they only assessed the effect of a single beat at the shorter cycle length. To our knowledge, the mode of adaptation of the HPS refractoriness from one steady state to another during a sudden acceleration of heart rate has not been evaluated in the human heart beyond the first beat of the shorter cycle length. The present study systematically evaluated the behavior of the human HPS relative refractory period (HPS-RRP) during a sudden rate acceleration. The data reported here present a new and unusual picture of the dynamic response of human HPS refractoriness to sudden rate acceleration that has not been previously reported. This response appears to be dramatically different than the behavior of ventricular myocardial refractoriness during identical rate accelerations.

Methods

Intracardiac electrophysiologic studies were performed in subjects in the postabsorptive state with recording and stimulating techniques that have been previously described.4,5 All cardioactive medications were withheld for at least five half-lives.

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The nature of the studies was explained and informed consent was obtained from each patient.

Fourteen consecutive patients with normal QRS duration on their surface electrocardiograms and normal HV intervals form the basis of this report. These patients underwent intracardiac electrophysiologic studies because of symptomatic or suspected cardiac arrhythmias. There were 10 men and four women. The pacing protocol used in this study was specifically designed to evaluate the mode of adaptation of the HPS-RRP (see definitions below) during a sudden acceleration of ventricular rate.

The HPS-RRP was chosen as an index of HPS refractoriness over the effective refractory period of the HPS (HPS-ERP) because, for the following reasons, the retrograde HPS-ERP does not seem to correlate well with refractoriness as measured in isolated Purkinje fibers. (1) There is frequently a large zone of coupling intervals between onset of retrograde HPS-RRP and occurrence of HPS-ERP, often as long as 100 msec. In isolated Purkinje fibers, the zone of coupling intervals in which premature beats would show conduction delay comparable to that found clinically is much narrower, usually no more than 20 to 30 msec. (2) In isolated Purkinje fibers, the relationship of conduction delay of a premature beat to its coupling interval is asymptotic. The corresponding relationship of \( V_{1H2} \) intervals to \( V_{1V2} \) intervals in the human heart is usually linear. (3) Finally, in the human heart, the retrograde HPS-ERP often occurs at the same coupling interval as the effective refractory period of the ventricular myocardium (ERP-VM). Refractory periods in isolated Purkinje fibers are always longer than those in the myocardium except perhaps at very fast pacing rates. These differences raise serious questions about the appropriateness of use of the retrograde HPS-ERP as a measure of refractoriness of the HPS. On the other hand, the HPS-RRP reflects retrograde conduction delay or block usually in the right bundle branch, and therefore is a more appropriate clinical measure of HPS refractoriness.

Figure 1 schematically shows the right ventricular apical pacing protocol. A basic ventricular drive (∆Si) of 6 beats at a cycle length as close as possible to the sinus cycle length as possible (within 50 to 100 msec) was used. The HPS-RRP of this basic drive was evaluated by the use of a premature ventricular beat (∆Si) (panel A). ∆Si was initially programmed in late diastole and its coupling interval was progressively shortened by 10 msec intervals until it failed to capture the ventricle. A train of ventricular beats (∆S1) at a shorter cycle length than the basic drive (range 400 to 600 msec) was then added to the end of the basic ventricular drive. The length of this train was varied from 1 to 6 beats, as illustrated in panels B through G, and the HPS-RRP of each successive beat of the accelerated train was determined in a similar manner by use of a premature ventricular beat (∆S1). Thus, the HPS-RRP of each successive beat of the train was determined up to 6 beats.

ERP-VM is the longest \( S_1S_2 \) interval, or \( S_1S_2 \) interval, during the accelerated train associated with absence of ventricular capture by \( S_1 \).

RRP-VM is the longest \( S_1S_2 \), or \( S_1S_2 \), coupling interval for which intraventricular conduction delay of \( V_2 \) can be measured on any of the ventricular electrograms.

All refractory periods were determined by 10 msec decrements of the \( S_2 \) coupling interval.

**Statistical methods.** Descriptive statistics are given as mean ± SD. Statistical analysis was performed by use of Student's paired t test corrected, where appropriate, for multiple comparisons.

**Results**

All patients underwent complete antegrade and retrograde conduction as well as refractoriness studies. However, only data relevant to this report will be presented here.

**Behavior of HPS refractoriness during sudden rate acceleration.** Table 1 lists the data on the HPS-RRP during the basic ventricular drive (∆Si) and following each successive beat at the accelerated rate (∆S1). The cycle length of the basic ventricular drive varied from 600 to 1000 msec (mean 757 ± 92 SD). The shorter cycle length of the accelerated train (∆S1) varied from 400 to 600 msec (482 ± 52). In each patient, the HPS-RRP of successive beats after the sudden rate acceleration behaved in a damped oscillatory fashion. With the first beat of the accelerated train, the HPS-RRP was dramatically lower than during the preceding constant ventricular drive. After the second beat of the same train, the HPS-RRP was always at its highest value of the entire accelerated train. Successive values after each additional beat were then alternately lower or higher, behaving in a damped oscillatory manner.

On the odd-numbered beats of the accelerated train (first, third, and fifth \( S_1 \) beats), the HPS-RRP was sometimes not reached even with the shortest \( S_2 \) coupling interval that produced ventricular capture. This was especially true for the first beat. In those cases, the HPS-RRP values were listed as less than the shortest coupling interval of \( S_2 \) producing ventricular capture. This value was used in table 1 for the purpose of calculating the means for the entire group. Continued conduction through the HPS down to the ERP-VM was verified in these patients by the presence of a retrograde atrial deflection or, when no retrograde atrial conduction was present, by the prolonged AH conduction of a subsequent spontaneous or programmed atrial beat.

**Figure 2** is a graphic illustration of the mean data from table 1. The mean HPS-RRP values during the accelerated trains were all statistically significantly lower than those during the basic ventricular drive (p
The HPS-RRP of each successive beat of the accelerated train was statistically significantly lower or higher than that of the corresponding preceding beat (p < .01 for all beats). The mean HPS-RRP of the fourth beat of the accelerated train was significantly lower than that of the second beat, but higher than that of the sixth (p < .01 for both), suggesting that this is a dampened oscillatory process.

Behavior of the retrograde HPS conduction time. A previous study has suggested that the retrograde HPS conduction times of a premature beat (S₂H₂) tended to increase by increments that were equal to the decre-

![Figure 1](http://circ.ahajournals.org/)

**FIGURE 1.** Pacing protocol. A. The pacing method used during the basic ventricular drive (S₁). A ventricular premature beat (S₂) was programmed in late diastole and its coupling interval was progressively shortened by 10 msec intervals to evaluate the HPS-RRP, ERP-VM, and RRP-VM. B through G. The pacing protocol used to evaluate the refractory periods of each successive beat during the accelerated train of 6 beats (S₁). This train was initiated at the end of a basic ventricular drive. A premature ventricular beat (S₂) was also used to evaluate the refractoriness of each beat of the accelerated train. For any coupling interval of S₂, the pacing protocol was repeated seven times, once with the basic ventricular drive, and once each with each additional beat of the accelerated train up to 6 beats. In this manner, refractoriness of the HPS as well as ventricular myocardium were determined after the basic ventricular drive and each beat of the accelerated train up to 6 beats.
TABLE 1

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All values in msec.

<sup>a</sup>Basic ventricular drive only.

<sup>b</sup><sup>p</sup> < .0001 compared with basic ventricular drive; <sup>c</sup><sup>p</sup> < .01 compared with mean value in the preceding column; <sup>d</sup><sup>p</sup> < .01 compared with 2 and 6 S' beats.

mements of the coupling interval of S<sub>2</sub>. Shortening of the HPS-RRP would tend to cause a similar shortening of the S<sub>2</sub>H<sub>2</sub> interval at a fixed S<sub>2</sub> coupling interval. One would therefore expect the S<sub>2</sub>H<sub>2</sub> intervals at a comparable coupling interval of S<sub>2</sub> following each successive beat of the accelerated train to have a pattern that reflects the oscillating pattern of the HPS-RRP. Figure 3 demonstrates such an oscillating pattern in patient 3.

Panels A through F show the behavior of the retrograde HPS conduction of S<sub>2</sub> after each beat of the accelerated train. The basic ventricular drive cycle length is 650 msec while the accelerated train has a cycle length of 400 msec. In each panel the S<sub>2</sub> coupling interval is 270 msec. Note in panel A that the retrograde H<sub>2</sub> has not emerged from the ventricular electrogram of S<sub>2</sub> after the first beat of the train. After the second beat of the train, as depicted in panel B, the retrograde H<sub>2</sub> as well as an RB<sub>2</sub> deflections are clearly visible. The RB<sub>2</sub> is followed by a macroreentrant V<sub>3</sub>. Panel C illustrates the effect of the third beat of the train on the retrograde conduction of S<sub>2</sub>. Note that the H<sub>2</sub> deflection is again not visible after the ventricular electrogram. Panels D through F reveal that the retrograde H<sub>2</sub> alternates from being within the ventricular electrogram to being clearly visible after the ventricular electrogram, thus behaving in an oscillatory fashion. The presence of the H<sub>2</sub> in panels A, C, and E, while not visible, can be inferred to be within the ventricular electrogram from the presence of the retrograde A<sub>2</sub>. It can also be noted in the same figure that the S<sub>2</sub>A<sub>2</sub> intervals behaved in a parallel fashion in comparison with the S<sub>2</sub>H<sub>2</sub> intervals. For comparison, the retrograde conduction of S<sub>2</sub> in the same patient during the basic ventricular drive is shown in figure 4. The HPS-RRP was 360 msec, as shown in panels A and B.
At an \( S_2 \) coupling interval of 300 msec (panel C), the \( S_2H_2 \) interval was 250 msec. With \( S_2 \) coupling intervals of 290 msec or less, the retrograde impulses were all noted to block below the His bundle. Therefore, during the basic ventricular drive, the retrograde \( H_2 \) emerged from the ventricular electrogram and blocked in the HPS at considerably longer coupling intervals of \( S_2 \) than those during the accelerated train.

Because of the wide range of oscillating HPS-RRP values in each patient, only four of the 14 patients had

![Image of Figure 3](http://circ.ahajournals.org/doi/abs/10.1161/01.CIR.36.5.912)

**FIGURE 3.** Oscillation of retrograde HPS conduction (\( S_2H_2 \)). The tracings are from patient 3. Surface electrocardiographic lead \( V_1 \) and right atrial (RA), His bundle (H), and right bundle (RB) electrograms are shown. The basic ventricular drive (\( S_1 \)) has a cycle length of 650 msec. The accelerated train (\( S_2 \)) has a cycle length of 400 msec. The atria were simultaneously paced during the basic ventricular drive and the accelerated train. In each panel, the coupling interval of \( S_2 \) (open arrow) is constant at 270 msec. A, The retrograde \( H_2 \) has not emerged from the ventricular electrogram (\( S_2H_2 < 140 \) msec) after 1 beat of the train. After 2 beats of the train (B), the retrograde \( H_2 \) has clearly emerged (\( S_2H_2 = 200 \)). As illustrated in C, the retrograde \( S_2H_2 \) interval following the third beat has again shortened such that \( H_2 \) cannot be seen (\( S_2H_2 < 140 \)). This alternating behavior of the retrograde HPS conduction of \( S_2 \) continues with each additional \( S_1 \) beat, as demonstrated in D, E, and F. Note that the \( S_2A_2 \) intervals also alternated in a parallel fashion.
measurable \(S_2H_3\) values for all 6 beats of the accelerated train available at a comparable coupling interval of \(S_2\). For those patients, the \(S_2H_3\) values for all 6 beats of the accelerated train at the longest comparable coupling interval of \(S_2\) are shown in figure 5. Note that a similar dampened oscillatory pattern exists, reflecting the behavior of the HPS-RRP in a parallel manner. Statistical comparisons were not made due to the small number of patients that could be included in this group.

**Behavior of ventricular refractoriness.** Data on the behavior of the ERP-VM and RRP-VM during the same pacing protocol were available in nine of the 14 patients. In the remaining five patients, the pacing protocol was discontinued before all the refractory period values were obtained because of the onset of ventricular arrhythmias. Data on the ERP-VM and RRP-VM are listed in table 2 and did not show any evidence of oscillatory behavior. Figure 6 graphically summarizes the mean data from table 2. The ERP-VM and RRP-VM tended to decrease with the first 2 beats of the accelerated train and then stabilized at a lower value. The ventricular refractory periods therefore appear to accumulate in a "cumulative" manner. The RRP-VM behaved in an identical manner to the ERP-VM except that it was 10 to 40 msec longer than the corresponding ERP-VM. Such a concordance of behavior is not surprising and has been previously reported.8

**Discussion**

Although refractoriness of the human HPS during steady-state pacing has been directly related to the cycle length,1 the dynamic aspect of the adaptation of this refractoriness when the cycle length is suddenly decreased has not been previously elucidated beyond

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**FIGURE 4.** Retrograde HPS conduction during the basic ventricular drive. This figure is from the same patient as in figure 3. A. The retrograde \(H_2\) has not emerged from the ventricular electrogram at an \(S_2\) coupling interval of 370 msec. With an \(S_2\) coupling interval of 360 msec (B), the \(H_2\) can be seen just emerging from the ventricular electrogram \((S_2H_3 = 150\) msec). As the \(S_2\) coupling interval is shortened to 300 msec (C), the retrograde \(H_2\) moves out even further \((S_2H_3 = 250\) msec) and is now followed by a macroreentrant \(V_3\). At coupling intervals less than 300 msec, \(S_2\) blocks below the His recording site. Thus, the HPS-RRP during the basic ventricular drive is 360 msec, a value considerably higher than that during the accelerated train. The \(S_2H_2\) interval of 250 msec in C is considerably longer than the ones seen in figure 3, despite the fact that the \(S_2\) coupling interval is longer by 30 msec.
**NUMBER OF BEATS ($S_1$) IN ACCELERATED TRAIN**

**FIGURE 5.** $S_2H_2$ conduction times at comparable $S_2$ coupling intervals. In four patients, $S_2H_2$ values at comparable $S_2$ coupling intervals were available for all 6 beats of the accelerated train. The mean values of the $S_2H_2$ intervals at the longest comparable $S_2$ coupling interval are illustrated on this graph, together with their standard deviations. Note that these retrograde HPS conduction times oscillated in a parallel fashion to the oscillations of the HPS-RRP shown in figure 2.

the first beat. While our findings on the “cumulative” behavior of the ERP-VM during sudden rate acceleration confirm those of previous investigators, the data on the behavior of HPS refractoriness present a new and dramatically different picture of the adaptation of the human HPS refractoriness to a similar rate change.

**TABLE 2**

**ERP-VM and RRP-VM**

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Mean ± SD

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<th>ERP-VM</th>
<th>236 ± 19</th>
<th>220 ± 19&lt;sup&gt;b&lt;/sup&gt;</th>
<th>216 ± 16&lt;sup&gt;c&lt;/sup&gt;</th>
<th>216 ± 16&lt;sup&gt;c&lt;/sup&gt;</th>
<th>214 ± 16&lt;sup&gt;b&lt;/sup&gt;</th>
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<td>243 ± 14&lt;sup&gt;b&lt;/sup&gt;</td>
<td>238 ± 11&lt;sup&gt;c&lt;/sup&gt;</td>
<td>238 ± 11&lt;sup&gt;b&lt;/sup&gt;</td>
<td>237 ± 11&lt;sup&gt;b&lt;/sup&gt;</td>
<td>237 ± 11&lt;sup&gt;b&lt;/sup&gt;</td>
<td>237 ± 11&lt;sup&gt;b&lt;/sup&gt;</td>
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All values are msec.

*Basic ventricular drive.

<sup>a</sup>p < .01 compared with basic ventricular drive; <sup>b</sup>p < .05 compared with the mean value in the preceding column.

**FIGURE 6.** Behavior of the ERP-VM and RRP-VM during sudden rate acceleration. Both refractory period measurements decreased after the first 1 to 2 beats of the accelerated train and then stabilized at a lower value for the remainder of the train. Thus, the ERP-VM behaved in a “cumulative” manner after the initiation of the accelerated train of $S_1$ beats. The RRP-VM behaved in an identical manner except that it was 20 to 25 msec longer on the average.

It would appear, at least within the cycle lengths used in this study, that human HPS refractoriness adapts in a dampened oscillatory fashion when its equilibrium is disturbed by a sudden rate acceleration.

Since the HPS-RRP is defined as the coupling interval at which the retrograde His deflection emerges from the ventricular electrogram, it can be argued that oscillatory changes in the duration of the ventricular...
electrogram with successive beats of the accelerated rhythm may artifactually create this behavior. This possibility was ruled out for the following reasons: (1) The ERP-VM and RRP-VM did not behave in an oscillatory manner. (2) At the cycle lengths used in this study, no oscillatory behavior of the ventricular electrogram duration of S₁ was noted. (3) The behavior of the S₂H₂ intervals (figure 5), a measurement that is independent of ventricular electrogram duration, was similar to that of the HPS-RRP in oscillating from beat to beat. (4) S₂A₂ conduction intervals, when available, also behaved in a similar manner, as illustrated in figure 3.

Refractoriness of Purkinje fibers at a particular pacing site is commonly considered to be closely related to its action potential duration. Therefore, any proposed mechanism to explain the observed oscillation of HPS refractoriness should, most likely, be based on oscillation of the HPS action potential duration during sudden rate acceleration.

Related studies in isolated Purkinje fibers. Several previous reports have described an “alternation” of action potential duration during high rates of pacing in cardiac tissues.¹⁰⁻¹⁴ Two of these studies specifically addressed the onset of this alternating behavior with sudden rate acceleration.¹¹,¹⁴ Vick¹¹ described the effect of the initiation of pacing at various frequencies on the action potential duration of canine Purkinje fibers after at least 3 min of electrical quiescence. At frequencies of two to three per second, he noted oscillation of the action potential duration during the initial portion of pacing. Boyett and Fedida¹⁴ described the time course of changes in action potential duration in isolated canine Purkinje fibers when the pacing rate was suddenly changed from 20 to 200 per minute. They noted that for about 30 sec after the increase in rate, there was an alternation in action potential duration.¹⁴

Neither of these studies are exactly analogous to the present report. The changes in pacing rate used in Boyett and Fedida’s study (20 per minute to 200 per minute) are quite large in comparison with the rate changes used in this study. The type of study performed by Vick required prolonged electrical quiescence of the Purkinje fiber before initiation of pacing and are, of course, impossible to achieve in a clinical study. Despite these differences, the underlying mechanism of oscillation of action potential duration and refractoriness may well be the same.

Role of diastolic interval in determining action potential duration. Various reports have suggested that cycle length is not the only factor involved in determining action potential durations.¹²,¹³,¹⁵,¹⁶ These studies have postulated that the diastolic interval (the interval from repolarization to the onset of the next depolarization) preceding a beat may have a significant contribution to the action potential duration due to its influence on the degree of “membrane recovery.” When the diastolic interval preceding a premature beat is short, the premature action potential may have an excessively abbreviated duration when compared with a steady-state action potential of identical cycle length. Gettes et al.¹⁶ and Elharrar and Surawicz¹⁷ have clearly demonstrated this in the pig and canine Purkinje fiber, respectively. Boyett and Jewell¹² have also used such a concept to explain the “electrical alternans” observed when pacing is initiated at a fast rate. They showed evidence to suggest that the first beat of a train with a short cycle length has a short preceding diastolic interval and therefore a short action potential duration. The diastolic interval after the first beat is thereby lengthened, causing the second beat of the train to have a longer action potential duration. Subsequent beats of the train would then alternately have a shorter or a longer action potential duration, depending on the preceding diastolic interval. They postulated that variations in the degree of recovery from inactivation of the slow inward current could account for this alternation. Hauswirth et al.¹³ suggested that variations in the outward current iₖ may be the main current involved in determining action potential duration. They showed that the time course of decay of iₖ corresponded to the zone of diastolic intervals where changes in the action potential duration occurred.

Postulated mechanism of HPS-RRP oscillation. In an analogous manner, the oscillation of the HPS-RRP during sudden rate acceleration observed in this study can be explained in terms of the effect of diastolic intervals on HPS refractoriness. Figure 7 is a schematic display of this proposed mechanism. Panel A shows the action potentials during the basic ventricular drive. With the first beat of the accelerated train of 6 beats (panel B), the action potential (and refractoriness) is shortened excessively due to marked shortening of the preceding diastolic interval (solid bar). The second beat of the accelerated train (panel C) is consequently preceded by a longer diastolic interval and therefore has a longer action potential. This process alternates with each additional beat (panels D through G), causing an oscillatory pattern to the action potential durations, and therefore also to the respective refractoriness. This oscillation dampens out gradually in a manner similar to that observed in the previously mentioned animal studies.

These types of oscillations have not been noted in all
FIGURE 7. Schematic illustration of the proposed mechanism for the observed oscillation of the HPS-RRP. The sequence of paced beats in these panels are the same as diagrammed in figure 1 except for the absence of $S_2$. Each beat, however, is represented here as an idealized action potential within the HPS. A, The action potentials during the basic ventricular drive. B through E, The proposed mechanism of alternation of action potential duration with the initiation of the accelerated train of beats. With the first beat of the accelerated train (B), the preceding diastolic interval is dramatically shortened. This results in an excessively shortened action potential when compared with the steady-state action potential at an identical cycle length (shown in dotted lines). Because of this shortened action potential, the diastolic interval preceding the second beat of the train is prolonged (C). In turn, this results in lengthening of the action potential of the second beat so that it is now longer than the comparable steady-state action potential. This process of alternating long and short action potentials continues as a consequence of a similar alternation in the diastolic intervals, thus creating the oscillatory pattern seen in D through G. These oscillations gradually dampen until the steady-state configuration of the action potential is achieved. This proposed sequence of events is the most likely explanation for the observed oscillation of the human HPS-RRP during sudden rate acceleration.

studies of isolated canine Purkinje fibers. Miller et al.\textsuperscript{17} evaluated the changes in action potential area after abrupt changes in frequency of stimulation from 30 to 60 beats/min. They noted a progressive decrease in action potential area until a new equilibrium was reached. Elharrar and Surawicz\textsuperscript{17} evaluated the response of canine Purkinje fiber action potential duration to a sudden decrease in cycle length of from 1500 to 500 msec. They also noted a progressive decrease in action potential duration. The different results noted in these two studies, however, may be explained by the design of the experiments. The frequencies of stimulation used by Miller et al. were considerably slower and not at all comparable to those used in our study. It is quite likely that a critically short diastolic interval, and thus also cycle length, must be achieved during the accelerated train of beats for this oscillatory behavior of the action potential duration, or refractoriness, to occur. In the study by Elharrar and Surawicz, the cycle length of the accelerated train of beats (500 msec) was not sufficiently short to generate an excessive shortening of the action potential duration of the first beat. The action potential duration restitution curves shown in that study indicated that the cycle length of the first beat of the train needed to be less than 400 msec before one could expect excessive shortening of action potential duration below that of the steady-state values. These reports therefore do not contradict the mechanism of oscillation of human HPS refractoriness proposed above. From the available data, it seems that the mechanism proposed would require that the cycle length of the accelerated train be short enough to produce excessive shortening of the action potential of the first beat of the train. This in effect primes the oscillatory mechanism and allows the generation of alternate long and short action potentials. In the human heart this critically short cycle length appears to be at least as long as 600 msec but may also be related to the cycle length of the basic ventricular drive. Furthermore, the number of beats that oscillation of refractoriness persists may also be related to both the cycle length of the accelerated train and the basic drive. It is of interest to note that only in patient 7, in whom the cycle length of the accelerated train was the longest, was there no difference between the HPS-RRPs of the fifth and sixth beats of the accelerated train. Thus, in this patient, these oscillations were observed to dampen out completely by the sixth beat. From observations in other patients studied in our laboratory, these oscillations appear to dampen out completely by 5 beats or earlier, whenever the cycle length of the accelerated train of ventricular beats is greater than 600 msec.
In summary, the data from this report reveal that refractoriness of the human HPS and ventricle behave in radically different manners when both tissues are subjected to sudden rate acceleration. While refractoriness of the myocardium appears to accommodate in a cumulative fashion, that of the HPS tends to accommodate in a dampened oscillatory manner.

Clinical implications. As opposed to the cycle length used in some of the quoted animal studies, the ones used in this study are commonly seen or used during clinical electrophysiologic studies. The range of cycle lengths used for the basic ventricular drive (600 to 1000 msec) are similar to the cycle lengths of most spontaneous sinus rhythms observed in the clinical electrophysiologic laboratory. The cycle lengths of the accelerated trains (400 to 600 msec) are also commonly used for pacing during clinical electrophysiologic studies. Therefore, the phenomenon reported in this study is not, at least in the human heart, related to the use of extremes in cycle lengths. Thus, in clinical studies of phenomenology of the HPS, it would be important to pay particular attention to the definition of baseline and steady states. Initiation of pacing at a rate much faster than the spontaneous rhythm, for example, may require a considerable number of beats before achieving a steady state in HPS refractoriness. In this regard, the basic ventricular drives in this study were purposely chosen to be as close to the underlying sinus rhythm as possible so as to avoid any drastic change in cycle length during the transition from sinus rhythm to paced rhythm.

Alternation of QRS morphology during, and especially at the initiation of, atrioventricular reentrant tachycardias involving an accessory bypass tract has been reported in the past. The mechanism of this alternation is unclear. The results of this study suggest a possible explanation of this phenomenon. These type of tachycardias can frequently be quite rapid, having cycle lengths of 300 msec or even less. With a sudden acceleration of rate such as at the initiation of the tachycardia, oscillation of the action potential durations within the HPS may be of considerable magnitude and may last for quite some time. This could conceivably cause the observed beat-to-beat alternation of the QRS morphology. However, it should be emphasized that no study has been performed to confirm this hypothesized mechanism and further systematic evaluation is necessary to verify this postulation.

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