Symposium on Cellular Aspects of Immunity, Wolstenholme, G. E. W., O'Connor, M., ed., Little Brown & Co., Boston, 1960, 198.

7. Morgan, J. F., Morton, H. J., Parker, R. C., Proc. Soc. Exp. Biol. and Med., 1950, v73, 1.

8. Stavitsky, A. B., J. Immunol., 1954, v72, 360.

9. Ambrose, C. T., Coons, A. H., Fed. Proc., 1963, v22, 266.

10. Ambrose, C. T., J. Exp. Med., 1964, v119, 1027.

11. Kritzman, J., Harper, A., Proc. Soc. Exp. Biol. & Med., 1966, v121, 489.

12. Halliday, W. J., Garvey, J. S., J. Immunol., 1964, v93, 757.

13. Wallace, J. H., Hanks, J. H., Science, 1958, v128, 658.

14. Ehrman, R. L., Gey, G. O., J. Nat. Cancer Inst., 1956, v16, 1375.

15. Gey, G. O., in Carcinogenesis: A Broad Critique (20th Annual Symposium on Fundamental Cancer Research), Univ. of Texas Press, in press.

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Series Elasticity in Cat Papillary Muscle: Increased Stiffness After Segmental Damage. (31958)

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Hill(1-4) has described active muscle in terms of a mechanical model with 3 functionally separate components: (a) an active contractile element (CE) which is assumed to be freely extensible at rest, but which can shorten and develop force with activation, (b) a passive series elastic element (SE) arranged in series with the CE, and (c) a passive parallel elastic element (PE) which sustains resting tension. During isometric contraction, the activated CE shortens and stretches the SE with the development of force in the series elastic in accordance with its stress strain relations. The rate of force development (dP/dt) is thus directly proportional to the CE velocity (dl/dt) and the stiffness of the SE (dP/dl):

$$dP/dt = (dl/dt)_{CE} \cdot (dP/dl)_{SE}$$

The shortening of the CE is described by a characteristic hyperbolic relation between force and velocity(1,7), and the SE behaves like an exponential spring with an extension of 4-5% of initial muscle length (in heart muscle) during an isometric contraction(5).

The mechanics of normal heart muscle have been described in considerable detail(6-9) but there is little information available about muscle mechanics in myocardial damage. In particular, a reduction in the rate of tension development (dP/dt) in damaged muscle might be due either to a reduction in CE velocity (dl/dt) or to a more compliant SE (dP/dl). For example, ventricular aneurysm may be considered as a "series elastic disease" of the intact heart, wherein the effective SE of the myocardium is overly compliant due to ballooning of the aneurysm in systole, thus resulting in a diminished rate of tension development. The possibility that damaged heart muscle might also be overly compliant prompted the present study.

Methods. Each of 5 papillary muscles was rapidly removed from the right ventricles of cats anesthetized with intraperitoneal sodium pentobarbital (25 mg/kg), and was quickly suspended in a 20 cc bath filled with Kreb's bicarbonate solution at a constant temperature of 30°C and bubbled with 95% O_2 and 5% CO_2. Muscle lengths varied from 5 to 8 mm (excluding the tendon) with an average calculated cross-sectional area of .98 mm^2. The non-tendinous end was held by a spring clip extension of a force transducer, while the tendinous end was attached to the tip of a muscle lever(10) with a short length(3-4 cm) of 4-0 silk. The muscles were stimulated with platinum mass electrodes using pulses of 7 msec duration, voltages not more than 20% above threshold, and a stimulation rate of 12/min. Lever movement was detected by a photoelectric transducing system, and preload and afterload were added to a weight holder

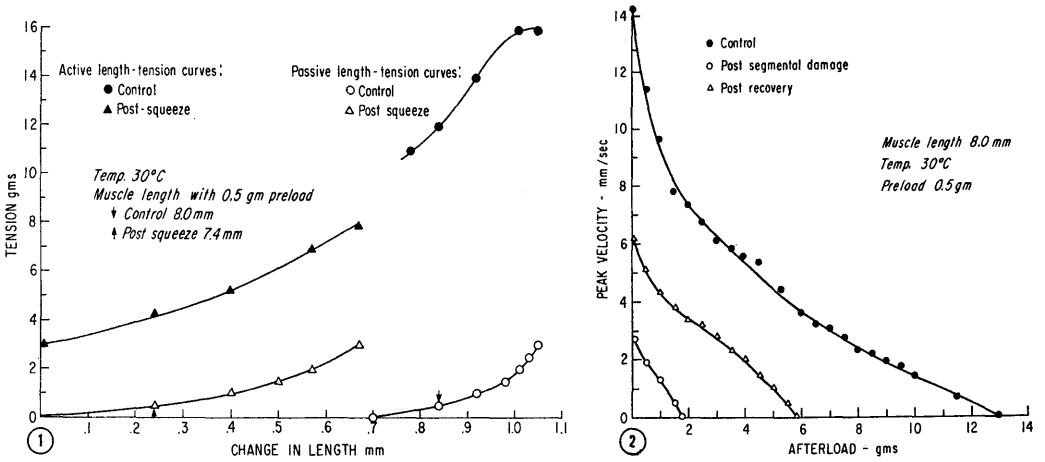

FIG. 1. Representative active and passive length-tension curves before and after segmental muscle damage.

FIG. 2. Representative force-velocity curves before, immediately after segmental muscle damage, and after maximum recovery.

suspended from the lever by a rubber band to produce damping. Force, muscle shortening, velocity of shortening, and a stimulation artifact were recorded on an Electronics for Medicine Recorder. During quick release experiments the muscle was stimulated but initially prevented from shortening by an air jet which held the lever against the micrometer stop. After a preselected delay, the air jet was diverted from the lever by a solenoid activated by a second stimulator, and the lever was free to move. Both rapid shortening and an instantaneous fall in tension occurred, representing the shortening of the SE component. A series of quick releases with afterload varied from zero to isometric force defined the SE extension curve. All measurements were made with a small preload (0.5 gm) so that the contribution of the parallel elastic could be neglected.

After initial stabilization, control force-velocity curves, active and passive length-tension curves, and series elastic extension curves by the quick release method were determined for each muscle. The muscle was then damaged by compressing an end segment of 15% of the muscle length with a pair of small tweezers, resulting in a tachyarrhythmia for about one minute before the muscle returned to the normal stimulated rate of 12/min. The studies done during the control period were then repeated and all data were corrected for the compliance of the equipment (5).

Results. Identical results were obtained in all 5 muscles and a representative experiment is illustrated. Fig. 1 shows the active and passive length-tension curves before and after segmental damage. Note the 0.6 mm passive shortening of the muscle and the marked reduction in developed tension. Fig. 2 illustrates force-velocity curves before, immediately after segmental damage, and after maximum recovery. Note the marked diminution in both velocity of shortening and isometric force development. Since time to peak tension was unchanged, the rate of tension development (dP/dt) was also decreased.

Fig. 3 illustrates quick release series elastic extension curves before, immediately after segmental damage, and after maximum recovery. The control passive length-tension curve is superimposed for comparison. Note that the SE is slightly stiffer than normal immediately following damage and tends to return towards normal with partial recovery of the muscle. If the vertical axis is changed to per cent of initial length, the three curves move closer together, since the muscle passively shortened due to contracture of the damaged segment and some normal muscle adjacent to it.

Discussion. The finding that overall series elasticity was slightly stiffer than normal after

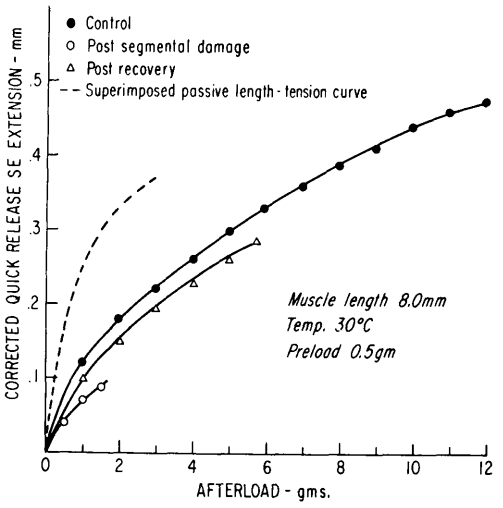

FIG. 3. Representative quick release series elastic extension curves before, immediately after segmental muscle damage, and after maximum recovery. The passive length-tension curve is superimposed for comparison.

damage rather than being more compliant indicates that the reduction in isometric force and rate of tension development were due entirely to a marked reduction in CE velocity. This occurred in spite of the fact that 85% of the muscle was undamaged by the segmental compression. With constant load, instantaneous muscle velocity is a function of instantaneous muscle length regardless of the initial length from which the muscle begins to shorten(9). Therefore, it would appear that much of the reduction in CE velocity after damage was secondary to passive shortening which caused the muscle to begin its active shortening from a decreased initial length. Part of this reduction in CE velocity, however, must also have been due to direct damage of a small portion of the contractile element.

Although these studies have no direct counterpart in the intact heart, it is of interest that recent work with experimental myocardial infarction in dogs(11) has shown that there is no change in the active stiffness of the damaged muscle for several weeks. Only later with healing and scar formation, does the damaged segment become more compliant than normal active muscle. It is conceivable, therefore, that the passive contracture of damaged heart muscle may serve to maintain the stiffness of the SE and thus protect that segment from excessive stretch during contraction of the normal muscle surrounding it. Such a mechanism may protect the heart from the development of ventricular aneurysm occurring as an inevitable sequelae of myocardial infarction.

Summary. After segmental compression damage of 5 cat papillary muscles *in vitro,* resting length shortened, contractility diminished, and the series elasticity (SE) became slightly stiffer as determined by isotonic quick release methods. The marked reduction in rate of force development was not due to an overly compliant SE, therefore, but rather to a decrease in contractile element (CE) velocity. A combination of direct damage to the CE, and the fact that the muscle contracted from a shorter initial length contributed to the reduction in both the contractile element velocity and the rate of tension development.

1. Hill, A. V., Proc. Roy. Soc., London, Ser. B, 1949, v136, 399.
2. ———, ibid., 1951, v138, 325.
3. ———, ibid., 1950, v137, 372.
4. ———, ibid., 1953, v141, 104.
5. Parmley, W. W., Sonnenblick, E. H., Circ. Res., 1697, v20, 112.
6. Abbott, B. C., Mommaerts, W.F.H.M., J. Gen. Physiol., 1959, v42, 533.
7. Sonnenblick, E. H., Fed. Proc., 1963, v21, 975.
8. ———, Am. J. Physiol., 1964, v207, 1330.
9. ———, Fed. Proc., 1965, v24, 1396.
10. Norris, G., Carmaci, P., J. Appl. Physiol., 1965, v20, 355.
11. Forwand, S. A., McIntyre, K. M., Lipana, J. G., Levine, H. J., Circ. Res., 1966, v19, 970.

Received December 5, 1966. P.S.E.B.M., 1967, v124.