Wolff-Parkinson-White Syndrome in Children: Electrophysiologic and Pharmacologic Characteristics

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SUMMARY Intracardiac electrophysiologic studies were performed on 28 infants and children, ages 1 month to 18 years, with the Wolff-Parkinson-White syndrome to try to determine 1) the electrophysiologic characteristics of the accessory connection and 2) the mechanisms of associated supraventricular dysrhythmias. Although the antegrade refractory periods of the normal conduction system were shorter than those found in adults, those of the accessory connection were slightly longer.

The mechanism involved reentry with antegrade conduction through the atrioventricular (AV) node and retrograde conduction through the accessory connection in 22. Eleven of these 22 had a wide QRS during tachycardia due to a bundle branch block. Three other subjects had wide QRS tachycardia, but the mechanism involved antegrade conduction through the accessory connection and retrograde through the AV node. The patient had AV node reentry tachycardia. Two patients did not have clinical VT, and in these two, VT could not be induced. Neither patient had retrograde conduction through the accessory connection.

The site of the accessory connection could be identified in 26 subjects by the sequence of retrograde activation of the atrium during VT or ventricular pacing. Digitalis shortened the refractory period of the accessory connection in five of the eight patients studied.

COMPLICATIONS of the Wolff-Parkinson-White syndrome (WPW) lead to significant morbidity and mortality in children. Supraventricular tachycardia (SVT) is common in children with WPW. Atrial flutter and fibrillation, although rarer, also occur.

The electrophysiologic characteristics, mechanisms of SVT, and responses to pharmacologic agents have been well described in adults, but not in infants and children. There are differing opinions as to the most effective approach to management of pediatric patients with WPW and VT. Mantakas et al. suggested that prospective randomized studies should be performed to resolve these issues.

In this paper we report the results of electrophysiologic studies in children with WPW at Texas Children's Hospital from January 1975 to October 1978. The response to intravenous ouabain and clinical characteristics are also presented.

Patients and Methods

Patients

Twenty-eight patients, ages 1 month to 18 years (median 8 years), with surface electrocardiographic evidence of WPW underwent invasive electrophysiologic studies. Eight patients had additional congenital heart defects. Three had a ventricular septal defect, two Ebstein's anomaly, one endocardial cushion defect, one univentricular heart and one tricuspid valve.

Electrophysiologic Studies

Since these studies were carried out over 3.5 years, there was some variation in technique. Our most recent technique is reported here. Cardioactive drugs were discontinued 48 hours before the procedure. Two to four electrode catheters were used percutaneously. In each patient a bipolar electrode catheter with both 1 mm and 10 mm interelectrode distances was inserted percutaneously into the right femoral vein. The catheter was advanced to the heart under fluoroscopic guidance and positioned across the tricuspid valve to record low septal right atrial (LSRA), bundle of His and right ventricular septal (V) electrograms. Each subject also had a quadrupolar catheter with interelectrode distances of 3 mm, inserted percutaneously from the left or right groin, placed near the sinus node (HRA). Twenty patients also had a quadrupolar catheter with 3 mm interelectrode distance inserted percutaneously from the left antecubital fossa and positioned in the coronary sinus to record left atrial and atrial septal activity. In 15 patients we placed a fourth quadrupolar catheter in the right ventricular apex for recording and stimulation. This catheter was moved during latter parts of the study to different locations in the right atrium to record the sequence of retrograde activation during paroxysmal VT (PSVT). Biplane fluoroscopy and cineradiography were used to define and record catheter position. Femoral arterial pressure was monitored continuously with an indwelling plastic cannula.

Three surface ECG leads were recorded simultaneously with three to six optically isolated intracardiac electrograms on a multichannel photographic recorder (Electronics for Medicine or Hewlett Packard) as previously reported. The intracardiac recordings were filtered below 30 Hz and above 250 Hz. Paper speeds from 100-500 mm/sec were used. A six-channel storage oscilloscope (Tektronix) was used to "freeze" the recordings for

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immediate analysis. A digital programmable stimulator (Medtronic 5325 or Bloom) was used for continuous pacing and to introduce single premature stimuli into sinus or paced rhythm. In nine patients atrial flutter or fibrillation was induced deliberately by pacing the atrium at a cycle length of 150 msec. In nine patients atrial flutter or fibrillation was induced deliberately by pacing the atrium at a cycle length of 150 msec. If induced, the SVT was terminated by single or multiple atrial or ventricular stimuli.

In 14 subjects, single premature ventricular beats were given during SVT at a time when the bundle of His was refractory to prove the presence of an accessory connection (AC) available for retrograde conduction and show the participation of the pathway in the SVT by shortening the atrial cycle length. The cycle length of SVT, as well as retrograde conduction time, was evaluated with and without bundle branch block in 16 cases. Ouabain 0.01 mg/kg was given intravenously to the most recent eight subjects and the electrophysiologic studies were repeated 30 minutes later.

Definitions

High right atrium (HRA): Depolarization of atrial muscle near the sinus node.

Low septal right atrium (LSRA): Depolarization of the atrial septum near the atrioventricular (AV) node.

Distal coronary sinus (DCS): Left atrial depolarization recorded from the pair of electrodes most distal in the coronary sinus; also records left ventricular basal depolarization.

Proximal coronary sinus (PCS): Atrial depolarization recorded from the area of the ostium of the coronary sinus, recording posterior atrial and ventricular septal activity.

Low lateral right atrium (LLRA): Depolarization recorded from the low lateral wall of the right atrium near its junction with the inferior vena cava.

LSRA-H interval: Records AV node conduction time; measured from the earliest depolarization of each electrogram.

HV interval: Measures conduction time through bundle of His and bundle branches.

Atrial-delta wave interval: Records conduction time through the AC; measured from the beginning of the atrial electrogram near the AV connection to the Δ wave on the surface ECG.

Ventricle-to-atrium interval: Measured from a stable ventricular electrogram (usually right ventricular apex) to the various atrial sites during retrograde conduction.

Effective refractory period (ERP): The longest premature interval cycle length of a structure which fails to conduct to the next most distal structure.

Functional refractory period (FRP): The shortest cycle length of the output of a structure in response to premature stimulation.

Results

In each patient the presence of an extranodal AC was proved by:

1) A shorter-than-normal HV interval (fig. 1). The HV intervals ranged from −10 to 20 msec. The H depolarization merged into the ventricular depolarization during premature atrial stimulation (fig. 1), but it did not follow the end of the QRS in any instance. The LSRA-H interval was normal (range 60–120 msec).
in 25 patients and abnormally short in three, compared with our normal intervals.  

2) Increased widening of the QRS with little or no change of the P-delta interval with either atrial pacing or premature atrial stimulation (fig. 1). At a critical coupling interval, the PR interval suddenly lengthened and the QRS narrowed, indicating failure of the AC to conduct (fig. 2). The QRS tended to be wider and the PR shorter when pacing was carried out in the atrium on the same side as the AC.

3) A constant ventriculatrial conduction time with incremental ventricular pacing and premature ventricular stimulation in the 26 subjects with retrograde conduction.

4) An asymmetric retrograde atrial activation sequence during ventricular pacing and/or reciprocating SVT (fig. 2).

Electrophysiologic Properties of the AC and the Normal Conduction System

The antegrade ERP and FRP of the AC, normal AV conduction system, and the atrial and ventricular muscle are listed in table 1. The antegrade ERP of the AC was the longest A1A2 interval that failed to conduct to the ventricle through the AC, as confirmed by the presence of a Δ wave (figs. 1 and 2). In the antegrade direction, the ERP of the AV node was shorter than that of the AC in 18 of 20 patients in whom it could be measured. The range of the difference between the AERP of the AC and of the AV node was 20–510 msec. In three patients, the ERP of the AC was shorter than that of the AV node by 10–50 msec. In five subjects, antegrade conduction was limited by the ERP of the atrial muscle. In four of 10 subjects in whom both the accessory pathway FRP and the AV node antegrade FRP were measured, that of the AC was shorter, while in one it was equal and in five the AV node had a shorter antegrade FRP. Thus, although the shortest cycle length at which the AV node could conduct was shorter than that of the accessory pathway, the greater delay in the AV node resulted in the impulse arriving at the ventricle later when it traversed the AV node. The retrograde ERP of the accessory pathway was shorter than its antegrade ERP in all of the 14 patients in whom both were measured (figs. 3 and 4). The retrograde FRP of the accessory pathway was also shorter in all patients.

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<tr>
<th>Table 1. Electrophysiologic Properties of the Accessory Connection and the Normal Conduction System</th>
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<td><strong>Electrophysiologic measurement</strong></td>
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<td>AERP accessory connection</td>
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<td>ERP atrium</td>
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<td>Tachycardia cycle length</td>
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Abbreviations: A = antegrade; R = retrograde; ERP = effective refractory period; FRP = functional refractory period; AV = atrioventricular.
than the antegrade FRP. The retrograde refractory periods of the AV node could not be measured. The shortest ventricular cycle length during atrial fibrillation or flutter induced by rapid atrial pacing had a wide QRS in each of the seven cases, indicating conduction over the AC. The shortest ventricular cycle length ranged from 200–302 msec (mean 248 msec). Atrial flutter or fibrillation could not be induced by single premature atrial stimulation. The atrial fibrillation self-terminated in each patient. Only two of these patients had clinical atrial fibrillation or flutter.

**Mechanism of Reciprocating Tachycardia**

Reciprocating tachycardia was induced in 26 of the 28 patients by premature atrial stimulation. In all 26 patients the mechanism was reentry, but the sites varied. In 22 of the 26 the reentry circuit was antegrade through the AV node, bundle of His, bundle branch, ventricle, and retrograde through the AC, atrium and back to the AV node (fig. 2). The method of induction of tachycardia in each of these 22 subjects involved a premature atrial contraction that blocked antegrade in the accessory pathway, but conducted through the AV node (fig. 2). The AC was therefore available for retrograde conduction, completing the reentry circuit. This was possible because the antegrade ERP of the AC was longer than that of the AV node in these patients. This mechanism was verified by the demonstration of a His bundle potential before each QRS, with a normal HV interval (indicating conduction through the AV node and His bundle in an antegrade direction with participation of the accessory pathway in the retrograde direction). The QRS morphology showed a bundle branch block pattern at some time in 11 of the 22 subjects.

In three subjects the reentry circuit involved antegrade conduction through the AC and retrograde through the bundle of His and AV node (fig. 5). In one subject, both wide and narrow QRS type of SVT could be induced at separate times during electrophysiologic study, but only the narrow QRS type was seen clinically. The mechanism of induction of SVT in these three patients involved a premature atrial complex that blocked antegrade in the AV node-bundle of His. The AV node-bundle of His was therefore able to conduct in a retrograde direction and complete the reentry circuit. This was possible because the antegrade refractory period of the AV node was longer than that of the AC in these patients.

One subject exhibited only AV node reentry tachycardia, as evidenced by a normal retrograde atrial activation sequence and 2:1 block below the His without interrupting the tachycardia (fig. 6). Participation of an AC in the tachycardia is excluded by 2:1 AV block because, if the ventricle is not depolarized, the ventricular end of the AC could not be depolarized.

In two subjects we could not induce reciprocating tachycardia in the catheterization laboratory. Neither of these patients had spontaneous SVT. Each had complete retrograde block in the AC, shown by the
The ventricle is again being paced at a cycle length of 540 msec and a premature stimulus, $V_2$, is entered at a cycle length of 270 msec. At this point the retrograde refractory period of the accessory connection (AC) has been reached. The atrium is now activated by the bundle of His, proximal coronary sinus, distal coronary sinus, and high right atrium. Thus, the retrograde effective refractory period of the AC in this patient is 280 msec. The demonstrated atrial activation sequence would be exactly as predicted during retrograde activation of the atrium in AV node reentry tachycardia.

Abbreviations: see previous figures.

Fact that during ventricular pacing at a rate faster than sinus rhythm there was no influence on the atrial rate. The AC therefore could not complete the retrograde limb of the tachycardia circuit as it usually does in patients with clinically evident SVT.

The fact that the AC was the retrograde limb of the reentry circuit in 22 subjects was shown by:
1) eccentric retrograde atrial activation in 22 subjects (fig. 2);
2) shortening of the atrial cycle length by a premature ventricular stimulus while the bundle of His was refractory during SVT in 14 subjects (fig. 7);
3) increased ventriculoatrial conduction time and tachycardia cycle length during ipsilateral bundle branch block in 10 subjects.

Location of the AC Determined in the Laboratory

The anatomic location of the AC was localized in the laboratory in 26 of 28 subjects. The sequence of retrograde atrial activation during SVT was the most successful method for determining the site of the pathway (22 subjects). The distal coronary sinus electrodes showed earliest activation in the left lateral and left posterior pathways. The ostium of the coronary sinus was the earliest site activated in posterior septal pathways. The right-sided pathways activated their respective parts of the right atrial endocardium early. When the AV node activated the atrium in a retrograde direction, the LSRA (as recorded by the His bundle catheter) was activated first (fig. 5). The mouths of the coronary sinus and atrial septum were sometimes simultaneous, but the coronary sinus was never earlier than the LSRA.

An additional confirmatory method of localizing accessory AV connections is to record the retrograde atrial activation sequence during ventricular pacing (figs. 3 and 4). This technique is more likely to be successful if pacing is carried out in the ventricle on the same side as the AC.

In the 16 patients who developed bundle branch block during SVT, the ventriculoatrial conduction
FIGURE 5. Example of antidromic tachycardia in a patient with Wolff-Parkinson-White syndrome. Pacing is being carried out from the high right atrium and there is maximal preexcitation. After cessation of pacing, a run of tachycardia with the same morphology as during high right atrial pacing ensues. The atrial activation sequence indicates retrograde activation by the AV node. Same format and abbreviations as in previous figures.

FIGURE 6. Example of atrioventricular (AV) nodal reentry tachycardia with 2:1 block below the His depolarization in a patient with Wolff-Parkinson-White syndrome. The atrial activation sequence is from low septal right atrium to proximal coronary sinus to distal coronary sinus and high right atrium, indicating activation of the atrium retrograde from the AV node. Same format and abbreviations as in previous figures.
time increased in all 11 with free wall pathways and none of five with septal pathways. The site of the AC as determined by the response to bundle branch block correlated completely with the site as determined by the other methods. The cycle length of the reciprocating tachycardia induced in the laboratory ranged from 190–420 msec (mean 291 msec), corresponding to a heart rate ranging from 315–142 beats/min (mean 206 beats/min).

Effect of Ouabain on Properties of the Accessory AV Connections

Ouabain, 0.01 mg/kg, was given intravenously to eight subjects. The results are shown in table 2. The AERP of the AC measured 30 minutes after ouabain shortened by 10–60 msec in five patients, lengthened by 10–20 msec in two patients and remained the same in one. The shortening was 20 msec or greater in only three subjects. The FRP of the AC shortened in three of four subjects given ouabain. The shortest ventricular cycle length during atrial fibrillation was unaltered by ouabain in any of the four subjects.

Clinical Course

Twenty-six of the 28 patients had reciprocating tachycardia clinically. Each of these 26 subjects received pharmacologic treatment. The tachycardia was controlled with one drug in 10 cases, two drugs in 11 cases, and could not be controlled by drugs in five cases. Three patients underwent mapping and division of the AC. The first is alive and free of WPW and SVT 2 1/2 years after surgery. The second patient died of a massive stroke 2 days after surgery. She also had closure of a "Swiss cheese" type of ventricular septal defect with a large Dacron patch on the left septal surface. There had been no WPW conduction of SVT postoperatively. Since her AC was on the right side, we suspect that the stroke was caused by the left ventricular surgery for the ventricular septal defects. The third patient is well and free of WPW and PSVT 6 months postoperatively.

One patient had a radiofrequency rapid atrial pacing implanted for overdrive of SVT. He had a univentricular heart and pulmonary atresia. He had had multiple episodes of ventricular fibrillation preoperatively that always followed episodes of reciprocating tachycardia. Despite treatment with quinidine and propranolol, he died suddenly and unexpectedly 18 months after pacemaker implantation.

One patient first examined at 13 months of age had no WPW when examined again at 18 months of age. He has had no WPW during the ensuing 2 years, either on routine ECG or multiple 24-hour ambulatory recordings. He has had no treatment for 2 years and has had no episodes of SVT.

Discussion

Electrophysiologic Properties of Accessory Connection

This report confirms that the electrophysiology of the WPW syndrome in children is qualitatively the
same as in adults,\textsuperscript{11} but differs quantitatively in several important aspects.

Although the antegrade AV node refractory periods in children were shorter than those in adults,\textsuperscript{22} the antegrade AC refractory periods were similar to or longer than those reported for adults.\textsuperscript{23} Tonkin et al.\textsuperscript{23} reported several patients with antegrade AC refractory periods shorter than 200 msec in adults, while we found only one such instance in children. This was not caused by the atrium limiting refractoriness in our study, nor was it caused by our lack of pacing near the atrial end of the connection, since this was done in each subject. The mean AERP of the AC in our series was 310 msec, while our estimate of the mean values in Tonkin’s series is 262 msec (calculated from his fig. 1). Conversely, we found more children with relatively long antegrade AC refractory periods (greater than 300 msec) than did Tonkin in adults. These findings did not influence the rate of tachycardia (which was faster in children than that reported in adults), since the AC was uninvolved in the antegrade pathway of SVT in most instances. The short antegrade AV node refractory periods in our patients may partially explain their rapid SVT. An explanation for our failure to identify pediatric age subjects with extremely short antegrade AC refractory periods is that such subjects do not come to medical attention until later in life when, with coronary or hypertensive heart disease, they are more likely to present with atrial flutter or fibrillation with rapid conduction to the ventricle. When subjects with short AERPAC are young, their normal short AERPAC may not provide the disparity in refractory periods necessary to allow induction of reciprocating SVT. Patients with longer AERPAC may present in infancy and childhood with reciprocating PSVT.

Our values in children for retrograde AC refractory periods are similar to those in adults. In each subject the retrograde refractory period was shorter than the antegrade, while in adults approximately half had shorter antegrade refractory periods, again suggesting that patients with a shorter antegrade refractory period do not come to medical attention until later in life.

\textbf{Localization of AC}

The anatomic distribution of the location of the AC was similar in children to that in adults\textsuperscript{11} (fig. 8), except right-sided pathways were slightly more prominent in children. The same techniques were feasible for localization of ACs in children as in adults.\textsuperscript{11, 24, 25} We could insert three catheters percutaneously in children as young as 2 years. In younger children, only two catheters were used and recordings were made sequentially\textsuperscript{26} rather than simultaneously, using a standard reference such as the His depolarization. When measurements from two times are compared sequentially, it is necessary to confirm a constant cycle length during the SVT. Although our experience with epicardial mapping and surgical division is small, we correctly predicted the site of the pathway preoperatively in each subject.

\textbf{Effect of Digitalis on AERP of the AC}

One of the most pressing problems we hoped to help answer with this study was the effect of digitalis glycosides on the antegrade AC refractory period in children.\textsuperscript{27–29} Ouabain has been reported to have a variable effect in acute and chronic studies in adults.\textsuperscript{27} In some patients ouabain has been reported to shorten the antegrade AC refractory period and result in ventricular fibrillation.\textsuperscript{27} Adult cardiologists, therefore, use digoxin infrequently in patients with WPW. However, pediatric cardiologists consider digoxin the drug of choice for treating SVT with or without WPW, largely because few problems are associated with use of digoxin in children.

Our findings are consistent with those of Sellers\textsuperscript{37} in that intravenous ouabain had a variable effect on the antegrade AC refractory period. In this small series we elected to withhold digoxin from clinical use in only four patients. In these patients ouabain shortened the antegrade AC refractory period in two, while in two other patients with a short resting antegrade AC refractory period ouabain was not tested.

Patients with a very short refractory period or a refractory period that shortens after ouabain or a very rapid ventricular response to atrial fibrillation should be treated with propranolol or quinidine rather than digoxin. Patients with SVT refractory to medical management or rapid response to atrial fibrillation should have epicardial mapping and division of the AC.

Children with congenital heart disease requiring intracardiac repair and WPW with absent or infrequent episodes of SVT are challenging problems.\textsuperscript{5, 8, 21} We and others have reported severe episodes of SVT in
such children and even death from SVT immediately after intracardiac operations.\textsuperscript{30} We recommend that the AC be mapped and divided during the same operation.\textsuperscript{30} This will prevent a rapid response to atrial fibrillation that can also appear for the first time postoperatively. A third reason for dividing the pathway is that mapping and division late postoperatively would be more difficult because of adhesions from the previous surgery.

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References

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