Entrainment as an Electrophysiologic Phenomenon*

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Waldo and his colleagues at the University of Alabama (1–3) observed that a critical rate of pacing was required to terminate atrial flutter. At the lower rates of pacing, continuation of the arrhythmia occurred immediately after cessation of pacing. Their observations had important clinical implications, including the recommendation for systematic prophylactic implantation of electrodes during cardiac surgical procedures to terminate arrhythmias by rapid pacing (3,4). A more complicated issue is the value of the rapid pacing technique to study mechanisms of arrhythmias. Waldo et al. (5) also suggested that the demonstration of transient entrainment supports reentry as the underlying mechanism of the arrhythmia. In this issue of the Journal, Waldo et al. (6) offer us a study of a unique case of ventricular tachycardia that could be transiently entrained and terminated by atrial pacing. Most important, the reentrant circuit could be reversed by rapid atrial pacing. In this article, we would like to discuss some aspects of the phenomenon of entrainment and some of its implications.

Definition of Entrainment

The ability to pace the heart during tachycardia has several consequences. First, it tells us that a gap of excitability is present during tachycardia in the chamber being paced. There is a time interval (gap of excitability) between the tail of refractoriness of the last tachycardia impulse and the time of arrival of the next tachycardia impulse during which stimuli can be given which depolarize the surrounding tissues. Second, the ability to deliver impulses during a tachycardia allows the study of site of origin, pathways and mechanisms of the arrhythmia (7).

Waldo et al. (5,6,8) defined transient entrainment of tachycardia with rapid pacing as "an increase in the rate of the tachycardia upon either abrupt cessation of pacing or slowing of the pacing rate below the intrinsic rate of the tachycardia." From this definition, it is clear that transient entrainment occurs at rates of pacing below those required to terminate tachycardia. To demonstrate entrainment is, however, much more complicated than simply pacing the heart during tachycardia. The observation that during tachycardia the heart can be paced is not the same as entrainment of tachycardia. It must be demonstrated that while the tachycardia is not terminated, the paced impulses have penetrated into the site of impulse formation, thereby accelerating the tachycardia to the pacing rate. As shown in Table 1, there are many different electrophysiologic phenomena that can occur during rapid pacing of a tachycardia.

In a patient with atrial tachycardia and no ventriculoatrial conduction, one can easily show during ventricular pacing that atrial tachycardia continues at its own rate while the ventricles follow the paced rate. There is, therefore, overt perpetuation of atrial tachycardia. Overt perpetuation can be very difficult to demonstrate in such a patient, however, during atrial pacing. We can pace from the right or left atrium and depolarize most of the atria, but not be able to invade the site of origin of the arrhythmia. There will be concealed perpetuation of tachycardia, which will regain control of the heart immediately after cessation of pacing. Concealed perpetuation (9) should not be taken for transient entrainment. Similarly, overdrive suppression, termination and reinitiation of tachycardia by subsequent impulses during pacing should be carefully excluded before diagnosing entrainment.

As pointed out, transient entrainment requires the ability to pace the heart during tachycardia to penetrate the area of impulse formation responsible for the arrhythmia, and acceleration of the tachycardia rate to the pacing rate without termination of the tachycardia on cessation of pacing.

How Can Entrainment Be Demonstrated?

The demonstration of entrainment during rapid pacing of tachycardia depends on the delicate interplay among different variables that must balance very accurately:

A. Pacing during tachycardia must be done from a site that allows penetration of the site of origin of the arrhythmia.
B. The site of origin of tachycardia must not be protected by entrance block.
C. A gap of excitability must exist at the site of origin of tachycardia to allow entry of paced impulses.
D. The paced impulses entering the site of origin must be able to accelerate the tachycardia rate to the pacing rate.
E. The paced impulses should not result in termination of tachycardia.

First criterion of entrainment. When all conditions are fulfilled, proof of entrainment depends on the demonstration that the tachycardia rate has been accelerated to the pacing rate without termination and reinitiation by subsequent impulses. We can demonstrate that the tachycardia has accelerated to the pacing rate when, in the available electrocardiographic leads, the complexes resulting from pacing and the complexes resulting from the tachycardia are initially very different in morphology. Then progressive fusion between the paced and tachycardia complex at different rates of pacing can be demonstrated. Progressive fusion between paced and tachycardia complexes at different rates of pacing constitutes the first of the three criteria for demonstration of entrainment (5,6,8). At the slowest rate of pacing, the observed complex is almost a pure tachycardia complex. At the fastest rate of pacing, the complex is almost a pure paced complex. At intermediate rates of pacing, different degrees of fusion complexes occur.

Second criterion of entrainment. After cessation of pacing, the first tachycardia complex occurs at the pacing rate and shows no fusion (5,6). This observation constitutes the second of the criteria to demonstrate entrainment. Demonstration of fusion usually requires pacing outside the site of origin of the arrhythmia. When the reentrant circuit is very large, however, fusion might be demonstrated by pacing from inside the circuit. When both the paced and the tachycardia complexes have a similar morphology, one is not able to demonstrate progressive fusion between the paced and tachycardia complexes. As will be discussed later, however, absence of fusion during pacing does not mean that entrainment is not occurring.

Third criterion of entrainment. During entrainment of reentrant tachycardia, every paced complex continuously invades and resets the reentrant circuit, resulting in acceleration of the rate of "tachycardia" to the pacing rate. This phenomenon can easily be demonstrated during rapid atrial pacing of the macroreentrant circuit present during circus movement tachycardia in the Wolff-Parkinson-White syndrome. Several recordings from different parts of the circuit can be obtained simultaneously during tachycardia. Entrainment of circus movement tachycardia in the Wolff-Parkinson-White syndrome was extensively studied by Waldo et al. (5). In patients with a left-sided accessory atrioventricular (AV) pathway, they showed that during circus movement tachycardia, rapid pacing from the right atrium resulted in different degrees of fusion P waves, depending on the pacing rate. The paced atrial impulses were conducted in an anterograde manner over the AV node to the His bundle and ventricles and also to the left atrium. In the left atrium, the resulting P wave was a fusion complex between activation from the paced impulse conducted in anterograde manner and the retrograde conduction of the previous impulse over the accessory pathway. Entrainment was demonstrated to occur up to the pacing rate at which the paced impulses resulted in bidirectional block (in the AV node-His-Purkinje system and in the left atrium or accessory pathway), thereby terminating tachycardia. In some cases, Waldo et al. could show fusion occurring at the ventricular level and temporal reversion of the circuit. As in the case presented in this issue of the Journal by Waldo et al. (6), and as previously shown in the Wolff-Parkinson-White reentrant circuit (5), reversion of the reentrant circuit during pacing resulted from localized block in the anterograde pathway of reentry, with sudden anterograde conduction over the pathway used in a retrograde manner during the spontaneous tachycardia. Demonstration of this localized block for one beat followed by subsequent activation of that blocked site from a different direction constitutes the third criterion for demonstration of transient entrainment (5,6).

Pacing inside the reentrant circuit. When pacing is performed during circus movement tachycardia inside the reentrant circuit—for example, from the coronary sinus close to the atrial end of a left-sided accessory pathway—fusion at the atrial level may not be demonstrated. The paced and the tachycardia P waves are similar. Entrainment may still be demonstrated, however, because several recordings are available from different sites of the reentrant circuit. The paced impulses travel in an anterograde manner over the normal AV pathway to the ventricles and collide in the accessory pathway with the impulse conducted in a retrograde manner. Entrainment cannot be diagnosed by analyzing electrograms recorded outside the reentrant circuit (surface electrocardiogram and recordings from the right atrium) unless the paced impulse is also able to travel in an anterograde direction to the ventricles over the accessory pathway, resulting in a fusion QRS complex. This stresses the importance of recording of local electrograms to help in the identification of entrainment.

Table 1. Possible Electrophysiologic Phenomena Occurring During Rapid Pacing of a Tachycardia

<table>
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<th>Phenomenon</th>
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<tr>
<td>1. Overt or manifest perpetuation</td>
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<td>2. Concealed perpetuation</td>
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<td>3. Overdrive suppression</td>
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<td>4. Overdrive acceleration</td>
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<td>5. Transient entrainment (continuous resetting)</td>
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<td>6. Termination with reinitiation by subsequent impulses</td>
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<td>7. Change to another tachycardia with same or different site of origin</td>
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<td>8. Termination</td>
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Let us now consider a different situation: a reentrant circuit located in the left ventricle occupying a small mass of tissue. In the intact human heart, simultaneous recordings from different parts of this reentrant circuit are not possible at the present time. Suggestive evidence of entrainment will depend on the observation of different degrees of progressive fusion between the paced and tachycardia complexes at different pacing rates, demonstration of entrainment of the first tachycardia complex after cessation of pacing and demonstration of localized block for one beat with reversal of the circuit. All these criteria are fulfilled in the case reported by Waldo et al. (6). Entrainment of ventricular tachycardia was also previously shown by these authors (8) by proving the presence of the first of these criteria. Although there are three criteria to diagnose entrainment, one should realize that entrainment can occur when only one or none of these criteria can be demonstrated (5).

Does Entrainment Mean That Reentry Is the Underlying Mechanism of the Arrhythmia?

Waldo et al. (1, 3, 5, 6, 8) suggested that the demonstration of entrainment argues in favor of reentry as the underlying mechanism of tachycardia. At present, we agree that entrainment is possible in reentrant tachycardias. It is known, however, that arrhythmias based on delayed afterdepolarizations reaching threshold levels can also be terminated by pacing, and a critical rate of pacing is required (10). It is not known what happens when rapid pacing does not result in termination of a tachycardia based on triggered activity. Jalife and Moe (11) demonstrated acceleration of an ectopic pacemaker, in both a mathematical and a biological model of parasystole. The implications of electrotonic modulation in clinical arrhythmias, as recently described by Rosenthal and Ferrier (12), are still unknown. It is unlikely that the strict criteria to diagnose entrainment offered by Waldo et al. can be fulfilled in these other arrhythmias, the mechanisms of which are different from reentry. We would like, however, to be better informed about that possibility.

Entrainment of Tachycardia by Modes of Pacing Other Than Rapid Pacing

The demonstration of entrainment of reentrant tachycardia does not always require rapid pacing. When activation at different parts of a reentrant circuit can be recorded simultaneously, a single premature beat can be shown to entrain the arrhythmia. Again, this can easily be demonstrated in the reentrant circuit of the Wolff-Parkinson-White syndrome. During a circus movement tachycardia, using in anterograde manner the AV node and in retrograde manner the accessory AV pathway, a ventricular premature beat will advance the next tachycardia QRS complex depending on the AV nodal and His-Purkinje conduction time of the atrial impulse caused by retrograde conduction of the ventricular premature beat. Tachycardia is reset by the premature beat. A single premature beat can thus entrain reentrant tachycardia. In this situation where activation from every part of the circuit can be recorded, the demonstration of fusion is not required; neither is it required to demonstrate reversal of the circuit after localized block.

Similar observations can be made when premature impulses are given during atrial, intra-AV nodal and ventricular tachycardias. They do not absolutely prove, however, that reentry is the underlying mechanism of the arrhythmia. The next tachycardia cycle can be advanced by a premature impulse in arrhythmias based on triggered activity, as in digitalis intoxication (13). The automatic rhythm of the sinus node can be advanced by a premature atrial beat to a less than compensatory pause (14).

Entrainment can be demonstrated by a single premature beat, but it requires analysis of activation at multiple sites at the site of origin of the arrhythmia to demonstrate that reentry is the mechanism. Unless these recordings are available, entrainment should, therefore, be studied by the rapid pacing technique.

How Useful Is the Concept of Entrainment?

Any good study asks more questions than it answers. Continuous resetting of a reentrant circuit results in acceleration of a reentrant tachycardia to the pacing rate. This is how the term "transient entrainment" was repeatedly used by Waldo et al. Electrotonic modulation, however, can also result in acceleration of the rate of a protected nonreentrant ectopic focus to the pacing rate. This phenomenon has also been called "entrainment" (11). This form of acceleration of the rhythm of an ectopic focus does not fulfill the criteria of Waldo et al. for the diagnosis of "entrainment." These differences in use of the term "entrainment" should also be kept in mind when trying to identify mechanisms of clinical arrhythmias by pacing techniques. Unless otherwise proved, demonstration of transient entrainment of tachycardia using the criteria of Waldo et al. is a very easy way to demonstrate that reentry is the underlying mechanism of the arrhythmia. However, the percent of patients with ventricular tachycardia entrainment is unknown at the present time.

References