His Bundle Electrograms in Two Cases of Wolff-Parkinson-White (Pre-excitation) Syndrome

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SUMMARY
The catheter technic for recording the electrical activity of the specialized conducting system in the human heart showed in two patients studied that ventricular pre-excitation was apparently due to a bypass of the His bundle. Intermediate forms of WPW complexes appeared to be combination beats resulting from the activation of the ventricles through impulses traversing both the His bundle and accessory communications. Preferential iatrogenic activation of an intra-atrial (and perhaps even of an atrioventricular) tract appeared to occur in one of the patients. The patients with the WPW (pre-excitation) syndrome and long histories of paroxysmal arrhythmias were successfully treated with a combination of oral propranolol and implanted (transvenous) demand pacemaker.

Additional Indexing Words:
Preferred intracardiac pathways
Atrial pacing

Several mechanisms have been invoked in the genesis of ventricular pre-excitation (Wolff-Parkinson-White) syndrome. Conventional electrocardiographic theory holds that the various clinical manifestations of this entity are due to existence of an accessory atrioventricular connection through which atrial impulses can bypass the normal A-V junction. The reports by Lau and associates and by Sherf and James, however, have challenged these traditional views. The present communication stresses the use of the recently introduced catheter technic of recording the electrical activity of the specialized conduction system of the heart. It offers important information regarding the mechanism and treatment of the Wolff-Parkinson-White (WPW) syndrome in man.

Methods
An extension of the original technics of His bundle recordings introduced by Scherlag and co-workers was used. The procedure was explained to the patients and consent was obtained. A tripolar electrode catheter was introduced through the right femoral vein under local anesthesia and positioned fluoroscopically close to the septal leaflet of the tricuspid valve. Two filtered (40 to 2,000 Hz) bipolar recordings were obtained (between electrodes 1 and 2 as well as between electrodes 2 and 3). In addition, two other bipolar catheter electrodes were introduced into an antecubital vein and positioned in the right atrium. One, in close proximity to the sino-atrial node was used to record the bipolar atrial electrocardiogram. Atrial pacing at varying rates was performed through the other catheter, also located high in the right atrium. Standard electrocardiograms (lead I, II, or III, or all three) were recorded on tape and on an Electronics for Medicine oscillographic instrument at variable paper speeds. In case 1, in the presence of sinus rhythm, the P-R and P-J intervals were measured...
from lead II. The P-H interval was determined from the beginning of the P wave in lead II to the upstroke of the rapid deflections which constituted the His bundle electrogram (HBE) in the intracardiac lead. The same measurements were made during atrial pacing except that the beginning of the stimulus (St.) was equated to the onset of the P wave. The values obtained at different paced rates were expressed in milliseconds. Case 2 had very small P waves in the standard leads. Therefore, the P-R and P-H intervals were measured from the onset of the P wave in the HBE to the beginning of ventricular depolarization in lead I.

Report of Cases

Case 1

The tracings presented in figures 1 to 4 were obtained from a 62-year-old man who had complained of paroxysmal rapid heart beating for 50 years. He had no past history compatible with rheumatic fever, syphilis, angina, or heart failure. A living son—now age 37 years—also had classical WPW syndrome and paroxysmal tachycardia. The patient's electrocardiogram showed sinus rhythm and WPW type A. He had been treated at one time or another, with different amounts of digitalis by mouth, quinidine, procainamide, diphenylhydantoin sodium, and potassium. Propranolol (40 mg daily in four doses) had been given. However, this treatment was stopped because of the development of sinus bradycardia. The various medications employed reduced the incidence of arrhythmias to some extent, but the patient still had daily attacks of palpitations even with the most effective drug combination. After careful analysis of the problem it was concluded that a temporary right ventricular pacemaker should be inserted so that larger amounts of propranolol could be administered without the dangers of symptomatic bradycardia.

Case 2

A 36-year-old female was admitted because of rapid heart action. She had been complaining of intermittent attacks of palpitations for the past 10 years. The frequency of the paroxysms was
SINUS WITH NORMAL A-V

RATE: 50/MIN.

NORMAL A-V

RATE: 60/MIN.

Figure 2

Case 1. Recording of His bundle electrograms during sinus bradycardia and atrial pacing. The left panel shows the standard leads and His bundle electrogram (HBE) obtained during sinus bradycardia (rate, 50/min) and normal intraventricular conduction. P and H represent P wave and His bundle deflections, respectively. In this and all figures, the intervals are expressed in milliseconds. The effects of atrial pacing at a rate of 60/min are shown in the right panel. At this pacing rate normal conduction still prevails. St. = pacemaker-stimulus artifact.

Results

Case 1

Recordings obtained during sinus rhythm and normal intraventricular conduction are shown in figure 2 (left). It was assumed that at this moment, conduction was occurring exclusively through the normal A-V junction. The His bundle potential consisted usually of a biphasic wave of around 15-msec duration and is in keeping with the findings of Scherlag and associates.8 Minor variations in the size of the His bundle electrograms were due to slight movements of the intracardiac electrodes. Changes in the different intervals and in QRS duration during electrical stimulation of the atria are shown in table 1.

The right panel in figure 2 shows the effects of atrial pacing at a rate of 60/min. Normal intraventricular conduction (80 msec) was reduced somewhat, but not completely abolished, by sedatives and quinidine.

An electrocardiogram after cardioversion showed sinus bradycardia (rate 40/min) and WPW type A (fig. 5).

The patient was given a test dose of propranolol (5 mg orally) and the rate dropped to 42/min. It was then decided to introduce a temporary transvenous pacemaker so that the dose of propranolol could be increased. As a secondary gain, the potentials from the specialized A-V conducting tissues could be studied.
Anomalous A-V conduction (An. A-V) appeared at a rate of 90/min as the atrial rate was increased from 90 to 100/min. The P-R interval remained the same, but the P-H interval lengthened. In the right panel the H deflections appeared after the onset of depolarization in the standard leads. This indicates that part of the ventricles were pre-excited ahead of the orthograde His bundle deflections.

Figure 3

Case 1. Recording of His bundle electrograms during atrial pacing at increasing rates. Anomalous A-V conduction (An. A-V) appeared at a rate of 90/min as the atrial rate was increased from 90 to 100/min. The P-R interval remained the same, but the P-H interval lengthened. In the right panel the H deflections appeared after the onset of depolarization in the standard leads. This indicates that part of the ventricles were pre-excited ahead of the orthograde His bundle deflections.

still present. Both P-R and P-H intervals had become longer after the rate was increased. This is the usual response to atrial pacing in patients without the WPW syndrome. Anomalous A-V conduction with the development of a delta wave occurred when the atrial rate was increased to 90/min (fig. 3, left panel). The P-R interval remained the same (200 msec) as it was during pacing at 60/min, but the P-H interval increased to 190 msec. Ventricular depolarization was more prolonged (100 msec). The P-J interval measured 300 msec. At rates of 100/min (fig. 3, right panel) and 125/min (fig. 4, left panel), the P-R interval did not change, but the P-H interval increased to 230 and 250 msec, respectively. The P-J intervals also increased to 340 and 360 msec at these rates. In addition, the His bundle electrogram appeared after the onset of depolarization in the extremity leads. This means that some parts of the ventricles had been pre-excited before the His bundle. It should also be noted that the QRS complexes became wider at the faster rates. Finally, at a rate of 145/min (fig. 4, right panel) the P-R interval remained the same, but the His bundle electrogram could not be identified. The QRS complexes were maximally distorted and widened as compared with control recordings (fig. 2). P-J duration
WPW SYNDROME

Figure 4

Case 1. Recording of His bundle electrograms during atrial pacing at increasing rates. In the left panel the H deflections occurred after the beginning of the QRS complexes in the standard leads. The His bundle deflections disappeared when the rate was 145/min (right panel), at a moment at which the duration of the QRS complexes and the P-J intervals was maximal (pure pre-excitation beats). It appears that minor degrees of Wolff-Parkinson-White type of conduction (left panel and fig. 3) resulted from the more or less simultaneous activation of the ventricles by impulse traversing the normal A-V junction and a His bundle bypass.

was 380 msec. These beats were believed to represent total activation of the ventricles through a His bundle bypass since Durrer and associates have emphasized that “with longer duration of the P-J and QRS intervals and concomitant increased deformation of the QRS complex, predominant or even exclusive excitation of the ventricles by way of the Kent bundle must be assumed.”

After completion of this study, the tripolar and one of the bipolar catheters were withdrawn, and the other bipolar electrode was advanced into the right ventricle. Demand pacing was instituted at a rate of 70/min. During the following days, the patient received progressively higher doses of propranolol. Palpitations were abolished only

Table 1

<table>
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<tr>
<th>Atrial rate</th>
<th>P-R interval</th>
<th>P-H interval</th>
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<td>145</td>
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after administering 160 mg daily (40 mg every 6 hours).

Yet, atrial extrasystoles with anomalous A-V conduction reappeared whenever the ventricular rate was reduced to below 75/min. In view of this situation, it was considered that the patient would benefit from the combination of permanent pacing and drug therapy. Hence, a transvenous adjustable rate Medtronic demand (ventricular-inhibited) pacemaker was implanted. The patient has remained symptom-free for 7 months since pacemaker implantation with pacing at a rate of 80/min. The dose of propranolol was maintained at 160 mg daily since atrial arrhythmias reappeared whenever the dose was decreased.

Case 2

The tracing obtained during sinus rhythm is presented in figure 5. Figure 6 shows the His bundle electrogram (HBE) during sinus (?) rhythm and varying degrees of pre-excitation. The onset of the P wave in the bipolar atrial electrogram (BAE) recorded from the higher portions of the right atrium preceded the one recorded from above the tricuspid valve (HBE) by an interval of 35 msec. The first QRS complex is less distorted and follows a different P wave from the second ventricular complex. Although the P-H interval was similar in both beats, the P-R interval was shorter in the second beat. In the latter, the HBE appeared 10 msec after the beginning of the QRS complex in lead I, indicating that part of the ventricles were pre-excited ahead of the His bundle. It appears that on both occasions the corresponding QRS complex was a “fusion” beat resulting from the more or less simultaneous depolarization of the ventricles through the normal A-V junction and through a bypass of the His bundle.

Figures 7 to 9 show the results of atrial pacing at increasing rates: Because the P waves were barely visible in lead I, the paced P-R and P-J intervals were measured from the beginning of the P wave in the HBE to the
onset of depolarization in lead I. Other reasons supporting this type of measurement will be presented below.

At a rate of 110/min (fig. 7) there was practically no pre-excitation since lead I showed an initial q wave. In both panels the P-R, P-H, and P-J intervals measured 110, 70, and 180 msec, respectively. However, with the same (artificial) pacemaker rate (110/min) there was an intermittent change in the stimulus to P (St.-P) intervals (from 50 to 100 msec) and in the morphology of the P waves. Yet, both P waves were conducted to the ventricles mainly through the His bundle (H). An interesting finding in this figure is that the shortening of the stimulus-to-QRS interval in the right-sided panel was due exclusively to a decrease in the St.-P, because the P-H and P-J intervals (measured in the bipolar lead recording the HBE) were similar in both panels. Regardless of the explanation for the variations in the St.-P (HBE) intervals in this case, it appears that the onset of the P wave was more exact than the emission of the stimulus to measure the P-R, P-H, and P-J intervals.

The results of atrial pacing at a rate of 155/min are presented in figure 8. The left panel shows that with an St.-P interval of 100 msec the P-R interval was similar to the one recorded at a rate of 110/min (fig. 7). The P-H interval had increased to 100 msec. The P-J interval measured 200 msec. Some degree of anomalous conduction was present since the q
Case 2. His bundle electrograms during atrial pacing at a rate of 110/min. Atrioventricular conduction is most probably occurring through the His bundle. There are two distinct P waves in the HBE, each with a different St-P interval.

The P wave had disappeared from lead I and had been replaced by a slurring in the upstroke of the R wave. After several seconds of pacing at the same rate, a similar phenomenon to that observed in figure 7 was noted: There was a change in morphology of the P wave associated with a shorter St-P interval (50 msec). Although the P-R interval did not change, the QRS complexes became wider while the P-J intervals increased from 200 to 215 msec. The His bundle electrogram could not be identified with certainty. Apparently (in the left panel) conduction was occurring through the A-V junction with His bundle bypass. The P-H interval (100 msec) was longer than it was when the rate was 110/min (70 msec in fig. 7). The widened QRS complexes and longer P-J interval in the right panel indicated that the ventricles were activated mainly by a His bundle bypass. They had been pre-excited ahead of the His bundle. The reasons as to why this occurs at the same pacing rate are not clear.

Finally, the effects of atrial pacing at a rate of 210/min are presented in figure 9. The exact duration of the P-R interval was difficult to determine since the upstroke of the R wave was superimposed on the preceding T wave. All QRS complexes (except the last) appear to be maximally distorted. The P-J interval was longer (245 msec) than with slower rates (200 and 215 msec in fig. 8). His bundle deflections were not visible. These findings suggested total activation of the ventricles through a His bundle bypass. In addition, the tracing showed a beat-to-beat alternating of St-P intervals. Neither type of P wave (regardless of the preceding St-P interval) was conducted through the normal A-V junction.

It appears that the fourth P wave was blocked to the ventricles when it encountered absolute refractoriness in the two pathways. In consequence, the following stimulus artifact occurred sufficiently late in diastole to produce a P wave able to be propagated through both routes. Favoring this assumption is the finding of the His bundle deflection preceding the moderately distorted ventricular...
complex. The corresponding P-J interval was shorter (190 msec) than that of previous beats (245 msec).

After recording the potentials from the specialized A-V conduction system, two of the catheters were withdrawn. The remaining catheter was advanced into the right ventricle. Its terminals were attached to a temporary demand (ventricular-inhibited) pacemaker (rate: 90/min). During the following days the dose of propranolol was increased progressively. Extrasystoles were not abolished until reaching a dose of 160 mg daily (40 mg every 6 hours). At this time conventional electrocardiograms showed pure pacemaker beats with persistent 1:1 retrograde (V-A) conduction to the atria. A few days later, a permanent transvenous, adjustable rate Medtronic demand (ventricular-inhibited) pacemaker was implanted. Its rate was set at 90/min. The patient was discharged with the dose of propranolol indicated above and has remained symptom-free for 3 months. Atrial extrasystoles have reappeared whenever the dose of propranolol has been decreased or the pacemaker rate reduced below 80/min. This seemed to be mainly due to the disappearance of the retrograde (1:1) conduction.

Discussion
Scherf and Cohen stressed that more than 60 theories have been proposed to explain the genesis of the pre-excitation (WPW) syndrome. Until recently, the most widely (al-
though not uniformly) accepted mechanism was that of an accessory atrioventricular connection bypassing the normal A-V junction.\textsuperscript{1} Two recent observations, however, have challenged the classical concepts. Lau and associates\textsuperscript{6} observed that atrial pacing at increasing rates did not change the P-R interval or QRS morphology of patients exhibiting the full blown picture of WPW syndrome in the control tracings. This behavior contrasted with that of persons who did not have the WPW syndrome in whom the catheter technic of His bundle recordings has shown that prolongation of the P-R interval occurs mainly at the expense of the P-H interval.\textsuperscript{9} Lau's group concluded that the WPW syndrome was not a fusion beat resulting from the activation of the ventricles through both accessory and normal A-V communications.\textsuperscript{6} They believed that the anomalous and normal components of the WPW beat were due to a complete bypass of the A-V node by the atrial impulse. However, they did accept the existence of an accessory A-V connection.

The interesting concept of "synchronized sino-ventricular conduction" was postulated by Sherf and James.\textsuperscript{7} According to these authors, an ectopic supraventricular impulse originating in one of the intra-atrial tracts which bypass the A-V node (posterior internodal tract), could arrive at the lower part of
Case 3. Inscription of an orthograde His bundle electrogram after the beginning of the QRS complex. This patient did not have a Wolf-Parkinson-White (pre-excitation) syndrome. The onset of ventricular depolarization can precede the His bundle deflections in the following conditions: (a) during ventricular pre-excitation (figs. 3, 4, 6, and 8), (b) during retrograde (V-A) conduction, and (c) rarely in the presence of late extrasystoles (falling after the P wave) provided that the atrial beats are able to stimulate (orthogradely) the His bundle before the latter can be excited retrogradely from the ventricles. This tracing shows the latter situation. Two sinus beats are followed by three ventricular paced beats. The stimulus artifact (St.) of the first iatrogenic extrasystole falls after the P wave. The orthograde P-H interval and the morphology of the H deflections do not change in this beat although the His bundle deflection appears after the onset of the QRS complex in lead II. It can be assumed that the His bundle was activated in a forward direction after parts of the ventricles had been depolarized by the ventricular pacemaker.

Figure 10

Case 3. Inscription of an orthograde His bundle electrogram after the beginning of the QRS complex. This patient did not have a Wolf-Parkinson-White (pre-excitation) syndrome. The onset of ventricular depolarization can precede the His bundle deflections in the following conditions: (a) during ventricular pre-excitation (figs. 3, 4, 6, and 8), (b) during retrograde (V-A) conduction, and (c) rarely in the presence of late extrasystoles (falling after the P wave) provided that the atrial beats are able to stimulate (orthogradely) the His bundle before the latter can be excited retrogradely from the ventricles. This tracing shows the latter situation. Two sinus beats are followed by three ventricular paced beats. The stimulus artifact (St.) of the first iatrogenic extrasystole falls after the P wave. The orthograde P-H interval and the morphology of the H deflections do not change in this beat although the His bundle deflection appears after the onset of the QRS complex in lead II. It can be assumed that the His bundle was activated in a forward direction after parts of the ventricles had been depolarized by the ventricular pacemaker.

this structure earlier than usual. Therefore, excitation of the A-V node would be different from normal, resulting in a distorted (and premature) arrival of the impulse to the His bundle, and the ventricular septum could produce ventricular pre-excitation. Later activation of the ventricles via the right and left bundle branches would be responsible for the inscription of the terminal part of the QRS complexes. This theory explains the characteristic features of ventricular pre-excitation: the short P-R interval (due to an A-V nodal bypass) and the abnormal QRS complexes (resulting from ventricular pre-excitation).7

Scherf and Bornemann14 believe that the ventricles can be pre-excited if there are tracts within the A-V node, His bundle, and bundle branches which connect with specific ventricu-
lar sites. According to Lepeschkin this type of bypass “within the normal A-V junction” is the only one compatible with the numerous observations of pre-excitation beats showing a normal or prolonged P-R interval.

The observations presented in this report seem to indicate that, in the patients studied, ventricular pre-excitation resulted from a bypass of the main His bundle, since in certain moments the ventricles were activated before the latter. In contrast, in the absence of the syndrome under consideration, the orthograde His bundle deflection invariably occurs before the onset of ventricular depolarization. An exception to this rule occurs occasionally in the presence of late ventricular extrasystoles (falling after the P wave). In some of these beats an orthograde His bundle electrogram can appear after the onset of the QRS complex if the retrograde activation of the bundle is sufficiently delayed (fig. 10).

Cases 1 and 2 show that the full blown image of ventricular pre-excitation did not occur until after the His bundle deflection had disappeared inside the ventricular complexes. Therefore, the less bizarre QRS complexes with shorter P-J intervals (which were preceded by His bundle deflections) most probably represented fusion beats resulting from ventricular activation through the normal A-V bundle (as evidenced by increasing P-H intervals with higher rates) and through the accessory communication (as indicated by the progressive increase in the delta portion of the QRS complexes). Finally, pure pre-excitation beats appeared when conduction failed completely through the A-V bundle. At very high rates A-V conduction did not occur through either communication. Significant differences between St.-P intervals appearing at the same rates have not been reported previously, so far as we know. Their being due to movements of the stimulating, or recording catheters, or both, cannot be completely excluded. A fatigue of conduction through the A-V junction or an enhancement of vagal effects could have delayed propagation sufficiently through the latter to allow conduction through the bypass; nevertheless, the short latency could be attributed to some degree of “supernormal” intra-atrial conduction or perhaps to direct stimulation of an intra-atrial tract which might have connected directly with the ventricles in a point not necessarily close to the His bundle.

Variations in the St.-P distance (latency) were not attributed to relative atrial refractoriness for two reasons: (1) the atrial rate was not high enough and (2) the intervals did not increase with higher rates (up to 210/min). It should be stressed that the St.-P interval represents the time between delivery of the impulse to a part of the right atrium and the moment in which the activation reached the bipolar recording lead (HBE) located in close proximity to the tricuspid valve. A high frequency of spontaneous ectopic atrial activity in ventricular pre-excitation was observed by Sherf and James. They postulated that ectopic supraventricular rhythms frequently originated in one of the tracts of fibers bypassing the A-V node (posterior internodal tract). It, therefore, might not be unusual for an artificial stimulus to have directly activated one of these preferential pathways resulting in decreased intra-atrial conduction time (fig. 8).

The results presented in this communication do not disprove the concept of “synchronized sino-ventricular conduction.” Apparent discrepancies can be reconciled by assuming the existence of an atroventricular connection bypassing both A-V node and His bundle. Moreover, the possibility that a group of His bundle fibers can conduct impulses in specific situations, such as during “synchronized sino-ventricular conduction”; a bypass within the A-V node region or functional longitudinal dissociation, and that their activity might not be detected by the catheter technic has to be considered. However, the reliability of this method for studying spontaneous (and artificial) atrioventricular and intraventricular conduction disturbances has been demonstrated by Damato and co-workers. Moreover, the finding in cases 1 and 2 should not be extrapolated to all patients with ventricular pre-excitation since the latter could be due to
several different mechanisms. Slight variations in size of the H deflections recorded in two patients are consistent with changes noted in our laboratory when using the catheter technic. The possibility that it might represent an orthograde right branch potential is unlikely, since we have not observed nor have found it reported [8-10, 17] that forward conduction through the right branch can follow the onset of ventricular depolarization.

Persistent ventricular arrhythmias occurring in this syndrome are difficult to control and have even required surgical treatment [18-20]. The combination of oral administration of propranolol with a permanent transvenous demand pacemaker, used by Gibson and Sowton [18] in one patient resulted in the complete suppression of otherwise intractable arrhythmias. If this therapy proves to be effective in the long-term management of pre-excitation arrhythmias, it will spare some patients the need of an intracardiac operation.

References

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