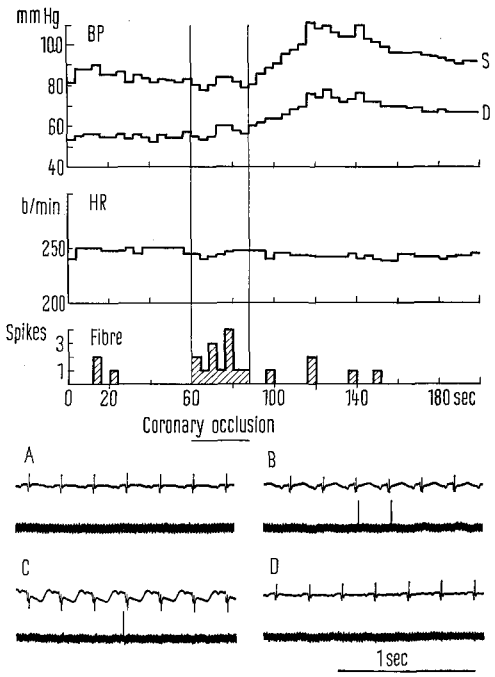
Reflex Activity of Single Preganglionic Sympathetic Fibres During Coronary Occlusion[1]

It is known that during myocardial infarction, resulting either from human disease[2] or from experimental coronary occlusion in animals[3,4] there are hemodynamic changes such as peripheral vasoconstriction, suggesting a reflex sympathetic discharge. This has commonly been interpreted as an effect of sino-aortic afferents compensating for the fall in arterial pressure caused by decreased cardiac output. However, local reflexes independent of general hemodynamics may also occur. Indeed BROWN has recently demonstrated[5] that a transient coronary occlusion provokes an increased discharge in sympathetic afferent fibres in cardiac nerves. We have therefore decided to study (1) whether sympathetic preganglionic fibres, likely to be related to the efferent innervation of the heart, are influenced by coronary occlusion, and (2) whether this reflex response may be independent of general hemodynamic changes and sino-aortic afferents. We concentrated our work on the activity of the left third thoracic (T 3) ramus communicans, which contributes importantly to the efferent innervation of the heart[6].

Method. Sixteen experiments were carried out on anaesthetized cats (pentobarbital sodium or chloralose-urethane), 3 additional experiments on decerebrate cats, and 2 on spinal cats. All animals were immobilized with gallamine triethiodide and artificially ventilated. A segment of the left coronary tree was dissected free of the surrounding myocardium and pericoronary nerve fibres. A thread was loosely passed around it, the ends of which were pulled through a rigid polyethylene tubing whenever the artery had to be occluded. The approach to T3 was retropleural. In most experiments very fine strands of fibres were split under a dissection microscope until a single active fibre was signalled by the recording system. In a smaller number of cases, filaments containing up to about 10 active axons were recorded in order to assess the responsiveness of a small population of fibres. Amplification, cathode-ray tube display (Tektronix 565) and film recording followed standard procedures. Blood pressure, ventilatory cycles, electrocardiogram (lead I) and heart rate (cardiotachogram) were simultaneously recorded on a multichannel inkwriter (Grass P-7). The spike activity was also used to trigger, by appropriate electronic devices, electric pulses corresponding to each spike and a continuous record of sympathetic activity was then obtained on the polygraph.

Results. We recorded from 21 single preganglionic sympathetic fibres, each of which could be recognized as a unit because of the excellent signal to noise ratio in our records (see example in lower part of the Figure). In agreement with previous descriptions[7,8], the spontaneous activity usually consisted of few spikes/sec, its frequency ranging from nearly no activity (as in the fibre shown in the Figure) up to, exceptionally, 50/sec. Several reflex stimuli were tested upon these fibres, as summarized elsewhere[9], but we report here the effects of coronary occlusion only. Occlusion lasted from 20–90 sec and was tested in 88 trials.

Various reflex responses occurred in different fibres, but increased sympathetic discharges predominated. The firing rate of 12 out of 21 fibres increased (tested in 53 trials). Only 2 fibres decreased their firing (6 trials), while the remaining 7 were unaffected (29 trials). In reflexly excited fibres firing rate never attained very high values: still the percent increase was quite marked (see the histogram in the Figure). The latency of this response was sometimes less than a second. An increased discharge was also obtained in spinal preparations. Recording from 3 multifibre strands (9 trials) confirmed that the most frequent reflex response to coronary occlusion is an increase in firing rate (2 strands were excited in 6 trials, while 1 strand was unaffected in 3 trials). Electrocardiographic signs of myocardial ischemia appeared during the occlusion (lower part of the Figure, B and C). Blood pressure and heart rate could both change in either direction, but in several



Upper part of Figure; systolic (S) and diastolic (D) blood pressure (BP) in mm Hg; heart rate (HR) in beats/min (averages of 4 sec epochs); firing rate (as number of spikes in 4 sec epochs) in a single T3 preganglionic sympathetic fibre, before, during and after occlusion of the left coronary artery (signalled by horizontal bar and 2 vertical lines). Lower part of Figure: cathode ray tube records of electrocardiogram (upper tracing) and sympathetic fibre activity (lower tracing), A, just before, B, 1 sec after, and C, 25 sec after beginning of coronary occlusion; D, 23 sec after end of coronary occlusion. Tracing of lower part of Figure are taken from the experiment summarized in the graphs of upper portion. Cat anaesthetized with pentobarbital sodium.

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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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