

V. TACHYCARDIAS – Rapid rhythm abnormalities

Tachyarrhythmias currently account for up to 350,000 deaths annually in the US. In addition to these clearly dangerous rhythm disturbances, other forms of more benign tachyarrhythmias are not uncommon in otherwise healthy persons. Knowledge of tachyarrhythmia mechanisms has increased dramatically in recent years. Appropriate acute therapy based on a proper understanding of the arrhythmia mechanism in a particular clinical setting can be life-saving; accurate knowledge of arrhythmia mechanism also impacts on choices for long-term therapy to prevent arrhythmia recurrences. It is thus important to understand, and be able to apply, some basic concepts relating to mechanisms of tachyarrhythmias.

At its simplest, a *tachycardia* is a heart rate exceeding 100/min, lasting for at least 3 beats. Some are nonsustained, terminating spontaneously. Other tachycardias last much longer than this (minutes to days to months). Tachycardias may originate in the atria, ventricles, or special conducting tissues; have regular or irregular rates; be physiologic or pathologic. Not all tachycardias cause symptoms. When they do cause symptoms, they range from a sensation of rapid heart beat (palpitations), to chest discomfort, dyspnea, lightheadedness, syncope, or cardiac arrest. The mechanism for isolated premature beats (such as premature ventricular complexes) may not be the same as for a similar-appearing tachycardia lasting minutes to hours. A *dysrhythmia* is an abnormal, maladaptive cardiac rhythm ("disturbed", "deranged", and "depraved" are also occasionally-applied modifiers – these terms are also often used to describe the behavior of clinical electrophysiologists by some of our colleagues). *Arrhythmia*, which technically means the absence of a rhythm, in practice is interchangeable with "dysrhythmia".

A. Mechanisms - General

A working classification for mechanisms of tachycardia consists of the following:

- 1) Automaticity
 - a. Normal
 - b. Enhanced normal
 - c. Abnormal
- 2) Reentry
 - a. Anatomic obstacle model
 - b. Functional model ("leading circle")
 - c. Anisotropic
 - d. Reflection
- 3) Triggered Activity
 - a. Early afterdepolarizations (EADs)
 - b. Delayed afterdepolarizations (DADs)

Of these, reentry is responsible for the majority of clinical arrhythmias. It should be recognized that the mechanism responsible for initiation of an arrhythmia might be different than the mechanism underlying maintenance of a tachycardia. Since the treatment of a particular rhythm disturbance may very much depend on the responsible mechanism, it is important to understand the major features of these mechanisms and appreciate similarities and differences.

B. Distinguishing Between Mechanisms

Automaticity

Automaticity can be defined as the occurrence of spontaneous phase 4 depolarization resulting in an action potential; that is, left alone, cells which possess automaticity will discharge repeatedly on their own. The rate of this firing depends on the type of cell, as well as the extracellular environment as illustrated earlier.

Action Potentials in Automaticity

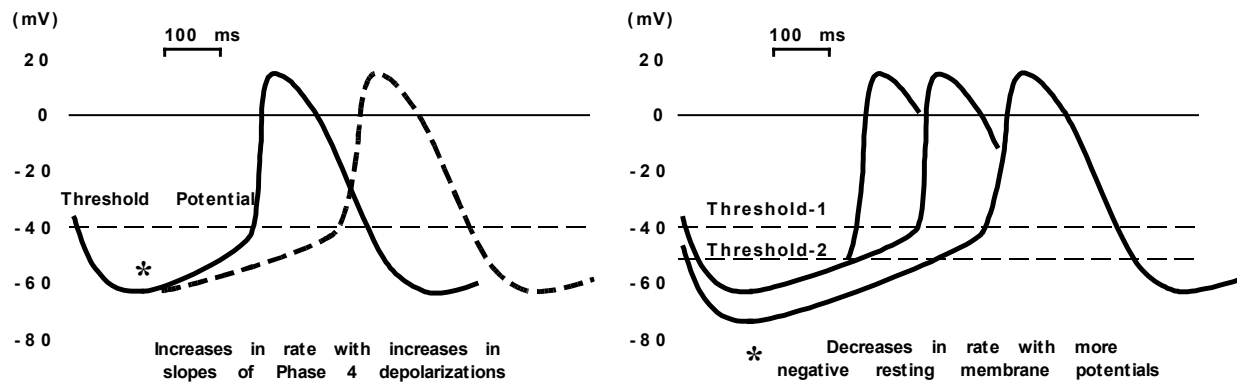


Fig. V-1. Different ways to alter automaticity. Action potentials (AP) from sinus node cells are shown. A voltage scale is shown at left, and threshold potential is indicated with horizontal dashed lines. *Left panel* - dashed AP - normal automaticity in a cell with normal resting membrane potential characterized by gradual phase 4 depolarization to the threshold potential, solid AP - an increased discharge rate due to increase in the slope of phase 4 (diastolic depolarization). *Right panel* - altered automaticity. The middle AP is that of a normally automatic cell with threshold potential 1. The left AP depicts that of a cell having a decreased in threshold potential (2), despite the same rate of phase 4 depolarization, resulting in an increased rate of firing. The right AP depicts a cell having more negative resting membrane potential becomes (hyperpolarized), the rate of cell firing will slow despite a normal slope of phase 4 depolarization and normal threshold potential (1).

Normal automaticity is a characteristic of sinoatrial, nodal and His-Purkinje cells as noted, but not other cells within the heart under normal conditions. The rate of firing of these cells can be increased by catecholamines (or sympathetic nerve stimulation); other factors tend to suppress normal automaticity, including parasympathetic (vagal) nerve stimulation, hyperkalemia, hypothermia, hypoxemia, acidosis, and some antiarrhythmic agents. *Abnormal automaticity* occurs in partially depolarized cells, and has been observed in cellular preparations of diseased human myocardium but its role in producing clinically relevant arrhythmias in man is unclear.

In the clinical realm, rhythm disturbances believed due to automaticity include:

- 1) paroxysmal sinus tachycardia (not physiologic sinus tachycardia--exercise)
- 2) some cases of atrial tachycardias
- 3) "junctional" or His bundle tachycardia (esp. after valve replacement surgery)
- 4) rare cases of ventricular tachycardia
- 5) premature depolarizations arising in the pulmonary veins of some patients may be responsible for initiation of atrial fibrillation

Since automaticity is such a prevalent mechanism (practically all of us are constantly under its influence -- i.e. normal sinus rhythm), it is relatively easily studied and understood. Unfortunately, it is not the most common mechanism responsible for clinical arrhythmias. This distinction belongs, in our current understanding, to *reentry*.

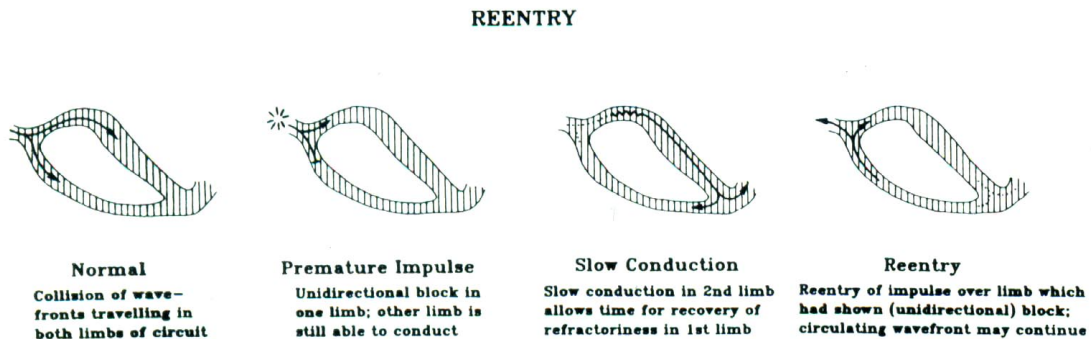
Reentry

Although accounting for a majority of arrhythmias, *reentry* is not a normally-occurring phenomenon, and cannot exist unless certain requirements are fulfilled:

- 1) a loop of excitable tissue, to serve as a pathway for impulse propagation
- 2) heterogeneity of electrophysiologic properties of tissue within the loop:
 - a) refractoriness - unidirectional block in some part of the circuit
 - b) conduction velocity - slow conduction in another part of the circuit
- 3) an initiating event, most commonly a premature beat

All these features must be present in order to initiate and sustain a reentrant arrhythmia; that is, a loop or circuit may exist within which are the necessary heterogeneous electrophysiologic properties, but without an initiating

event it remains dormant and no reentry or arrhythmia occurs. These principles are illustrated in the following figure. (V-2)

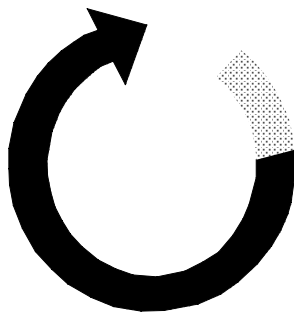


Once reentry is established, it continues in the same path and direction until one or more of the required conditions is no longer satisfied. If, for example, a medication is given which prolongs refractoriness in one portion of the circuit, the reentering wavefront may encounter tissue which has not yet recovered excitability from the previous beat and at that time reentry stops suddenly. There is no reason that the circulating wavefront must always travel in the same direction in a reentrant circuit, although the balance of electrophysiologic properties is often not conducive to initiating this type of arrhythmia.

Two primary models of reentry have been described:

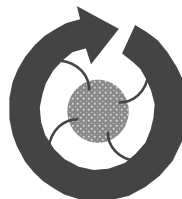
Fig. V-3

Circus movement around anatomical obstacle
(Mines 1913)



- fixed circuit length
- cycle length a properties and size of anatomical obstacle
- excitable gap exist
- separate "entrance" and "exit" are possible

Leading circle model without anatomical obstacle
(Allessie 1977)



- circuit length may be variable
- cycle length a refractoriness and conduction velocity
- no full excitable gap exist
- circuit may be mobile

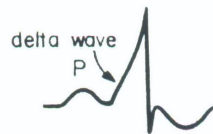
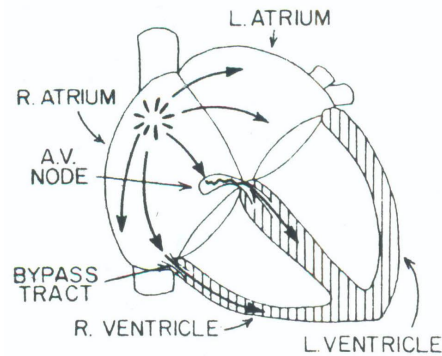
Fig. V-3. Models of reentry. On the left, the *anatomic obstacle model*, in which the circuit exists around a non-conducting central obstruction (such as a scar or a vena caval orifice), is easiest to

understand. The advancing end of the wavefront is shown by the arrow, the blackened area behind it completely refractory tissue, and the stippled area is partially refractory. In the "leading circle" model, or *functional reentry*, the advancing wavefront is always impinging upon partially refractory tissue acts as functionally inexcitable "obstruction" around which the wavefront circulates. No part of the circuit is ever completely recovered in excitability; a precise balance of conduction velocity and refractoriness is thus necessary in order for reentry to continue in this model. ("Cycle length" refers not to circuit length; rather the time needed to complete one cycle, and thus is the inverse of rate.)

Reentry in the Wolff-Parkinson-White syndrome is a good example of reentry dependent upon an "anatomic obstacle", in that there is an obligatory path length for the circuit which cannot be "short-circuited" (the atrial and ventricular cavities forming the obstacle).

Fig. V-4

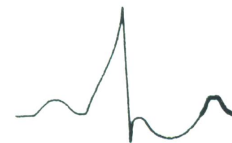
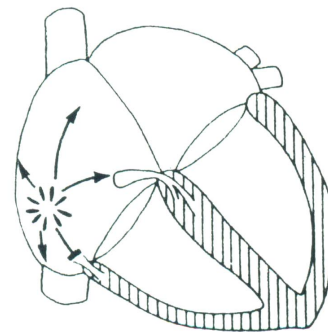
A.



Normal

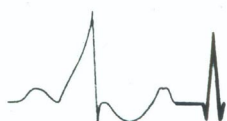
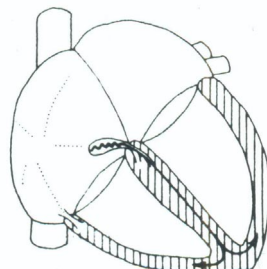
Collision of wavefronts
travelling down both the
AV node and bypass tract

B.



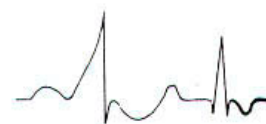
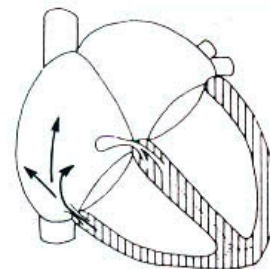
Premature Impulse
Unidirectional block
in bypass tract only

C.



Slow Conduction
Slow conduction over AV node,
spread of wavefronts through
His-Purkinje and ventricles

D.



Reflection is a model of reentry in which partially depolarized tissue acts on itself to produce a 2nd, reflected action potential. While this phenomenon has been observed in laboratory preparations, it is poorly understood, and does not seem to have clinical relevance at present.

An additional mechanism of reentry has received much attention lately is anisotropic reentry. An anisotropic substance is one which demonstrates different reactions to the same stress when applied from different directions (for example, wood resists breaking when bent in one direction better than in another, depending on the grain). In cardiac muscle, this concept translates as follows: differences may exist in conduction velocity and refractoriness in normal or diseased tissue which are determined solely by the spatial orientation of myocardial fibers. This is demonstrated in the following figures.

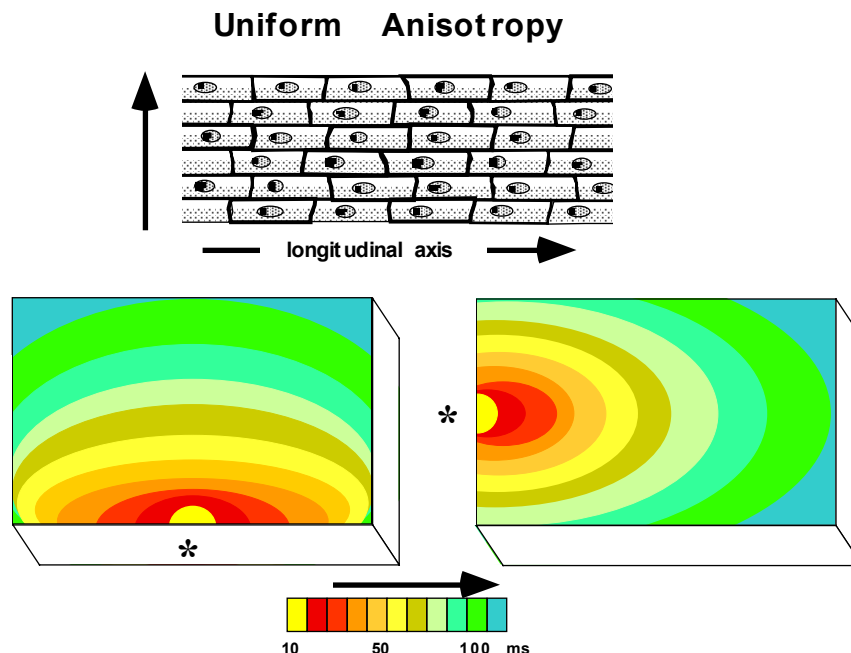


Fig. V-5 (*above*). In normal myocardial cells, conduction proceeds parallel to the long axis more rapidly than in the transverse direction, but a premature impulse along this axis may encounter refractoriness when an impulse of the same prematurity but the perpendicular direction may conduct, albeit more slowly (higher "safety factor"). This "uniform anisotropy" is a feature of normal myocardium.

Fig. V-6. (*below*). A sheet of infarcted, canine myocardium is depicted in which a stimulus is applied and the resultant spread of the electrical wavefront shown. (*right-hand figure*) a stimulus applied from the left end (*) is rapidly conducted parallel to the long axis of the fibers. (*left-hand figure*) The same stimulus applied 90° to the example above, along the transverse axis; conduction proceeds very slowly through the same sheet of cells.

Anisotropic reentry may be an important mechanism in many human arrhythmias. The disparity in conduction and refractoriness may be such that a premature impulse occurring at one point may encounter block during its propagation along the "long axis," but spread transversely--slower than normal. It can then make its way around the initially blocked region and if this region can recover excitability, reentry can occur. This tissues involved may exhibit only minimal or no abnormalities in conduction during normal sinus rhythm.

Many clinical arrhythmias in man appear to be due to reentry. Good evidence exists for this in the following:

- 1) sinoatrial nodal reentry
- 2) some atrial tachycardias
- 3) atrial flutter
- 4) AV nodal reentry (reentry occurring entirely within the AV node)
- 5) atrioventricular tachycardia as in Wolf-Parkinson-White syndrome; usually the circuit path is atrium→AV node→His-Purkinje system→ventricle→bypass tract→back to atrium
- 6) most ventricular tachycardia tachycardias

There is some evidence that reentry is operating in the following:

- 7) atrial fibrillation
- 8) polymorphic ventricular tachycardia (each beat a different shape)
- 9) ventricular fibrillation

As noted earlier, reentry appears to be the most prevalent mechanism responsible for clinical arrhythmias in man.

Triggered Activity

In the last several years, a completely different mechanism of arrhythmia has been studied. This mechanism, *Triggered activity*, has several characteristics:

- 1) The presence of *afterdepolarizations*, which occur near the end of the action potential: either "early" (EADs) or "late" (DADs).
- 2) Afterdepolarizations may, under appropriate circumstances, reach threshold potential and result in the generation of a second action potential or a sustained, ongoing tachycardia.
- 3) Afterdepolarization

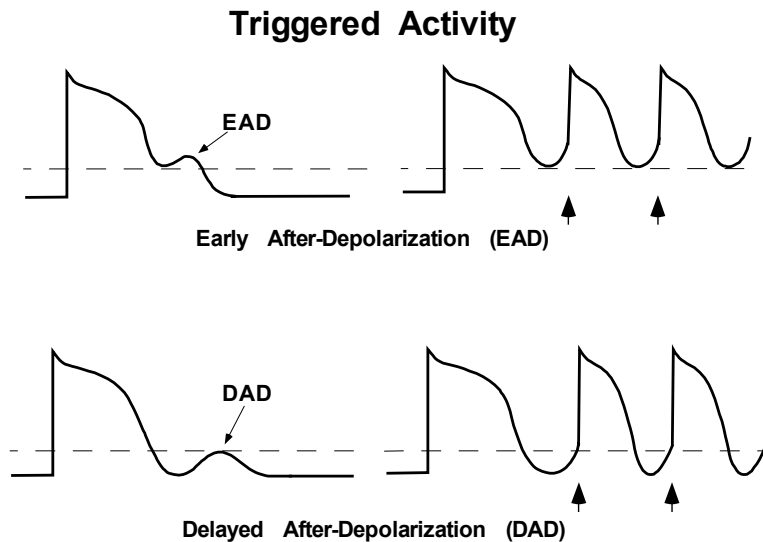


Fig. V-7. Representation of afterdepolarizations (arrows) responsible for triggered activity. Action potentials are shown with voltage scale. Early afterdepolarizations (top) are small depolarizing waves occurring before the cell has fully repolarized; delayed afterdepolarizations (bottom) occur after repolarization is complete.

EADs appear to be most prominent and of highest amplitude (most likely to reach threshold) at slower heart rates; in contrast, DADs are most frequently observed, and reach higher amplitudes, at faster heart rates or with catecholamine infusion. The most common setting in which arrhythmias conclusively due to triggered activity are observed is in the basic science laboratory, although several varieties of clinical arrhythmias are believed due to triggered activity; confirmatory evidence is very hard to obtain, though.

Clinical arrhythmias *potentially* due to triggered activity include:

- 1) polymorphic ventricular tachycardia of the torsades de pointes variety, when associated with a long QT interval on the ECG (EADs implicated)
- 2) digitalis-toxic atrial, junctional, and ventricular tachycardias (DADs implicated)
- 3) multifocal atrial tachycardia (DADs implicated)

B. Distinguishing Between Arrhythmia Mechanisms

The mechanism responsible for clinical arrhythmias can occasionally be discerned from characteristic features of the arrhythmia:

- 1) Mode of initiation

automaticity - enhanced or abnormal - spontaneous onset of tachycardia (that is, no premature beats leading to the arrhythmia), as well as a gradual increase in the rate of the arrhythmia over the first 5-10 beats ("warm-up"); the ECG appearance of the 1st tachycardia beat is identical to subsequent beats.

reentry - initiation is with a premature beat followed by a slight pause, then the arrhythmia (corresponding to premature beat, unidirectional block, slow conduction). "Warm-up" is less common, and the ECG appearance of the 1st tachycardia beat (the premature beat) need *not be* identical to the rest.

- 2) Mode of termination in response to overdrive pacing (pacing the heart at a rate faster than the tachycardia rate)
 - a) automaticity - often shows "overdrive suppression" (the arrhythmia seems to be terminated by pacing, only to return after several seconds with a gradual resumption of the pre-pacing rate). This is related to increased activity of the $\text{Na}^+\text{-K}^+$ pump with Na^+ loading, causing the cell to have a more negative resting membrane potential and taking longer to reach threshold.
 - b) reentry - often terminates in response to overdrive pacing, but without subsequent arrhythmia resumption. The tachycardia stops because paced impulses have entered the circuit in both limbs, causing bi-directional block.

The precise role of triggered activity as a mechanism of human arrhythmias has not been studied in adequate detail to characterize nodes of initiation or response to pacing. Other means exist to more clearly differentiate arrhythmia mechanism, at the time of invasive electrophysiologic study.

C. Treatment Strategies Based on Arrhythmia Mechanism

If the clinical setting or ECG features of an arrhythmia suggest a particular mechanism, specific forms of therapy can be selected. Examples of this would be:

- 1) Enhanced normal automaticity due to an increase in the rate of phase 4 depolarization - treatment could entail: decreasing the rate of phase 4 depolarization by administration of 1) Ca^{++} channel blocking agents (in the case of Ca^{++} -dependent depolarization), 2) Na^+ -channel blocking agents, or 3) beta-adrenergic blocking agents to antagonize effects of circulating catecholamines or increased sympathetic nervous system tone.
- 2) Reentry may be treated by (a) drugs which increase refractoriness (Type 1A or 1C agents) to an extent that the amount of slow conduction produced by a premature impulse is insufficient to allow for recovery of excitability in the tissue in which unidirectional block occurred (thus never getting reentry started), (b) using pacing to terminate reentry, or (c) destroying a part of the circuit, and thereby preventing reentry, using catheter-delivered energy (usually radiofrequency today) or surgical procedures.
- 3) In triggered activity due to digitalis-related delayed afterdepolarizations, withhold further glycoside therapy.

A note of caution: although antiarrhythmic drugs may be quite useful in treating many clinical arrhythmias, one of the principal toxic side effects is a tendency to exacerbate rhythm disturbances. This feature has been termed a "pro-arrhythmic effect". Examples of this include digitalis-induced atrial, junctional, and ventricular tachycardias thought due to triggered activity; polymorphic ventricular tachycardia due to QT interval prolongation engendered by Type 1A and Type 3 drugs; and more frequent episodes of uniform-morphology ventricular tachycardia due to the effects of Type 1 or Type 3 drugs (increased refractoriness some/slowing conduction more, thus allowing reentry to start more easily and be more stable).