THE CLASSIC DEFINITION of parasystole implies the existence of an automatic focus which, although protected from extraneous depolarizations, can activate the surrounding myocardium to produce propagated responses.1 Parasystole is diagnosed when occasional ectopic beats occur with varying coupling intervals (including fusion beats) and when the interectopic intervals are multiples of a common denominator presumed to represent the ectopic cycle length.1

Before the work initiated in Moe's laboratory in 1976,2 several mechanisms had been postulated to explain the nature of parasystolic protection. Kaufman and Rothberger3 assumed the existence of a zone of protective, or entrance, block surrounding the focus in all directions. Vedoya4 believed that there were two zones of block around the focus, each one with different degrees of refractoriness. According to Scherf and Schott,5 the focus had a lower excitability compared with that of the oncoming impulses. The studies of specimens of canine His-Purkinje cells 24 hours after ligation of the anterior descending artery performed by El-Sherif et al.6 revealed the existence of automatic cells showing both entrance and exit block (parasystole). The most plausible explanation for these phenomena was considered to have been the depressed (slowing rising) "slope of diastolic depolarization of the pacemaker cells."6

Scherf and Schott5 considered none of these assumptions necessary to explain the rapid "parasystole" that they produced by topical application or subepicardial injection of sodium chloride and veratrine. They suggested that the fast rate per se accounted for both protection and exit block, since the focus would be surrounded by refractory tissues as a result of its fast rate of impulse formation.

Because of the variety of mechanisms that could be involved in the genesis of this phenomenon, Scherf and Schott preferred the term "protection" over "protective block."5

Classic parasystole may be considered one in which the rate of discharge is regular.1 If, as suggested by Jalife, Antzelevitch and Moe,7 one permits the variations of the ectopic cycle length not to exceed ± 5% for an average cycle of 2000 msec (certainly an allowable biologic variation), then there are examples that indeed fit the classic criteria. Such cases have been reported by Katz and Pick,1 Scherf and Schott5 and Pick and Langendorf.8

In these cases of classic continuous parasystole with or without type II (Mobitz) exit block, the almost constant ectopic cycle lengths imply that the focus has the intrinsic ability to form impulses regularly and that the regularity can occur (and be maintained) because the focus is not affected by (or totally insulated from) extraneous impulses for relatively long periods of time. The mechanisms of the classic parasystole that occur in the absence of acute myocardial infarction or ischemia are unknown. It probably does not result from protected automatic activity arising from spontaneous depolarization in the range of −90 to −70 mV.

However, in most cases, when parasystole is diagnosed, the ectopic cycle lengths are not regular.5,6 Even in classic parasystole, 24-hour Holter recordings show fluctuations in rate (in patients not receiving drugs and without electrolyte imbalance), presumably due to variations in autonomic discharge. For example, the parasystolic rate may decrease at night during sleep. This phenomenon, which usually occurs in association with a reduction in sinus rate, may result not only from an enhanced vagal tone, but also from an associated decrease in sympathetic activity.

The irregular rate of discharge that occurs in nonclassic parasystole may reflect, in addition to variations of automaticity, the fact that the focus is affected by extraneous depolarizations. The latter probably is what occurs in the so-called intermittent parasystole, either of the type where the ectopic focus "produces manifest impulses only intermittently so that the arrhythmia occurs only periodically,"15 or of the type in which resetting occurs only during the terminal portions of the ectopic cycle because protection is limited to the first half of the cycle.5 In both types, intermittent affectation of the focus does not allow the necessary time for a relatively regular automatic activity to develop.

There are many tracings obtained from nonmedicated patients in which ectopic beats show characteristics that are suggestive of parasystole (markedly varying coupling intervals and fusion beats), but in which the absence of a common denominator precludes the diagnosis of classic, regular parasystole. In our experience, these tracings are more common than those in which parasystole can be diagnosed.

It is in this regard that the article by Rosenthal and Ferrier,10 published in this issue of Circulation, assumes particular importance. This study, climaxing the line of work initiated by Jalife and Moe in 1976,2 deals with the role of variable exit and entrance phenomena on the arrhythmogenesis of focal automaticity produced either by local application of 3000-msec positive current pulses or by exposure of the preparations to Tyrode solution containing 1.5–2.0 mM KCl. Rosenthal and Ferrier demonstrated that in the "two-dimensional" model used, protection of depolarized foci depended on the existence (within the
region of one-way conduction) of a gradient of membrane potential between depolarized tissue and more normal tissue surrounding the focus. Protection was also dependent on the occurrence of a low resting potential since this property was lost when the membrane potential shifted to higher values.

As in experiments using the sucrose gap technique, they observed that electrotonic depolarizations propa-
gating from the normal tissues traversed the affected area and reached the focus to produce a variety of phenomena. Foremost among these was the so-called "pacemaker annihilation" (the termination of abnormal automaticity by premature impulses). This phenomenon is clinically significant because it represents another situation (in addition to triggered activity due to delayed afterdepolarizations) in which premature impulses can abolish a nonreentry arrhythmia.

Electrotonic modulation of the focus may cause irregular interectopic intervals capable of being interpreted as resulting from a variable rate of discharge and even of making the diagnosis of parasystole virtually impossible. Moreover, modulation is a likely explanation for intermittent parasystole due to the occurrence of protection only during the initial portions of the cycle. According to Jalife et al., this is likely to occur when a relatively great distance between the focus and the affected regions causes enough asymmetry so as to attenuate or abolish the early phase of delay (the resulting effect being protection during the initial portions of the cycle). Persistence of the late accelerat-
ing phase (resulting in capture of the focus) would then be equivalent to what is clinically known as "reset-
ting."

One-to-one entrainment of the focus (with the ecto-
ic discharges occurring during the effective refractory period of the beat producing the entrainment) leads to periods of intermittency during which no manifest parasystolic discharges occur. The surface electrocardio-
graphic features will be those of intermittent parasys-
tole, in which the "ectopic" focus produces manifest impulses only "intermittently." Intermittent reflection may explain why parasystole has been seen to change into coupled extrasystoles. Persistent reflection may produce continuous bigeminy, trigeminy and even (by virtue of causing a special type of to-and-fro "reciprocation") sustained tachycardia.

Rosenthal and Ferrier also showed that exit conduc-
tion was a function of a critical level of low resting potential. When the latter was reduced below this (critical) level, complete exit block ensued. This, too, could lead to periods of parasystolic intermittence. Moreover, even when complete exit block was present, electrotonic depolarizations leaving the focus were responsible for the excitation of the normal distal myocardium, provided that the tissues between the focus and normal myocardium showed phase 4 depo-
larization.

We believe that the future will reveal the clinical counterparts of most of these experimental phenomena. Currents of 3000 msec duration are not delivered to, nor is Tyrode's solution applied on, the human heart; but similar degrees in reduction in membrane potential, coexisting with focal automaticity and entrance and exit phenomena, have been observed in cells of diseased atria12, 13 and in ventricular and His-Purkinje cells obtained from ischemic, infarcted or traumatized areas. Therefore, the findings under consideration may be expected to occur in the corresponding clinical settings.

Classic regular and irregular parasystole probably represent specific cases in the range of possible behaviors of abnormally depolarized foci. However, whether all of the arrhythmias discussed by Rosenthal and Ferrier should be considered "parasystolic" should stimulate debate. But that is another story.

References
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