De Subitaneis Mortibus
XXII. Intractable Paroxysmal Tachycardias Which Proved Fatal in Type A Wolff-Parkinson-White Syndrome

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Summary Paroxysmal tachycardias proved fatal in a middle-aged man with type A Wolff-Parkinson-White syndrome. Efforts to control his arrhythmias included a surgical incision into the left atrium, based on discovery of early left ventricular activation during epicardial mapping. The incision did not alter any electrocardiographic or clinical feature; at later necropsy examination it was found that the incision had not cut a nearby left atrioventricular (A-V) connection. Serial section study of the entire A-V rings and septal junction of this heart also demonstrated a second unusual A-V connection, between the atrial septum and the region of the His bundle. This latter connection was anatomically eccentric to the normal organization of this region and may have caused an alteration in the local electrophysiological behavior. The left lateral A-V connection may have been of no electrophysiological significance since it was composed of ordinary working myocardial cells. These and other possible correlations are discussed in the context of the clinical features, numerous electrophysiological observations, and the meticulously determined anatomical findings.

It is now widely believed that electrical instability of the heart is a fundamental causative mechanism of sudden unexpected death. How often the lethal electrical instability may have begun as some form of paroxysmal tachycardia is difficult to determine in most cases, and is by definition virtually impossible to know from cases of sudden unexpected death. From its earliest clinical description it has been known that paroxysmal tachycardia was a cardinal feature of the Wolff-Parkinson-White (WPW) syndrome.1 There is growing clinical evidence that the WPW syndrome is in exceptional instances fatal, and that the terminal electrophysiologic mechanism was either paroxysmal tachycardia or was initiated by tachycardia. Although most patients with paroxysmal tachycardia can be treated successfully and many do not even require treatment, there are patients who are exceptions to this rule. Such patients often include ones with the WPW syndrome. In this report we present the clinical, electrophysiological, and postmortem correlative findings in one patient with type A WPW syndrome who had life-long paroxysmal tachycardia which eventually became intractable and caused his death.

Case Report

A 46-year-old policeman was first admitted to the University Hospital at Tours because of repetitive bouts of tachycardia which had been recognized at least from the age of 14. A brother was known to have paroxysmal atrial flutter, and a daughter had had surgical repair of a ventricular septal defect. In the beginning the patient's tachycardias were infrequent and seemed to follow episodes of unusual fatigue or either physical or emotional stress, would terminate spontaneously within about 15 minutes, and were followed by polyuria. For the past ten years, and especially in the previous two years, the paroxysms of tachycardia increased in frequency until they were occurring two or three times a week. At the same time the duration of the individual attacks became longer so that they lasted up to two days. The bouts of tachycardia also became associated with profuse sweating, vomiting, chest pain, significant hypotension, and in the episode just before admission, with syncope.

There were no abnormal physical or laboratory findings except those associated with the heart. During any episode of tachycardia, the cardiac rhythm was regular and varied in rate from 140 to 300 beats/min. Both the onset and termination of tachycardia were abrupt in nature. During sinus rhythm, there were varying degrees of pre-excitation producing type A WPW complexes (figs. 1 and 2). Two different types of tachycardia were observed: 1) Paroxysmal supraventricular (reciprocating) tachycardia with a narrow QRS complex and a heart rate of 170 beats/min. 2) Paroxysmal atrial flutter usually accompanied by a pre-excitation QRS pattern and conducted either 2:1 or 1:1, so that the corresponding ventricular rates were 130-150 or 260-300 beats/min. When the ventricular rate was the most rapid, the patient usually lost consciousness. The very rapid forms of tachycardia progressively became more frequent and severe, and decreasingly responded to any form of pharmacological therapy, including rather high concentrations of digitalis or propranolol or ajmaline.

Because the clinical condition of the patient was deteriorating, special electrophysiological studies were conducted preparatory to a consideration of cardiac surgery. Recordings from the region of the His bundle and with an intracavitary lead in the right atrium are illustrated in figures 2 to 4 during sinus rhythm, during paroxysmal tachycardia and atrial flutter, and also in response to special premature stimulations. Early atrial stimulation increased the magnitude of the delta wave, exclusively attributable to

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prolongation of conduction time in the A-V (atrioventricular) node. The refractory period of the accessory pathway was so brief that we were unable to measure it accurately. At the shortest coupling intervals the stimulus was blocked due to the refractory period of the right atrium. We were unable to terminate the supraventricular tachycardia with a premature atrial stimulus. Attempts to produce supraventricular tachycardia with a premature atrial stimulus actually caused atrial flutter. When atrial flutter was conducted 1:1, it was possible to distinguish this rhythm from ventricular tachycardia only by simultaneously recording intracardiac electrograms from the right atrium (fig. 4).

Because premature ventricular stimulation (fig. 3) was successful in either starting or stopping a paroxysm of supraventricular tachycardia, it seems likely that the spontaneous bouts were also reciprocating tachycardias.

Six months after the initial admission cardiac surgery was performed. After suitable exposure of the heart, epicardial mapping was conducted and the results are illustrated in figure 5. Abnormally early excitation was found in the left ventricular epicardium near the obtuse margin of the heart. An incision was made in the left atrial myocardium just above this point and extended parallel to the A-V sulcus as indicated in the drawing. This incision caused no change in the configuration of the P wave, did not abolish the delta wave present during sinus rhythm and did not alter the P-R interval. In the postoperative period bouts of supraventricular tachycardia and of atrial flutter persisted, essentially the same as before surgery. New treatment was then begun with verapamil and in amounts of 700 mg per day this was successful in reducing the frequency of the paroxysmal tachycardias to a tolerable level.

Three years later the arrhythmias again became a problem. Bouts of atrial flutter with 1:1 conduction were occurring several times a day. Various medications were utilized in an attempt to control this problem, eventually in association with the use of a right ventricular catheter placed to provide support pacing as necessary. Anti-arrhythmic medications included ajmaline, verapamil, pindolol, propranolol, disopyramide, and potassium. Despite various combinations of these drugs and their use in maximally tolerated concentrations, there was little or no significant effect on the arrhythmias. The terminal episode was a bout of atrial flutter in 1:1 conduction during which syncope and then cardiac arrest occurred and all efforts at resuscitation failed.

At necropsy examination the important findings for this report were limited to the heart. Chamber size and volume, all major coronary arteries, both the interatrial and interventricular septa, and all four cardiac valves were normal. Special blocks were prepared for serial sectioning of six regions: 1) the sinus node; 2) the entire junction of atrial and ventricular septa; 3) the left posterior and lateral A-V ring; 4) the left anterior A-V ring; 5) the right anterior A-V ring; and 6) the right posterior A-V ring. A description of the technique utilized has been published previously and this was modified only to include microscopic examination of every section. More than 16,000 slides were studied.

**Figure 1.** Despite the pre-excitation during sinus rhythm, the P-R interval is not shortened but normal (150 msec), due in part to the large amplitude of the P wave. The positive delta wave in V1 and negative one in V6 make this type A WPW. Pre-excitation is not present during paroxysmal supraventricular tachycardia.

**Figure 2.** Without other tracings in this patient it would be difficult to diagnose the WPW syndrome from this ECG alone. P-R interval (130 msec) is not shortened and QRS duration (100 msec) is not prolonged. On comparison with other records, however, the generous amplitude of the R wave in V1, with negative delta wave in III and V6 here can be recognized as pre-excitation. In the His bundle electrogram the A-H interval is rather short (55 msec) but the H-V interval is normal (50 msec).
There was more than normal fibrosis in the sinus node (fig. 6) and in many portions of the internodal pathways. Focal degeneration and fibrosis of the internodal pathways was particularly prominent just above the A-V node. Some foci of degeneration and fibrosis were present in both atrial free walls, but not nearly so extensive as in some previous examinations of the heart in fatal WPW syndrome. Focal fibrosis and degeneration was also present to a minor degree in the ventricular myocardium. The His bundle and its right and left branches were normal, except for an unusual connection to the His bundle which will be described below. Within the A-V node there was focal fibrosis and abnormal deposits of fat (fig. 7); numerous bypass tracts entered the right side of the A-V node including its inferior margin, just as they do in normal hearts.

Two unusual A-V connections were found, one in the left A-V ring near the obtuse margin of the left ventricle, and the other connecting the atrial septum to the His bundle region. The left lateral A-V connection was located 4.5 cm from the crux of the heart (figs. 8–10). It coursed from the left atrium deep to the coronary sinus and entered the epicardial margin of the left ventricular myocardium (figs. 9 and 10).

**Figure 3.** Premature atrial stimuli (marked Ps in panels A and B) caused enlargement of the delta wave. A premature ventricular stimulus (Rs with dotted vertical line in panel C) terminates a paroxysm of supraventricular tachycardia. H-V intervals of the His electrogram (A-V) can be compared in these several circumstances: during supraventricular tachycardia (panel C) it is 60 msec; during sinus rhythm (panel A) it is only 50 msec but the delta wave has a 10 msec duration; exaggeration of the delta wave by premature atrial stimulus (panels A and B) is proportional to the decrease of the H-V interval from 50 to 0 msec. During the paroxysmal tachycardia in the left of panel C, note the alteration of ventricular cycle length.

**Figure 4.** During paroxysmal atrial flutter there was highly variable A-V conduction. In the first three beats shown there is a normal QRS pattern with 2:1 A-V block, but the following beats exhibit a maximal degree of pre-excitation. Shortly thereafter (right half of upper strip) A-V conduction changes from 2:1 to 1:1 with a ventricular rate of 270 beats/min, lasting only a few seconds until sinus rhythm resumes. The lower channel in each strip is an intracardiac right atrial recording (RA).
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FIGURE 5. Locally measured P-R intervals during epicardial mapping at the time of surgery are indicated on these two drawings of the anterior and posterior surfaces of the heart. The earliest epicardial activation site was associated with a P-R interval of 150 msec, and its proximity to one of the unusual A-V connections (A-V #1) is illustrated. The interrupted line shows the location of the left atrial incision. RA = right atrium, LA = left atrium, RV = right ventricle, LV = left ventricle.

One must visualize, however, that the epicardial margin of the left ventricular myocardium at this location is still some distance from the actual epicardium of the heart, all that space being occupied by fat. This lateral A-V connection did not penetrate the mitral valve anulus. It was composed exclusively of working myocardial cells (figs. 11 and 12) and specifically did not contain either Purkinje cells or P cells or transitional cells.7 Closely adjacent to the left lateral A-V connection, however, and embedded within the collagen of the mitral valve, there were a few islands of slender tran-

FIGURE 6. The sinus node is shown here at low magnification between the two arrows in A. Pericardial fibrosis from the old surgery is visible above the sinus node. A small area of abnormal fibrosis and fatty replacement boxed in A is seen at higher magnification in B; a nerve involved by this process at the atrionodal junction is indicated with a black arrow. Goldner trichrome stain in this and all subsequent photomicrographs; magnifications indicated with reference bars.
FIGURE 7. Focal degeneration and fatty replacement within the A-V node (open arrows in A) are illustrated at higher magnification in B (same area boxed in A). The A-V node artery (asterisk in A) is slightly thickened but its lumen was only moderately narrowed. CFB is central fibrous body.

FIGURE 8. This drawing illustrates the location of both unusual A-V connections: the one at the left lateral A-V sulcus is #1 and the one between the atrial septum and region of His bundle is #2. Other abbreviations: CS = coronary sinus, Ao = aorta, SVC = superior vena cava, and AVN = A-V node. The location of the surgical incision is indicated and extends with dashed lines over the schematic cutout of the posterior left atrial wall.
area should properly be called an abnormally forward persistence of A-V node (as the cytology would suggest), or an unusual composition in the histology of the proximal His bundle (as the anatomical location would suggest). In either event, the existence of the connection is distinctly unusual and perhaps of even more electrophysiological significance than the other A-V connection.

**Discussion**

Although all cases of the WPW syndrome have certain fundamental similarities, each also has its own special features. Every patient with the WPW syndrome, therefore, poses a new set of electrophysiological puzzles. Any knowledge which can help in the solution of these puzzles will offer useful clues not only to a fuller understanding of the WPW syndrome generally but also to the nature of all cardiac electrical activity, including that responsible for lethal arrhythmias and sudden death. In the present case the presence of two unusual A-V connections offers a special anatomical basis for considering the possible pathogenesis of some of the electrophysiological abnormalities and their consequent clinical problems.

In contrast to most examples of the WPW syndrome where the P-R interval is characteristically short when a delta wave is present in the QRS complex, in our patient the P-R interval was often not shortened when a delta wave was present. Only a small part of the lengthened (relatively) P-R interval could be attributed to a generous amplitude of the P wave. There was some abnormal fibrosis in the sinus node, particularly at its atrionodal margin, and also some focal degeneration and fibrosis in portions of the internodal pathways. Both of these abnormalities could have contributed to a delay of atrial conduction of the sinus impulse. Focal degeneration and fatty replacement in the A-V node was even more impressive and this must have contributed to delayed conduction proximal to the His bundle. These same anatomical abnormalities may have deranged the sequence of atrial conduction in a manner conducive to the production of atrial flutter or other supraventricular arrhythmias.

At some times in the present case the P-R interval was rather short (130 msec) and the delta wave was very small (fig. 2); at such times the A-H interval was also short, measuring 55 msec. A ready explanation for this situation would be the unusual connection between the atrial septum and the region of junction between the A-V node and His bundle. Indeed, the anatomical existence of just such a connection has been predicted on the basis of physiological evidence and deductive logic from previous examples of partially concealed pre-excitation. We believe that the unusual connection found in the A-V septal junction of our patient was therefore functionally significant. Why it functioned intermittently rather than constantly is uncertain. The rarity
of this type of A-V septal connection may be appreciated from the fact that only two such examples have been encountered in a carefully examined series of 687 human hearts, and it is especially significant that in one of these two the patient had a short P-R interval and died from supraventricular tachycardia.9

While the A-V septal connection in our patient is useful in explaining the short P-R and A-H intervals when they were present, and could contribute to an explanation of the QRS changes if one assumes there was eccentric activation of a longitudinally partitioned His bundle as has been postulated to occur in some examples of the WPW syndrome,10-12 there were times when the P-R interval was not short. There are at least two possible explanations for this latter observation.

FIGURE 10. The left lateral A-V connection is shown in more detail in these three photomicrographs encompassing the same region as in figure 9. Reversal in viewer orientation for these photomicrographs (compared to fig. 9) is due to difference in photographic method, but the identifying labels are correct. A is from the same histologic section as figure 9A and B the same as 9B, but C here is from a section made between 9B and 9C. Course of the A-V connection is indicated with an open arrow, and magnification in A, B, and C is the same as indicated in B. The two boxes in B mark areas shown at higher magnification in figure 11 to demonstrate the histology in detail.

FIGURE 11. There is a tiny node-like structure embedded within the mitral anulus and comprised of a few slender interweaving transitional cells (A). The lateral A-V connection is comprised entirely of working myocardial cells (B). The boxed areas are shown at still higher magnification in figure 12 to illustrate the cytology.
The facility of atrial conduction from the sinus node to the A-V junctional region may simply have varied from time to time for unexplained reasons. A second explanation may be offered from the observations that the A-H interval could be prolonged with a premature atrial stimulation, indicating that the refractory period of the A-V septal connection was long, possibly longer than that of the focally diseased A-V node itself. A long refractory period for the A-V septal connection could also help explain the alternating long and short cardiac cycle lengths sometimes observed during tachycardia. The intracavitary recording showed that the alteration involved only the P-H interval, since the H-V and V-P (retrograde) intervals remained constant. With such an explanation we postulate that antegrade conduction could have alternately occurred via the unusual A-V septal connection and then via the A-V node.

What may seem the most tempting explanation for many of the electrophysiological abnormalities is the left lateral A-V connection. It was in the vicinity of the abnormally early activation of the left ventricle, and the existence of three different pathways has been suspected in previous observations of paroxysmal supraventricular tachycardia with alternating cycle lengths. However, both the delta wave and the supraventricular tachycardia were unchanged by a rather long incision above the lateral A-V connection. The atrial incision clearly did not cut the left lateral A-V connection, but one would expect that spread of any atrial activation to it should have been impaired, as should spread of any ventricular activation passing via that connection back into the atria. Furthermore, all the cells in the left lateral A-V connection were working myocardial cells, no different from those in areas elsewhere in the heart expected to conduct rather slowly instead of unusually rapidly. Thus, there are two plausible explanations for the failure of the
surgery to improve the clinical course of this patient: the incision may have been ineffective because it failed to cut the connection at fault, or this left lateral A-V connection may have been of no electrophysiological significance. Despite the compelling attractive logic based on demonstrated early activation of the left ventricle just in the vicinity of this left lateral A-V connection, direct evidence that the anatomical connection was in fact responsible for that early activation is lacking and evidence to the contrary, although not proof, cannot be ignored.

If the left lateral A-V connection was not responsible for producing the delta wave when it was present, then how did it occur? Reasons have been presented previously to explain how all components of the WPW syndrome can be mediated within the region of the A-V node and His bundle, without the necessity of invoking lateral A-V connections on either the right or left side. While reported successes in the surgical treatment of some cases of WPW syndrome would seem to indicate that lateral A-V connections do play a physiological role in the pathogenesis of the clinical problem, it must be kept in mind that there have also been many surgical failures based on exactly the same logic and one may suspect that more failures have occurred than have been reported in publications. Furthermore, even in the experience of those most adept at such surgery it has been found that A-V septal (rather than lateral) connections are indeed a frequent cause of the WPW syndrome (figure 18 in reference 15). One of the key concepts to support electrophysiological explanations of the WPW syndrome on the basis of abnormal structure and/or function in the region of A-V node and His bundle is the concept that longitudinal dissociation normally is present in the His bundle. If that concept is correct, then not only re-entrant tachycardias but also virtually all degrees of distorted patterns of ventricular activation are possible. A recent carefully conducted electrophysiological experimental study demonstrated that ven-

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**Figure 14.** The second unusual A-V connection was between the atrial septum and the proximal portion of the His bundle (open arrows in A). Difficulty in anatomically distinguishing precisely where A-V node stops and His bundle begins is discussed in the text. Collagen surrounding the structure in A would suggest that it is His bundle, and direct connection above with interatrial septum (IAS) is distinctly unusual. The His bundle photomicrograph in B shows complete normal separation from the interatrial septum (IAS) by collagen and is from a histological section made 112 microns anterior to the one in A. IVS in B is interventricular septum.

**Figure 15.** Histological and cytological detail of the second A-V connection (corresponding to #2 in the drawings of figures 5 and 8) is shown here. The cells continuing from the interatrial septum into the His bundle region are slender transitional cells, similar to A-V node, as is much of the "His bundle" itself illustrated in B from this same histological section. Potential electrophysiological significance of this histological organization and cytology is further discussed in the text.
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Much remains to be learned about the true pattern of conduction within the human His bundle, but cases such as the present one represent experiments of nature which merit continued examination of all plausible explanations for the WPW syndrome and its complications.

References

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