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THE DELAYED ANAEROBIC HEAT PRODUCTION OF STIMULATED MUSCLE.

By H. BLASCHKO[1].

(*From the Department of Physiology and Biochemistry, University College, London.*)

THE delayed anaerobic heat production (d.a.h.p.), after a tetanic stimulus in muscle, has been the object of several investigations since the first description of it by Hartree and Hill [1922]. Various explanations of it have been proposed, none of which, however, is very convincing. In their last paper on the subject Hartree and Hill [1928] suggested that the delayed heat might be due to an excessive stimulus of those muscle fibres which lay immediately on the electrodes. This explanation, however, had to be abandoned when Hartree [1929] showed that the same phenomenon occurs after stimulation of the muscle through its nerve.

The present experiments represent a critical examination designed to answer the question whether the effect is really due to an active process of some kind, or whether its appearance is artificial and caused by some peculiarity of the apparatus or of the method of calculating the results. Several possible causes have been examined, none of which gives a satisfactory explanation of the d.a.h.p., and we are again forced to the conclusion that its appearance after a tetanic stimulus is genuinely due to some process occurring in the muscle.

(*a*) *A temporary rise in the osmotic pressure.* It has been shown by Hill [1929, 1930] that a rise of osmotic pressure in a muscle on a thermopile causes an apparent heat production due to a decrease in the vapour pressure and a consequent difference in the rate of condensation of water on its surface. This rise of osmotic pressure has been recognized as the explanation of the increment in resting heat rate resulting from anaerobic stimulation. It seemed possible, therefore, that the d.a.h.p. was due to a temporary rise of osmotic pressure lasting for a few minutes after a contraction: such a rise might be caused, not perhaps by a change in the concentration of lactic acid, but by some other chemical process

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occurring within the period stated, *e.g.* by an alteration in the phosphagen system of the muscle.

The possibility, however, of water condensation as an explanation could be excluded by placing the thermopile carrying the muscle in an environment in which water evaporation did not occur. Experiments were made, not as usual in an atmosphere of nitrogen saturated with water vapour, but in a chamber filled with liquid paraffin oil, anaerobic conditions being guaranteed by bubbling nitrogen through the chamber. The results were indistinguishable from those obtained in a long series of recent observations by Mr W. Hartree, of Cambridge, with a muscle in nitrogen. I have found the following percentage values for the d.a.h.p.:

9, 4½, 12, 12, mean 9[1]

in paraffin oil. Mr Hartree in his series of experiments (unpublished) found as *minimum* values:

5, 6, 3, 9, 6, 0, 6, 7, 10

in nitrogen. The mean of his whole series in nitrogen, in close agreement with mine in paraffin, is 9 to 10 p.c. The possibility, therefore, that the effect can be attributed to water condensation caused by a temporary change of vapour pressure can be dismissed.

(*b*) *Non-uniform heat production during activity.* The method of determining the amount of heat set free in a given period of observation is based upon a comparison of the time course of the galvanometer deflection in the experiments on the living muscle with a curve obtained from artificial heating of the dead muscle by means of an electric current of short duration. The application of this method is justifiable only if the heat produced in contraction appear in the same part of the muscle as the heat arising in calibration, *i.e.* in particular if in both cases the liberation of heat be uniform over the whole muscle. This assumption is certainly not strictly realized. The living muscle contracts and, therefore, also produces heat, over its entire length, whereas in the control the heating current passes between the two electrodes, so that in the latter case no heat is set free in the extremities of the muscle. The reason why the warming current is not applied over the whole length of the muscle is that the final portion of the latter is of diminishing cross-section, and the heat produced in it by a given current would be greater, and the rise of temperature still greater, than in the central portion. The error due to non-uniform heating of the ends would be at least as bad as that due to not heating them at all.

[1] These and all my other experiments were made at room temperature (*c.* 18° C.).

It was possible, therefore, that in the case of an active muscle there might be sufficient conduction of heat from the extremity to the thermopile, which did not occur in the control heating, to give the appearance of delayed heat production. It was *a priori* unlikely that this could provide a satisfactory explanation of the phenomenon in question, because in the new all-metal type of thermopile [Hill, 1928] a silver frame of high heat conductivity and comparatively large heat capacity protects the thermopile elements from any heat liberated beyond the limits of the frame. In order, however, to make sure that no effect of this kind occurred, the upper end of a dead muscle was heated with an alternating current between the upper electrode and the extremity. In this way the part of the muscle which is not usually heated in a control observation was heated, while the part which is usually heated, namely the part on the thermopile, was left unheated. For reasonable strengths of current the galvanometer did not deflect at all, but several seconds of heating with a very excessive current caused at first a very small positive deflection, which was followed after about 10 seconds by a much larger and long-lasting negative one. The explanation of the latter is that the shielding of the thermopile by the silver frame is so good that no considerable amount of heat reaches the hot junctions directly, even when the rise of temperature of the outside portion is very great. Indirectly, however, by warming up the whole instrument it causes a greater rise of temperature in the "cold" junctions than in the "warm" ones, since the latter are protected to some degree from a rise of temperature by the heat capacity of the cold muscle lying on them[1]. The phenomenon observed is, in any case, in the wrong direction to explain the usual delayed heat production, and it occurs only when the heating at the extremities is excessive. It is quite clear that in the experiments as usually conducted no effect at all is produced at the junctions by not warming the extremities in the control observations.

Mr Hartree informs me that he has made similar observations from time to time, warming only the extremities of the muscle, and that he agrees with the conclusion just given.

It seemed possible, however, that the d.a.h.p. might be caused by a layer of the muscle lying in immediate contact with the thermopile not contracting as vigorously as more distant parts. During dissection and preparation slight injury at the surface might have occurred, and so led

[1] The experiments were made with a so-called differential thermopile which is used with only one muscle, the "warm" junctions lying on one face, the "cold" junctions on the opposite face.

to a smaller response of the layer of muscle immediately on the thermopile. The heat conducting up from the more distant portions which contracted more strongly might then appear to have been produced after contraction was over. In the usual arrangement the surface of the muscle in contact with the thermopile is that which lies free in the frog's body immediately under the skin. In dissection it is certainly less exposed to danger of injury than the interior surface which is outside on the thermopile. We should expect, indeed, that the part of the muscle in immediate contact with the thermopile would contract better than the other part. The delayed heat production, therefore, might be considerably increased if the inner face of the muscle were placed against the thermopile instead of the outer. Experiments were made with the muscle reversed in this way, and it was found that the d.a.h.p. was of the usual size.

The result was not unexpected: the very slow decline in the rate of the d.a.h.p. and its long duration are hardly compatible with the assumption that its appearance is controlled by heat conduction over a distance of less than 1 mm., namely, the thickness of the muscle. That a weaker response of the superficial layer is not, in any case, the cause of the phenomenon could be verified directly by experiments in which the difference between the control curve and the curve from the live muscle was exaggerated artificially by placing a conducting but non-contracting layer between the muscle and the face of the thermopile.

For this purpose a strip of filter paper was fixed by spots of paraffin over the hot junctions, *i.e.* between the muscle and the surface of the thermopile. When, in this case, the muscle was stimulated the heat due to contraction reached the thermopile only after conduction through the filter paper, whereas in the control heating the filter paper, which was saturated with Ringer's solution, conducted the current as well as the muscle and was, therefore, heated at the same time.

In this case a delayed appearance of heat was observed due to lag in conduction, in addition to the usual d.a.h.p.: the character, however, and the extreme rapidity of its appearance showed it to be certainly due to conduction, and were so entirely different from those of the d.a.h.p. that the same reason could not possibly explain them both. The apparent delayed heat production caused by the presence of the filter paper between muscle and thermopile surface occurs during a short interval only after contraction, and is practically complete in 0·1 minute, whereas the usual d.a.h.p. is much slower in its occurrence and diminishes gradually to zero during several minutes. Mr Hartree has made similar experiments with the same result.

The same conclusion that non-uniform contraction of the muscle over its cross-section is not the explanation of the d.a.h.p. can be reached by an approximate mathematical calculation of the time in which heat liberated in the outer half only would become uniformly distributed; assuming the usual coefficient of thermal conduction for water as applicable to muscle, the time involved in the equalization of the heat would be much too short to afford the required explanation.

The failure of all such attempts to explain the d.a.h.p. as an artefact forces us to conclude that in the normal muscle after a tetanus under anaerobic conditions a delayed heat production does really occur. The present experiments do not contribute any new evidence as to the processes involved in it or its significance. Presumably some chemical reactions at present unknown must follow contraction and be completed in the 3 or 4 minutes occupied by the d.a.h.p.

SUMMARY.

The delayed anaerobic heat production after a tetanus has been subjected to a critical examination. It is not due to condensation of water vapour caused by a possible temporary rise of osmotic pressure, nor is it due to non-uniform heat production in contraction or control. Its occurrence has been verified, and it has exhibited the usual variability and order of size. It seems to be due to some real process occurring in the muscle.

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