Wolff-Parkinson-White Syndrome

Introduction and epidemiology

Supraventricular tachycardias (SVTs) denote all tachyarrhythmias that originate from supraventricular tissue or require it to be a part of the re-entrant circuit. These arrhythmias are frequently encountered in otherwise healthy patients without structural heart disease. The prevalence of SVT is estimated to be 570,000 in the US population with about 89,000 new cases diagnosed annually. The three most common cause of paroxysmal SVT include atrioventricular nodal re-entrant tachycardia (AVNRT) (56%), followed by atrioventricular re-entrant tachycardia (AVRT) (27%) and atrial tachycardia (AT) (17%).

Most SVTs are due to either abnormal automaticity or reentry. Automatic SVTs are relatively uncommon, except in acutely ill patients (metabolic disturbances, myocardial ischemia, acute exacerbations of chronic lung disease, acute alcohol ingestion and electrolyte disturbances). The vast majority of SVTs seen in ambulatory patients are due to reentry and are seen in patients who are not acutely ill and free of chronic heart disease. The reentrant substrate for supraventricular arrhythmias tends to be congenital. Thus, the typical patient with reentrant supraventricular tachycardia is young and healthy.

Mechanism of SVT also appears to be influenced by age and gender: SVT using accessory pathway (AP) are most common in the paediatric population; the age of onset of symptoms in patients with AVNRT is almost a decade later than those with AP-mediated tachycardias. Incidence and prevalence of SVTs increases with advancing age; for all age groups, women are twice more likely to develop SVT than men. Wolff-Parkinson-White syndrome tends to be more frequent in males than females, although the difference is reduced with increasing age due to the loss of pre-excitation. In contrast, both AVNRT and AT are more frequent in females than males.

In 1930, Drs Wolff, Parkinson and White reported on 11 young and healthy patients with peculiar ECG findings that included short PR interval and bundle branch block. These patients suffered from paroxysms of SVT. This eventually became known as the Wolff-Parkinson-White (WPW) syndrome. The wide QRS patterns were initially thought to be related to a short PR and bundle branch block; extranodal atrio-ventricular connections accounting for ventricular pre-excitation were first proposed by Kent.

A major reason for the interest in the WPW syndrome and AVRTs over the years is their associated morbidity and mortality. There is a well-established relationship between the presence of symptoms and the risk of sudden death (SD). In asymptomatic WPW patients the SD rate is low and is estimated to be about 1 per 1,000 patient-years. In a symptomatic young patient with WPW syndrome, the lifetime incidence of SD has been estimated to be approximately 3% to 4%. In some patients, ventricular fibrillation was the first manifestation of this syndrome.

While electrophysiologic (EP) study and AP ablation is well established in symptomatic patients with WPW syndrome, the approach to asymptomatic patients is less clear. The improved safety of EP study and catheter-based ablation techniques provide an impetus for prophylactic pathway ablation. To support this, randomized studies have shown that in experienced arrhythmia centres prophylactic ablation in asymptomatic patients who are found to be at high risk for arrhythmias reduces the risk for life-threatening arrhythmias. Whether this proactive approach can be applied to all asymptomatic patients is not clear. Based on recommendations from the 2003 ACC/AHA/ESC guidelines, asymptomatic pre-excitation is associated with a class IIa indication for catheter ablation.
**Clinical presentation**

The WPW syndrome is associated with numerous medical conditions, including various forms of congenital heart disease. Numerous reports delineate the association of Ebstein anomaly with WPW syndrome with up to 5% affected with both conditions in some case series. In adults, an association with the left-sided bypass tracts and mitral valve prolapse has been noted. Left-sided bypass tracts appear to be the most common, however, and because mitral valve prolapse is also common in the patient population, their association may in fact represent the coexistence of two relatively common conditions.

The **WPW pattern** refers to ventricular preexcitation on the ECG, while the **WPW syndrome** is the association of symptoms with the WPW pattern.

Of all patients who show signs of preexcitation on the surface ECG, only about 50% develop symptoms during their life. Since the preexcitation syndrome is characterized precisely by the association of electrocardiographic changes and arrhythmias, it can be said that only 45-50% of patients presenting preexcitation on 12-Leads ECG is suffering from WPW syndrome.

**Pathophysiology**

Preexcitation exists when, in relation to atrial events, all or some part of the ventricular muscle is activated by the atrial impulse sooner than would be expected if the impulse reached the ventricles only by way of the normal atrioventricular (A-V) conduction system.

The preexcitation syndromes previously were classified on the basis of proposed anatomic connections described by the eponyms Kent fibers, James fibers, and Mahaim fibers. Subsequently, the European Study Group for Preexcitation devised a new classification of the preexcitation syndromes based on their proposed anatomic connections (1). These connections are (a) A-V bypass tracts forming direct connections between the atria and ventricles, (b) nodoventricular fibers connecting the A-V node to the ventricular myocardium, (c) fasciculoventricular connections from the His-Purkinje system to the ventricular myocardium, and (d) A-V nodal bypass tracts, direct communications from the atrium to the His bundle or from the atrium to the lower A-V node via a specialized internodal tract or via specialized intranodal tracts with rapid conduction. Subsequently, connections defined pathophysiologically as atriofascicular and nodofascicular (i.e., from the atrium or A-V node to the right bundle branch (RBB) or adjacent myocardium) have been described and distinguished from nodoventricular fibers. Physiological (to be distinguished from anatomic) A-V connections produce the classic Wolff-Parkinson-White (WPW) syndrome; nodoventricular, atriofascicular, nodofascicular, and fascicular-ventricular connections (which were frequently referred to as “Mahaim fibers”) produce WPW variants, and A-V nodal bypass tracts may produce the so-called Lown-Ganong-Levine syndrome. Of note is that many of the fibers actually described by Mahaim have been demonstrated to exist anatomically in the absence of electrophysiologic function (2). Hence, anatomic descriptors will be retained but applied only when the accessory pathways demonstrate electrophysiologic function. Because these pathways appear to represent developmental abnormalities, it is not surprising that multiple types of accessory pathways may exist in any individual patient.
Electrophysiologic Evaluation in Patients with Wolff-Parkinson-White Syndrome

Electrophysiologic studies in patients with WPW are useful for confirming the diagnosis, studying the mode of initiation of tachycardias, localizing the bypass tract, demonstrating that the bypass tract participates in the tachycardias, evaluating the refractoriness of the bypass tract and its implication for risk of life-threatening arrhythmias, terminating tachycardias and aiding the development of pharmacologic, pacing, or ablative therapy for arrhythmias associated with WPW syndrome.

The typical AP (bundle of Kent) is a muscle fiber that bridges the atrio-ventricular groove providing electrical continuity between the atrium and ventricle in parallel to the AV node-His-Purkinje axis.

APs are composed of microscopic strands of morphologically normal myocardium that are located along the cardiac annulus or septum. More than 50% of APs are located at the left free wall, 20% to 30% at the posterosheetum, 10% to 20% at the right free wall, and 5% to 10% at the anteroseptum. It can conduct antegradely, retrogradely or bidirectionally. Antegradely conducting APs show ventricular pre-excitation on the 12-lead ECG and are, therefore, “manifest” (AP conducts more rapidly in the antegrade direction than the AV node, resulting in a discernible delta wave on the surface ECG). In sinus rhythm, there are some secondary repolarization changes in pre-excitation, represented by negative asymmetric (secondary) T waves, whose direction is opposite to that of the delta wave; this evident when pre-excitation is maximal. There are other T wave changes that occur in “intermittent” pre-excitation. When pre-excitation disappears after being present for a long period, narrow complexes, representing normal intraventricular conduction, show evident T wave abnormalities. The direction of the T wave vector during normal conduction is the same as that of the delta wave during pre-excitation. For example, when there is a posterosheetal accessory pathway, at the end of pre-excitation, there will be negative T waves in D2, D3 and aVF, as during pre-excitation delta waves were negative in those leads (Fig.1). This is due to the “electric memory” effect, which is also evident in the intermittent left bundle branch block, electric ventricular stimulation and ventricular tachycardia. If APs conduct only in the retrograde direction, they do not cause pre-excitation and are, therefore, called “concealed” (AP only conduct in the retrograde direction). When the AP is concealed, there is no delta wave on the ECG at baseline, in response to atrial decremental or extrastimuli pacing, or whit vagal maneuvers. “Latent” APs are those that have the capability to conduct in the antegrade direction. Latent pathways are most often far left lateral pathway where the conduction time to the AV node is much shorter than to the AP. Pacing closer to the pathway may elicit pre-excitation. In some patients, the absence of overt retrograde conduction over AP may be due a low resting sympathetic tone. Restoration of retrograde conduction with isoproterenol is not unusual and is most likely to be seen in those individuals with clinically documented SVT related to exercise. Adenosine can be a useful diagnostic tool: it can be used to unmask ventricular pre-excitation in patients with a minor degree of pre-excitation. Episodes of re-entrant tachycardia can start from early infancy, but their onset is more common during adolescence or adulthood; paroxysmal atrial fibrillation, on the other hand, appears almost exclusively in adults. It is not rare to see ECG pre-excitation signs at birth, which disappear after a few time, as the accessory pathway degenerates and fibrosis takes place, becoming unable to conduct; however the disappearance of ECG signs of pre-excitation does not necessarily mean that there is a complete elimination of conduction over Kent’s bundle, since both non manifest and concealed pre-excitation do not associate with the typical ECG pattern (delta wave, short P-R interval, etc.) but are both able to induce arrhythmias.

AV re-entrant paroxysmal tachycardia causes typical symptoms such as palpitations, dyspnea, hypotension and even syncope; the latter is probably neuromediated, rather than due to the low cardiac output secondary to the high heart rate (3). An extremely low percentage of patients with...
pre-excitation dies suddenly due to ventricular fibrillation. The mechanism is almost certainly an atrial fibrillation with a high ventricular response, which then degenerates into a ventricular fibrillation due to the high ventricular frequency. This is a dramatic event that can occur even in asymptomatic subjects, with an incidence of 1 subject out of 1000 per years. It was observed that all patients with pre-excitation that were resuscitated from a cardiac arrest had a short (<250 ms) antegrade refractory period of the accessory pathway; based on these data it was proposed to consider ‘at risk’ patients with this electrophysiologic finding (4). However the positive predictive value of this parameter is very low, since about 20% of the subjects who undergo an EP study have these features and should therefore be considered at risk, while the actual incidence of sudden death is considerably lower.

![Fig.1](image)

**Fig.1** In this ECG the first three ventricular complexes are pre-excited, whereas in the following beats pre-excitation disappears, the QRS normalize and the T vector exactly reproduces the direction of the QRS vector during pre-excitation.

### LOCALIZATION OF ACCESSORY PATHWAYS

Accessory pathways can be found anywhere along the tricuspid or mitral annuli except at the aorto-mitral continuity. The ECG clues to identify the approximate location of an AP are 1) delta-wave axis during manifest preexcitation and 2) P-wave axis during orthodromic AVRT.

**Delta-Wave Axis**

The horizontal QRS transition in the anterior precordium (V1-V4) differentiates left-, septal-, and right-sided APs, while the vertical delta-wave axis determines its anterior or posterior location along the annulus. Early QRS transition (at or before V1) indicates a left-sided AP because initial ventricular forces are directed anteriorly toward the right ventricle. Negative delta waves in the
lateral (I, aVL) or inferior leads identify a left free wall or left posterior AP, respectively. Horizontal transition at V2, which overlies the interventricular septum, indicates a right postero- or mid-septal AP. Late transition (at or beyond V3) indicates a right-sided AP. Anteroseptal APs show a “Left Bundle Brunch Block (LBBB)” type pattern transitioning before V4, sum of delta wave polarities in the inferior leads (II, III, aVF) ≥ +2, and a frontal QRS axis +30 to +120 degrees (Fig. 2).

P-Wave Axis

P-wave polarities during orthodromic AVRT also differentiate left-, septal-, and right-sided APs. A rightward axis (positive in aVR, negative in aVL) indicates eccentric atrial activation arising from a left-sided AP, while a leftward axis (positive in aVL, negative in aVR) identifies eccentric activation from a right-sided AP. Postero- and mid-septal APs generate a midline, superior axis (equally positive in aVL and aVR), while anteroseptal APs produce positive P waves inferiorly.
Errors in AP localization are usually due to minimal pre-excitation on the surface ECG, multiple APs (2-20% of patients) and thoracic deformity or congenital cardiac disease. Thus, detailed intracardiac mapping is required for successful pathway ablation.

The intracardiac hallmark of preexcitation is a short (<35 ms) or negative HV interval. Because atrio-ventricular APs originates above the His bundle, His extrasystoles conduct to the ventricle without preexcitation. A preexcited His bundle extrasystole identifies an AP originating below the His bundle (fasciculo-ventricular AP).

**Endocavitary mapping**

The ECG can help in localizing the AP, however the electrophysiologic study gives precise data on its position. In order to define the exact location of the Kent bundle, mapping of the AV annulus is performed in order to find the point with the shortest A-V interval during antegrade conduction over the Kent bundle or the shortest VA interval during ventricular stimulation or orthodromic tachycardia. This type of mapping can be performed using bipolar or unipolar recordings and it’s based on the principle that earliest chamber activation (ventricular during antegrade conduction, atrial during retrograde conduction) allows to localize the AP insertion in the chamber. Therefore the ablator catheter needs to be positioned on the right or left AV annulus, in contact with the endocardium, and then moved around until the shortest conduction interval is found. The position of the catheter is confirmed by the fluoroscopy and by the recorded potential which is composed of two deflections, the atrial and ventricular one. If the catheter is on the Kent bundle it’s easy to record almost fused A and V waves, indicating the extremely short conduction time. Sometimes it’s even possible to record the Kent bundle potential, seen as a rapid deflection of short duration, between the A and the V, expressing the depolarization of the AP: the A and V waves and the Kent potential are continuous, and the different components are hard to separate. The identification of such continuous electrical activity strongly indicates the presence of an accessory pathway.

**Antegrade mapping**

The earliest site of ventricular activation during manifest preexcitation (preexcited sinus rhythm, antidromic AVRT) identifies the ventricular insertion site of the AP. Target site criteria for ablation during antegrade mapping include: 1) AP potential (Kent potential), 2) earliest local ventricular activation relative to onset of the delta wave (pre-delta), and 3) fusion of atrial and ventricular electrograms. Accessory pathway potentials reflect rapid local activation of the AP and are sharp, high frequency deflections between atrial and ventricular electrograms that precede onset of the delta wave. The earlier the local ventricular electrogram on the ablation catheter precedes onset of the delta wave, the higher the probability of success. Relying on AV fusion alone, however, can be misleading, especially with slanting (oblique) and slowly conducting APs where fusion might be absent at the site recording an AP potential.

**Retrograde mapping**

The earliest site of atrial activation during retrograde conduction over the AP (ventricular pacing, orthodromic AVRT) identifies its atrial insertion site. A limitation of mapping during ventricular pacing, however, is the possibility that retrograde conduction over the AV node can interfere with identifying the earliest site of atrial activation over the AP (particularly, septal APs). Potential solutions include pacing at a faster rate (to cause decrement or block in the AV node), administration of drugs that slow AV nodal conduction, or mapping during orthodromic AVRT (where retrograde conduction occurs only over the AP). Target site criteria for ablation include: 1) AP potentials, 2) earliest site of atrial activation, and 3) fusion of annular (A and V) electrograms.
**Ablation**

Electrogram stability is an important determinant of success during radiofrequency (RF) delivery. After ablation, adenosine-induced AV and VA block provides further confirmation of success. If an AP is resistant to a particular ablation strategy, options include changing 1) mapping criteria (antegrade versus retrograde), 2) annular approach (e.g. transeptal versus transaortic) and 3) type of ablation catheter.

**Atypical accessory pathways**

**Permanet form of junctional reciprocating tachycardia (PJRT)**

PJRT is a nearly incessant type of orthodromic AVRT utilizing a concealed, slowly conducting and decremental AP. The AP is usually (but not always) located in the posteroseptal region and is mapped by identifying the earliest site of atrial activation during ventricular pacing or tachycardia. Fusion of atrial and ventricular electrograms is absent because AP conduction is slow and decremental. Successful target sites might show a fragmented atrial electrogram or possibly an AP potential.

**Mahaim fibers**

Mahaim fibers refer collectively to variant APs generally with decremental, antegrade-only conduction, originating or inserting into or near the right bundle. **Atrio-fascicular** APs can be targeted at its atrial insertion site by mapping along the antero- to posterolateral tricuspid annulus and identifying the site demonstrating 1) Mahaim potentials between atrial and ventricular electrograms (“His bundle-like” electrograms), 2) shortest stimulus-delta wave interval during constant atrial pacing, 3) longest coupled AVJ-refractory APD that preexcites the ventricle during antidromic tachycardia, and 4) susceptibility to mechanical block with catheter manipulation. **Nodo-fascicular** (or **nodo-ventricular**) APs can be targeted by selective ablation of the slow AV nodal pathway in the midseptum.

**Unusual locations**

Some posteroseptal APs course subepicardially and require ablation within the coronary venous system (middle cardiac vein, coronary sinus diverticulum). 12-Lead ECG features suggesting a posteroseptal AP within the coronary sinus are 1) negative delta wave in lead II, 2) steep (≥45 degree) positive delta wave in lead aVR, and 3) deep S wave (R≤S) in lead V6. Successful ablation sites can show relatively large AP potentials (AP/A and/or AP/V amplitude ratios ≥1). The presence of fused atrial and ventricular electrograms can be misleading and may not coincide with a successful ablation site. RF delivery should start with low energy (≤30 Watts) and titrated upwards gradually (“low and slow”). Some APs are **anteroseptal** in location where RF delivery can damage the His bundle. **Parahisian APs** are defined as APs associated with a His bundle potential ≥0.1mV at its atrial or ventricular insertion site. 12-Lead ECG features suggesting a parahisian AP are 1) positive delta waves in leads I, II and aVF, and 2) negative delta waves in leads V1, V2, and sometimes V3. Anteroseptal APs are prone to mechanical block with catheter manipulation suggesting that they course superficially in the subendocardium in contrast to the deeper penetrating His bundle within the central fibrous body. Recording an AP potential and the smallest possible His bundle potential are important target site criteria for successful ablation without creating AV block. RF delivery with low (initially 5-7 Watts) incremental energy is important and should be terminated immediately with onset of a junctional rhythm or persistence of AP conduction after 10 sec.
Multiple accessory pathways

In about 10-15% of subjects with pre-excitation, multiple APs are present. Histopathologic data show a higher frequency of multiple APs than those observed clinically. The presence of APs increases the incidence of symptoms and is associated with a higher risk of sudden death due to atrial fibrillation degenerating into ventricular fibrillation. Patients with pre-excitation resuscitated from sudden death had a higher incidence of multiple APs than the control group that did not have a cardiac arrest (5). Diagnosis of multiple APs on the ECG is possible but not in all cases. The following criteria should be used:

a) two different pre-excitation morphologies during atrial fibrillation. In this case atrial frequency is high and the two APs compete between themselves and the AV node-His pathway to conduct the impulse to the ventricles. The variation of the pre-excited QRS complex shows that atrial impulse reaches the ventricles over different paths. The diagnosis of a double AP requires two different complexes, each with typical features of a Kent bundle location. Sometimes it’s also possible to observe beats with an intermediate morphology, which express a fusion of the two types of ventricular activation. Variability of the pre-excited QRS morphology by itself is not sufficient for the diagnosis of multiple APs, as this phenomenon can also be caused by a fusion between a single AP and the His bundle;

b) the lack of correspondence between the site of the AP determined by the polarity of the P waves during an orthodromic tachycardia and the one determined by the QRS morphology during sinus rhythm or atrial fibrillation or pre-excited tachycardia;

c) the presence of two different P waves during different episodes (or even during the same episode) of orthodromic tachycardia;

d) the sudden change, from an orthodromic tachycardia to an antidromic tachycardia or from an antidromic tachycardia to a different antidromic tachycardia;

e) the presence of an antidromic tachycardia. Its presence does not necessarily mean that multiple APs are present, however in a high percentage of cases an orthodromic tachycardia uses another AP for the retro-conduction of the impulse rather than the AV node-His pathway.

Accessory pathway-mediated tachycardias

The most common tachycardias associated with the WPW syndrome are the circus movement tachycardias, 95% of which are orthodromic; that is, they conduct antegrade down the normal A-V conducting system and retrogradely up the bypass tract. The relationship of conduction and refractoriness of the normal A-V conducting system and the bypass tract, as well as the site of stimulation, determine both the ability to initiate circus movement tachycardia and, theoretically, the type of circus movement tachycardia. Conduction and refractoriness of the bypass tracts in most cases behave like working muscle; therefore bypass tracts demonstrate rapid conduction, and have refractory periods that tend to shorten at decreasing pacing cycle lengths (PCLs). The WPW syndrome allows one to actually see all the requirements for a reentrant rhythm: (a) two anatomic or functionally determined pathways of conduction; (b) unidirectional block in one of the pathways (in this instance, either in the accessory pathway or in the A-V nodal His pathway); (c) sufficient slowing in a part of the circuit to overcome refractoriness ahead of the circulating impulse; and (d) conduction time of the impulse must exceed the longest effective refractory period of any component in the circuit. Both antegrade and retrograde refractory periods of the accessory pathway are major determinants of (a) the ability to initiate and sustain circus movement SVT, and (b) the ventricular responses to atrial tachyarrhythmias (e.g., atrial fibrillation, atrial flutter, and atrial tachycardia).
AVRT is a re-entrant arrhythmias and is categorized into orthodromic and antidromic variants. During orthodromic tachycardia, the antegrade limb is the AV node-His-Purkinje system and the retrograde limb is the AP. Conversely, during antidromic tachycardia, the antegrade limb is the AP and the retrograde limb is the normal conduction system. Orthodromic AVRT constitutes approximately 95% of spontaneous and laboratory-induced AVRTs. For tachycardia initiation, an atrial premature complex (APC), either spontaneous or induced by pacing, blocks at the AP and travels down the AV node-His-Purkinje system. The conducted impulse reaches the ventricle and travels back up to the atrium over the AP, which has now recovered its excitability. The impulse then reenters the AV node-His-Purkinje system, perpetuating the tachycardia. Orthodromic tachycardia can also be initiated by a premature ventricular complex (PVC). In this case, the PVC blocks the His-Purkinje system but travels over the AP up to the atrium. If the AV node-His-Purkinje system has recovered excitability, the impulse then travels down the node and reenters the ventricle and orthodromic tachycardia is started (Fig.3).

**Fig.3** Induction of orthodromic AVRT by atrial premature complex (a) or by ventricular premature complex (b).

**Bundle Branch Block (BBB)**

Orthodromic AVRT involves the shortest circuit capable of sustained reentry and, therefore, incorporates the bundle branch ipsilateral to the AP as an integral part of its circuit. Spontaneous or induced bundle branch block during orthodromic AVRT can also provide important diagnostic
clues. Lengthening of the tachycardia cycle length is seen in cases of AVRT when bundle branch block occurs ipsilateral to the free wall pathway. During tachycardia, development of BBB ipsilateral to the AP forces antegrade conduction over the controlateral bundle and enlarges the circuit, with resulting increase in VA interval and tachycardia cycle length (6). The degree of VA interval increase depends on the location of the AP. Accessory pathways located along the free wall increase the VA interval >35 ms; in contrast, septal APs increase the VA interval <25 ms. Development of BBB controlateral to the AP does not affect orthodromic AVRT, as the controlateral bundle is a bystander to the tachycardia circuit (Fig.4).

Pacing maneuvers

The diagnosis of a narrow complex tachycardia (NCT) is facilitated by pacing maneuvers delivered from the ventricles. Preexcitation of the atrium without a change in the atrial activation pattern by His refractory ventricular premature depolarizations (VPDs) confirm the presence of an AP and, if the tachycardia is reset or terminated, the AP is likely required for the tachycardia circuit. In this case, retrograde conduction can occur only via an AP as the His bundle is refractory.

Spontaneous and laboratory-induced atrial fibrillation (AF) has been reported to occur in up to 32% to 52% of patients with the WPW syndrome. Several mechanism have been proposed: 1) premature atrial complex (PAC)-induced degeneration of AVRT to AF; 2) PVC-induced atrial depolarization during the atrial vulnerable period leading to AF; 3) a reentrant circuit within the atrial branching insertion sites of the AP fibers. In patients without structural heart disease, susceptibility to subsequent AF is low (6% to 10%) after successful AP ablation. However, despite successful pathway ablation, some patients still have recurrence of AF. The characteristics of these patients include older age (>50 years old), a history of paroxysmal AF and presence of structural heart disease, no antegrade conduction in the AP, slow ventricular response during AF and inducible AF after AP ablation.

Risk of sudden death

Unlike the AV node, APs do not demonstrate rate-dependent, decremental conduction that slows with faster atrial rates. The following features identify a low risk AP: 1) intermittent preexcitation, 2) exercise-induced AP block, 3) shortest preexcited RR interval during AF >250 ms, and 4) loss of preexcitation with procainamide, ajmaline or disopyramide (7). Intermittent preexcitation

![Fig.4 Effect of Bundle Branch Block on orthodromic AVRT cycle length.](image)
demonstrates that AP is incapable of sustaining 1:1 conduction during sinus rhythm, and, therefore, cannot conduct rapidly during AF. Similarly, abrupt loss of preexcitation during exercise demonstrates that the AP is incapable of sustaining 1:1 conduction during exercise-induced sinus tachycardia. During exercise, abrupt loss of preexcitation (rate-dependent AP block) should be differentiated from gradual loss of preexcitation (pseudonormalization) that is due to enhanced AV nodal conduction. During pseudonormalization, the AP continues to conduct antegradely, but the delta wave slowly disappears as the contribution to ventricular activation by the AV node-His-Purkinje system increases. Because the antegrade effective refractory period (ERP) correlates with the shortest preexcited RR interval during AF, an antegrade AP ERP or shortest atrial pacing cycle length maintaining 1:1 AP conduction >250 ms is a reasonable but not ideal surrogate to the shortest preexcited RR interval when AF is absent. Finally, the ability to alter AP conduction with Na channel blocking drugs suggests a low risk AP although this is controversial.

Therapy of the pre-excitation syndrome

The therapy of pre-excitation has four different objectives:
1. To cure the symptoms;
2. To prevent the risk of sudden death;
3. To prevent or cure, in case of a chronic tachycardia, the worsening of the ventricular function;
4. Allow subjects with pre-excitation to carry out all the activities that are otherwise forbidden by law when pre-excitation is present on the ECG.

In the other cases, a therapy is not indicated: particularly in asymptomatic subjects, who only have ECG anomaly, do not need any treatment, except from rare case, since their risk of developing ventricular pre-excitation is very limited.

There are three different kinds of therapeutic approaches: antiarrhythmic drugs, catheter ablation, surgical ablation of the AP. Electrical therapy (cardioversion, pacing) is considered separately.

Pharmacologic treatment

In orthodromic AVRT, the AV node is the weak link and drugs that prolong AV nodal refractoriness or depress its conduction can lead to block in the node resulting in tachycardia termination. Vagal maneuvers terminate tachycardia by causing block in the node. First-line drugs that are effective in acute termination of orthodromic AVRT include I.V. administration of adenosine, verapamil or diltiazem or beta-blockers. I.V. digoxin is less effective due to its delayed onset of action. I.V. procainamide is a viable alternative: it depresses conduction, prolongs refractoriness in most cardiac tissue (i.e. atrium, ventricle and His-Purkinje system) and also blocks conduction in the AP. Oral class Ic drugs are more efficacious than class Ia drugs in blocking AP conduction; however, they should be avoided in patients with structural heart disease. Amiodarone has various electrophysiologic effects but is not more effective than class Ic drugs used alone or in combination with beta-blockers. In general, amiodarone should be reserved for those who are drug-refractory, elderly and not suitable candidates for ablative therapy. Sotalol can be effective in preventing tachycardia, although it is associated with a 4% risk of torsades de pointes, especially in those with significant structural heart disease and congestive heart failure. Oral digoxin is not effective as monotherapy for orthodromic AVRT and, by its direct effects on the AP, this drug may actually accelerate conduction over the AP during atrial fibrillation. Therefore, digoxin should never be used for the treatment of patients with pre-excitation.
In **antidromic** AVRT, retrograde AV nodal conduction may be the weak link. I.V. calcium-channel blockers, beta-blockers and adenosine can be used for acute termination of tachycardia. I.V. procainamide is the drug of choice in the acute treatment of antidromic AVRT. Even this drug does not terminate the tachycardia, it may slow the tachycardia rate. In the absence of contraindications, class Ic drugs are the drugs of choice for long-term oral treatment of antidromic tachycardia.

**Catheter ablation**

Catheter-based ablation is the procedure of choice for patients with symptomatic WPW syndrome and for those who respond poorly to medical therapy. In most experienced centers, the success rate is 95% to 97% with a recurrence rate of 6%.

Successful ablation is critically dependent on accurate localization of the AP. Preliminary pathway localization can be obtained from delta wave and QRS morphologies. When pre-excitation is not maximal, rapid atrial pacing or I.V. adenosine can be used to obtain full pre-excitation so as to improve localization accuracy. This is especially useful in left lateral APs in which pre-excitation may be enhanced with left atrial pacing (from the coronary sinus, CS, catheter). Intracardiac electrogram criteria (8) used to identify appropriate target sites for ablation of manifest pathways include presence of an AP potential (Fig.5), early onset of local ventricular activation relative to the delta wave onset, electrogram stability and antegrade continuous electrical activity (fused atrial and ventricular electrograms). Electrogram criteria have also been used to identify appropriate target sites for ablation of concealed pathway and include retrograde AP potential, retrograde continuous electrical activity with ventricular pacing or during tachycardia and electrogram stability. **Left free wall pathways** constitute the majority of APs. Ablation can be guided by the CS catheter that is used to bracket the pathway’s location. It can be ablated via either a transeptal or a retrograde transaortic approach depending on the operator’s experience and preference. In the absence of a PFO, the transeptal approach involves the puncture across the fossa ovalis. With the transaortic approach, the tip of the ablation catheter is curved into a “pigtail” to avoid damaging the coronary arteries, advanced retrogradely across the aortic valve into the left ventricle and positioned along the mitral annulus using posterior and counterclockwise torque.

Catheter ablation is associated with a very high success rate. Successful ablation of **right free wall** pathways requires detailed mapping of the lateral tricuspid annulus. The overall success rate for right free wall pathway ablation is the lowest of any of the AP's with an average of 90% and a recurrence rate of 14%. Reasons for reduced success rate include catheter instability and lack of a right-sided CS structure that parallel the tricuspid annulus to aid in mapping.

Ablation of **anteroseptal and midseptal** pathways can be challenging due to their proximity to the AV node and His bundle; nevertheless it is associated with overall success rate of 95% to 98% and a 1% to 3% risk of permanent AV block.

Ablation of **posteroseptal** pathways can be challenging due to the complex anatomy at the posteroseptum. Most posteroseptal pathways can be ablated from the right side, although in up to 20% of cases a left-sided approach is needed (Fig.6). ECG and EP clues that suggest a left-sided approach include a positive delta wave or a positive QRS complex in V1, earliest retrograde atrial activation at the CS ostium and increase in VA interval with LBBB during orthodromic tachycardia. Between 5% to 17% of posteroseptal and left posterior APs are located **epicardially** and ablation in the CS (most commonly the middle cardiac vein) is needed. A manifest AP that may require ablation within the CS is suggested by a negative delta wave in lead II.
It appears that a small percentage of APs are epicardial. This is suggested by the finding of a small or no pathway potentials during endocardial mapping and large pathway potentials in the CS. Left-sided pathways can be successfully ablated within the CS at sites with large AP potentials. However, successful ablation of APs at other epicardial sites may require a percutaneous epicardial approach, as an alternative to cardiac surgery.

Overall, ablation of AP is associated with a **complication rate** of 1% to 4% and a procedure related death rate of approximately 0.2%. The complication of complete AV block occurs in about 1% of patients and is seen most frequently in patients undergoing ablation of septal pathways. Autonomic dysfunction and inappropriate sinus tachycardia are rare complications of radiofrequency ablation of AP and are less frequent than that seen in slow pathway ablation for AVNRT.

Today, **advances in catheter design, energy delivery systems, mapping systems and remote navigation systems** have made catheter ablation the therapy of choice for a majority of SVTs.

**Surgical ablation**

The elective surgical treatment of WPW has basically been abandoned. Until 1980’s several patients underwent surgical interventions in order to interrupt conduction over the AP, but since catheter ablation became available it was universally accepted that the risk/benefit ratio of such surgical intervention was unacceptable, since better results were obtained using simpler and less traumatic methods.

**Electrical therapy**

Electrical therapy of pre-excitation is based on cardioversion, that is used in case of pre-excited atrial fibrillation and rarely for AVRT, and on atrial or ventricular pacing in case of a re-entrant tachycardia. Atrial stimulation can be performed via the endocavitary or transesophageal route, while ventricular stimulation only via the endocavitary one. This kind of approach is advisable in subjects in whom drug administration is not possible, or an AVRT doesn’t cease after vagal maneuvers and it’s not well tolerated.
Fig. 5 From top to bottom are leads I, III, V1 and electrograms from the proximal His bundle area (HBE p), proximal to distal coronary sinus (from CS 7-8 to CS 1-2), proximal and distal Ablator (ABLp and ABLd) and right ventricular apex (RV Ap): the distal Ablator records a rapid potential (Kent potential, K) between atrial (A) and ventricular (V) electrograms.
Fig. 6 Ablation of a manifest left posteroseptal AP by retrograde transaortic approach (LAO projection). The ablation catheter is positioned along the posteroseptal mitral annulus where it records an AP potential between atrial and ventricular electrograms. Application of RF energy at this site caused loss of preexcitation in few seconds. The CS catheter provides a useful reference landmark to the mitral annulus.
Bibliography


