MELTZER\(^1\) introduced the term "factor of safety" into physiologic thinking—a term used in engineering to indicate the margin by which the strength of material or structure exceeds the actual working stress to which it is submitted in normal use. In the case of the heart, an impressive number of such factors of safety have been recognized. Among these we might cite: (1) the ability of cardiac muscle to respond with increased liberation of energy to increased degrees of diastolic stretch, commonly designated as Starling's Law of the Heart, (2) the existence of neural and humoral mechanisms capable of inducing great accelerations in the rate of heart beat, (3) the dilatory response of the coronary circulation to greatly increase blood flow during anoxemia and when metabolic needs become excessive, (4) the potential contractile force of the atria which, though making a relatively minor contribution to ventricular filling under normal circumstances,\(^2\) may assume a considerably more important role in such conditions as mitral stenosis, (5) the morphologic property of heart muscle to exhibit hypertrophy under conditions of maintained stress, (6) the awakening of ectopic rhythmic foci to initiate rhythmic impulses in the event of failure of the normal sinus pacemaker, (7) the physiologic properties of the A-V bundle which limit the number of impulses that can reach the ventricles, (8) the ability of the heart to maintain effective mechanical beats so as to preserve adequate circulation to the organism despite the presence of significant areas of infarction which cause the ventricular wall to bulge during systole\(^3\)\(^4\) in early stages and form fibrotic scars within the muscle mass in later stages.

Recognition of these factors of safety does not imply that our knowledge of them is complete or even adequate. It is of interest to note, for example, that though the Starling Law relationship was one of the earliest clearly documented properties of heart muscle, its details are still the subject of intensive investigations, as evidenced by the study by Ferguson, Shadle and Gregg\(^5\) on this general problem appearing in the first issue of this journal. In the important and relatively commonplace phenomenon of cardiac hypertrophy, existing knowledge is grossly inadequate, particularly as to the precise factors responsible for this manifestation.\(^6\)

In addition, it appears justified to suggest that there are still further cardiac factors of safety whose operation is appreciated only dimly, if at all. In the list given above, the absence of biochemical factors of safety is to be noted. That there are biochemical factors of safety in the myocardium, however, is strongly suggested in various ways. For example, the observations of Khairallah and Mommaerts\(^7\) reported in the first issue of this journal indicate that only one tenth of the available ATP is apparently dephosphorylated during each contraction. Furthermore, the recent studies of Hajdu and Szent-Györgyi\(^8\) suggested the possibility that changes in membrane permeability and consequent changes in the ionic atmosphere in which actomyosin contracts may underlie the ability of the myocardium to regulate quickly the intensity of its contractions. However, the studies of Taeschler and Bing\(^9\) on extracted heart muscle reported in the current issue indicate that many of the reactions of normal heart muscle (for example, increased response to stretching) are due to inherent
qualities of the contractile proteins. Though Nature has appeared exceedingly jealous in guarding her inner secrets, the intensive investigations being directed toward these problems in many laboratories must surely yield at least a partial answer in the foreseeable future.

For those whose interest is focused on the dynamics of cardiac contraction, any complacency that some might have had as to the completeness with which they understood dynamic factors of safety must surely have been shaken by the observation that massive cauterization of most of the outer wall of the right ventricle produces little dynamic alteration, as first reported by Starr and subsequently confirmed by Bakos and Kagan. Bakos offered the plausible suggestion that compensation for the destroyed muscular tissue might be achieved by the contracting muscle bands of the left ventricle as they encircle the right ventricle. Against such an explanation are the experimental facts (a) that in systole the cauterized right ventricle bulges and the superficial fibers lengthen, (b) that experimental increase in pulmonary resistance is followed immediately by increased right ventricular response, and (c) that right and left ventricular pressures are known to alter independently and often in opposite directions. Kagan suggested that the energy for right ventricular ejection in these hearts might be derived from bulging or shortening of the intact ventricular septum during systole, but the observations of Rushmer and his associates reported in this issue do not offer support for the view that septal bulging takes place. There must certainly be more evidence brought to the fore to explain the factors of safety which permit a right ventricle with 70 to 80 per cent of its outer wall destroyed by cautery to accomplish a nearly normal compensatory action.

A final source of unrecognized factors of safety may reside in the process of ventricular relaxation. Attention has been almost wholly focused upon the process of ventricular relaxation. Attention has been almost wholly focused upon the process of ventricular contraction, in spite of the classic studies of Henderson which indicated that the stroke volume depends basically on the degree of diastolic filling. This latter relationship clearly empha-
sizes that, should ventricular relaxation be subject to physiologic variations, it could have profound dynamic consequences. A recent report of Opdyke has suggested the possibility of such a physiologic mechanism in that epinephrine appears to produce a marked change in the nature of ventricular relaxation. Behind this fragmentary report there may well be lurking important cardiac factors of safety that have so far received little attention.

One of the major responsibilities of the physician is to aid the cardiac patient in taking full advantage of these factors of safety. It would be foolish to predict that further elucidation of the nature of any specific factor of safety would necessarily offer him practical assistance in this task; it would be equally foolish to ignore this possibility.

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Cardiac Factors of Safety
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