EDITORIAL

Reentry: Slow Conduction, Summation and Inhibition

PREMATUR E systoles may arise through activity of an automatic focus of the sort normally present in the sinoatrial node or they may arise through reentry. A reentrant extrasystole is assumed to arise when the impulse that caused the previous systole lingers somewhere in the heart long enough to be able to emerge and reexcite the heart after the end of the refractory period.

The familiar extrasystole with fixed coupling has long been regarded as possibly reentrant since it only appears following a previous impulse and appears at a fixed time after that impulse; whether reentrant or not, such an extrasystole certainly seems to be the direct result of the previous impulse. The difficulty in regarding this or any arrhythmia as reentrant stems from the fact that the refractory period of cardiac tissue is so long. In the human heart over 0.3 sec must elapse after excitation before ventricular muscle is again excitable. The normal wave of excitation travels between 1 and 4 m/sec in the ventricular conducting system and between 0.5 and 1.0 m/sec in the myocardium. Were the impulse responsible for reentry to travel at such speeds it would have to find a path between 15 cm and 1 m long in which to travel to be able to reexcite after the refractory period. That so long a path, however circuitous, could exist in functional isolation from the rest of the heart has never seemed likely.

The possibility of reentry only demands, however, that the impulse survive in some manner until the refractory period is over. Travel at normal velocity is not the only way in which an impulse might occupy itself during the refractory period; nor is the refractory period fixed in length. The refractory period might be shortened, either locally or throughout the heart, or the impulse might linger in a small part of the heart for a long time, traveling very slowly over a short path. Many coupled extrasystoles that might be considered reentrant are, however, seen following cardiac cycles in which the Q-T interval, and therefore the refractory period, are of normal duration. However, in spite of some persuasive early studies, doubts have often been expressed that very slow conduction can occur anywhere in the heart except in the atrioventricular node.

Various investigators have, therefore, ruled out the possibility that the impulse causing reentry is conducted at normal speed on the grounds that great length of path is required, ruled out the role of a shortened refractory period on the grounds that many possibly reentrant beats follow cycles in which there is
no shortening of the refractory period, and ruled out very slow conduction on the grounds that it has been demonstrated only in nodal tissue and is inherently improbable. To thus rule out as impossible, or of rare occurrence, all the mechanisms that might allow of reentry is to rule out reentry as an important cause of arrhythmias. However, reentry has been produced in recent laboratory studies, and it may be a far more common cause of ventricular arrhythmias than would have been thought possible a few years ago.

It has been shown, for example, that the refractory period of fibers of the ventricular conducting system varies along the course of the fiber, becoming longer as the impulse passes from the bundle of His toward the periphery and becoming shorter again very near the myocardium; moreover, the various peripheral twigs of the ventricular conducting system do not have identical refractory periods.1 Such variation in the length of the refractory periods of normal fibers might, under certain circumstances, facilitate reentry. It has also been shown that premature excitation may result in marked shortening of the action potentials of Purkinje fibers without a correspondingly great shortening of the action potentials of myocardial fibers so that the refractory period of the ventricular conducting system becomes less than that of the ventricle.2 Such a reversal of the normal relationship of those refractory periods could predispose to certain kinds of reentry. Finally, it has been found that two or three premature excitations of the heart in quick succession may shorten the action potential enough to facilitate reentry and reentry has actually been demonstrated under such circumstances.3

In the normal heart the entire ventricle is, however, activated relatively quickly so that the variations in refractoriness described above can arise only from variations in the duration of action potentials that begin at about the same time. Almost no matter how short the action potential may become, or how great the variation in duration among the refractory periods of different fibers may be, a reentrant impulse must still either find a moderately long path or be conducted slowly. During a refractory period as short as 50% of the normal value, an impulse conducted as slowly as 0.5 m/sec would still travel nearly 8 cm. While shortening or heterogeneity of refractory periods certainly facilitates reentry, it is quite possible that the series of premature excitations in the experiments described above4 produced not only shortening of the refractory period but also localized slow conduction. In general, if ventricular activation is normal, the presence of reasonably normal refractory periods and of reasonably rapid conduction does seem to protect the heart against reentry (reference 2, p 84).

On the other hand, one-way block in combination with slow conduction ought to be able to produce reentry even in the presence of refractory periods of normal duration. We have shown that one-way conduction and conduction even slower than that normally seen in the atroventricular node can readily be induced by depression of excitability in short segments of the ventricular conducting system.4 Delayed transmission of excitation results partly from a marked slowing of ordinary conduction and partly from a previously undescribed phenomenon in which two blocked impulses can create a new impulse by summation beyond the point of block.5 The delay caused by slow conduction plus the further delay associated with summation may result in effective conduction velocities as low as 0.02 m/sec. An impulse with that conduction velocity would travel only 6 mm during a refractory period lasting 0.3 sec. The delays and one-way block necessary for reentry can occur as the result of the depression of excitability in a segment of Purkinje fibers depolarized by exposure to high external K+,4 i.e. by depolarization of the sort found in Purkinje fibers subject to ischemia in vivo. Marked slowing of conduction has also been seen to result from spontaneous depolarization in isolated Purkinje fibers.

The newly discovered phenomenon of summation is seen in the situation in which a pair of fibers merge to form a single fiber.6
The impulse in each of such a pair of fibers may be blocked in a depressed area and yet the subthreshold depolarizations spreading forward from each blocked impulse may add or summate to evoke a new impulse in the fiber formed by the union of the two branches. Transmission by summation introduces an element of delay that is exquisitely sensitive to changes in rate and rhythm because the impulse evoked by summation arises with a latency that is very sensitive to any asynchrony in the time of arrival of the impulses via the merging fibers. Shifts of only 10 msec in the arrival of one or the other of the impulses may delay the appearance of the summated response by nearly 100 msec. Indeed, under certain circumstances, the early arrival of one impulse may depress the area where the fibers join and prevent the transmission of an impulse that would otherwise have been propagated, giving rise to a type of inhibition not previously known in the heart. Summation also provides a mechanism by which one-way block may arise since it is effective at a given site only when excitation travels in the direction that the fibers travel to reach their point of merger.

Summation may cause some fibers to be excited long after excitation of the rest of the heart, while inhibition may cause failure of excitation in a small part of an otherwise fully excited heart. That mechanisms exist capable of bringing about so marked a degree of dispersal of excitability and refractoriness strongly favors reentry as the basis of fibrillation. The heterogeneity of refractoriness in question may arise even if all fibers in a network of cardiac cells have refractory periods of normal duration, since the dispersal in the recovery of excitability arises from a dispersal in the times of onset of excitation. The fact that impulses that enter a fiber through which they cannot propagate show markedly shortened action potentials points to another source of heterogeneity of refractoriness that may be of particular importance in fibrillation.

That depressed cardiac fibers can show properties that are sufficient to cause reentry has thus been experimentally demonstrated; equally important, it has been shown that, when one-way block, slow conduction, summation, and inhibition are induced by depressing the excitability of a peripheral twig of the ventricular conducting system, classic reentry does occur with regularity. Furthermore, reentry at one or more sites can become self-sustaining when each reentrant impulse evokes the next reentrant impulse, thus creating a tachycardia. Further investigation of the role of heterogeneity of refractoriness and further investigation of the nature of slow conduction, summation, and inhibition in depressed fibers may greatly enlarge our understanding of arrhythmias and may also increase our ability to prevent and control them.

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References
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