Influence of Hyperthermia on Myocardial Contractility

The influence of hyperthermia on the contractility of isolated heart muscle has not been extensively studied, and the results of the few investigations reported are inconclusive. For example, HOLLANDER and WEBB[1] noted a decrease in the developed tension of rat heart muscle when the bath temperature was raised from 37 °C to 42 °C. On the other hand, LOCK[2] reported an increase in tension of isolated hens auricles when the temperature was raised from 38 °C to 40 °C. Furthermore NAJAD[3] found, in the heart-lung preparation of the guinea-pig, that performance was unchanged or reduced from 39 °C to 42 °C, while from 43 °C to 44 °C a consistent and marked improvement of performance occurred. They concluded that 'although such high temperature is detrimental to the organism, as far as the heart alone is concerned, this improvement in the heart's performance has a possible survival value' (ref.[3], p. 766).

An understanding of the behavior of the myocardium at higher than normal temperatures is of specific interest in considering the depression of contractility which occurs in an area of the heart subjected to coronary occlusion. It is not known, for instance, whether the depression is due directly to a resultant hyperthermia per se (possible continued residual metabolism without tissue perfusion), to the associated hypoxia, to shifts of tissue pH, or etc.

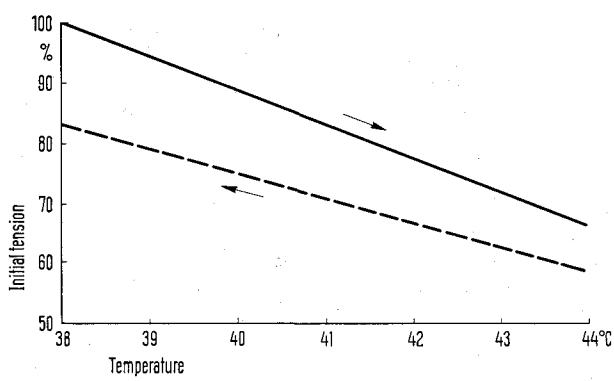
The paucity and inconsistency of data pertaining to the behavior of the heart at elevated temperatures, together with the importance of the subject, have therefore prompted us to undertake the experiment here reported.

Methods. Male Sprague-Dawley rats weighing 100–150 g were used in the experiment. Each animal was decapitated, the heart removed, and the trabecular carneae from the posterior wall of the left ventricle immediately excised. The preparations were placed in a Ringer's bath gassed with 100% O_2, and subjected to a resting tension which stretched the tissue to a length where a nearly maximum isometric contractile response was observed. The muscles were stimulated via punctate electrodes at a rate of 1 stimulus per 2 sec. Characteristics of the preparation and other general details of the technique have been described previously[4].

Twenty muscles were introduced into the bath at 38 °C for a 10 min equilibration period, after which the bath temperature was raised 1 degree every 5–7 min, to 44 °C, while developed isometric tension was continuously recorded. When the muscles had been at 44 °C for 3 min, the bath temperature was returned to 38 °C at the same rate, again with continuous recording of developed tension. Additional preparations were introduced into the bath directly at 44 °C for varying periods of time to check the durability of the tissue at that elevated temperature.

Results and discussion. The Figure shows the influence on isometric tension of increasing the bath temperature from 38 °C to 44 °C. It is apparent that an elevated temperature has a detrimental effect on the contractility. (The slope of the linear regression line was significant, $p < 0.001$.) The Figur also shows that the temperature effect is partially reversible, i.e., the isometric tension for the same preparation increases again as the bath temperature is lowered, the slope of the regression line also being significant, $p < 0.001$. The tension does not recover fully however, and two possible explanations for this 'hysteresis' effect immediately present themselves. First, the effect could simply represent a time decay of tension, irrespective of the induced temperature change. A second possible explanation is that the higher temperatures have in part an irreversible effect on tension development. Both explanations probably have some validity. For example, preparations kept for 30 min or more at 38 °C show a slight but definite loss in developed tension, while those at 44 °C show a steady decline in tension to essentially zero after 15 min. When these later preparations are returned to a bath temperature of 38 °C the tension fails completely to recover. A prior experiment[5] on the same preparation moreover gave indication that the developed tension in the isolated rat myocardium is less stable at higher than at lower temperatures. There seems to be no question but that the increased temperature has a deleterious effect on tension, nevertheless, as the Figure shows, if the time spent at the higher temperature is not prolonged more than a few min, the effect is partially reversible.

The significance of these results with regard to the intact heart relates to the mechanisms by which the myocardium dissipates its heat; i.e., via the coronary circulation and by thermal conductivity through adjacent tissues. One study[6] has shown that the amount of heat removed from the heart via coronary blood flow is proportional to the flow, and that under normal conditions this amounts to about 40% of the total. 60% therefore would be removed by the thermal conductivity through adjacent tissue. With reduced coronary flow an even greater percentage of heat would undoubtedly be removed by thermal conductivity, a less efficient means of heat loss than through the coronary circulation. Under such circumstances one would anticipate an elevated myocardial temperature and as a consequence an impairment of contractility. It has been found in fact, that with complete coronary occlusion in dogs there is an initial and transitory rise in temperature of the occluded area[7]. Considering the result of our experiment then, it is



Influence of temperature on isometric developed tension of isolated rat heart preparations. Solid line obtained from least squares regression analysis as temperature was elevated from 38°C to 44°C; dotted line from regression analysis as temperature was returned to 38°C. Both regression analyses incorporate values from every preparation at each temperature.

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certainly possible that in conditions of partial coronary occlusion modest hypothermia could prove beneficial.

Résumé. On a étudié la tension isometrique des fibres trabéculaires isolées du myocarde du rat, en fonction d'une température de 38–44 °C. On a trouvé que la contractilité était nettement affaiblie aux températures supérieures à 38 °C. Après une courte durée, l'effet est en partie reversible.

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Excitability Changes in Spinal Cutaneous Primary Afferent Terminals Induced by Acoustic Stimuli

Heterosensory presynaptic inhibition at the level of the spinal cord was first demonstrated by Mallart[1] when he recorded lumbar dorsal root potentials (DRPs) in the chloralose-anesthetized cat after acoustic as well as photic stimulation. Recently, Chu[2] studied the effects of auditory and visual inputs on lumbar DRPs and spinal reflexes and found that a conditioning stimulus in either one of these two special senses, which in itself did not evoke lumbar DRPs, inhibited segmentally evoked DRPs while producing a biphasic effect on spinal reflexes. This biphasic effect consisted of an early facilitation of mono- and polysynaptic reflexes at 30–80 msec followed by a depression which reached a maximum at about 300 msec. It became of interest to study the effects of a conditioning auditory input on the excitability of cutaneous primary afferent terminals in the lumbosacral spinal cord. In the following experiments we tested the excitability of sural presynaptic terminals by the method of Wall[3].

Six adult cats were anesthetized by i.p. administration of α-chloralose (40–50 mg/kg), immobilized with gallamine triethiodide (Flaxedil), and artificially respired (4% CO_2 in expired air). The lumbosacral cord was exposed by laminectomy and covered with mineral oil maintained at a constant temperature of 37 °C. Body temperature was also maintained close to 37 °C by a heating pad placed under the cat. Ventral roots of L_6, L_7 and S_1 were sectioned on one side. A branch of the ipsilateral sural nerve was isolated, crushed peripherally, and placed on platinum hook electrodes in a mineral oil pool. DRPs were recorded from a cut dorsal L_7 filament. The excitability of the sural nerve afferent terminals was tested by delivering strong pulses of 0.1 msec duration and 10–50 volt strength through a low resistance 4 *M* NaCl glass microelectrode introduced into the spinal cord just medial to the entry of dorsal L_7 and directed laterally following the technique of Wall[3]. The best response was obtained at a depth of about 1.25 mm. The acoustic stimulus consisted of a train of clicks of various frequencies (300–1000 cycles/sec) and duration (10–40 msec) delivered through a loudspeaker placed about 10 cm away from the ipsilateral ear. The higher frequencies were usually more effective.

A train of clicks produced negative DRPs in a lumbar dorsal rootlet as originally reported by Mallart[1]. When acoustic stimulation preceded sural nerve stimulation, the conditioning auditory input inhibited segmentally-evoked DRPs. This inhibition reached a peak around 50 msec and persisted for over 400 msec. Its time course suggested the presence of a presynaptic inhibitory pathway.

Since cutaneous presynaptic inhibition is effected by depolarization of afferent fibers at their terminals[4], auditory conditioning should increase the excitability of these terminals when tested by direct electrical stimulation. The test pulses delivered through a microelectrode were always submaximal to allow for the recruitment of more fibers in the stimulated area as a result of their depolarization by the conditioning input, and only the fastest, synchronized group of antidromic impulses was considered. Several tracks and depths of sural terminations were explored. At some sites within certain tracks, little or no increase in excitability was observed. But at most sites,

Maximal increase (%) in excitability of sural terminals after acoustic stimulation at conditioning-test intervals of 50, 58 and 75 msec

Experiment	50	58	75
1	67	85	56
2	40	51	36
3	29	80	61
4	14	53	53
5	78	300	210
6	80	204	111

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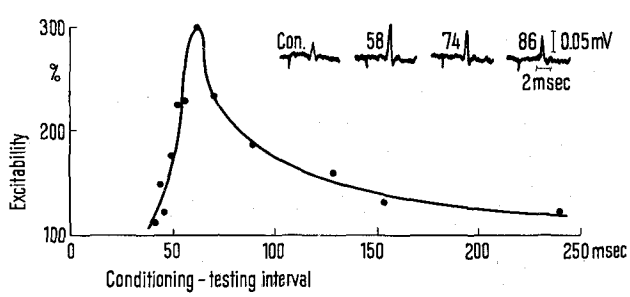

An experiment showing the time course of the increase in excitability of sural afferent terminals after conditioning acoustic stimulation. A low resistance microelectrode was inserted into the dorsal horn and used for test stimulation, the antidromic response being recorded in the ipsilateral sural nerve. This antidromic response was taken as control, and the increase in its size by conditioning acoustic stimulation is expressed as percentage on the ordinate, while the conditioning-test intervals are indicated on the abscissa. The inset shows at left the control antidromic response after stimulation of the sural terminals, followed by the response at the indicated intervals.