instances of increased sympathetic discharge (as in the case of the Figure, at the time of occlusion) they remained unmodified.

We conclude that T3 sympathetic fibres, probably related to the efferent innervation of the heart, are frequently activated by coronary occlusion. This increased discharge is independent of sino-aortic reflexes, as demonstrated by its occurrence in spinal animals. The results obtained in the spinal preparation support the concept that a cardio-cardiac reflex may also occur at a purely spinal level. Reflex reduction in firing rate also occurred, but at variance with what reported by other authors[10,11], it was not the most frequent response. As stimulation of the left stellate ganglion, to which T3 distributes, is known to induce a predominant augmentor effect on the heart[12] it might be suggested, as an hypothesis, that reflex firing in T3 fibres during coronary occlusion might represent an immediate compensatory reaction to decreased contractility of injured myocardium.

Résumé. La décharge de fibres sympathiques préganglionnaires isolées, faisant probablement partie de l'innervation efférente du cœur, a été étudiée sur des chats, soit anésthésiés, soit décérébrés, soit spinalisés, par rapport à l'occlusion d'un segment de l'artère coronaire de gauche.

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Cardiac Muscle: Changes in Optimal Length During Inotropic Interventions[1]

STARLING showed that the energy of contraction of the mammalian heart is a function of the diastolic volume and thus of fiber length[2]. The relationship is such that, as in the case of skeletal muscle, the isometric tension developed during contraction decreases if fiber or muscle length is either greater or less than an optimal value (L_0). There is direct evidence for skeletal muscle that this length-tension relationship depends on changes in sarcomere length and thus on the position of the thick and thin filaments relative to each other[3]. Indirect evidence for the same mechanism has been presented for heart[4]. It has been assumed that changes in the contractile state of heart muscle do not alter L_0: for example, SONNENBLICK has reported that calcium ions and norepinephrine had little effect on the optimal length of cat papillary muscle contracting at 30 beats/min at 25 °C[5].

Because this assumption is crucial to an understanding of the performance of the heart, we have developed a technique which permits repeated, precise determination of the length-tension relationship and L_0 for isolated preparations of cardiac muscle during continuous, programmed increases and decreases in fiber length[6]. This report summarizes the results of 17 experiments on cat papillary muscles in which comparison was made between the length-tension curves obtained before and after an inotropic intervention. In 9 of these experiments there was a significant change in L_0, i.e. after the inotropic intervention the maximum tension developed during isometric contraction was recorded at a muscle length and resting tension remarkably different from the control values.

Papillary muscles were obtained from the right ventricles of cats anesthetized with pentobarbital sodium (30 mg/kg). Muscles were stimulated to contract under isometric conditions at a rate of 45/min in a muscle bath maintained at 37 °C and perfused with a modified tyrode solution[6]. After performance of each muscle had become stable, length was increased and decreased between fixed maximum and minimum values at a constant rate to provide a large series of length-tension curves. Figure 1 A and B shows the results obtained during 10 successive lengthening cycles for 2 different muscles. It is clear that, under constant experimental conditions, both diastolic (resting) and developed systolic (active) tension bear a consistent relationship to muscle length. Figure 2 shows both the control data for another muscle which was stretched just to L_0, the peak of the length-tension curve and the results obtained when norepinephrine ($1.2 \times 10^{-7} M$) was added to the perfusate. The norepinephrine caused the expected increase in developed systolic tension at all lengths and also, as we have shown in previous studies, caused an increase in diastolic compliance such that, at lengths approaching L_0, resting tension was reduced. At the maximum length studied the decrease in diastolic tension was 0.3 g. This change in compliance would have an appreciable effect on the pressure-volume relationship for the intact heart.

However, in relation to the pressure-volume curve and the performance of the intact heart, the most important finding is that after exposure of the muscle to norepinephrine, the apex of the length-tension curve shifted to the left and L_0 decreased by approximately 200 μ. Similar shifts in L_0 were obtained when either paired stimulation or calcium ions were used to increase compliance and developed tension. For the experiment shown in Figure 2 the net effect of the increase in compliance and the shift in L_0 was to decrease the tension required to bring the muscle to optimum length from 9.7 g/mm^2 to 3.2 g/mm^2; the difference between these two values,

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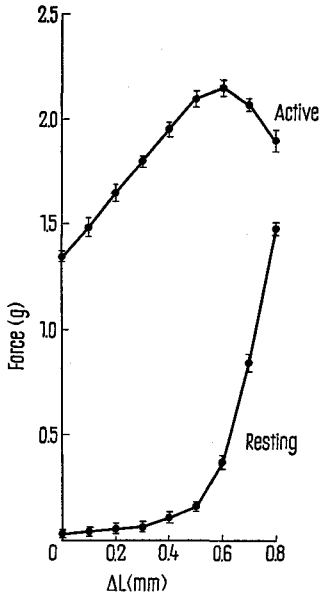

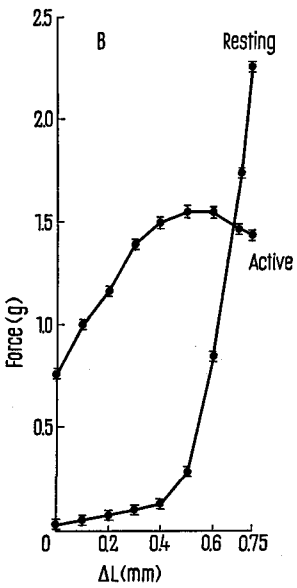

Fig. 1. Data from 10 consecutive lengthening cycles (0.1 mm/15 sec) from each of 2 cat papillary muscles; temperature, 37 °C; stimulation frequency, 45/min. Muscle dimensions, (A) 5.2×0.8 mm; (B) 4.8×0.75 mm. Data are plotted as the mean and range of both active and resting tension (force) at each length.

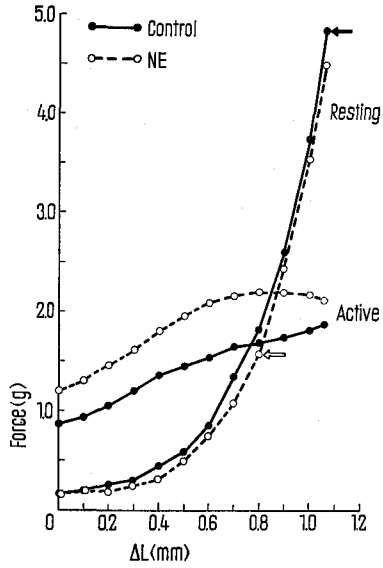

Fig. 2. Data from a control and an experimental cycle of length change (0.1 mm/15 sec) of a cat papillary muscle. Control data are shown by solid lines and filled circles; data during perfusion with norepinephrine ($1.2 \times 10^{-7} M$) are shown by dashed lines and unfilled circles. Temperature, 36.5 °C; stimulation frequency, 45/min; muscle dimensions, 8×0.8 mm. Note the increase in developed systolic tension (force) and decreased resting tension (increased diastolic compliance) during the catecholamine intervention. Also note the decrease in optimal length (length at which maximum systolic tension is developed) during perfusion with the drug. The horizontal filled arrow shows the resting tension at optimal length during the control cycle and the unfilled arrow shows the resting tension at the shorter optimal muscle length during perfusion with the catecholamine.

6.5 g/mm², provides some indication of the change in diastolic pressure which might be required to bring the intact ventricle to the peak of the STARLING curve.

Studies on the cause of the variability in L_0 are in progress and preliminary results suggest that one important factor is variable residual interaction between the contractile elements[7,8] such that elongation of the muscle may cause varying degrees of change in the overlap of the thick and thin filaments. However, even without an understanding of the mechanism responsible for the phenomenon, it is clear that, since an increase in diastolic compliance may be associated with a change in the relationship between muscle length and developed tension, even small changes in compliance, of the magnitudes we have reported[9] may have profound effects on the pressure-volume relationship of the intact heart. Further, one must consider the possibility that decreases in compliance, of similar magnitude, may contribute to the high diastolic pressure developed during cardiac failure and to the progressive impairment of cardiac function. Finally, since it has been shown that the relationship between developed systolic tension and muscle length is not constant for cardiac muscle, this variable must be studied when the contraction of cardiac muscle is influenced by drugs and other experimental variables.

Résumé. Des courbes exprimant le rapport longueur-tension dans le muscle papillaire du chat furent étudiées en comparant des changements successifs de longueur. En traitant la préparation avec des substances inotropes, on produisit souvent des modifications marquées de la longueur optimale. Ces modifications peuvent avoir une importance dans la relation volume-pression du cœur intact.

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