Some Mechanical Properties of Isolated Mammalian Cardiac Muscle

By Brian F. Hoffman, Arthur L. Bassett, and Herbert J. Bartelstone

ABSTRACT

Isolated preparations of mammalian cardiac muscle have been employed to study possible mechanisms responsible for changes in diastolic compliance. Muscles have been studied at rest and during isometric and afterloaded contractions, at fixed initial length and during programmed, cyclic changes in length, and under the influence of paired stimulation, catecholamines, and elevated extracellular calcium concentrations. The results obtained indicate that, although there is a series viscous element in cardiac muscle, which accounts for stress-relaxation, some changes in compliance apparently result from alterations in the extensibility of the contractile element. This conclusion is based primarily on experiments showing shifts in the apex of the length-tension curve produced by action of inotropic agents which alter diastolic compliance and on experiments showing that the rate and extent of relaxation of afterloaded contractions depend on the extent of shortening during contraction.

ADDITIONAL KEY WORDS cat dog cardiac muscles contractility variable diastolic compliance isometric, afterloaded contractions paired stimulation catecholamines calcium muscle models postextrasystolic potentiation series and parallel viscous elements

During the past forty years a variety of considerations have suggested that the diastolic pressure-volume relationship for the mammalian ventricle might vary as a result of some change in the characteristics of the myocardium (1-8). Moreover, it was recognized early that under appropriate conditions variability in the pressure-volume relationship would influence both the performance of the heart as well as any evaluation of performance which employed measurement of end-diastolic pressure as an index of fiber length. A change in the pressure-volume or length-tension relationship might result either from an alteration in the contractile elements or from a change in other components of the myocardium. Meek (1) concluded that tonus did not vary in mammalian hearts; as he defined tonus ("... a condition of sustained diastolic contraction ..."), this conclusion excluded the possibility that a change in the pressure-volume relationship might result from an active change in the contractile elements. Others, whose studies have been reviewed by Blinks and Koch-Weser (9), showed that variations in pressure-volume and length-tension relationships might be caused either by changes in passive components of the myocardium or by incomplete relaxation of the contractile elements. In spite of this evidence, after introduction of the ventricular function curve as a measure of the contractile state of the ventricles (10), many investigators assumed that there was a constant relationship between end-diastolic pressure and fiber length. This belief was reinforced by the studies of Mitchell et al. (11) which failed to demonstrate any effect of stimulation of the stellate ganglia or vagal nerves on extensibility of the ventricular myocardium.
We began studies on this problem several years ago when, during studies on the effects of paired stimulation and postextrasystolic potentiation on the canine heart in situ, we obtained results which indicated that the diastolic pressure-volume relationship varied as a result of paired stimulation (12). At that time we chose to describe the change by the term variable diastolic compliance to indicate clearly that the results obtained indicated a change in the length-tension relationship for ventricular muscle during the diastolic interval and not a change in the pressure-volume relationship which resulted from alterations in the shape or size of the ventricular chamber. In selecting the term compliance, we were guided by the glossary prepared by Landowne and Stacy (13) and the definitions given by Blinks and Koch-Weser (9); we defined compliance, as did the latter, as the ratio of the change in length to the change in extending force.

At the same time, on the basis of studies of isometric contractions of isolated papillary muscle, Sonnenblick (14) concluded that paired stimulation caused no change in diastolic compliance. Because of the obvious disagreement between his results and ours (12), we subsequently extended our studies to the isolated cat papillary muscle. Using isometric recording techniques we demonstrated that, in vitro as in vivo, paired stimulation and the resulting postextrasystolic potentiation caused a marked increase in diastolic compliance (15). Also, it was possible to show that the change in compliance was not necessarily dependent on an increase in active tension developed by the preceding contraction. This result was confirmed by Feigl (16) who showed that when paired stimuli were used to activate a muscle studied under isometric conditions, there was a clear decrease in diastolic tension after the first premature stimulus and prior to any change in developed systolic tension. Further studies by ourselves (17) and Koch-Weser (18) have shown that diastolic compliance is changed not only by paired stimulation but also by a number of inotropic agents including digitalis and catecholamines. Here, again (17), it was shown that the change in diastolic tension at constant length was not necessarily related to either an increase or a decrease in tension developed during contraction.

Most recently, Sonnenblick (19) has repeated his studies on isolated papillary muscles and, further, has conducted studies similar to those of Bartelstone et al. (12) on the intact canine ventricle. In this paper he concludes that diastolic compliance does indeed vary as a result of postextrasystolic potentiation, the action of catecholamines, calcium, and other experimental procedures. Thus, the observation that diastolic compliance varies is no longer open to question. However, there is disagreement about the mechanisms underlying the observed changes.

Sonnenblick (19) has found that, in his experiments, the changes in compliance are apparent only if the magnitude of tension developed during contraction is allowed to vary. In studies of the isotonic or afterloaded contractions of papillary muscles, he has not observed changes in diastolic length or tension, respectively. Moreover, he has suggested that the changes in compliance recorded under conditions which permit an increase in tension developed during contraction result because the augmented tension causes elongation of a viscous element which is in series with the contractile elements of the muscle.

Because some of his results still were in disagreement with ours and because his interpretations of the mechanism responsible for alterations in compliance (19) are different from ours (15, 17), we undertook further studies of this problem. We repeated many of our earlier experiments which were designed to determine whether or not changes in diastolic compliance result solely from alterations in developed systolic tension. In addition, we have conducted studies on the phenomenon of stress relaxation, on the changes in diastolic tension of afterloaded muscles, and on the effects of elongation and shortening on diastolic tension and developed systolic tension. The results of studies on
MECHANICAL PROPERTIES OF ISOLATED CARDIAC MUSCLE

293

Muscles contracting isometrically are presented because they confirm our earlier findings, in terms of the experimental data, and because they support the hypothesis we have advanced (15, 17), i.e., that diastolic compliance of cardiac muscle is determined in part by residual interaction between the contractile elements and that changes in such interaction will alter both diastolic compliance and developed systolic tension. The results of experiments on afterloaded muscles are presented because they demonstrate an important relationship between extent of shortening and diastolic tension and because they clarify the basis for disagreement between data published by others (19) and by us. The results of studies on stress relaxation are presented because they provide new data on the changes in developed systolic tension which result from this characteristic of cardiac muscle, a matter about which there has been some disagreement, and because they provide a convenient model on which to base discussion of all our findings. The results of all the studies are discussed in relation to our hypothesis which assumes that a variable degree of interaction between the contractile elements may modify the diastolic compliance of cardiac muscle. We believe the results clearly demonstrate that a change in a series viscous element is not sufficient to explain all alterations in diastolic length-tension relationships recorded under isometric and afterloaded conditions, and we strongly suggest that the relationship between cardiac muscle length and sarcomere length need not be constant.

Methods

Muscles were obtained from the right ventricle of cats anesthetized with sodium pentobarbital, 25 to 30 mg/kg ip, or the right atrium of dogs anesthetized with sodium pentobarbital, 30 mg/kg iv. For studies on ventricular tissue we employed thin papillary muscles or trabeculae carneae; for studies on atrial muscle we used thin trabeculae from the right appendage. The muscles were mounted in a muscle chamber with a volume of 8 ml and perfused with modified Tyrode solution containing, in mM: NaCl, 137; NaHCO3, 12; NaH2PO4, 1.8; KCl, 2.7; CaCl2, 2.7; glucose, 5.5; and MgCl2, 0.5. The solution was equilibrated with 95% O2, 5% CO2 and maintained at desired temperature. Flow rate through the tissue bath was 6 ml/min.

One end of the muscle was directly attached by means of a tie of 6-0 silk thread to a steel hook which extended through a diaphragm in the bottom of the perfusion chamber. The other end of the hook was affixed to a Statham bi-directional transducer (model UC-2). The other end of the muscle was tied directly to a fine golden chain which was attached to a light isotonic lever. The lever system was designed for studies on skeletal muscle (20); for our experiments the lever arm was made of magnesium and somewhat reduced in length and mass. The extent to which the effective mass of the lever caused variations in load of afterloaded contractions can be seen in the records of such contractions. Appropriate mechanical stops permitted us to study either isometric contractions or contractions under constant afterload. Stimuli were delivered through large platinum plates to the entire muscle; stimulus duration was 5 or 10 msec, and stimulus strength was always above threshold.

The transducer and other equipment have been described elsewhere (17). The unit permitted measurement to be made at constant length or during programmed cyclic increases and decreases in length. Systolic and diastolic isometric tension, recorded at high and low sensitivity, diastolic length, changes in length, temperature, time of stimulation, and rate of change of either systolic tension or length were recorded on an Electronics for Medicine DR-8 recorder. For some records of isometric contractions during programmed changes in muscle length, the output of the force-displacement transducer was direct-coupled to one recording channel and condenser-coupled to another which was set at higher gain. The time constant of the R-C coupling was 125 msec. The R-C coupling provided a constant baseline at the temperature and stimulation rate used, and thus permitted graphic display of the changes in developed systolic tension. All changes in magnitude of developed systolic tension shown in the condenser-coupled records are also shown by the simultaneous direct-coupled records; all measurements were made from the latter. Measurements of diastolic tension were made at sensitivities up to 25 mg/cm chart; measurement of changes in diastolic length were accurate to within 2 /u. Compliance of the recording system in the absence of a muscle was <15 /u/gm. For this measurement one end of the gold chain was tied directly to the hook on the force transducer and the other end of the chain tied to the isotonic...
lever. Dry, 6-0 silk was used. Compliance was measured as the change in length/g load between 0 and 2 g. This measurement of compliance was chosen because inclusion of tendon from the papillary muscles would imply that all such tendons are uniform in dimensions and composition, and because it has been known for many years that attachment of a thread or clamp to muscle causes injury and introduces a new, indeterminate compliance (21).

The maximum diameter of the muscles employed, under a load of 1 g, was 0.35 to 1.0 mm. This measurement was made while the muscle was in the tissue bath. Muscle length varied from 4 to 8 mm for ventricular tissue and 8 to 15 mm for atrial trabeculae. Most experiments were conducted at a temperature of 37°C and stimulation rates of 25 to 60/min. Exceptions are noted in the Results.

**Definitions and Conventions**

The term tension will be employed to describe the linear strain in the muscle in conformity with traditional usage, i.e., the length-tension relationship. Tension will be expressed as total tension since, at constant length, neither the cross-sectional area nor the cross-sectional shape are constant for a given muscle over its length and since, when length is altered, neither the cross-sectional area nor the shape vary in a uniform manner at different cross sections. The term diastolic tension will be employed rather than resting tension because we wish to identify an interval and not to characterize the state of the muscle. The terms active or developed systolic tension and total tension (the sum of diastolic and developed tension) are employed in the usual sense. In the text the term “systolic” is employed when we wish to call attention to the characteristics of the contractile apparatus; the term is synonymous with active tension. The terms preload and afterload are employed in the usual sense. Although it is obvious that, in our usage, load and tension are synonymous, the former term is less cumbersome since standard use of a term such as afterload has provided accurate and precise definition.

The term compliance is used to describe, for the diastolic interval, the general relationship between the force or forces acting on the muscle and the extent of linear deformation. As we have used it, the term has no connotation that would suggest a mechanism for changes observed. The term tonus has not been employed because its precise definition by Meek (1) would exclude many of the conditions which we wish to consider. The terms incomplete relaxation, partial contraction, and aftercontraction impose restraint in terms of a particular biological process. Although each of these processes would modify compliance during any diastolic interval, the change in compliance, as we will show, need not result solely from the action of any one. For example, a change in compliance noted at the end of a given diastolic interval might result from both a change in the terminal rate of relaxation and a force-dependent change in a passive viscous element in series with the contractile element. The term contraction, which is used, is discussed elsewhere.

The symbol $L_o$ indicates the muscle length at which developed systolic tension is greatest, $L_i$ indicates the initial length of the muscle for each experiment in which the length-tension curve was determined. $L_i$ is not the slack length, the length obtaining under zero load.

**Results and Discussion**

**STUDIES ON STRESS-RELAXATION**

Analysis of the mechanical behavior of striated muscle customarily has employed an analog consisting of an elastic element in series with the contractile element and a second elastic element in parallel with both the contractile and series elastic elements (22). In descriptions of the force-velocity relationships for cardiac muscle and in characterization of its contractile and elastic properties (23, 24, 25), these three elements usually have been arranged in the manner shown in Figure 1, A. However, it also is possible that a more appropriate analog might be formed if the three elements were arranged in the manner shown in Figure 1, B (9, 26, 27), and several recent studies of cardiac muscle have suggested that, under appropriate conditions, either or both might...
MECHANICAL PROPERTIES OF ISOLATED CARDIAC MUSCLE

Diagrams of possible mechanical analogs of cardiac muscle. For A to D: PE = parallel elastic element; CE = contractile element; SE = series elastic element; SV = series viscous element; E = elastic element in parallel with SV. Note that in A, SE is in series only with CE; while in B, SE is in series with both CE and PE. In C, a viscous element has been added in series with PE; in D the viscous element is in series with both PE and CE. In E and F are shown the effects of elongation of the series viscous element in C and D, respectively, on muscle length (L_m), sarcomere length (L_s), resting tension (T_R), and developed systolic tension (F_s). Note that only for the model shown in D would an elongation of SV result in the changes in resting tension and developed systolic tension which are shown in Figure 3. See text for discussion.

The muscle is at rest the length of the contractile element (i.e., sarcomere length) will bear a linear and predictable relationship to total muscle length, at least over the greater part of the length-tension curve (31). Thus, the contractile element will have no effect on the length-tension relationship of quiescent muscle (22), and the active tension developed during contraction will depend on the length of the muscle prior to excitation (31, 32).

In terms of the model, if a suitable preparation of cardiac muscle were brought rather slowly from one length of a greater length, the diastolic tension would be expected to change from its initial value to a new value and then remain constant. Also, tension developed during systole would be proportional to the

FIGURE 2

Records of length and high and low sensitivity records of tension (force) recorded from quiescent cat papillary muscle. The top trace is a superimposition of the record of length and a reference line; increase in length is indicated by a downward deflection. The next trace from the top is a high sensitivity tension trace, the next is a reference line and the bottom a low sensitivity tension trace. At the upward arrow length was increased by slightly more than 200/L, at the downward arrow length was returned to the control value. During elongation the high sensitivity tension trace was driven off the record. The dashed vertical line indicates the moment when length reached the control value, ±2/L; the horizontal dashed line indicates the level of tension recorded at low sensitivity prior to elongation. Temperature, 35°C. (Slight variations in length and tension result from the fact that length was changed manually.)
new muscle (and sarcomere) length and would not change as a function of time. A number of studies have shown that this is not the case for cardiac muscle (7, 8, 33, 34, 35, 36) and that there may be stress-relaxation or "creep" after elongation. The records shown in Figure 2 demonstrate this phenomenon for quiescent cat papillary muscle studied under isometric conditions. When length is increased rather abruptly, diastolic tension increases. Then, although the muscle is kept at the same length, diastolic tension decreases first rapidly and then progressively more slowly. Also, when muscle length is returned to the control value, tension falls below that recorded for the same length prior to elongation and then slowly increases. These time-dependent changes in tension would not result from the behavior of the undamped elastic elements in the model in Figure 1, A and are not due to properties of the recording apparatus. To explain them it is necessary to assume that there is in cardiac muscle another element which has viscous properties. Such a viscous element might have several locations in an analog. In terms of the model in Figure 1, A, the results obtained from studies of quiescent muscle would not differentiate between Figure 1, C, where the viscous element is in series only with the parallel elastic element, and Figure 1, D, where the viscous element is in series with both the parallel and series elastic elements. In either case it is necessary to assume that there is an additional elastic element in parallel with the viscous element so that, when force on the system is decreased, the viscous element will return to control length. A choice between these two possibilities for locating the viscous element (Figs. 1, C and D) can be made if the length of the muscle is varied, as in the experiment shown in Figure 2, during regular isometric contractions and if the experiment is repeated with the initial muscle length set first on the ascending limb, then at the peak and finally on the descending limb of the length-tension curve. The results of such an experiment are shown in Figure 3. In Figure 3, A the muscle length was changed between two values on the ascending limb of the length-tension curve; after elongation there was, as expected, an increase in developed systolic tension and a progressive decrease in diastolic tension as the muscle was maintained at the new length. When length was returned to the initial value and diastolic tension fell below the control, it is clear that developed systolic tension was reduced with respect to the control value obtained at the same muscle length. Developed systolic tension then increased slowly as diastolic tension increased towards the control value. The records in Figure 3, B were obtained when the muscle length was varied between two points near the peak of the length-tension curve and those in Figures 3, C and D when length varied between two points on the descending limb of the curve. In Figure 3, B the changes in length have little if any effect on the active systolic tension even though there are time-dependent changes in diastolic tension after both elongation and shortening. However, in Figure 3, C it is evident that active tension developed during systole was decreased after the muscle had been elongated. This is to be expected since the muscle was on the descending limb of the length-tension curve. The significant observation (Figs. 3, C and D) is that when muscle length was returned to the control value, active tension developed during systole was greater than that recorded prior to elongation. With the passage of time, as diastolic tension increased there was a decrease in the developed systolic tension.

For the models in both Figure 1, C and Figure 1, D an imposed change in muscle length would result in a change in the length of the contractile element. As a result there would be a change in developed systolic tension appropriate to the position of the muscle on the length-tension curve. Thus a change in developed systolic tension would be expected to follow immediately on lengthening or shortening. Also, in terms of either model, an increase in length would be expected to result in a gradual, force-depen-
Effects of increases and decreases in length on diastolic and peak developed systolic tension of cat papillary muscle as a function of initial muscle length.

A and B: Rate, 60/min; temperature, 35°C. From above down the traces show the record of muscle length (increase downward), superimposed on a reference line, stimulus artifacts on a second reference line, and a record of isometric tension (force). Horizontal dashed line shows level of diastolic tension prior to stretch, and vertical dashed line the moment when length returns to the control value. In A, prior to stretch the length of the muscle was less than $L_o$, i.e., the muscle was on the ascending limb of the length-tension curve. For A, the values of developed systolic tension at points 1, 2, 3, and 4 are 0.64, 1.14, 0.51, and 0.62 g respectively. In B, the control muscle length is near $L_o$. Note decreased sensitivity on tension trace. After elongation developed systolic tension is slightly reduced. Although there is marked stress-relaxation, after the muscle is returned to control length in spite of a lower diastolic tension, developed systolic tension is approximately equal to the control value. For B, the values of systolic tension at points 1, 2, 3, and 4 are 1.15, 1.02, 1.12, and 1.13 g, respectively.

C: Records from a different preparation. Rate = 45/min, temperature, 36°C. Stimulus artifacts at bottom of record. Prior to stretch the muscle length is slightly greater than $L_o$. After returning to control length there is the usual decrease in diastolic tension but a slight, persistent increase in developed systolic tension. The values of developed systolic tension at points 1, 2, 3, and 4 are 1.51, 1.32, 1.54, and 1.58 g, respectively.

D: Experiment on another muscle. Temperature, 35°C; rate, 60/min. Tension recorded at both high and low sensitivity. Prior to elongation the muscle has been brought to a point on the descending limb of the length-tension curve, i.e., to a length > $L_o$. During elongation only the bottom of the low sensitivity tension trace is seen. Stress-relaxation is marked. After returning to control length diastolic tension is markedly reduced and developed systolic tension is considerably increased. The values of developed systolic tension at points 1, 2, and 3 are 1.30, 1.43, and 1.43 g, respectively.
changes in the length of the contractile element. Therefore the model in Figure 1, C could not account for either the slow changes in developed systolic tension which were seen after the imposed elongation or shortening or the fact that, when the muscle had been returned to control length, developed systolic tension was not the same as that recorded prior to elongation.

The results of the experiment shown in Figure 3 thus suggest that the viscous element behaves as though it has the location shown in Figure 1, D, in series with both the parallel and series elastic elements, and thus in series with the contractile element as well. Changes in length of such a series viscous element would permit the length of the contractile element to vary and thus cause the changes in developed systolic tension shown in Figure 3. After elongation of the muscle, a gradual increase in length of the series viscous element would permit shortening of the contractile element. After the muscle had been returned to control length, because of the elongated series viscous element, the contractile element would be somewhat shorter than expected on the basis of muscle length. By equating contractile element length and sarcomere length, it is reasonable to expect that at points on the ascending limb of the length-tension curve elongation of a series viscous element would cause a reduction in the active tension developed during contraction while, at points on the descending limb of the curve, elongation of the series viscous element would permit the sarcomere to shorten, and the shorter sarcomere would develop more tension during systole. Although there has been some disagreement between results of previous experiments in terms of the change in active tension caused by stress relaxation (33, 34), the results shown in Figure 3 are characteristic for isolated preparations of mammalian cardiac muscle. Although they do not exclude other possible causes for changes in diastolic and active systolic tension during stress relaxation (see Figure 9), they are compatible with a model similar to that shown in Figure 1, D. More important, selection of this model permits certain predictions about the behavior of cardiac muscle which are subject to test...
and have direct bearing on our thoughts about the nature of changes in diastolic compliance.

**CHANGES IN DIASTOLIC COMPLIANCE AFTER PAIRED STIMULATION**

If there is in cardiac muscle an element which has, at least, the properties of the series viscous element in Figure 1, D, the following prediction seems reasonable: Within the limits imposed by the extensibility of the series viscous element, any change in the force developed during contraction would result in a change in the length of this element. Such changes in length of the series viscous element would have a variety of effects on the development of active systolic tension and on the diastolic compliance of the muscle. We propose to consider only the latter at this time. The records in Figure 4 show isometric contractions of cat papillary muscle during a control period and after initiation of paired stimulation. It is evident that the paired stimuli cause, in addition to postextrasystolic potentiation of contraction, a decrease in diastolic tension. We have described this decrease in diastolic tension which occurs at constant muscle length as an increase in diastolic compliance (15) and have suggested that it might result from variations in residual interaction between the contractile elements (15, 17). Sonnenblick (19) has studied the same phenomenon and has found that, although there was an increase in diastolic compliance when paired

**FIGURE 5**

Records of tension and shortening of afterloaded cat papillary muscle. A: From above down the records show tension recorded at high sensitivity and at low sensitivity, length, and a stimulus artifact. Temperature, 37°C; rate, 45/min; PS, paired stimulation. Note that with the onset of paired stimulation there is an increase in shortening and an increase in the time during which the muscle bears the afterload. B: Records from the same preparation obtained at a lower paper speed and with a smaller pre-load. Note that after initiation of paired stimulation shortening increases more markedly and there is in the top trace a change in both the terminal rate of relaxation and the end-diastolic tension. The dashed line permits the decrease in diastolic compliance (increase in diastolic tension) to be measured.

Circulation Research, Vol. XXIII, August 1968
stimulation caused an increase in developed systolic tension (i.e., under isometric conditions), if the muscle contracted isotonically or against an afterload of constant magnitude the diastolic length or tension did not vary during or after application of paired stimuli. These results led him to conclude that the change in compliance caused by paired stimulation resulted from force-dependent changes in length of a series viscous element similar to that shown in Figure 1, D.

We have made similar studies on changes in diastolic tension at constant diastolic length under isometric and afterloaded conditions. Some of our results have direct bearing on the models proposed in Figure 1 and on an analysis of the proposition that all changes in diastolic compliance are a result of force-dependent hysteresis. The records in Figure 5 show afterloaded contractions of isolated cat papillary muscle during regular stimulation and after initiation of paired stimulation and the resulting sustained postextrasystolic potentiation. It can be seen that, during the period of paired stimulation, the magnitude of the afterload is constant. However, the pattern of paired stimulation causes a fairly marked second contraction. As a result, the muscle bears the entire afterload for a greater fraction of each cycle during paired stimulation than under control conditions (Fig. 5, A). In terms of the model shown in Figure 1, D, each of the potenti ated contractions caused by the paired stimulation would be expected to increase the length of the series viscous element. This is so because, under these conditions, even though the magnitude of the afterload is constant, the time during which the afterload acts on the series viscous element is increased. One thus would expect that, by increasing the time during which the muscle supported the afterload, paired stimulation would have caused a decrease in diastolic tension (increased diastolic compliance). In fact, in most of our experiments the records show either no change (Fig. 5, A) or a progressive decrease (Fig. 5, B, Fig. 6) in diastolic compliance instead of the expected increase; in the latter, after each of the potentiAted contractions diastolic tension is higher than during the preceding diastole. Under these experimental conditions we have recorded an increase in compliance of extremely small magnitude and then only rarely. The fact that neither our experiments nor those of others (19) have demonstrated a consistent increase in diastolic compliance under these conditions may not be used to support the argument that all changes in diastolic compliance are force-dependent. An increase in compliance would be expected if changes in this property resulted solely from a series viscous element. Indeed, the experimental results suggest that something other than a series viscous element is important in determining the diastolic compliance of cardiac muscle. The records show one possible mechanism. When, under conditions of constant afterload, paired stimulation was initiated, the resulting postextrasystolic potentiation caused the expected increase in the velocity and extent of shortening, in addition to the effect on the time during which
Records of afterloaded contractions of cat papillary muscle. Temperature, 36°C; rate, 25/min. Traces from above down show tension at high and low sensitivity, length, and a stimulus artifact. A: A single pair of stimuli (PS) cause an increase in terminal relaxation rate (top trace, solid arrow); the subsequent, potentiated contraction results in greater shortening and a decrease in the terminal rate of relaxation (top trace, unfilled arrow). B: Maintained paired stimulation causes more rapid relaxation and increased compliance after the first premature contraction and then, as shortening increases, a decrease in the terminal rate of relaxation and a decrease in compliance. These changes persist for several cycles after the end of paired stimulation, when the duration of contraction has returned to the control value.

Several other aspects of these records require comment at this time. First, although paired stimulation causes an increase in the duration of contraction (by adding a second mechanical event), under isometric conditions the terminal rate of relaxation either is increased or unchanged (Fig. 4). Second, the changes in diastolic tension shown in Figures 5 and 6 do not appear to result solely from the abbreviation of the diastolic interval. Figure 7 shows records from a different preparation. In Figure 7, A, a single pair of stimuli is introduced. During the cycle containing the premature contraction the muscle bears the afterload for an increased time and the terminal rate of relaxation is increased. During the next cycle, the potentiated contraction is not increased in duration but shortening is augmented. The terminal rate of relaxation is decreased markedly (compare with Fig. 4). The same changes are shown in Figure 7, B, during sustained paired stimulation. After the first pair of stimuli, relaxation is accelerated and end-diastolic tension reduced. During subsequent cycles, with increased shortening, the terminal rate of relaxation is reduced and end-diastolic tension rises. The most marked changes in diastolic compliance are seen after the end of paired stimulation, when the duration of contraction returns to normal but shortening is still greater than under control conditions. Further, a similar progressive beat-to-beat increase in the diastolic tension of the afterloaded muscle is observed if a catecholamine is used to cause an increase in shortening (Fig. 8, A). This is so even though catecholamines typically increase the rate of both contraction and relaxation and thus, at constant frequency of contraction, under isometric conditions increase the duration of diastole relative to that of systole. In the presence of low concentrations of catecholamine, an additional decrease in compliance results from initiation of paired stimulation (Fig. 8, B).

Although we have not proven, here, a causal relationship between extent of shortening and changes in diastolic compliance, it is of some interest to examine the possibility that changes in extent of shortening are the immediate cause of the demonstrated alteration in diastolic length-tension relationship.
Records of afterloaded contractions of cat papillary muscle. Temperature, 36°C; rate, 45/min. Traces from above down show tension, at high and low sensitivity, length, a stimulus artifact and a marker. Paper speed varied to show duration of contraction. A: At the mark (arrow), isoproterenol was added to the bath to give a final concentration of $1.5 \times 10^{-7}$M. Note that as shortening increases, terminal relaxation is delayed and end-diastolic tension increases. B: The pre-load has been increased slightly to diminish shortening and the afterload increased. Isoproterenol, in a final concentration of $5 \times 10^{-6}$M, added at the mark (first arrow). (The top trace shows a movement artifact caused by addition of the drug.) Isoproterenol causes a slight increase in shortening and a small decrease in diastolic compliance. Initiation of paired stimulation causes a further increase in shortening and a more marked decrease in compliance. The dashed line has been drawn for reference to show the decrease in compliance.

in the afterloaded muscle (Figs. 5, 6, 7, and 8) and to refer again to the muscle models which we have considered. The model shown in Figure 1, D is not sufficient to explain this relationship. However, (Fig. 9, A) addition of an additional viscous element in parallel with the contractile element (and the parallel elastic element) would change the properties of the model so that under afterloaded conditions the rate of elongation might depend on the extent of shortening. With greater shortening, and perhaps with a greater duration of the period of shortening, the viscous element might assume a shorter length than under control conditions and this would retard relaxation.

THE COMPLIANCE OF THE CONTRACTILE ELEMENT

As in the case of the postulated series viscous element, a viscous element in parallel with the contractile element would modify several of the characteristics of the model. However, again we will limit our consideration to argument bearing on the nature of changes in diastolic compliance. A parallel viscous element might be passive, in the sense that the traditional elastic elements and our postulated series viscous elements are passive, or it might be active. By active we mean that it might represent a variable degree of persistent interaction between the contractile elements. We have conducted one group of experiments which have some bearing on this question. Two models are shown in Figure 9. In Figure 9, A there is one passive viscous element in parallel with the contractile element and another passive viscous...
FIGURE 9

A and B show diagrammatic representations of two possible sites for a viscous element (PV) which would dampen the length changes of the contractile element (CE). Other abbreviations as in Figure 1. In A the PV is represented as a passive element in parallel with the parallel elastic element, PE. In B the viscosity (PV) is represented as a property of the contractile element of each sarcomere, and is shown diagrammatically as cross-links. In each model the length of CE is intended to represent sarcomere length. The diagram in C shows the changes in length of CE which would occur if an increase in compliance were to result only from the action of increased force on SV, the series viscous element causing it to elongate. That in D shows the changes in length of CE that would result if a similar increase in compliance were caused by a change in the compliance of CE itself. See text for discussion.

element in the location suggested by the experiments on stress-relaxation (see Fig. 1, D). In Figure 9, B we have attempted to indicate that the contractile element itself may contribute to the diastolic compliance of the muscle because of variable residual interaction. For the model in Figure 9, A, under ideal isometric conditions, a change in diastolic compliance would result from force-dependent changes in the length of the series viscous element or from changes in the rate of relaxation which might be caused by slight differences in the extent of shortening of the contractile element. In the case of an observed increase in diastolic compliance, we must assume that the series viscous element has been elongated. A necessary consequence of such elongation of the series viscous element is that, for any muscle length, sarcomere length will be less than that obtaining prior to the increase in compliance (Fig. 9, C).

Conversely, if one assumes that variability of diastolic compliance may result from changes in the compliance of the contractile element itself (Fig. 9, B), an increase in diastolic compliance would result in a longer sarcomere, at any muscle length, than prior to the change in diastolic compliance (Fig. 9, D). In terms of the two models, then, an increase in diastolic compliance would have opposite effects on the relationship between muscle length and sarcomere length and thus on the active isometric tension developed during contraction at any muscle length. This difference is difficult to quantify when the muscle is kept at a fixed length since the means we have used to alter diastolic compliance (paired stimulation, catecholamines, etc.) also have direct effects on contractility. However, regardless of the direct positive inotropic actions of the measures used to increase diastolic compliance, each of the mechanisms considered as possible causes of the change (Figs. 9, C and D) would have different effects on the relationship between maximum active tension and muscle length. An increase in compliance due solely to force-dependent elongation of the series viscous element would be expected to shift the length-tension curve so that maximum active systolic force appeared at a muscle length greater than that demonstrated under control conditions since, for any muscle length, the sarcomere length would be less (Fig. 9, C). An increase in compliance caused by a change in the compliance of the contractile element would have the opposite effect: peak active isometric tension would appear at a muscle length less than that obtaining under control conditions since sarcomere length would now be greater for any muscle length (Fig. 9, D). We have attempted to test these two possibilities by varying muscle length in a controlled manner and recording length as well as systolic and diastolic tension over the greater part of the length-tension curve. The technique employed has been described in detail (17, 37)
but some comments should be made here in relation to the experiments to be considered.

The records in Figure 10 show isometric contractions and changes in length during two of a series of programmed increases and decreases in length. It is clear from the record that, during lengthening, the muscle has not been carried over the peak of the length-tension curve. If the rates of elongation and shortening are not excessive, consistent results can be obtained from a large number of such cyclic changes in length. The reproducibility of the curves shown in Figure 10 is supported by data published elsewhere (17, 37); similar reproducibility is obtained even if the muscle is stretched over the peak of the curve. Evidence for the consistency of $L_0$ under control conditions is provided by Figure 11, A and C. The length-tension curves plotted from the results of a series of such determinations, prior to and after experimental intervention, permit one to assign some...
FIGURE 11

A: Record of contractions of cat papillary muscle during a lengthening-shortening cycle and repetitive single stimulation. Temperature, 36.5°C; rate, 45/min; muscle length, 8 mm. Traces from above down show rate of change in length (0.1 mm/sawtooth), stimulus artifact, and tension at low and high sensitivity. On the high sensitivity trace of tension, only the peaks of the contractions are displayed. This high sensitivity trace was obtained by condenser-coupling the output from the strain gauge channel before amplification. Thus, a steady diastolic baseline was maintained and the display of the peaks of the contractions led to immediate visualization of the apex of the length-tension curve. Note that the apex of the length-tension curve is shown between the arrows just above the high sensitivity tension trace.

B: Record of contractions of the same muscle during a subsequent lengthening-shortening cycle using repetitive paired stimulation. Calibrations and displays same as A. Note the marked shift in the apex of the length-tension curve to a shorter length during paired stimulation. The apex of the curve is again shown between the arrows just above the high sensitivity tension trace. Thus the muscle developed maximum systolic tension at a shorter length, during the lengthening portion of the cycle, as a result of paired stimulation. The increase in diastolic compliance at the maximum length is 900 mg. Note the decrease in hysteresis during the shortening half of the cycle, in relation to the control.

C: Another control record from the same cat papillary muscle during another lengthening-shortening cycle and single stimulation. All calibrations and displays are the same as in A and B. Again note that the apex of the length-tension relationship is indicated between the two arrows just above the high sensitivity tension trace.

D: The same muscle during exposure to norepinephrine (1.2 \times 10^{-7} M). Note again the marked shift in the apex of the length-tension curve to a shorter length during norepinephrine infusion. Thus, the muscle developed greater systolic tension at a shorter muscle length during exposure to catecholamine. The increase in compliance (as shown by the decreased diastolic tension) at maximum length is 300 mg.
significance to even rather small changes in the relationship between muscle length and maximum active isometric tension. This technique has been used to determine the effect of changes in diastolic compliance on the muscle length at which peak active tension is recorded. Figure 11 and Table 1 show the results of a number of such experiments.

In all experiments which compared the length-tension curves inscribed during regular stimulation and paired stimulation (Table 1) the paired stimuli increased developed systolic force and increased diastolic compliance over the entire curve. Also, paired stimulation shifted the peak developed tension to a shorter muscle length: i.e., \( L_0 \) decreased. This suggests that the increase in compliance permitted the sarcomere length to become greater, for any muscle length, over the entire ascending limb of the curve. In other studies, isoproterenol, norepinephrine, and calcium were used to increase diastolic compliance. These agents have a strong, positive inotropic effect. This complicates the experiment since a marked increase in systolic force is expected to act on the series viscous element and shift the peak of the length-tension curve to a greater muscle length, i.e., to increase \( L_0 \). In contrast, were these same agents to increase compliance by diminishing residual interaction in the contractile element, they would shift the peak of the length-tension curve in the opposite direction and decrease \( L_0 \). Depending on the concentration of either agent employed, the two opposing effects might cancel each other or one or the other might predominate. In Figure 11, C and D, norepinephrine (\( 1.2 \times 10^{-6} \text{M} \)) has shifted the peak of the length-tension curve to the left (decreased \( L_0 \)).

In fact, we found that when contractile force at rest length was not maximally increased (Table 1), isoproterenol, norepinephrine, and calcium caused an increase in diastolic compliance over the entire curve.

**Table 1**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Tension (g)</th>
<th>Rate/min</th>
<th>Peak tension (g)</th>
<th>( L_0 - L_s ) (mm)</th>
<th>Change, diastolic tension (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>Ca++ 2.7 mM</td>
<td>5 \times 0.7</td>
<td>37</td>
<td>1.4</td>
<td>0.85</td>
</tr>
<tr>
<td>Test</td>
<td>Ca++ 5.4 mM</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>Ca++ 2.7 mM</td>
<td>5.2 \times 0.6</td>
<td>36</td>
<td>1.2</td>
<td>0.55</td>
</tr>
<tr>
<td>Test</td>
<td>Ca++ 5.4 mM</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>Isoproterenol (( 10^{-6} \text{M} ))</td>
<td>6.5 \times 0.9</td>
<td>30</td>
<td>2.6</td>
<td>0.65</td>
</tr>
<tr>
<td>Control</td>
<td>Ca++ 2.7 mM</td>
<td>7.5 \times 1.0</td>
<td>30</td>
<td>8.8</td>
<td>0.90</td>
</tr>
<tr>
<td>Test</td>
<td>Ca++ 8.1 mM</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>Single Stimulation</td>
<td>8 \times 0.8</td>
<td>36.5</td>
<td>2.6</td>
<td>0.65</td>
</tr>
<tr>
<td>Test</td>
<td>Paired Stimulation</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>Norepinephrine (( 1.2 \times 10^{-6} \text{M} ))</td>
<td>8 \times 0.8</td>
<td>36.5</td>
<td>1.8</td>
<td>1.05</td>
</tr>
<tr>
<td>Test</td>
<td>Acetylcholine (( 8 \times 10^{-6} \text{M} ))</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>Single Stimulation</td>
<td>8 \times 0.8</td>
<td>36.5</td>
<td>1.8</td>
<td>1.10</td>
</tr>
<tr>
<td>Test</td>
<td>Paired Stimulation</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>Norepinephrine (( 4 \times 10^{-7} \text{M} ))</td>
<td>7.5 \times 1.0</td>
<td>39</td>
<td>1.3</td>
<td>0.75</td>
</tr>
</tbody>
</table>

\( L_0 = \) Length for maximum force, \( L_R = \) Initial length. Data show change in length required to attain peak of length-tension curve (i.e., \( L_0 \)).

*Change in diastolic tension at maximum length studied.

Circulation Research, Vol. XXIII, August 1968
and decreased $L_o$ by shifting the peak active isometric tension to a shorter muscle length. Higher concentrations of the same agents, which produced a maximal increase in contractility, either failed to shift the peak of the curve or displaced it in the opposite direction, increasing $L_o$. This was true particularly when the preparation was maintained at low temperatures. Under these conditions isoproterenol, norepinephrine, and calcium consistently shifted the curve so that $L_o$ was increased. These results are those which would be expected if the model in Figure 9, B is an appropriate analog and if a change in diastolic compliance can indeed result either from effects on a force-dependent series compliance.

**FIGURE 12**

A: Graph of the changes in diastolic and developed systolic tension of a cat papillary muscle during elongation and shortening at a rate of 0.6 mm/min. Filled triangles and solid lines show data obtained during lengthening, open triangles and dashed lines show data obtained during shortening. Arrows indicate direction of change in length for each curve. Note that during shortening, for any chosen length, resting (diastolic) tension is less and developed systolic tension is higher over the greater part of the curve. Stimulus rate, 60/min; temperature, 36°C. Insert shows data obtained during lengthening and shortening. Dashed lines show data during shortening, open circles show data during shortening.

B: Similar data obtained from the same muscle during exposure to isoproterenol, $3 \times 10^{-5}$M. Filled circles show data obtained during lengthening, open circles show data obtained during shortening. Insert shows data plotted in a manner similar to the records in Figure 10. Note that differences between the developed systolic tension during lengthening and shortening almost have disappeared and that diastolic tension during shortening still is slightly less than during lengthening. The horizontal arrow shows the resting tension at maximum length in A, under control conditions, to permit some appreciation of the increase in compliance caused by isoproterenol.

*Circulation Research, Vol. XXIII, August 1968*
viscous element or from changes in compliance of the contractile element due to alterations in residual interaction. The fact that an increase in compliance, even if it is accompanied by a simultaneous increase in the developed systolic force, may shift the peak of the length-tension curve to a shorter muscle length convinces us that the compliance of the contractile element must be variable. The fact that a marked increase in developed systolic force shifts the curve in the opposite direction is expected (Fig. 1, D and Fig. 9, D) and does not negate or modify the first conclusion.

Several other characteristics of the records shown in Figures 10 and 11 appear to support the idea that the compliance of the contractile element may vary. Under control conditions, during the shortening half of each cycle end-diastolic tension was less and developed systolic tension was greater at any muscle length than at the same muscle length during the preceding or subsequent lengthening cycle. This is also shown in Figure 12, A. If one assumes that the increase in compliance during the shortening cycle, demonstrated by the reduced diastolic tension at each length, has resulted from elongation of a series viscous element, one would expect sarcomere length to be less at each point on the abscissa during shortening than had been the case during lengthening. Obviously, on this basis, one would expect developed systolic force to be reduced. Over a wide range of rates of elongation and shortening, we have found the opposite result. We are forced to conclude that sarcomere length is greater when compliance is greater during the shortening half of the cycle and that therefore the change in compliance cannot be a result solely of elongation of the series viscous element. This would suggest the elongation of the sarcomeres, during the lengthening of the muscle, has made them more compliant. As a result, during the subsequent programmed decrease in muscle length, sarcomere length is greater at any muscle length than it was at the same length during the prior programmed stretch. Further support of this proposal is provided by experiments in which curves were obtained under control conditions and after exposure of the preparation to agents such as isoproterenol, which increase both diastolic compliance and contractility. The data shown in Figure 12 were obtained from such an experiment. They clearly show (Fig. 12, B) that under the influence of isoproterenol the hysteresis during the shortening half of the cycle is markedly reduced for any muscle length, i.e., end-diastolic tensions are more nearly the same during both lengthening and shortening. Also, developed systolic tension at a given muscle length is nearly the same on both sides of the curve. In terms of the model, these results suggest that isoproterenol directly increases the compliance of the contractile element, and for this reason sarcomere length bears a more nearly constant relationship to total muscle length during both elongation and shortening. A similar effect is shown in Figure 11. For each of the control curves (Fig. 11, A and C), during the shortening half of the cycle Lₒ is smaller than during the lengthening half of the cycle. Also, after paired stimulation or norepinephrine (Fig. 11, C and D), during the shortening half of the cycle the developed systolic tension is more nearly equal to that recorded during lengthening, and the difference in Lₒ for the lengthening and shortening halves of the sequence is reduced in comparison to the control curves.

Concluding Remarks

For some time there has been argument about whether the diastolic compliance of cardiac muscle was constant (14) or variable (12). As a result of more recent studies the fact that diastolic compliance varies is generally accepted (19). However, there has now arisen disagreement concerning the mechanism or mechanisms responsible for this variability. In part, this results from lack of agreement on terminology. We have used the term compliance to mean quite simply the extent of deformation resulting from an applied force. We have suggested that changes in diastolic compliance might result,
MECHANICAL PROPERTIES OF ISOLATED CARDIAC MUSCLE

at least in part, from different degrees of residual interaction between the contractile elements. Such residual interaction might be due to incomplete relaxation from a preceding contraction, from the redevelopment of interaction as seen in aftercontractions (38), or from differing degrees of steady interaction as seen in partial contracture. The question which we have attempted to answer is whether changes in diastolic compliance result solely from changes in a series viscous element, as postulated by Sonnenblick (19), or whether they also may result from variations in the diastolic compliance of the contractile element. In the experiments described here, we have attempted to evaluate observed changes in diastolic properties in terms of muscle models which contain, in addition to the usual contractile element and parallel and series elastic elements, series and parallel viscous elements. The results permit certain general conclusions about cardiac muscle and, although they do not indicate that the analog we have suggested is either sufficient or unique, they do appear to rule out certain possibilities.

First, our results from experiments on stress-relaxation show that cardiac muscle cannot be described in terms of the three element models. They show that there is a viscous element in series with both the parallel elastic and contractile elements. On this basis it is inevitable that there will be, at least under some conditions, force-dependent changes in compliance. However, results from experiments on muscles contracting under constant afterload show that the avoidance of change in either resting or active tension may not be sufficient to permit a conclusion concerning the presence or absence of other causes for the variability of diastolic compliance. This is so because relaxation under the same conditions of loading may be changed by the extent of shortening during the previous contraction. This finding can be accounted for by placing a second viscous element in parallel with the contractile element. Such an element might be "passive" or might represent the degree of persistent interaction in the contractile element. Other types of studies have suggested that the contractile element has viscous properties (8). Our own results indicate that the viscous element in parallel with the contractile element does indeed represent an active property of the contractile element. After a variety of interventions have caused an increase in diastolic compliance, during gradual elongation of the muscle, the maximum active systolic tension is developed at a shorter muscle length than prior to the change in compliance. This shift in the peak of the length-tension curve on the length axis is assumed to reflect a change in the relationship between sarcomere length and muscle length; the direction of the shift is opposite to that which would result from the action of increased systolic force on the series viscous element. It is obvious that an increase in diastolic compliance will decrease the force exerted on the series viscous element during diastole at any length; however, the means we have employed to increase compliance also cause a sufficient increase in systolic force to more than outweigh this effect. Moreover, with greater increases in contractility the peak of the length-tension curve shifted in the opposite direction showing that elongation of the series viscous element does have the expected effect.

The means used to increase diastolic compliance also changed the hysteresis observed when muscles were stretched and then allowed to shorten at varying rates. The fact that, during shortening, diastolic tension was less and active systolic tension greater than the values recorded at the same length during extension is not what our model would predict if the change were due only to the effect of increased diastolic and peak tension on a series viscous element. Rather, the observation suggests that gradual elongation of the muscle increased the compliance of the contractile element so that, during the subsequent shortening half of each programmed cycle of length changes, the sarcomeres were longer at any muscle length than had been the case during elongation. One might assume
that, as the muscle was stretched, internal shortening during the isometric contractions was reduced and thus relaxation was more complete. As a result, the contractile elements were more compliant. Since agents which increased diastolic compliance diminished this hysteresis, it is tempting to assume that they changed the compliance of the contractile element and thus permitted a better correlation between muscle length and sarcomere length during elongation.

Some comment seems indicated on the experiments designed to test whether or not changes in compliance were associated with a shift in the relationship between muscle length and peak active force. The experiments in which paired stimulation was used to change compliance gave results which were quite consistent; however, we recognize that they may not be perfectly reliable since the increase in contractility caused by paired stimulation might have changed during the period of elongation. It is clear that a decrease in contractility during maintained paired stimulation would cause a spurious shift in the peak of the active tension curve. However, when an increase in calcium ion concentration or a catecholamine was used to change contractility and compliance, this problem did not arise since the positive inotropic effect of either was constant for a period much longer than the time required to inscribe the curve relating active tension to length. The results obtained with positive inotropic interventions other than paired stimulation strongly suggest that the results obtained during paired stimulation were not due to the artifact mentioned above.

Some comment on the adequacy of the preparation is appropriate. Some years ago (39) it was shown that, at temperatures similar to those we have employed, oxygenation of quiescent cat papillary muscle was adequate only if the diameter of the muscle was considerably less than 1.0 mm. The same studies suggested that the maximum permissible diameter for muscle contracting at a rate of 30 to 60/min was less than 0.5 mm. More recently, studies relating maximum isometric force to cross-sectional area (40) have suggested a similar maximum diameter. Many of the muscles we have used have exceeded these limits; the actual range of diameters has been 0.35 to 1.0 mm. These figures are somewhat misleading since most trabeculae and many papillary muscles are ovoid in cross section. Nevertheless, it may be true that, for some muscles under some of the test conditions, the core was both anoxic and inadequately perfused. Thus, some of the changes in compliance we have observed may reflect such conditions. The basic problem is the normalcy of isolated preparations of mammalian cardiac muscle. Since the studies of Cranefield and Greenspan (39) many workers have been concerned about the relationship between the thickness of isolated preparations of cardiac muscle and the adequacy of oxygenation (9). The studies by Fisher et al. (40) show that, in terms of maximum developed isometric tension, such concern is justified. However, a ready solution to the problem is not apparent to us. Few muscles obtained from adult cats are thin enough to meet the strictest criteria (39) for maximum permissible diameter. Although thinner muscles can be obtained more often from kittens (18), we have not employed such muscles because their higher rate of oxygen utilization (39) may more than negate any advantage afforded by their smaller diameter. We have not limited our studies to muscles maintained at low temperatures, as have others (16, 19) because at comparable rates of stimulation the contractions of the cool muscle are increased in strength and duration and the resulting increase in oxygen consumption per beat may more than offset the decrease in resting oxygen uptake which results from the lower temperature (9). We realize that most, if not all, isolated preparations of mammalian cardiac muscle are abnormal in some sense. We believe, however, that the properties demonstrated by the muscles we have used, even to the extent that they result from inadequate diffusion, also may be properties of the heart in situ. Indeed, it is intriguing...
to speculate on possible relationships between changes in the heart produced by ischemia, hypoxia, drugs, or disease and changes in diastolic compliance. Regardless of the conditions primarily responsible for the changes in diastolic compliance, we believe that such changes are real.

If we are correct in assuming that a variable degree of persistent interaction between the contractile elements is responsible for some of the changes in diastolic compliance demonstrated in our records, then it may be correct to ascribe the changes in compliance of the contractile element to various degrees of contracture. We would prefer to restrict the use of this term to a steady change in diastolic compliance (9) and to recognize that at least two other phenomena, delayed relaxation and the development of aftercontractions, may also influence the diastolic compliance of mammalian myocardium and the extent to which the heart will fill with blood when it is acted on by a given force for a given time. We would conclude, in relation to one of the questions posed in the introduction, that the pressure-volume relationship for the heart in situ may vary over quite short periods of time as a result both of geometric changes and changes in diastolic compliance. We believe that the latter may be of considerable importance in the presence of disease, when there are alterations in pressure, flow, and perfusion and when the heart is acted on by drugs.

References


Some Mechanical Properties of Isolated Mammalian Cardiac Muscle
BRIAN F. HOFFMAN, ARTHUR L. BASSETT and HERBERT J. BARTELSTONE

Circ Res. 1968;23:291-312
doi: 10.1161/01.RES.23.2.291
Circulation Research is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1968 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7330. Online ISSN: 1524-4571

The online version of this article, along with updated information and services, is located on the
World Wide Web at:
http://circres.ahajournals.org/content/23/2/291