RESPONSES OF THE CONTRACTILE MECHANISM OF UNSTRIATED MUSCLE

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UNSTRIATED muscle which has been killed by heat, is a suitable preparation for the study of certain effects of substances on the contractile mechanism (Singh, 1954 *a*, *b*, *c*; 1955 *b*). Thus substances which denature proteins, cause it to lengthen actively; certain substances which coagulate proteins, cause it to contract. Of particular interest is the contraction produced by strong hydrochloric acid; it simulates the contraction produced through the excitatory mechanism (Singh, 1955 *a*). Heat also produces contraction. In the present research the properties of this heat induced contraction have been investigated.

EXPERIMENTAL

The experimental procedure has been described previously (Singh and Singh, 1954 *b*, *c*). These experiments were performed on strips of circular muscle from the stomach of the frog, *Rana tigrina*, and from dog's stomach. The muscles were killed by heating to 50° C. for 10 minutes. To produce the contraction by heat, the heat killed muscles were suspended in air at room temperature (18–20° C.), and then the contraction was produced by immersion in saline of the required temperature.

RESULTS

Effect of heat.—The effect of heat depends upon the temperature to which the muscle had been previously treated. If the unloaded muscle is killed by heating to 50° C., and then restored to 20° C., heating it again to 50–60° C. under loaded conditions, causes it to relax only (Fig. 1). Unloaded muscle previously killed by heating to 50° C. relaxes actively if heated to 60° C. (Singh and Singh, 1954 *a*, *b*, *c*). Active relaxation is best demonstrated on frog's stomach muscle; it is abolished if the muscle is heated to 65–70° C.

If heated to 65–70° C., the muscle behaves quite differently. It shows a reversible contraction with increase of temperature (Fig. 2). In these experiments the muscle was initially kept at 20° C., after being killed by heating to 70° C. The temperature was then raised to 40° C. and higher

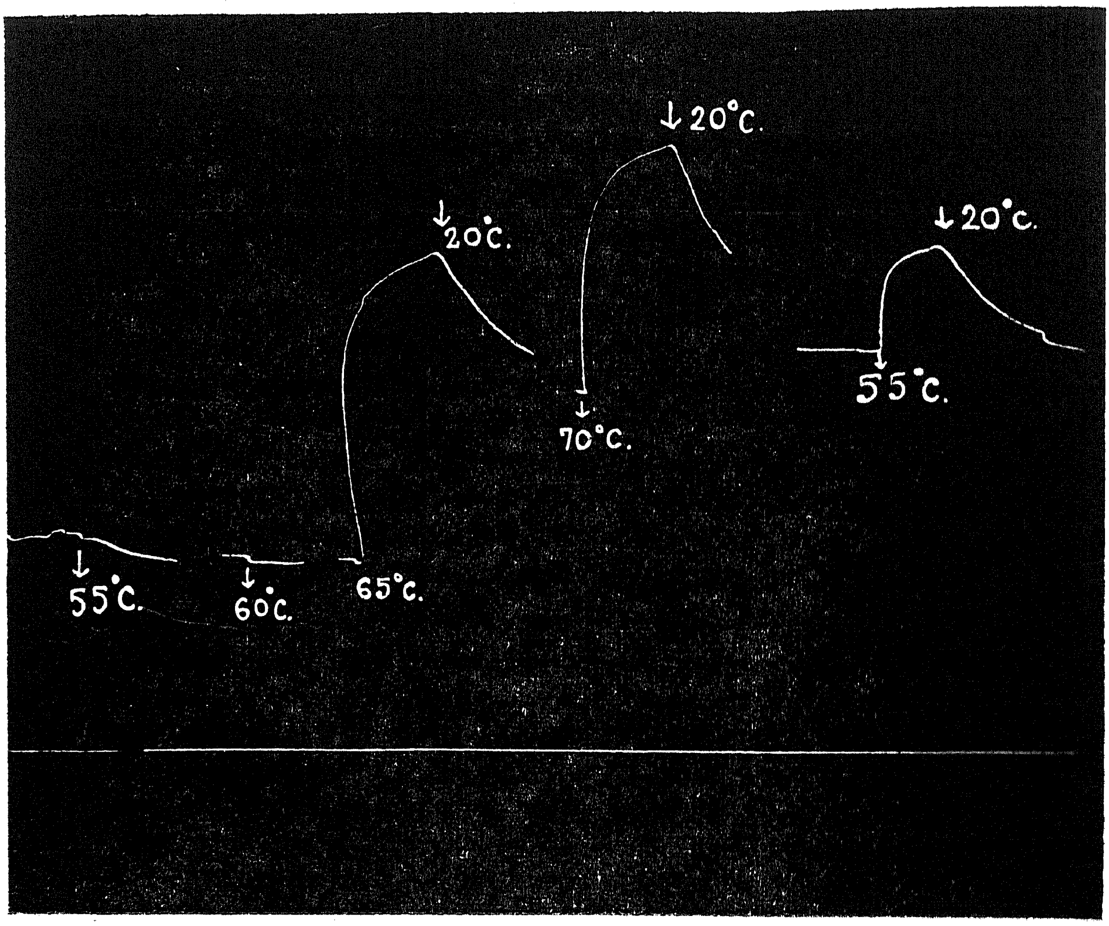

FIG. 1. Dog's stomach muscle killed by heating to 50° C. and then suspended at 20° C. after each response the muscle is brought back to 20° C. At first 55° and 60° C. cause relaxation only. After the muscle is heated to 70° C., they cause contraction.

values up to 98° C. These values were increased in steps of 5° C. from 40° C. onwards. The tension varies linearly with temperature up to 80° C.

For further study, the thermal contraction was produced by raising the temperature of the heat-killed muscle to 70° C. each time, the initial temperature being 20° C.

Sensitivity of different parts of the stomach.—The thermal contraction of heat killed dog's stomach muscle is maximum at the cardiac end; it diminishes towards the pyloric end, though at this end also, the response may increase. These effects resemble those produced by hydrochloric acid (Singh and Singh, 1955 *a*). This shows that the contractile mechanism of unstriated muscle is a variable entity. The muscle from the cardiac end, though it contracts powerfully relaxes comparatively slowly, when compared with that from other parts of the stomach. Striated muscle from dog's rectus abdominis also contracts powerfully and relaxes very slowly. This

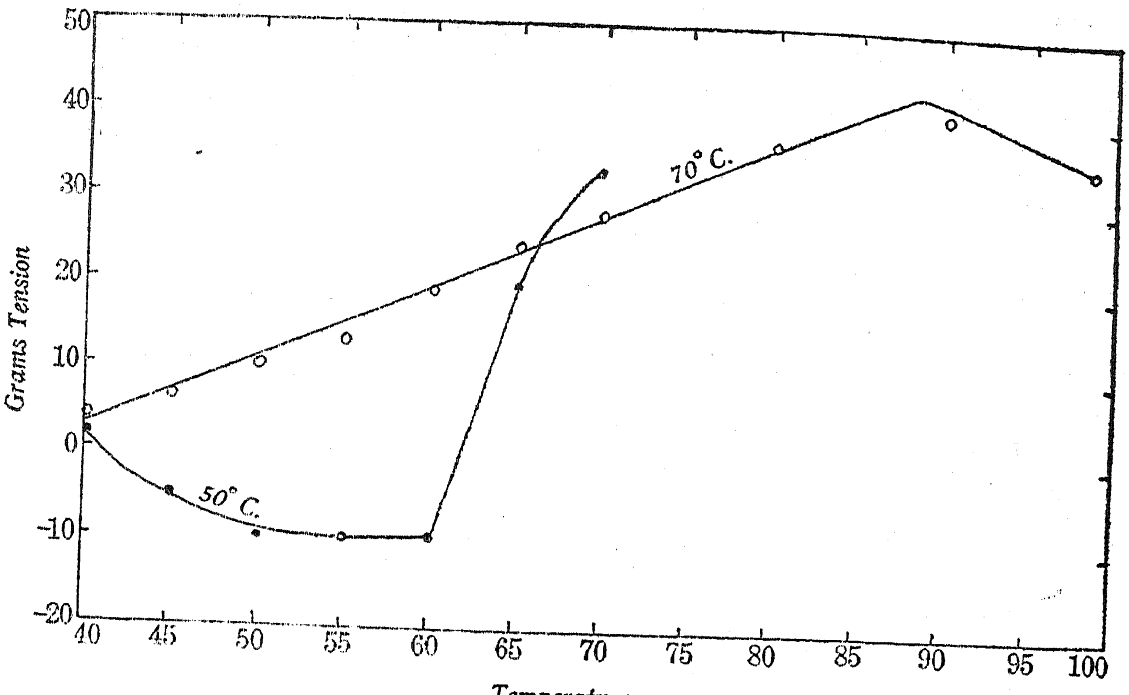

FIG. 2. Dog's stomach muscle killed by heat. Upper curve produced by varying temperatures in muscle at first heated to 70° C. Lower curve by muscle killed by heating to 50° C.

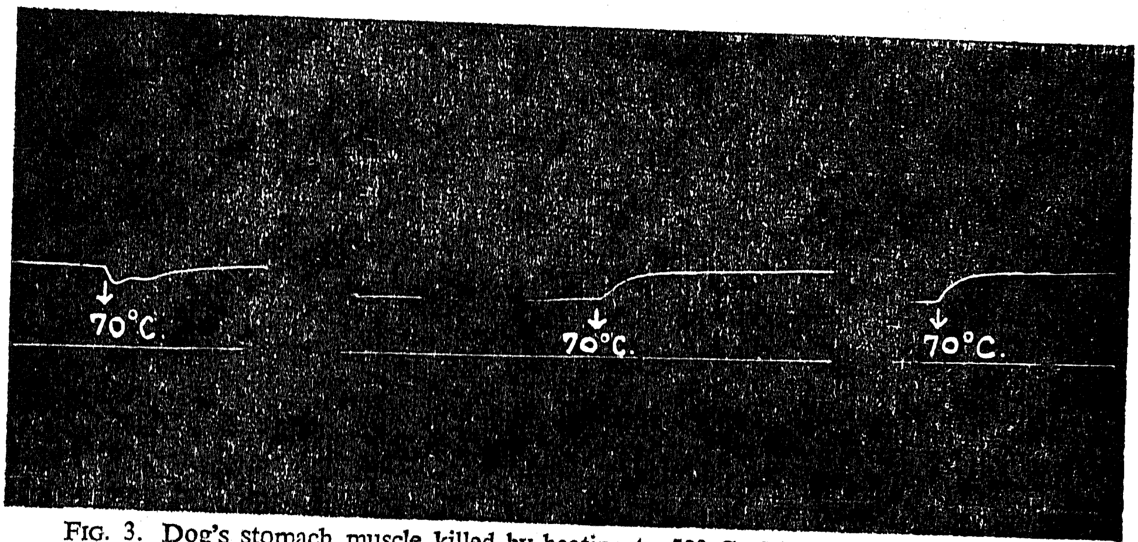

FIG. 3. Dog's stomach muscle killed by heating to 50° C. The second and third responses show the beneficial effect of contraction. The initial dip in the first response is a buoyancy effect, due to immersion of the muscle from air into heated saline.

suggests that the normal response of the contractile mechanism of unstriated muscle is the net result of two opposing forces, which may operate simultaneously; one produces contraction and the other relaxation. The contraction is more powerful if the relaxation is slow, that is, if it is not partially antagonised by simultaneous rapid relaxation. The muscle may, therefore, be contracting and relaxing simultaneously. This explains the difference between the sensitivity of muscle from various parts of the stomach.

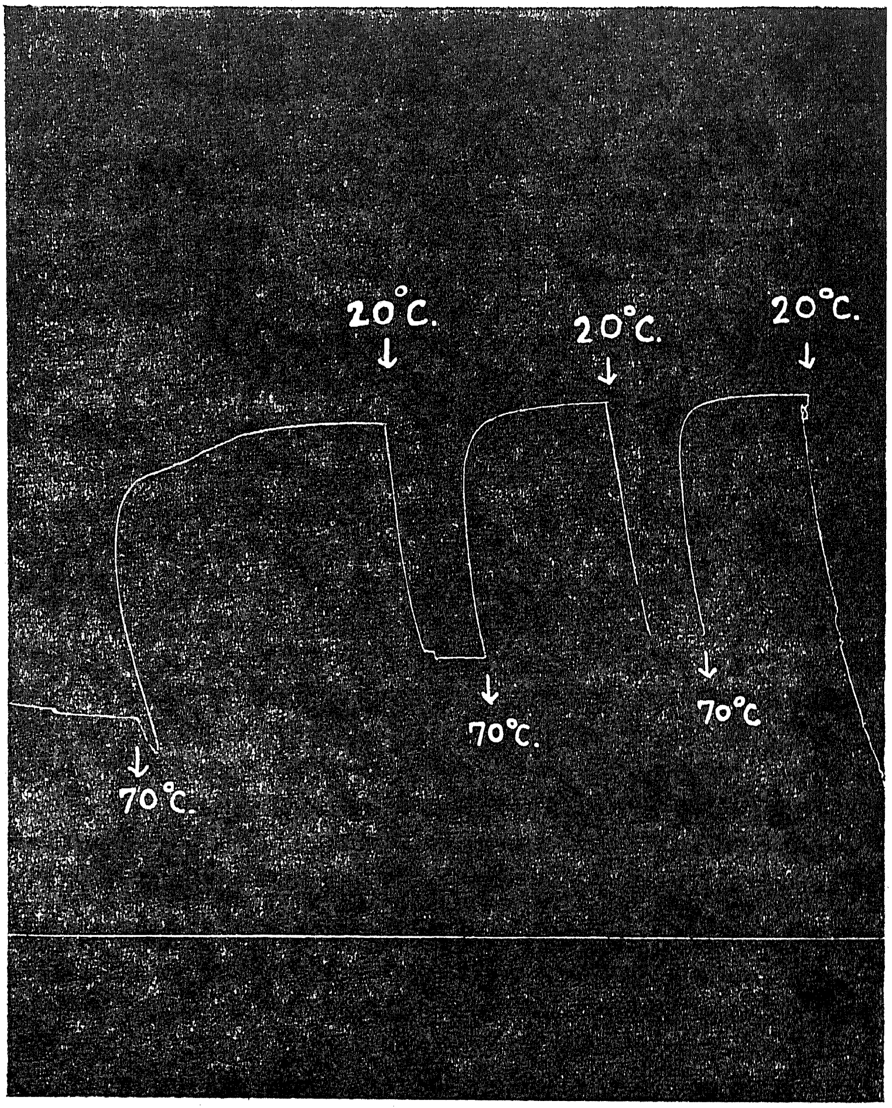

FIG. 4. Dog's stomach muscle from the cardiac end, killed by heating to 50° C. shows fatigue.

Staircase.—The staircase phenomenon or the beneficial effect of contraction is shown by the thermal contraction of dog's stomach muscle (Fig. 3). This effect, shown by living muscle, therefore appears to be a property of the contractile mechanism. This is further suggested by the fact that the staircase effect in dead muscle is most marked when the initial response is small, as in muscle from middle part of the stomach or from near the pyloric end. This exactly resembles the staircase effect in living muscle.

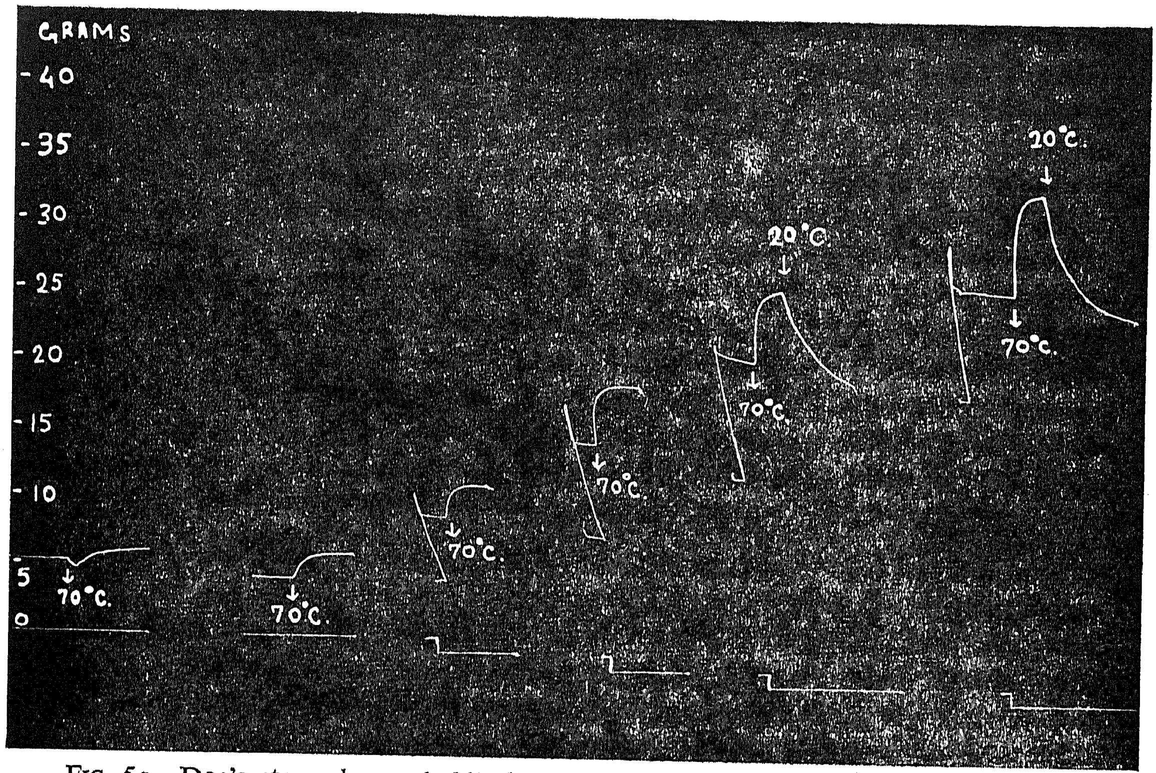

FIG. 5*a*. Dog's stomach muscle killed by heating to 50° C.; shows the effect of initial length on tension.

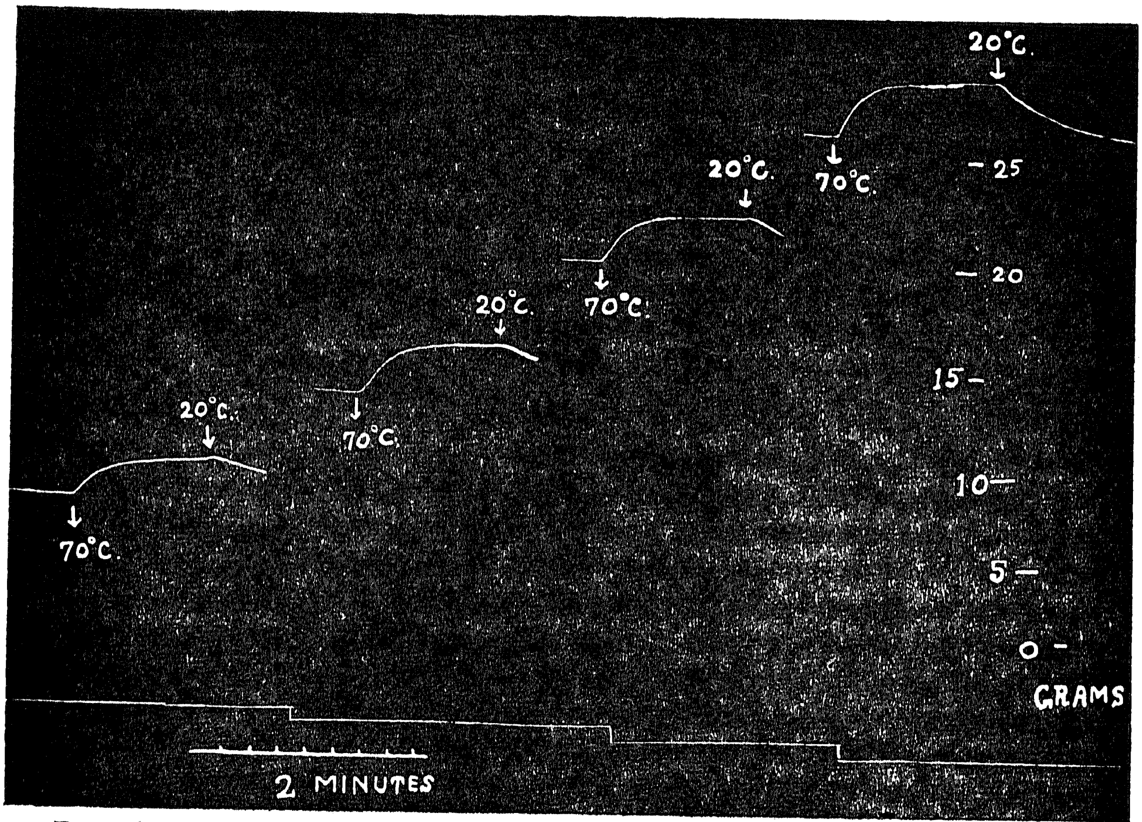

FIG. 5 *b*. Frog's heart killed by heating to 50° C. (*Rana tigrina*). Suspended as an ordinary piece of unstriated muscle. Effect of initial length on tension. Length increased by 3-4 per cent each time. Note last contraction is double the first.

In living muscle the staircase effect is most marked if the initial response to alternating current is small. If the response is initially large, then by a little excess of potassium in the saline, or other depressant ions, the initial response of the living muscle can be depressed; the staircase effect is then very pronounced.

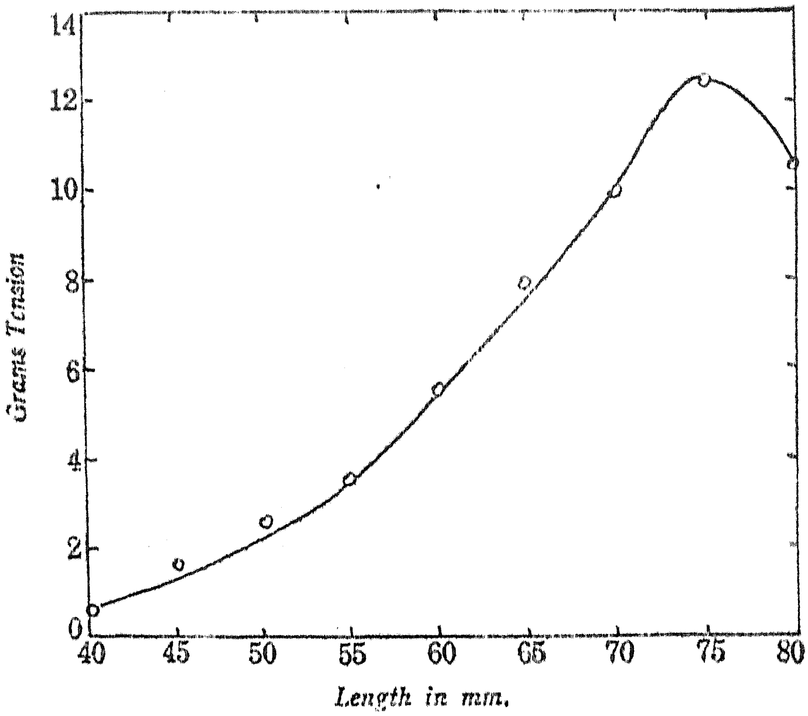

FIG. 6. Dog's stomach muscle killed by heating to 50° C.; shows the effect of initial length on tension.

Fatigue.—If the heat killed dog's stomach is made to contract frequently, then "fatigue" sets in. Relaxation becomes incomplete, so that the muscle passes into a contracted state (Fig. 4). This occurs especially in muscle from the cardiac end, in which the thermal response is large. These phenomena simulate those found in living muscle. In living muscle it is found that if the initial contraction is large, then fatigue sets in rapidly, and relaxation may be incomplete. Some changes in fatigue which are shown by living muscle, are therefore due to the contractile mechanism.

Effect of initial length.—The thermal response of dead muscle increases with the initial length up to a certain point (Fig. 5 *a*, *b*) therefore, there is an optimum length for contraction (Fig. 6). These effects, therefore, resemble those produced by hydrochloric acid (Singh and Singh, 1955 *a*). This property, found in living muscle, therefore, resides in the contractile mechanism.

It was not possible to demonstrate this property in striated muscle, as the relaxation is very slow. In dog's heart muscle, the thermal contraction was feeble owing to non-linear arrangement of fibres in the pieces of muscle used. The effect of initial length is best demonstrated with pieces of muscle obtained by transverse sections of the right ventricle. The whole of the frog's heart can be used and suspended like a strip of unstriated muscle (Fig. 5 *b*). In striated muscle, the heat contraction is not reversible as indicated by the

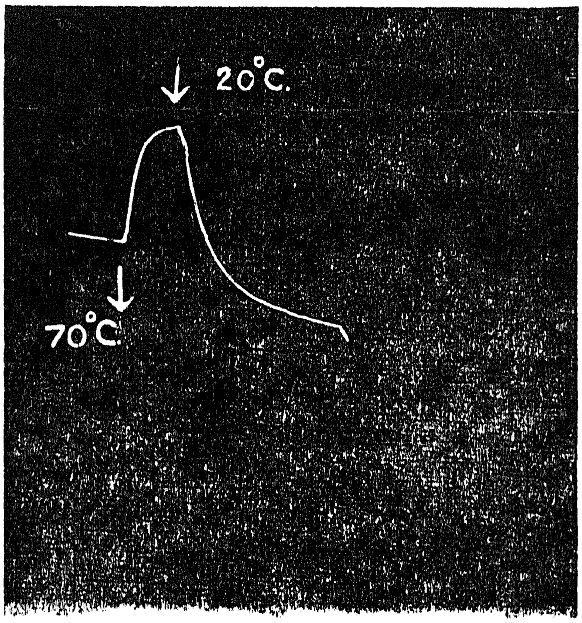

FIG. 7. Dog's stomach muscle killed by heating to 50° C.; shows the relaxation of the thermal contraction beyond the starting point.

slow relaxation, and in cardiac and some unstriated muscles it is partially reversible; this results in a partial tonic contraction, on which reversible contractions can be superimposed, and thus the responses of the contractile mechanism studied. Starling's law of the heart is well demonstrated in this way. It was also demonstrated by contraction produced by hydrochloric acid (Singh and Singh, 1955 *a*).

Antagonism to tonus.—The thermal contraction of dead muscle appears to be antagonistic to tonic contraction. In living muscle, tone decreases after a response to alternating current (Singh, 1938 *a*, *b*). If initially tone is great, then the response to alternating current is small, but the subsequent relaxation is more marked. These effects have been ascribed to decrease in viscosity (Winton, 1937). These results are also shown by dead muscle. The muscle continues to relax beyond the starting point after a thermal contraction (Fig. 7). If the initial response is small due to greater tone, then the subsequent relaxation is more marked (Fig. 8).

Relaxation.—The relaxation of dead muscle when heated to 50–60° C. is active (Singh and Singh, 1954 *a*, *b*, *c*). But if the muscle is heated to

65–70° C., then the relaxation of the thermal contraction is passive. By active relaxation of dead muscle is implied that it relaxes without the application of an external force.

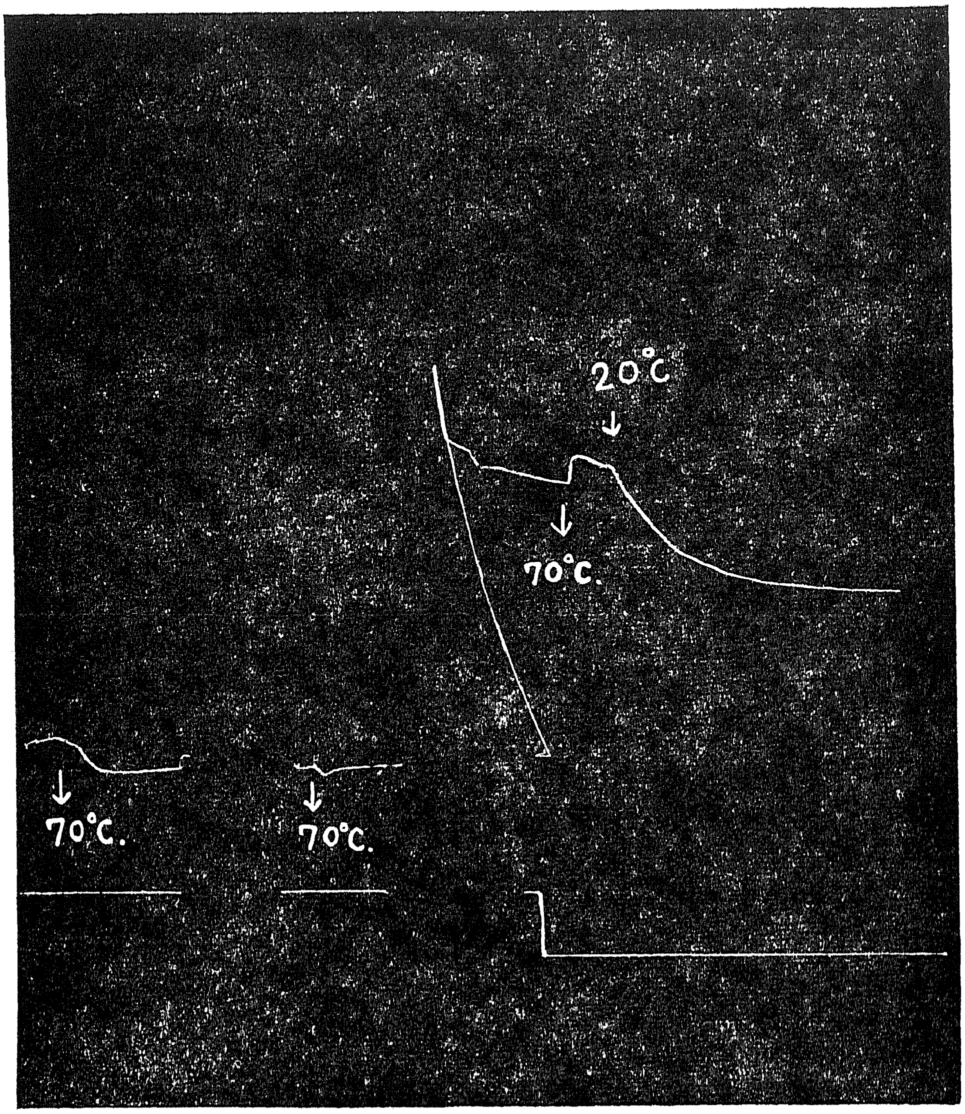

FIG. 8. Dog's sromach muscle killed by heating to 50° C. The muscle is not very sensitive; so the initial length is increased. The initial tension now increases. The thermal response has now increased. But the muscle relaxes much beyond the starting point.

It has been shown above that if the muscle has been previously heated to 50° C. then heating to 50–60° C. produces only relaxation or a feeble contraction. After one of the relaxing mechanisms has been inactivated by heating to 70° C., the thermal response increases. This again suggests that the normal response of unstriated muscle is the net result of two opposing forces. One produces relaxation and the other contraction; if the former is inactivated, then the contraction is increased. The muscle may thus be contracting and relaxing simultaneously. The relaxing mechanism may also be inactivated by increase in initial length; this is probably one of the causes which produces increasing tension with increase in initial length. The effect of increase in initial length in antagonising inhibition, is well shown in living muscle.

Discussion

These experiments show that the contractile system of unstriated muscle consists of two components; in one the relaxation is active and in the other passive. The former is inactivated by heating to 70° C. Further the contraction of dead muscle, in which the relaxation is passive, resembles the twitch contraction. These experiments, therefore, substantiate the views mentioned previously that unstriated system consists of two systems; in one the relaxation is active and in the other, passive (Singh and Singh, 1950, 1951 *a*; 1952; Singh, 1953).

The system in which the relaxation is passive, consists of two components; one component is inactivated by heating to 70° C., as the relaxation becomes very slow. Striated muscle contains predominantly this component, and this may therefore be termed as striated muscle component (SMC). In some unstriated muscles, there is a component relaxing passively, which is not inactivated by heating to 70° C.; this may be considered as a pure unstriated muscle component (UMC). Cardiac muscle and some unstriated muscles are of intermediate variety. It is interesting to note that histologically also, cardiac muscle is intermediate between striated and unstriated muscles. There is thus a correlation between histological appearance and the response of the contractile mechanism of muscle. Muscle therefore appears to be made of two structural components (SMC and UMC), which relax passively, in addition to the component which relaxes actively (ARC, active relaxation component). Different muscles differ in having these in different proportions.

The properties of the thermal contraction show that the staircase effects and fatigue phenomena are at least partially due to the contractile mechanism, though the excitatory system may also be involved in living muscle. Contractions produced by heat and by hydrochloric acid show that the increasing tension produced by increase in the initial length, is due to the contractile mechanism.

These experiments also show that the contractile mechanism of unstriated muscle is a variable entity; this was also shown by contraction of dead muscle produced by hydrochloric acid,

SUMMARY

1. The properties of the contractile mechanism of unstriated muscle have been studied by recording the contraction of heat killed muscle, produced by raising its temperature to 70° C.

2. The effects of heat show that the contractile mechanism of unstriated muscle consists of two components; in one the relaxation is active and in the other passive. The latter again consists of two parts one of which is activated by heat.

3. The thermal contraction of heat killed unstriated muscle resembles the phasic response of living muscle.

4. The thermal response of heat killed unstriated muscle shows staircase and fatigue effects. It increases with initial length up to a certain point, so that there is an optimum length of muscle for its production. These phenomena in living muscle are therefore properties of the contractile mechanism.

5. Starling's law of the heart is also shown by thermal contraction of dead muscle.

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