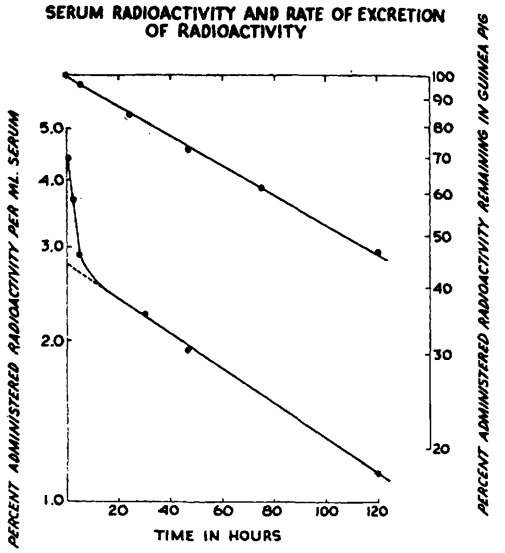

FIG. 1. Serum radioactivity and rate of excretion of radioactivity in 5 guinea pigs following intravenous administration of I^{131} trace iodinated rabbit globulin.

being pooled in the thyroid or in other tissues. Kreiger *et al.*(13) have shown that I^{131} labelled protein slowly enters the thoracic duct lymph and has correlated this initial rapid rate of disappearance of activity with the dilution of the labelled protein in the lymph space. In view of these findings extrapolation of the slower rate to zero time should yield the total volume into which the protein mixes. This calculation, based on a composite curve of 5 guinea pigs, yields a final protein dilution volume of 7.58 cc/100 g body weight, if the concentration of the foreign protein in this larger volume is the same as in the blood. The estimated value gives a minimum volume, since this volume is inversely proportional to the concentration of protein found in this fluid. The 8 to 15-minute dilution volume (peripheral plasma volume) therefore constitutes a maximum value of 59% of the total body fluid volume into which the protein is diluted. The "globulin space" is probably made up of an undetermined number of compartments, which include liver lymph, thoracic duct lymph and other extravascular globulin spaces, since the initial rapid decrease in the serum activity curve is not a single exponential rate.

Summary. (1) The blood and plasma volumes of guinea pigs were determined by the dilution of I^{131} trace iodinated rabbit globulin. (2) The average 8 to 15-minute dilution blood volume was found to be 7.53 $\pm$ 0.71 cc† per 100 g body weight, and the average plasma volume was 3.94 $\pm$ 0.37 cc† per 100 g body weight. (3) The labelled protein was found to mix slowly over a period of 20 hours into a larger body fluid volume which was found to have a minimum value of 7.58 cc/100 g body weight, which includes the peripheral plasma volume and a number of undetermined compartments.

Received September 6, 1951. P.S.E.B.M., 1951, v78

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Shortening of Uterine Muscle at Different Temperatures. (19041)

ARPAD CSAPO* AND GEORGE W. CORNER.

From the Department of Embryology, Carnegie Institution of Washington, Baltimore, Md.

The experiments here reported show that the amount of shortening of uterine muscle when contracting *in vitro* is a function of temperature. There are no previous reports on this question as regards uterine muscle. On smooth muscle in general there is only one report(1), on the dog's retractor penis, and this deals with only a narrow temperature range (16°-35°C). The literature on the relation between temperature and shortening of

* Lecturer in Obstetrics, Johns Hopkins University.

1. Winton, F., *J. Physiol.*, 1927, v63, 28.

skeletal muscle is summarized by Fenn(2) and by Hajdu and O'Sullivan(3). The question has an important bearing upon the thermodynamic concept of muscle contraction, recently emphasized by Szent-Györgyi, which has led to new experimental approaches. Varga, in association with Laki(4), found that the degree of shortening of washed frog and rabbit muscle, elicited by adenosine triphosphate, is a function of temperature. The same was found true of the contractile substance of skeletal muscle in a state still further removed from the living condition, *i.e.*, threads of actomyosin extracted from the muscle. Szent-Györgyi(5) made the assumption that the contractile matter is built of small units which obey an equilibrium reaction of the first order, and that the shortening of the whole muscle is the expression of the shortening of these units, which have been called autons. The autons are supposed to act in all-or-none fashion. Under these assumptions, the length of the muscle indicates the relative number of relaxed and contracted autons, which is the equilibrium constant (K) of the reaction. Since equilibrium reactions are directly influenced by temperature, the graph of log K plotted against 1/T should give a straight line.

These assumptions, and the general justifiability of applying thermodynamics to muscle, have been criticized by Hill(6) and restated by Szent-Györgyi(4). Recently Hajdu(7), Hajdu and O'Sullivan(3), and Varga(8) have extended their observations to living muscle of the frog and rat and to glycerol-treated rabbit muscle. They find that both the tension and the shortening developed by these muscle preparations depend quantitatively upon temperature. Although the present authors are not prepared to discuss the applicability of thermodynamics to muscle contractions, the present experiments are presented as relevant to the discussion.

Strips of uterine muscle were prepared from rabbits in estrus. Immediately after mating the animal was anesthetized with intravenous Nembutal. The uterine horns were quickly removed and immersed in pre-oxygenated modified Locke solution at 0°C at pH 7.0 (NaH_2PO_4 buffer). Identical segments 2.5 cm long, 0.5 cm wide and weighing about 2 g were cut from the uterine horn, and placed in 50 ml tubes of the recording apparatus. The tubes were filled with the modified Locke solution, which was kept oxygenated at 2.0 vol. %. The bath temperature was 35°C. A constant load of 3 g (including friction) was applied. Two strips were used simultaneously as mutual controls. The length of the writing lever and other kymographic details were kept constant. For a detailed description of the method see Csapo and Corner(9). Electrical stimulation was provided by 20 volt, 60-cycle alternating current passed through the tissue between the 2 platinum hooks. Stimulation was applied for a 5-second period once every 2 to 4 minutes, depending upon the speed of a single contraction-relaxation cycle, which also varies with temperature. Since a stimulation-potential of 10 to 15 volts causes maximal amplitude of contraction, the 20-volt stimulus is supermaximal, and thus it may be assumed that the whole mass of contractile substance is reacting. The relatively high potential also assures a pattern similar to that of spontaneous contractions. After recording 3 contractions at a given temperature, the temperature of the water bath surrounding the tubes was changed in about 2 minutes and an additional 8-minute period was allowed for adjustment to the new temperature. Observations were begun at 35°C and the temperature was decreased by 5°C at each step to 5°C. Then, in order to exclude changes in amplitude due to fatigue the temperature was raised by 5°C steps to 45°C, recording 3 contractions at each temperature as before.

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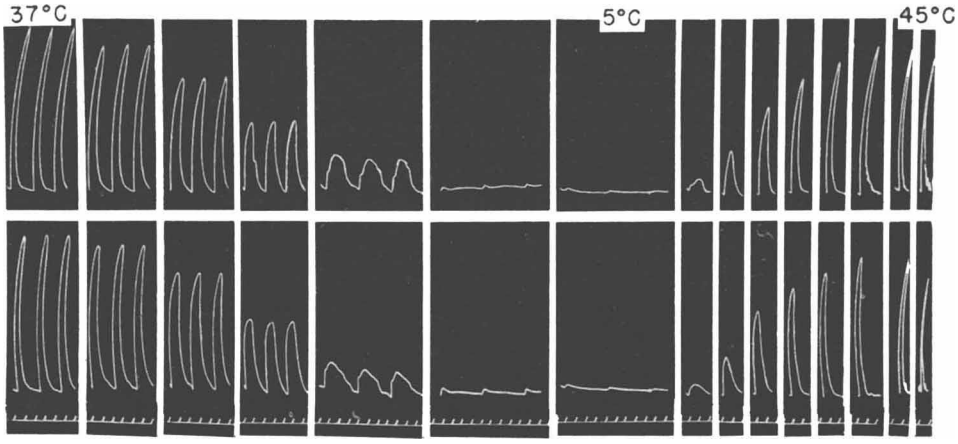

FIG. 1. Amplitude of electrically-stimulated contractions. Simultaneous runs with identical strips from an estrous rabbit. Temperature changes, by 5° steps, indicated by vertical white spaces. Time intervals, 1 min.

After several preliminary experiments on sows' and rabbits' uteri, 8 strips were recorded from 3 rabbits in estrus and from one 28 days pregnant. Fig. 1 represents two runs. As the temperature is decreased the amplitude (extent of shortening) simultaneously decreases step by step until at 5°C the shortening, even though magnified by the lever, is scarcely noticeable. As the temperature is again increased, the amplitude increases up to 35°C. At 40°C however, the behavior of the muscle changes and instead of increase in amplitude there is a decrease, which goes further with increasing temperature. It can also be seen that the speed of both contraction and relaxation decreases with decreasing temperature.

The experimental apparatus and conditions having been carefully standardized, it is possible to combine the results in a plot of amplitude against temperature. Fig. 2, summarizing the outcome of 14 experiments on the 8 strips used, shows graphically the relation described above. This curve has two directions of slope from the peak at or near 35°C. Only that phase between 5° and 35° has thus far been studied in detail.

Fig. 3 compares the amplitude of spontaneous contractions with those electrically induced and shows they are alike both in amplitude and in the speed of contraction and relaxation. This indicates that the reaction (or series of reactions) resulting in spontaneous contraction is also dependent upon temperature.

The amplitudes in the temperature range 10°-35°C were plotted against 1/T, by the formula log A/B in which A is the recorded amplitude at each temperature and B the maximal amplitude minus A. A straight line was obtained as in the work on skeletal muscle cited above. It should, however, be mentioned that use of the logarithmic quantity tends to lessen the fluctuations of the curve and thus to straighten it out.

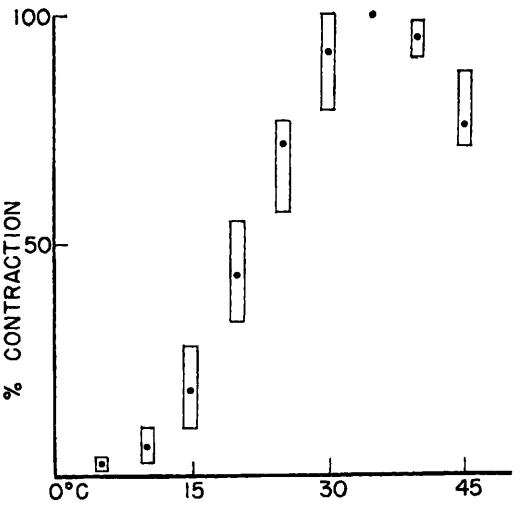

FIG. 2. Extent of contraction at each temperature, plotted as % of maximum, against the temperature. Dots indicate averages of 14 experiments, bars indicate ranges observed.

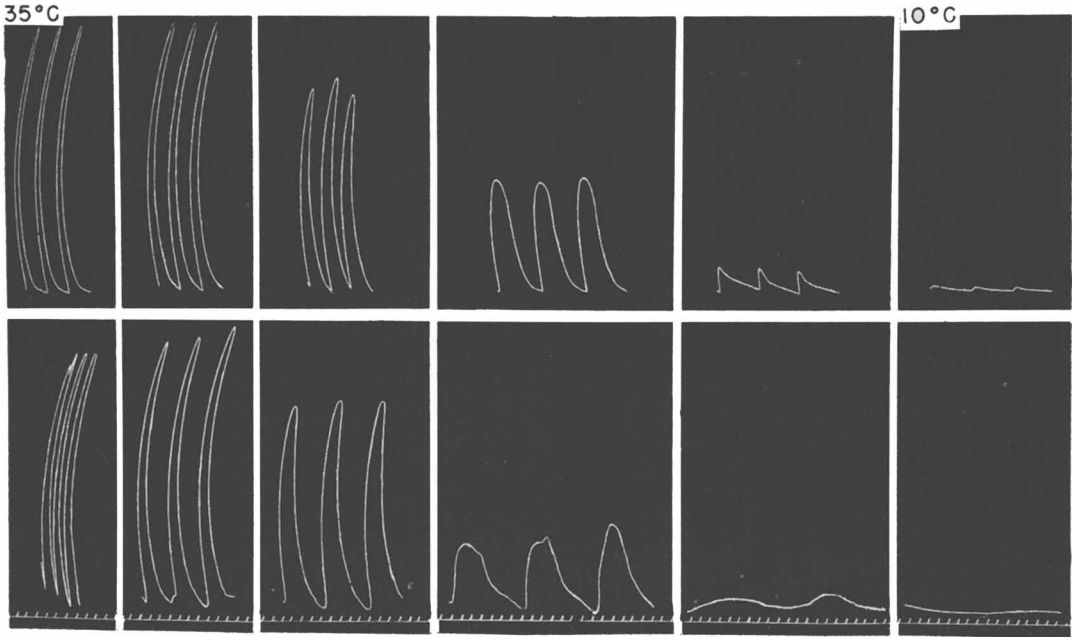

FIG. 3. Comparison of spontaneous with electrically-stimulated contractions. Rabbit 28 days pregnant. Temperature changes, by 5° steps, indicated by vertical white spaces. Time intervals, 1 min.

Summary. In agreement with the observations of others on skeletal muscle, strips of uterine muscle from rabbits in estrus undergo changes in the extent of shortening in relation to temperature. The speed of contraction and relaxation also varies with temperature. These effects occur equally whether the contractions are spontaneous or electrically simulated.

Received September 6, 1951. P.S.E.B.M., 1951, v78.

Invasiveness of Fibrosarcomata in Mice.* (19042)

LEONELL C. STRONG.

From Yale University School of Medicine, New Haven, Conn.

It has been shown that the characteristic of invasiveness of chemically induced fibrosarcomas (the presence of discrete nodules in the abdomen derived either by direct extension of the tumor or by the process of metastasis) is partially determined by some new principle found in the host which had been derived from its ancestry and differentially determined by litter seriation(1). These conclusions were based upon observations on 788 mice of 2 descents (Prunt and 2Prunt), which were genetically related to each other (17 generations of inbreeding in common).

In the first analysis of an association between invasiveness of fibrosarcomas and litter

* This experiment has been made possible by grants from The Anna Fuller Fund, The Jane Coffin Childs Memorial Fund for Medical Research, and The James Hudson Brown Memorial Fund of Yale University School of Medicine. The statistical analysis of the data has been done by Dr. H. Auerbach of Yale University, School of Public Health.

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