Early history of the pre-excitation syndrome

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Abstract This brief review discusses the interesting early history of the pre-excitation syndrome. In 1913 Cohn and Fraser published the first patient with a short P-R interval, wide QRS complexes, and paroxysmal tachycardia. This was followed by other cases of pre-excitation syndrome, all of which were considered to be due to bundle branch blocks. In 1930 Wolff, Parkinson, and White reported 11 patients with the syndrome, which came to bear their name. Two years later, Holzmann and Scherf suggested bypass tracts as the most likely mechanism of pre-excitation syndrome. In 1942, Wood et al. documented the first accessory connection at autopsy. Despite these early studies supporting the bypass theory, the quest for alternative mechanisms continued until the 1970s when electrophysiological studies and surgical therapy confirmed accessory connections as the mechanism of pre-excitation syndrome.

KEYWORDS
WPW syndrome; pre-excitation syndrome; early history; accessory connections

Introduction

Pre-excitation syndrome has an interesting and remarkable history. Early descriptions of this phenomenon date back more than 80 years to the first isolated cases reported by Wilson [1], Wedd [2], and Hamburger [3]. The more comprehensive description by Wolff, Parkinson, and White in 1930 brought this syndrome to prominence. Wolff and coworkers [4] reported 11 mostly young, healthy subjects with a short P-R interval, wide QRS complexes, and paroxysms of tachycardia. This pattern, which later came to be known as the Wolff—Parkinson—White (WPW) syndrome, was the first characterized pre-excitation syndrome.

In 1944, Ohnell [5] introduced the term pre-excitation syndrome for an electrocardiogram (ECG) manifested by a short P-R interval and a wide QRS complex, regardless of the presence or absence of tachycardia. That same year, Segers and coworkers proposed the term delta wave for the initial slurred component of the QRS complex [6]. The aim of this review is to discuss some of the notable historical aspects of pre-excitation...
syndrome, specifically the early misconceptions regarding the basis of the electrocardiographic abnormalities and arrhythmias associated with this condition [1,2,7,8].

**Early reports of pre-excitation syndrome**

Cohn and Fraser [7] in essence reported the first case of pre-excitation syndrome in 1913. These authors presented two patients with paroxysmal tachycardia, terminated by vagal stimulation. In the first patient, the resting ECG showed right bundle branch block (RBBB) and the second patient’s ECG revealed a slurring of the initial portion of the QRS complex (Fig. 1). In 1915, Wilson [1] published a patient with pre-excitation and episodes of supraventricular tachycardia, which were terminated by the Valsalva maneuver. This patient also had spontaneous and atropine induced AV junctional rhythm. These two reports [1,7] were followed by additional cases of pre-excitation syndrome in 1921 and 1926, all of which were classified as bundle branch block (BBB) [2,8].

**Anatomical substrate of pre-excitation syndrome**

Kent dramatically advanced the understanding of intracardiac conduction with his study of auriculoventricular (A-V) muscular connections. Kent proposed that there were multiple muscular links, which crossed the A-V groove. Specifically, he focused attention on a muscular connection between the right auricle and right ventricle at the lateral right border of the heart [9]. Thomas Lewis, who in 1925 did not find adequate anatomical or physiological evidence to support this hypothesis [10], questioned the role of “Kent’s bundle” in A-V conduction. Despite this scepticism, the notion that these bundles might play a role in A-V conduction continued to be studied [11,12]. Fifty years after Kent’s first work on the subject was published, Mahaim stated, “If conduction by Kent’s fibres is accepted (and it has still not been proved that these fibres regularly exist, and one can even doubt it), it should be regarded as an accessory form of conduction: para-specific conduction” [13].

A significant development occurred in 1942 when Wood and coworkers [14] reported the first histological proof of muscular connections between the right auricle and the right ventricle in a human autopsy specimen. The patient was a 16-year-old boy with episodes of paroxysmal tachycardia. Three years after the initial presentation, he presented with palpitations, severe substernal distress, and a heart rate over 150 beats per minute (bpm). The patient died 2 h later after drinking cold water. Autopsy revealed a normal heart with three muscular A-V connections between the right atrium and ventricle.

In the subsequent years, accessory connections were documented in series of patients with pre-excitation syndromes [15-18]. Despite these findings, Lev [15] in 1966 stated, “the anatomical base of the WPW syndrome is today unknown” and seven years later, “one must not overlook, however, the concept of Sherf and James of a physiological bypass within the conduction system” [16]. In other words, according to Lev, accessory connections were not the only means of pre-excitation.

**The mechanism of pre-excitation syndrome**

Interestingly, two groups working independently in the early 1930s proposed that the muscular connections described by Kent might be used to conduct an auricular impulse to the ventricle. Holzmann and Scherf [11], in 1932, were the first

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**Figure 1** Rhythm strip showing three pre-excited beats followed by a ventricular premature, which initiates a run of narrow complex tachycardia (from Cohn and Fraser [7] with permission).
Holzmann and Scherf, in addition to their pioneering theory on the mechanism of pre-excitation, also discussed the possibility of an "excitable centre" [11]. A properly timed atrial contraction could initiate a ventricular impulse from an excitable ventricular centre, thereby causing a short P-R interval and a delta wave. Sodi-Palares offered a similar mechanism in which electrotonus from the depolarized atrium triggers a ventricular impulse [20]. Further, according to Prinzmetal et al., a short P-R interval and a delta wave could be due to an accelerated atrial impulse stimulating the summit of the intraventricular septum [21]. The initial slurring of the QRS complex during stimulation of the intraventricular septum in patients undergoing right heart catheterization supported this concept [22]. Finally Sherf and James developed the "synchronized sino-ventricular conduction" theory [23]. According to these authors, an impulse originating in the posterior intranodal bundle preferentially activates the ventricle and causes pre-excitation.

Substantial support for the accessory pathway theorists arrived in 1942 when Butterworth and Poindexter published the first experimental animal study using an "electric bypass between the atrium and ventricle" [24]. The investigators were able experimentally to generate tracings similar to the previously described WPW syndrome.

Thus, A-V bypass tracts as the mechanism of pre-excitation was not generally accepted until the 1970s. A major advance was achieved when Durrer and Roos performed epicardial excitation mapping on a patient with the WPW syndrome [25]. Mapping was performed on a 21-year-old woman during surgery for a large atrial septal defect. The right ventricle was activated earliest as a result of conduction of the atrial impulse through a connection near the right lateral atrio-ventricular sulcus. This finding laid the foundation for later invasive electrophysiological studies [26–29], which not only clarified the underlying abnormality but also confirmed reentry as the mechanism of paroxysmal tachycardias in the WPW syndrome. These studies also became the basis for the surgical and catheter ablation therapy of the pre-excitation syndrome. It is most likely that James, in 1976, more than 80 years after Kent's original publications, wrote the last article challenging accessory connection as the mechanism of pre-excitation syndrome [30].

Another interesting aspect of the history of pre-excitation syndrome is the role of accessory connections within the specialized conduction system (nodoventricular, nodofascicular, and fasciculo-ventricular connections). According to Ferrer,
WPW syndrome could either be due to a Kent bundle or a combination of James’ posterior intranodal tract with Mahaim fibres [31]. Lev et al. documented this combination in a patient with pre-excitation syndrome who subsequently developed complete A-V block [32]. The role of the Mahaim fibres was also considered in patients with accessory pathways and decremental conduction properties. However, electrophysiological studies and surgical results in the 1980s and 1990s challenged the participation of Mahaim fibres in the pre-excitation syndrome [33,34].

Wide QRS complex tachycardia in Wolff–Parkinson–White syndrome

Studies have repeatedly shown that wide QRS tachycardias are seen in patients with the WPW syndrome. Early reports diagnosed these rhythms as ventricular tachycardia.

In 1929, Hamburger reviewed four cases of “Intraventricular block showing some interesting and unusual features” [3]. The “most interesting” case was of a 4-year-old boy with palpitations and difficulty breathing. The electrocardiogram revealed paroxysms of wide QRS complex tachycardia with a short P-R interval. Dr. Hamburger made a presumptive diagnosis of auricular tachycardia with right bundle branch block due to a respiratory infection [3].

In 1941, Levine and Beeson reported three patients with paroxysms of tachycardia classified by the authors as “ventricular tachycardia” [35]. All of their patients had pre-excitation and irregular wide QRS complex tachycardia, most likely due to atrial fibrillation. The most notable patient was a 36-year-old steamfitter who “while lifting a heavy box, suddenly became conscious of a “knock” in the centre of his chest”. The initial ECG showed “ventricular tachycardia,” which was treated with 0.8 mg of oral digitalis (Fig. 3). After restoration of sinus rhythm the ECG showed a short P-R interval and bundle branch block, with an infarct pattern. The patient was hospitalized for six weeks with the diagnosis of acute myocardial infarction. However, according to Levine, who saw the patient two months later, the diagnosis of

![Figure 3](http://example.com/figure3.png)
myocardial infarction was erroneous. He still believed however, that the clinical syndrome could be attributed to "an attack of ventricular tachycardia" [35]. The case was recognized for its similarity to those described by Wolff, Parkinson, and White, in that the young steamfitter was free of organic heart disease, yet a ventricular origin for the arrhythmias was assumed.

These wide complex rhythms initially thought to be ventricular in origin are in fact, the result of a supraventricular rhythm inducing a ventricular complex that is broad and slurred. Additional reports detailing ventricular tachycardia and fibrillation in WPW syndrome abound [3,35–41]. However, as understanding of the condition advanced, retrospective review of the rhythms reported as ventricular in origin called these diagnoses into question [42].

Conclusion

In summary, pre-excitation syndrome has a long and interesting history. This ECG abnormality was originally classified as BBB. Two years after Wolff and coworker’s classic article, Holzmann and Scherf and then Wolferth and Wood suggested accessory connection as its cause. In 1942, Wood et al. first reported the human anatomical substrate of the pre-excitation syndrome. However, even after documentation of accessory pathways, the search for alternative mechanisms continued. Finally, electrophysiological studies and ablative surgical therapy confirmed accessory A-V connections as the underlying mechanism of pre-excitation syndrome and put the debate to rest.

References


