Elucidation of Prinzmetal’s Variant Form of Preexcitation

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Background In 1952, Prinzmetal induced preexcitation in the normal dog heart using subthreshold stimulation (SS) delivered to the right ventricle.

Methods and Results In 12 dogs we recorded ECG leads II, aVR, His (Hb) and proximal right bundle potentials with electrode catheters at the aortic root and a special electrode that was inserted through the right ventricular (RV) free wall. In 12 others, SS was delivered to the Hb area by a catheter placed under the septal leaflet of the tricuspid valve. During SS, the HV interval shortened from 35±4 milliseconds (mean±SD) to 19±7 milliseconds (P=.0001), but AH intervals were unchanged. The ECG showed delta waves with aberrant QRS complexes. Endocardial electrograms showed that the origin of activation in the preexcitation beats was localized to the muscle adjacent to the Hb or proximal right bundle. When vagal stimulation induced sudden AV block, no ventricular excitation was seen, confirming the subthreshold nature of the applied stimulation. By adjusting the levels of SS, latent forms of preexcitation could be induced, e.g., early local septal muscle activation but no change in the ECG leads. Premature ventricular stimuli delivered to the RV apex or outflow tract could cause manifest preexcitation in the ECG leads or inhibit expression of latent preexcitation in endocardial recordings.

Conclusions SS delivered to the RV apex or Hb area causes ventricular preexcitation, as shown previously by Prinzmetal et al. SS delivered at the insertion sites of an accessory pathway may facilitate localization of such abnormal connections, particularly when preexcitation is concealed. (Circulation. 1994;89:2380-2389.)

Key Words • preexcitation • electrocardiography • His bundle

In the present study, we attempted to repeat some of the experiments of Prinzmetal et al with some important modifications. Intracardiac activations were recorded to determine and validate the means by which SS induced preexcitation patterns in the normal dog heart. In addition, latent forms of preexcitation were induced and methods described for converting latent forms to manifest preexcitation. The latter may have clinical usefulness in localizing and manifesting accessory pathways in humans, particularly in those with concealed accessory connections or in patients in whom incomplete ablation has been performed.

Methods

Application of Subthreshold Stimulation to the RV Apex

Twelve adult mongrel dogs weighing 12 to 25 kg were anesthetized with sodium pentobarbital 30 mg/kg IV. With the dog in a supine position, a 12-lead set of ECGs was recorded before the start of each experiment. The left femoral vein was dissected and cannulated for delivery of intravenous fluids and drugs. The left femoral artery then was cannulated for monitoring central aortic blood pressure through a Statham-Gould pressure transducer. The left common carotid artery was dissected, and the vagosympathetic trunk was isolated. Teflon-coated silver wires were inserted into the vagosympathetic trunk to decrease heart rate and/or block AV conduction. The vagosympathetic trunk was stimulated at 20 Hz with pulses of 0.05-millisecond duration and a voltage range of 2 to 20 V. A tripolar catheter was inserted into the left common carotid artery and advanced to the aortic root to record His bundle activity. The tip of this catheter was wedged at the junction of the noncoronary and right coronary cusps. The dog then was turned onto the left side. Under positive-pressure ventilation, a right thoracotomy was performed at the fourth intercostal space. The pericardium was opened to expose the right atrium and base of the right ventricle. A four-
or six-ring electrode catheter with a 4-mm-long electrode at the tip was introduced into the right femoral vein and advanced to the apical area of the right ventricle (Fig 2). A plunge-wire electrode was inserted in the high right atrium near the sinus node for pacing the atrium. In eight experiments, a special multipolar, tubular electrode was introduced through the free wall of the right ventricle near the anterior AV junction. It was held in place by a purse-string suture into the free wall of the right ventricle so that the electrode would be in stable contact with the proximal right bundle branch (Fig 2). Initially, we determined the threshold for pacing at the RV apex. The first channel of a Grass S-88, two-channel stimulator that delivered stimuli to drive the train was also set to trigger pulse trains from the second channel to the RV electrodes at 1000 Hz, with a delay of 80 to 100 milliseconds from the atrial pacing impulse. Each pulse of the train was 0.5 millisecond in duration, and the duration of the pulse train was 50 milliseconds. The large tip was used as the cathode, and the other seven electrodes were connected to form a large anode (Fig 2). In most cases, constant DC was also delivered to the RV apex either during sinus rhythm or during atrial pacing at various pacing rates.

**Application of Subthreshold Stimulation to the His Bundle Area**

Another group of 12 mongrel dogs was anesthetized as described above. The same procedures for delivery of drugs, blood pressure recording, ECG, and His bundle recordings were used as described previously. The right heart was exposed by thoracotomy at the fourth intercostal space, and plunge-wire electrodes were placed into the RV epicardium at the RV apex and outflow tracts for introduction of premature ventricular stimuli. A deflectable-tip electrode catheter (four or six rings, 4 mm apart) was introduced through the right jugular vein into the right ventricle. In six dogs, the tip was placed under the septal leaflet of the tricuspid valve to record His bundle activity at the crest of the interventricular septum. SS in the form of pulse trains (as described above) was delivered to the electrodes under the tricuspid valve with the tip electrode serving as cathode and the other three or five electrodes serving as a combined anode. Each train was coupled to a high right atrial pacing stimulus with a delay of 60 to 80 milliseconds. Another form of SS was delivered to this same electrode arrangement as a constant DC pulse of variable duration (30 seconds to 2 minutes). During SS, premature ventricular beats (PVB) were elicited by suprathreshold stimuli delivered to the RV apex or outflow tract. These PVBs were delivered after every eighth atrial paced beat, with variable coupling intervals ranging from the ventricular functional refractory point to that producing fusion with the next paced beat.

To verify that SS was truly subthreshold, two tests were applied: (1) During SS that induced ECG changes indicative of preexcitation, AV conduction was abruptly blocked by strong vagosympathetic truck stimulation. (2) When subthreshold pulse trains coupled to an atrial pacing stimulus induced preexcitation, atrial pacing was discontinued, thereby allowing the pulse trains to traverse the cardiac cycle, including the diastolic interval.

All recordings were monitored on an Electronics for Medicine oscillographic/photographic recorder that was interfaced to a Gould ES1000 monitor/recorder to obtain hard copy of the data on electrostatic paper at speeds ranging from 25 to 250 mm/s. ECGs were recorded with standard filters at 0.03 to 250 Hz; electrograms were recorded with filter settings of 30 to 250 Hz.

Animal studies were performed in accordance with guidelines established by the National Institutes of Health and state regulations from the US Department of Agriculture. In addition, all protocols were approved by the Animal Studies Subcommittee and the Research and Development Commit-
Fig 3. Tracings obtained by Prinzmetal et al to illustrate formation of ventricular preexcitation complexes and the effect of sectioning of the His bundle. A, Normal sinus rhythm with PR interval of 0.08 second. B, Complexes produced by subthreshold DC stimulation of apical endocardium of the right ventricle at 50 V and 0.5 mA. Note the short PR interval (0.04 to 0.06 second) and delta wave. C, After the His bundle was sectioned, no preexcitation complexes were seen even though the same current was applied.

Statistical Methods

Data are expressed as mean±SD. Statistical analyses were performed using a paired Student’s t test (two-sided). Differences were considered significant at values of P<.05.

Definitions

Right bundle branch block (RBBB) in the dog shows a widening of the QRS complex from a mean of 50 milliseconds to >65 milliseconds but <75 milliseconds for incomplete bundle branch block and >75 to 80 milliseconds for complete bundle branch block. The changes in the ECG leads II and aVR are fairly characteristic during the evaluation of RBBB in the dog heart. Lead II in the control state shows diminished R waves and deep, wide S waves, whereas aVR is a mirror image of lead II. The RV apex was determined using pulse trains of square wave pulses triggered by each atrial pacing stimulus was then delivered to the RV apex (Fig 4B). The duration of each square wave was 0.5 milliseconds, the frequency of the pulses was 1000 Hz, and the duration of the train was 50 milliseconds. Each pulse train (0.1 mA) was delayed 80 to 100 milliseconds from the atrial pacing impulse to fall during the HV interval. Note that this SS was associated with a shortened PR interval because of a decrease in the HV interval from 40 milliseconds (control) to 25 milliseconds and was associated with a LBBB pattern in the ECG leads. In this case, a small delta wave preceded the aberrant ventricular depolarization. The onset of vagosympathetic trunk stimulation resulted in one beat, with a prolonged AH interval of 110 milliseconds and a negative HV interval of 15 milliseconds. Note that all the other AH intervals in the control state and during the Prinzmetal effect were the same: 90 milliseconds. These findings will be discussed in detail below.

The threshold (in milliamperes) to induce constant ventricular pacing from the RV apex was determined using a 2-millisecond pulse (Table 1, first column). The level of stimulation in milliamperes required to produce the Prinzmetal effect was determined using pulse trains or constant DC current (Table 1, second column). There was a significant difference between threshold and subthreshold levels of stimulation (P=.007). One of the consistent responses to SS, which caused PR shortening at any given heart rate, was the concurrent shortening of the HV interval. Table 2 shows the results of a paired t test applied to the changes in the HV interval before and after the application of SS to the RV apex. The mean HV interval during the control state...
was 35±4 milliseconds (mean±SD) versus 19±7 milliseconds in response to SS (P=.0001).

Not all results of SS at the RV apex were associated with typical delta waves in leads II and aVR. In Fig 5, an alternating form of preexcitation similar to that described by Prinzmetal et al was seen during delivery of constant DC current of 0.2 mA to the catheter in the RV apex. In addition to the ECG and His bundle recordings, we used a special tubular electrode (Fig 2) that could be inserted, rotated, and fixed against the basal RV septum so that one or more bipolar pairs would record potentials from the proximal right bundle branch. Application of DC constant current induced a shortened PR interval and aberrant ventricular depolarization that was preceded by an abbreviated positive delta wave followed by a large, wide Q wave in lead II. This response occurred in only 2 of 10 cases. The QRS duration was 85 milliseconds compared with the normal duration, 50 milliseconds, and its morphology allowed a classification of LBBB. The intracardiac recordings clearly show the maintenance of the normal sequence of His bundle and right bundle activation. However, a prominent "slow" deflection arising in the vicinity of the proximal right bundle was observed in this and other experiments. In this case, the HV interval decrease from 30 to 5 milliseconds was atypical (Table 2). In all cases, the appearance of a slow potential in the vicinity of the proximal right bundle branch distorted the normal isoelectric RbV interval. These potentials were consistently coincident with the onset of delta waves on the surface ECG associated with the shortened PR intervals. The significance of these slow waves will be discussed below.

In all cases, the subthreshold nature of the stimulus was attested to by the response to vagally induced complete AV nodal block (Fig 6). The first beat shows normal PQRS (ECG leads I to III) and HV interval (30 milliseconds) during atrial pacing at 150 per minute. In response to a coupled pulse train (0.34 mA) delivered during the latter half of the PR segment, the HV shortened by 10 milliseconds and the QRS showed a

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**Table 1. Suprathreshold Pacing and Prinzmetal Effect With Subthreshold Stimuli**

<table>
<thead>
<tr>
<th>Dog</th>
<th>Regular Pacing, mA</th>
<th>Prinzmetal Effect, mA</th>
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<tbody>
<tr>
<td>1</td>
<td>3.3</td>
<td>2.0</td>
</tr>
<tr>
<td>2</td>
<td>1.0</td>
<td>0.7</td>
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<tr>
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<td>1.2</td>
<td>0.7</td>
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<tr>
<td>5</td>
<td>1.3</td>
<td>0.3</td>
</tr>
<tr>
<td>6</td>
<td>1.3</td>
<td>0.2</td>
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<tr>
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<td>0.2</td>
</tr>
<tr>
<td>8</td>
<td>0.4</td>
<td>0.3</td>
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<tr>
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<td>0.1</td>
</tr>
<tr>
<td>10</td>
<td>2.4</td>
<td>1.0</td>
</tr>
</tbody>
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Mean±SD 1.3±0.9 0.6±0.6  

P=.007

**Table 2. Alteration In HV Interval During Prinzmetal Effect**

<table>
<thead>
<tr>
<th>Dog</th>
<th>Control, ms</th>
<th>Prinzmetal Effect, ms</th>
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<tbody>
<tr>
<td>1</td>
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<td>25</td>
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<tr>
<td>2</td>
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<td>10</td>
<td>35</td>
<td>10</td>
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</table>

Mean±SD 35±4 19±7  

P=.0001
Fig 5. Alternating form of preexcitation and normal beats during Prinzmetal effect while recording His bundle (Hb), proximal (prox), and distal (dist) right bundle (Rb) activations. Subthreshold DC current (0.2 mA) induced alternating aberrant and normal beats (beats 1 and 3). The fourth beat is a ventricular ectopic beat probably arising in the right ventricular apex. In beats 1 and 3, the onset of ventricular activation is simultaneous on the proximal right bundle recording and ECG leads (dashed vertical line). Note the antegrade H-Rb1-Rb2 activation sequence. Also, a large endocardial muscle activation (*) occurs in the vicinity of the proximal Rb1. In contrast, the ventricular ectopic beat shows endocardial activation originating before Rb2 with retrograde Rb2-H activation. In this beat, the onset of ventricular activation to H is 25 milliseconds. The AH interval (65 milliseconds) is constant throughout.

LBBB pattern with a deep and widened Q wave, as seen in Fig 5. With the onset of vagally induced AV nodal block, no ventricular excitation was observed until normal conduction resumed intermittently three atrial paced beats later. This response to complete AV block during the Prinzmetal effect was not seen often. More commonly, there was a transient continuation of AV conduction with aberrant ventricular depolarizations (for one or more beats). However, complete or high-grade block always superseded, as seen in Fig 6.

Subthreshold Stimulation to the His Bundle Area

Manifest forms of preexcitation were seen in 4 of 12 dogs as a result of SS applied to the His bundle area. Although the effects of SS were generally similar to SS delivered at the RV apex, there were some specific differences. Fig 7 shows the effects of a constant DC current (0.25 mA) delivered to the catheter electrodes under the septal tricuspid leaflet. As with SS to the RV apex, preexcitation is evident by delta waves (Fig 7B), HV shortening (30 to 10 milliseconds), and an unchanged AH interval (45 milliseconds). However, the ventricular depolarization showed much less change in the degree of aberration and prolongation of duration with SS applied to the His bundle area than that observed during SS applied to the RV apex.

An examination of the His bundle electrogram provides some basis for these differences. The last deflection of the ventricular potential in the control state (Fig 7A) occurs after the end of the surface ventricular complex. With the local application of constant DC current (0.25 mA), the previously late septal crest potential now preceded the onset of ventricular depolarization (Fig 7B) and coincides temporally with the
delta waves. This response to SS, that is, alterations both in the ECG and His bundle electrogram, were seen in 4 of 12 dogs.

In 6 of 12 cases, latent forms of preexcitation induced by SS were seen that consisted of a shortened HV interval without noticeable change in the recorded surface ECG leads. In Fig 8A, 0.65-mA pulse trains coupled to each atrial pacing stimulus were delivered to the electrodes under the septal leaflet of the tricuspid valve. No changes either in the ECG leads or the HV interval were noted (HV, 30 milliseconds, as in the nonstimulated state). In Fig 8B, when the subthreshold stimulus intensity was raised to 0.80 mA, the septal crest potential shifted from the end toward the beginning of ventricular depolarization with a shortened HV interval of 20 milliseconds. However, no changes in the QRS complexes were seen during latent preexcitation. Two of the six dogs showed both latent and manifest forms, depending on the level of the subthreshold stimuli applied.

That the stimuli inducing these effects are truly subthreshold was evident in another experiment when atrial pacing was terminated during manifest preexcitation. In Fig 9, the pulse train (current level, 0.5 mA), when uncoupled from the atrial pacing stimulus, tracked through the cardiac cycle. Only when the subthreshold pulse train fell within the PR segment was there an alteration of either the His bundle electrogram, that is, advance of the septal crest potential (Fig 9A, first to third beat), or both the His bundle electrogram and ECG (Fig 9A, fourth and fifth beat). When the pulse train fell during the diastolic period, the TP interval (Fig 9B), no electrophysiological changes were seen, thus verifying the subthreshold level of these pulse trains.

Under conditions of constant SS that induced only latent preexcitation, the delivery of a strong (28-mA) stimulus to the ventricle converted the latent to a manifest form of preexcitation. In Fig 10, the first two beats exhibit latent preexcitation induced by the sub-

![Fig 8. Latent preexcitation induced by subthreshold stimulation (SS). A, SS (0.65 mA) delivered to the basal ventricular septum induces no change in ECG leads or His bundle recording (Hbeg). Note late septal activation (*). B, SS (0.80 mA) induces no change in the ECG leads, but in Hbeg, septal activation shifts to the left and the HV interval decreases from 30 to 20 milliseconds (latent preexcitation).](image)

![Fig 9. Uncoupling of the subthreshold pulse train from the atrial pacing stimulus to verify that the pulse train stimuli are truly subthreshold. A, When atrial pacing was discontinued, the subthreshold pulse train (0.5 mA) "tracked" across the cardiac cycle. Only when the train fell during the PR segment was latent or manifest preexcitation seen. B, When the same level of pulse train occurred during diastole, no depolarizations were induced. SS indicates subthreshold stimulation; L-2, lead II ECG; and Hbeg, His bundle recording.](image)

![Fig 10. Conversion of latent to manifest preexcitation by a premature ventricular beat (PVB). Traces from above: ECG leads II (L-2), aVR; and His bundle electrogram (Hbeg). The delivery of a 50-millisecond pulse train (1000 Hz, 0.4 mA) coupled to each atrial pacing stimulus induced latent preexcitation, as seen in the shortened HV interval (20 milliseconds) and early activation of the septal crest potential in the Hbeg (*). The introduction of a PVB was followed by an atrial paced beat manifesting preexcitation in the ECG leads (*, delta wave, aberrant ventricular activation) as well as the short HV (20 milliseconds).](image)
Discussion

Effects of Subthreshold Stimulation in the Normal Dog Heart

In his monograph, Prinzmetal and his associates described chemical, mechanical, and electrical stimulation of the RV endocardial surface that induced a consistent shortening of the PR interval associated with WPW-like changes in the QRS complex. Before our awareness of these investigations, reports from our laboratory detailed similar changes, particularly regarding delta wave induction in dog hearts, in which the interface between the His bundle and ventricular septum had been damaged by chemical means, ie, by lidocaine or ischemia. We coined the expression "ectopic conduction" to describe the premature exit of the impulse from the normal conduction pathways to adjacent myocardium. However, in these cases, there was an associated prolongation of the PR interval mainly caused by a marked intra-His bundle block.

As originally described by Prinzmetal et al, the application of subthreshold DC current to the RV endocardium was the most effective means of producing what appeared to be the ECG manifestations of the WPW syndrome. It should be stated that in these experiments, as in the present studies, no arrhythmias were induced. However, in the present studies, additional electrical recordings were made from the His and right bundle branches. Our findings for the most part confirm and extend the results and some of the conclusions of Prinzmetal et al. Delivery of SS in the form of DC constant current or pulse trains synchronized to an atrial pacing spike consistently shortened the PR interval, as found by Prinzmetal et al. The His bundle recordings alone allowed us to determine that AV nodal conduction, that is, the AH interval, was consistently unaffected, whereas the HV interval was significantly shortened (Table 2). Thus, these data do not support the original postulation by Prinzmetal et al that accelerated AV nodal conduction is the explanation of the effect but do indicate that the site of preexcitation was localized in proximal portions of the His-Purkinje system. Even when SS was applied at the RV apex, localization of preexcitation was found in recordings from the area of the proximal right bundle branch and its adjacent septal muscle. The Prinzmetal effect was consistently associated with the appearance of a relatively slow depolarization in the vicinity of the proximal right bundle branch even though the site of subthreshold application was 3 to 4 cm distant to that site. Thus, the sequence of His bundle-right bundle activation was maintained in the abnormal beats, and the slow wave, recorded endocardially, was always coincident with the delta wave seen in the surface ECGs. It is important to point out that when subthreshold stimuli were applied to the RV apex, the delta waves were not uniform. The different varieties are shown in Figs 4 and 5. Either there was a typical initial slurred onset of the ventricular depolarization (Fig 4B) or an attenuated slurred R wave followed by an S and R' (Fig 5). In the first instance, the ventricular depolarization took the form of functional LBBB, that is, early activation of the right septal surface and late activation of the left septal surface. This would result in the diminution of the initial left to right septal vector (Q wave). The RSR'
configuration may represent a fusion complex between initial but incomplete septal activation close to the proximal bundle and normal activation of the rest of the ventricles.

That either form of ventricular aberration was not due to direct stimulation of the right ventricle at the apex (where the subthreshold stimuli were delivered) is evidenced by (1) the normal sequence of His and right bundle activation during the Prinzmetal effect. If the ventricular beat had been directly excited at the RV apex, then the activation sequence would have been reversed as seen in the fourth beat (Fig 5), which is a ventricular ectopic beat probably arising from the apex.

(2) Vagal stimulation, a form of entrainment of atrioventricular node pacemaker activity, also failed to show the expected ventricular response. Thus, there was no evidence of a direct excitation of the right ventricle by vagal stimulation.

There was at least one ventricular excitation that occurred immediately after the onset of vagally induced AV block (Fig 4B). Characteristically, this beat showed a prolonged AH interval and a greater degree of LBBB than the beats before the onset of vagal stimulation. Thus, unlike the Prinzmetal effect, which presumably induced premature exit of the propagating sinus impulse at the proximal right bundle to adjacent myocardium, this excited beat probably arose in the vicinity of the tip of the electrode catheter at the RV apex, that is, at the site of delivery of SS. Such a transient excitatory effect of SS has been described under various circumstances in nerve and heart as the Wedensky effect. Briefly stated, it is the concept that some ectopic beats can be due to a local change in excitability, in this case caused by the subthreshold stimulus. The source of the subthreshold stimulus can serve as a site of "cathodal block," with a resulting increase in excitability just distal to that blocked site. Excitability at such a site immediately after a conditioning threshold or subthreshold stimulus is markedly decreased and with time increases to threshold and even above threshold levels. Importantly, this altered excitability is dependent on a dominant or triggering impulse. Also, it has been noted that these beats are transient, which is in keeping with the gradual increase in excitability described above.

As might be expected, these findings on the effects of SS in the normal heart raised many questions: What is the mechanism by which the impulse can prematurely exit from supposedly insulated portions of the AV conduction system in response to a supraventricular beat and background SS? In our previous studies, damage to the interface between the His bundle and underlying septal crest muscle or the right bundle and adjacent myocardium induced ectopic conduction without the need for subthreshold stimuli. This effect occurred in about 40% of the experiments. In the present studies, it is difficult to accept that subthreshold stimuli could have induced damage of adjacent Purkinje and muscle membranes so that ectopic conduction could occur within the period of a few beats. Perhaps the presumed electrical insulation between Purkinje and muscle cells, particularly at the proximal portions of the His-Purkinje system, is relative as a high-resistance connection that can be altered by the interaction of a supraventricular beat and SS applied locally or even at a distance. Baird and Robb showed in the dog heart that the His bundle and the proximal portions of the right bundle are not separated by a connective tissue sheath, as is the case in the more distal parts of the bundle and its arborizations. Lev also showed similar findings in humans. Thus, the cardiac impulse that consists of a passive or electrotonic component and an active component can have the former summed with the artificially induced subthreshold stimulus. This summed electrotonic influence could cross the interstitial space, that is, Purkinje and muscle cells that are separated by a relatively inexcitable gap. If this activation (represented by the slow, relatively low-level deflection seen in Figs 5 and 6) caused the membrane potential of the muscle to reach threshold, it can be depolarized before its normal activation from the more peripheral Purkinje-muscle junctions.

Recent studies by Antzelevitch and Mo have shown that subthreshold stimuli can be summed with local electrotonic currents to successfully bridge an inexcitable gap artificially created in the middle of an isolated Purkinje fiber. Excitation of the distal side of the gap was thereby achieved. Our preliminary studies in vitro have clearly reproduced the Prinzmetal effect in the isolated tissue preparation. However, in these preparations from normal heart, we have not been able to localize the cellular features associated with the supposed electrotonic crossover from proximal bundle to adjacent muscle. In our previous studies of damage-induced ectopic conduction, we found foot potentials at the site of "slow conduction" between Purkinje cells of the right bundle branch and adjacent myocardium. More in vitro studies are required to clarify the cellular correlates of the Prinzmetal effect.

Interaction of Wedensky Phenomenon and the Prinzmetal Effect

The previous discussion has already implicated the role of the Wedensky phenomenon, that is, transient enhanced excitability distal to a site of the block caused by SS. In the experiments in which the subthreshold stimuli were delivered under the tricuspid septal leaflet, premature ventricular stimuli provided further evidence of interaction between the Prinzmetal and Wedensky effects. In our studies, titration of subthreshold stimuli to the ventricular septal crest induced a local Prinzmetal effect, that is, shift of septal activation from the end toward the beginning of ventricular depolarization (Figs 8 and 9). However, the amount of tissue activated was apparently too small to alter the body surface recordings (Fig 8); thus, preexcitation was latent in the ECG. We postulate that the introduction of a PVB even at a distance from the interventricular septal crest serves as another conditioning component whose electrotonic contribution further enhances excitability in the critical area, thereby potentiating excitation of the region. A greater area now activated, a more intense excitation, or both lead to manifest preexcitation in the surface ECG leads.

A similar observation has been made in patients showing antegrade block of accessory pathway conduction at particular heart rates. A PVB could restore antegrade accessory pathway conduction, albeit in a series of paced beats subsequent to the ectopic beat.
Possible mechanisms for this response were “peeling” back of a refractory barrier, supernormal conduction, or Wedensky facilitation.35 The apparent induction of inhibition of latent preexcitation by premature beats delivered at the RV apex or outflow tract is more difficult to explain. Although it would seem to be an example of Wedensky inhibition, the possibility of catheter movement caused by postextrasystolic-enhanced contraction cannot be ignored. Further studies in vivo, particularly with multielectrode mapping techniques, and in vitro should be carried out to fully explore the basis for Wedensky facilitation and inhibition in the context of the Prinzmetal effect.

Clinical Implications

Inhibition of left-sided accessory pathway conduction has been described by Gang et al36 using SS applied to the coronary sinus area. Reciprocating tachycardias were terminated using this method in 7 of 10 patients. More recently, Fromer and Shenasa37 used subthreshold stimuli applied to the proximal coronary sinus or low atrial septum to terminate AV nodal reentrant tachycardia in 15 patients. These authors found that facilitated conduction, manifested in shortening of the tachycardia cycle length before termination, may have played a role in termination. They specifically cite the Prinzmetal effect as a possible mechanism for these findings. In this regard, SS could be used as a reproducible means to determine which of various sites at the AV junction are optimal for radiofrequency ablation.38

Another possible use for SS would be its application at ventricular insertion sites of concealed accessory bypass tracts, for example, those showing only retrograde conduction. Would SS at this site result in successful antegrade propagation over the accessory pathway, thus pinpointing the target for ablation? SS delivered to the accessory pathway insertion in patients with intermittent preexcitation, directly converting normal conduction to consistent preexcitation,38 demonstrates the feasibility of this approach. The ability of PVB to convert normal conduction to preexcitation in patients with latent preexcitation has already been cited.35 With further basic studies and greater understanding of the mechanisms of the Prinzmetal effect, new clinical uses may be found for this unusual response to SS.

Acknowledgments

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