612.74:612.26

THE EFFECT OF LENGTH ON THE RESTING METABOLISM OF MUSCLE.

By T. P. FENG[1].

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

During a study of the thermo-elastic properties of muscle (see the following paper), using the sartorius of *R. temporaria,* I noticed that a permanent deflection of the galvanometer occurred in the "heating" direction when the muscle was kept stretched. On release the "heating" disappeared. This observation was regarded at first with suspicion as possibly originating in some error, and various controls were made to prevent if possible its occurrence. These, however, all failed to do so. Further experiments soon demonstrated beyond doubt that in the case at least of English *temporaria* there is a genuine relation between the resting metabolism of a muscle and its length. This paper reports these experiments and similar ones on Dutch and Hungarian *R. esculenta.*

Fig. 1 shows the original observation. A pair of sartorii of *R. temporaria* were mounted on a thermopile and loaded with 100 g. A progressive rise of heat rate occurred, reaching a maximum, then settling down to a lower level which, however, was considerably higher than the original resting one. On release, after a sharp kick in the heating direction —probably a thermo-elastic effect—the galvanometer returned to—or as was more often the case, nearly to—where it was before the stretch. When the return of the galvanometer was incomplete after release, there was also incomplete restoration of the length of the muscle. Fig. 2 shows a more conspicuous case obtained in later experiments and illustrates the effect of increasing and decreasing the load by successive steps of 10 g. All observations were made at 20° C., unless otherwise stated.

The following sources of error may be considered:

(1) *Creep of galvanometer zero.* This may be dismissed immediately, for the Downing moving-magnet galvanometer employed usually kept its zero within 2 mm., at the sensitivity employed, throughout the whole day. Moreover, one cannot conceive that the creep should always coincide with the stretch and the release of the muscle.

---

[1] Tsing Hua University Fellow.

(2) *Stretching a muscle may change its contact with the thermopile surface.* The muscle was stretched by weighting one end of an isotonic lever, pivoted in its middle, whose other end was connected to the muscle sometimes by a thread, sometimes by a wire, over 2 ft. long. The amount of stretch was seldom more than 1 cm., usually about 5 mm. The lateral displacement of the muscle, therefore, was negligible. An important result of stretch is that the muscle becomes thinner and narrower and consequently less of it lies on the thermopile. This, however, other things being equal, and, for a given rate of heat production, would cause a decrease and not an increase of the galvanometer deflection. If the face of the thermopile were slightly irregular, the muscle would lie more intimately in contact under capillarity with a low than with a high tension: with a high tension it would tend to bridge over a gap. The worse contact with the higher tension would diminish the deflection for a given heat rate, not increase it.

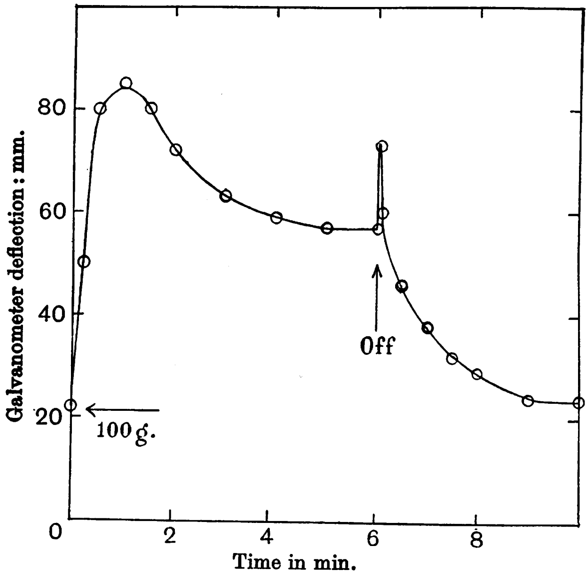

Fig. 1. Sartorius of *R. temporaria* in O_2 at 15° C., showing prolonged heat production while the muscle is kept loaded with 100 g. On unloading, the heat rate falls to the original resting level.

(3) *There might be insufficient equalization of temperature, and a hotter portion of the muscle might be brought into contact with the thermopile when it was stretched.* This is most unlikely, since the constant temperature

bath employed regulated within 1/500th of a degree. Furthermore, observations made in Ringer's solution, unstirred or vigorously stirred, gave results entirely similar to those in a gas.

(4) *Stretching the muscle might cause twitching,* either directly (by acting as a stimulus) or by some attendant irritation, such as rubbing of the muscle against thermopile or electrodes. This is made very improbable by the permanency of the increased rate of heat production following a stretch. Curarization, moreover, or rendering the muscle inexcitable by increasing the KCl content of the Ringer's fluid to about five times its normal amount or by soaking in isotonic sugar solution, all failed to abolish the phenomenon.

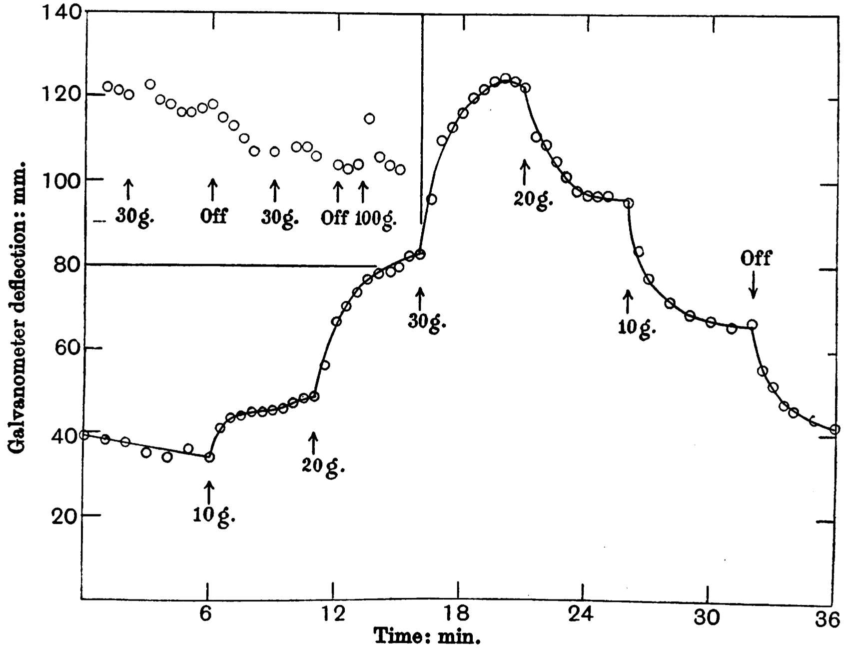

Fig. 2. Sartorius of *R. temporaria* in O_2 at 20° C., showing the effect on resting heat rate of loading and unloading the muscle by 10 g. steps. Inset showing the disappearance of the effect after the muscle was electrocuted.

(5) Finally, in an *electrocuted or chloroformed muscle* stretching no longer causes any rise of its resting metabolism. This will be discussed more fully later: it is quoted here merely to show that the phenomenon is not due to extraneous error.

Its existence being certain, attempts were made to gain some insight into the nature of the phenomenon which, for want of a better name, will be referred to as the "stretch response." If the increment of resting heat rate due to stretch be of the same nature as the original resting heat itself, it is to be expected that, for a given stretch, (*a*) it should be greater in oxygen than in nitrogen and (*b*) that if the stretch were done in nitrogen it should cause an extra oxygen debt which would show itself later, on admitting oxygen, in the form of extra recovery heat. All this was actually realized. Fig. 3 shows the relative magnitude of the stretch response to 20 g. loading in oxygen and in nitrogen. The former is about twice the latter, as it should be perhaps, since the usual resting heat rate in oxygen is about twice that in nitrogen. Fig. 4 shows the recovery

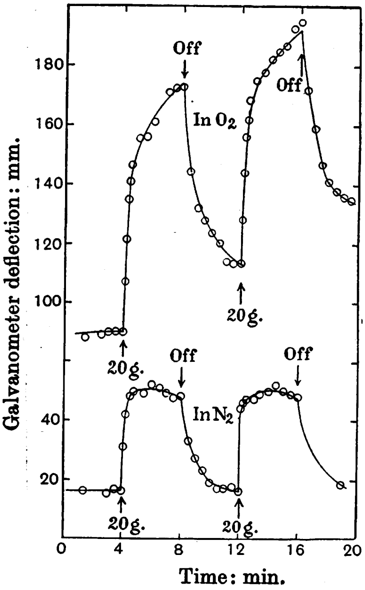

Fig. 3.

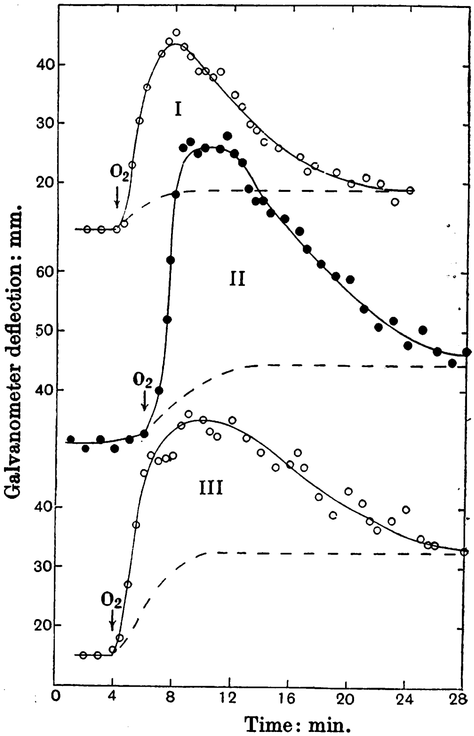

Fig. 4.

Fig. 3. Showing the relative magnitude of the stretch response in O_2 and N_2.

Fig. 4. Recovery heats: I and III after 40 min. unloaded anaerobiosis, II after anaerobiosis lasting 40 min., during 30 min. of which the muscle was loaded with 50 g. I, II and III observed in succession and all with muscles unloaded.

heat on admitting oxygen (galvanometer deflection, unanalysed) after the same period of oxygen want under different conditions. I represents the amount after oxygen want unloaded for 40 min.; II that after oxygen want for 40 min. during 30 min. of which the muscle was loaded with 50 g.; and III that after unloaded anaerobiosis again. II is obviously very much greater than I, in this particular case about twice as great: III is also somewhat greater than I, the anaerobic heat rate after stretch not having returned completely to the original level. It should be noted that the recovery heats were measured always with the muscle under the same conditions, namely unloaded, so that the difference between I and II must be due to the conditions obtaining during previous oxygen want and not to the conditions existing at the moment, which were the same in both.

It is quite clear, therefore, that stretching the muscle does increase its oxygen requirement. For further demonstration an independent method was sought and measurements made directly of the oxygen consumption of a muscle when stretched and when unstretched respectively. A Barcroft differential manometer was employed with special chambers, as shown in Fig. 5. The chambers were of approximately equal size, containing about 14 c.c. A glass rod, bent somewhat to one side, and provided with two glass hooks, was sealed to the stopper *A*. The apparatus was particularly designed for the double sartorius preparation. The small portion of pelvic bone joining the two muscles rested against the lower hook, while the free ends of the muscles were slung over the upper hook and tied, by means of thread, on to a rod projecting from a bottom stopper. Turning the latter winds up the thread and stretches the muscle: release is simply effected by turning the stopcock in the opposite direction. In this way stretch and release can be carried out without opening the chamber and repeated as often as desired. During an experiment about 0·3 c.c. of 0·7 p.c. KOH, having approximately the same vapour pressure as the muscle, was placed in the bottom

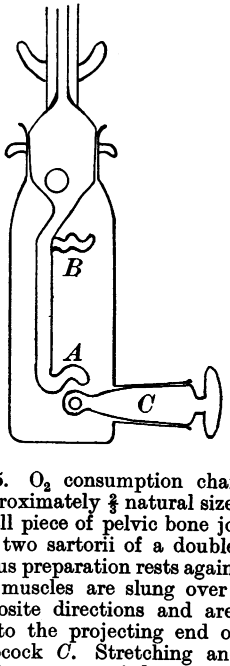

Fig. 5. O_2 consumption chamber, approximately $\frac{3}{4}$ natural size. The small piece of pelvic bone joining the two sartorii of a double sartorius preparation rests against *A*; the muscles are slung over *B* in opposite directions and are tied on to the projecting end of the stopcock *C*. Stretching and releasing are carried out without opening the chamber, simply by turning *C*.

of the chamber and served to absorb CO_2 as well as to keep the chamber moist. The chamber containing the muscles was always filled with oxygen, the compensation chamber holding about 0·6 c.c. of KOH solution and air. The chambers were immersed in a water bath at room temperature and shaken by a to-and-fro movement about once per second. The manometer was read every 10 min., both sides being recorded and the average taken.

Some results are shown in Fig. 6. Oxygen consumption in any interval is expressed simply in mm. displacement of the meniscus of the manometer, no calibration being made. The amount of stretch applied was not accurately known but was of the order of that due to 30 to 60 g. hung on a pair of sartorii weighing about 160 mg. As shown, stretching the muscle increases its oxygen consumption two to fourfold.

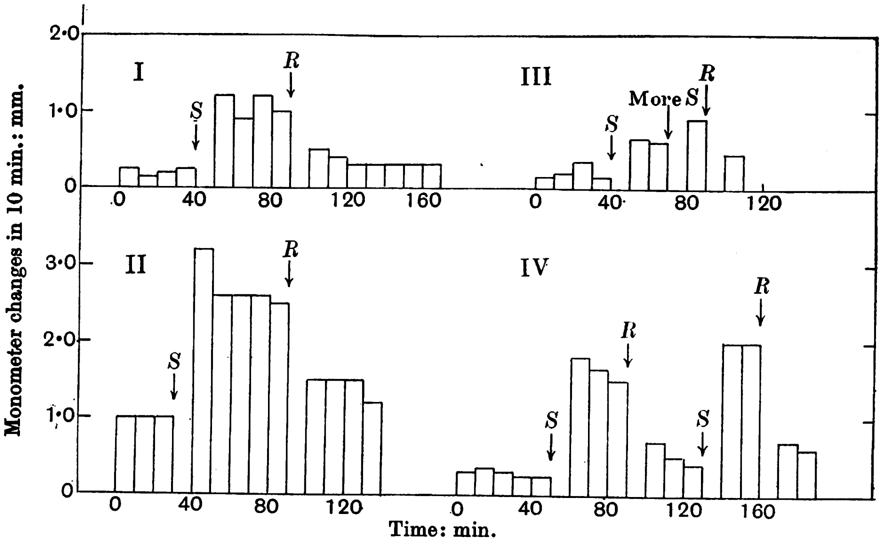

Fig. 6. Sartorius of *R. temporaria* at room temperature, showing the effect of stretch on the O_2 consumption. I, II, III, IV are four individual experiments. *S* = stretch, *R* = release. O_2 consumption expressed in mm. displacement of meniscus, each block representing 10 min.

The next step in the effort to understand the stretch response was to see what change in the condition of the muscle itself could influence it. As mentioned already, the response was abolished altogether by electrocution or by chloroform, but still existed when the muscle was rendered inexcitable by soaking in high-KCl Ringer's fluid or in sugar solution. Clearly the mere ability of the muscle to contract when stimulated is not a necessary condition of the stretch response. Its disappearance after electrocution and chloroform may of course be correctly stated as due to the muscle being dead. More probably, however, it may be attributed to the muscle being completely exhausted. The question then arises whether partial exhaustion will partially abolish it. Experiment showed this to be the case. Fig. 7 is one experiment on a muscle in nitrogen, showing how the stretch response is much diminished with each series of 50 twitches. On allowing the muscle to recover in oxygen the stretch response also recovers; often it appeared larger after oxidative recovery following stimulation than at the beginning, as in the case shown.

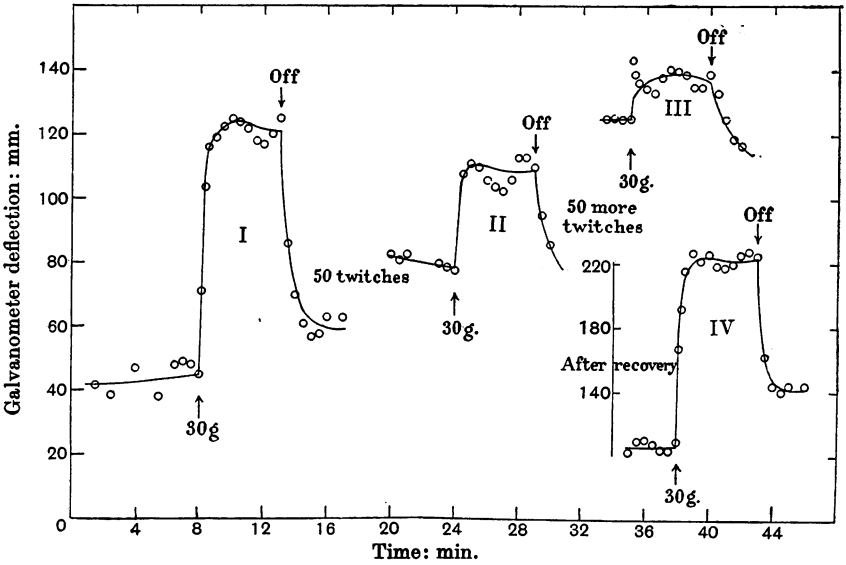

Fig. 7. Sartorius of *R. temporaria* in N_2, showing the effect of previous activity on the size of the stretch response to a load of 30 g. I, fresh muscle; II, after 50 twitches; III, after another 50 twitches; IV, after 2¾ hours' oxidative recovery. Note that the scale of the ordinates for IV is half as large as for the others.

Muscles poisoned with iodoacetic acid give a full-sized stretch response. The effect, however, of stimulation is more pronounced, and once diminished by stimulation oxidative recovery of the response does not occur (see Fig. 8).

Ringer's fluid containing 120 mg. of extra KCl per 100 c.c. appears to make the muscle give a considerably larger stretch response to a given load. Soaking in isotonic KCl solution, however, even for 5 min., seems to diminish it, certainly not to increase it. Ringer's fluid containing

300 mg. of extra $CaCl_2$ per 100 c.c., and pure isotonic $CaCl_2$, leave the stretch response unaltered. Pure CO_2 definitely diminishes it.

The experiments reported so far were all made on *R. temporaria*. When similar experiments were tried on the large Hungarian *R. esculenta* I was surprised to find generally no stretch response at all, occasionally a small and doubtful one. The results obtained before August with this species of frog were as consistently negative as with *R. temporaria* they were positive. There was no prolonged heating effect when the sartorius of a Hungarian frog was stretched, even by a relatively much greater amount than was usually applied to the English ones. The recovery heats, moreover, after a given period of oxygen want were the same whether the muscle was stretched or not. The oxygen consumption of the muscle also was unaffected by stretching. This specific difference was most unexpected and puzzling. One would naturally be inclined to suppose that the particular batch of Hungarian frogs, at the time they were used, were in bad condition, or more precisely, in a partially exhausted condition, since, as shown above, exhaustion is so effective in diminishing or abolishing the stretch response. Actually they were not in the best

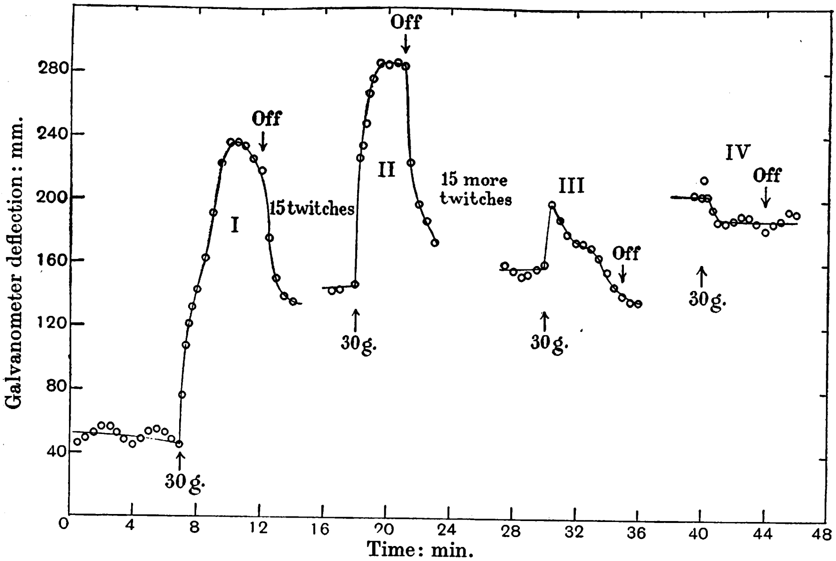

Fig. 8. Sartorius of *R. temporaria* poisoned by iodoacetic acid, in N_2. The effect of previous activity on the response is similar to that in normal muscles but more pronounced: I, before stimulation; II, after 15 twitches; III, after another 15 twitches; IV, after 45 min. in O_2; in contrast with normal muscle no oxidative recovery takes place.

of condition as they had been in the laboratory two and a half months, but still their muscles contracted strongly when stimulated. Later, in September, a new batch of Hungarian frogs was obtained. These were certainly in excellent condition, and nine experiments were made on their sartorii. In two cases I found definite evidence of the stretch response; in two others none at all, while in the remaining five the response appeared to be present but small and doubtful. After these new experiments, in which there was no question about the condition of the animals, I feel compelled to conclude that the muscles of Hungarian *R. esculenta* generally do not show, or show only to a very slight degree, the stretch response so conspicuously manifested by *R. temporaria*.

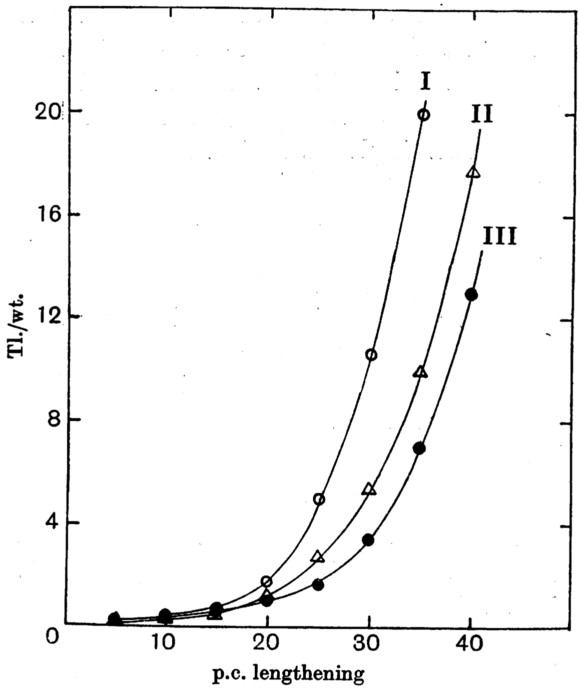

Fig. 9. Average tension-length curves of resting sartorii. I, Hungarian *R. esculenta* (average of 5 curves); II, Dutch *esculenta* (average of 4 curves); and III, English *temporaria* (average of 4 curves). Ordinate, Tl./wt., which is roughly proportional to the tension in g. per sq. mm.; abscissa, percentage lengthening reckoned from length at zero tension.

A few experiments also were made late in September on Dutch *R. esculenta* which were not available in the months before August. The sartorii of this species in the half-dozen cases examined showed the stretch response indeed but to a considerably less extent than those of *R. temporaria.* Two experiments on the biceps cruris of the tortoise and one on the rectus abdominis of the mouse at 20° C. gave negative results.

Large specific differences therefore exist. What can be their cause? In handling the various kinds of muscles one gains a general impression that those of Hungarian frogs are considerably and those of Dutch frogs appreciably less extensible than those of English ones. This is borne out by experiment. Fig. 9 shows average tension-length curves of resting sartorii of the three species of frogs. For the better comparison of muscles of different weights and lengths, the tension per unit of cross-section (actually Tl./wt.) is plotted against the percentage lengthening. The curve for Hungarian sartorii is steepest, that for Dutch comes next, while that for English is the lowest. It is not unreasonable to suppose that the stretch response would be more prominent in more extensible muscles, and that this might be the basis of the specific difference in question. Against this, however, it may be urged that a load of 20 g. caused a conspicuous stretch response in *R. temporaria,* while 150 g. failed to evoke any response at all in Hungarian *R. esculenta.* Such differences must presumably be based upon some factor in addition to extensibility.

DISCUSSION.

That stretching a muscle may increase its metabolism has been suspected from time to time ever since Weber first systematically investigated the extensibility of muscle. Suggestive evidence of various kinds appeared in the literature at intervals. Meyerstein and Thiry [1863] found that when a muscle was extended by a relatively large weight there was at first a slight cooling, generally followed by some heating, and they concluded that muscle, at the moment of being stretched, offered an active though weak resistance; once stretched, the muscle was thought to carry the weight passively. Schmulewitch [1867] observed a larger heat production on extending a living muscle than a dead one. Westermann [1868], however, found that thermal effects of stretch and release were the same in living and in dead muscles. A rise of temperature in a muscle when it was stretched was noticed by a number of other workers, but there is no point in enumerating all the instances here. Most probably these older observations showed only the thermo-elastic and frictional heat later studied by Hill and Hartree [1920] and gave no definite evidence of any active heat production due to stretch. Gotschlich in 1894 (quoted by Eddy and Downs, 1921 *b*) found a production of lactic acid by a muscle when loaded.

More recently Eddy and Downs [1921 *b*], using Tashiro's barium hydroxide technique, showed that a stretched muscle liberates about four times as much CO_2 in a given time as an unstretched one. These authors used gastrocnemii and weights of 50 g. to stretch them. The fact that gastrocnemii have obliquely arranged fibres and are so rich in strong inextensible connective tissue that a weight of 50 g. will hardly extend the muscle fibres at all, makes their result, if it be correct, very striking. It is possible that American frogs greatly surpass even English *R. temporaria* in the prominence of the stretch response. More probably, however, the method employed showed a much greater difference in CO_2 output between stretched and unstretched muscles than really existed. If Gotschlich be right, an unknown fraction of the CO_2 output by stretched muscles must be due to preformed CO_2 driven out by lactic acid.

In another paper Eddy and Downs [1921 *a*] reported that gastrocnemii, previously loaded by 100 g. for periods from 30 min. to 3 hours, were fatigued by stimulation in less time than unstretched muscles. The average time to complete fatigue for unstretched muscles is 19·25 min. and that for stretched ones 16·53 min. Their results, however, showed very large individual variations: in a number of cases it took a longer time to fatigue a stretched muscle than an unstretched one. And even if the average difference be significant, it is still not necessary to conclude that the difference is due to partial depletion of available energy store in the case of stretched muscles, as the authors did.

The question will naturally be asked, how does stretch bring about an increase in the resting metabolism of a muscle? In this form the question can no more be answered than why does stimulation cause contraction and attendant energy liberation? Stretching a muscle is known [Hill, 1925] to affect the heat liberated in response to a stimulus. In this case, however, the heat increases with the stretch up to a certain quite low limit and then decreases considerably as the muscle is further stretched. With the loads used in the present experiments the heat liberated in an isometric twitch would be less and not more than that of the unloaded muscle. It is possible to discuss whether the increased length itself, or the tension causing it, is the determining factor in the stretch response. Naturally in a resting muscle tension and length vary in the same direction and there is no way to separate them. There might, however, be a simple relation between the one, or the other, and the resting metabolic rate.

In Fig. 10 is shown an experiment in which the load on the muscle was increased progressively by 10 g., and the resting heat rate following each increment observed. There is no simple proportion between heat rate and load; nor, however, it can be similarly shown, is there between heat rate and length. It is impossible in this way to decide which relation is the more fundamental.

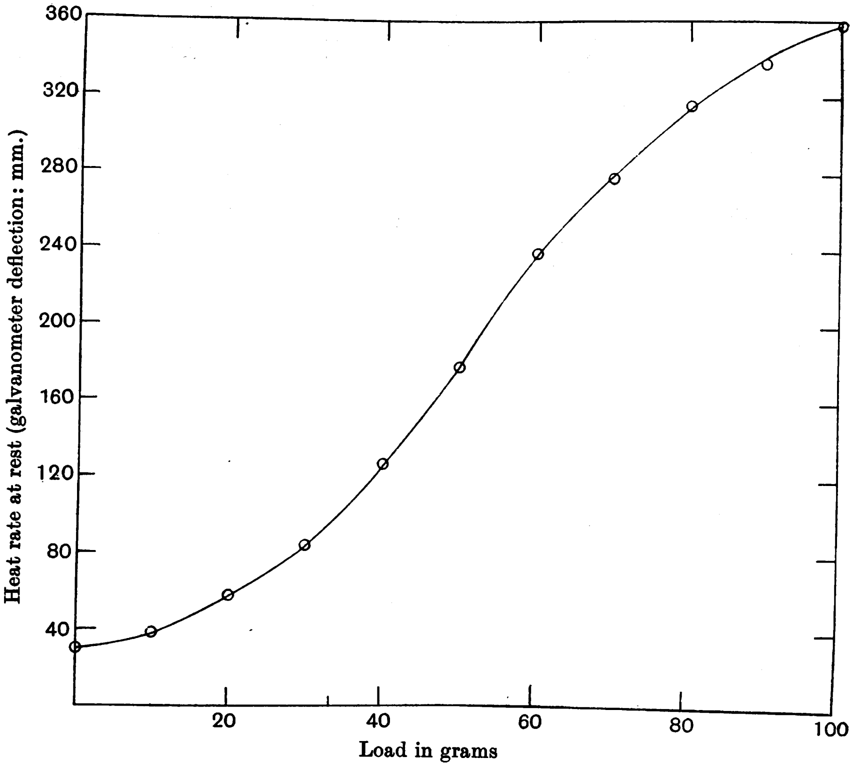

Fig. 10. The relation between resting heat rate and load. Curve starting with 2·5 g. initial load, in air.

The most striking evidence of the nature of the effect described is its intimate dependence on the previous activity of the muscle. Fifty twitches of a muscle in nitrogen often diminish the stretch response to a half or less, and this at a stage of fatigue when the ability to contract was entirely unimpaired, often indeed greater than at the beginning. If the source of energy for contraction and stretch response be one and the same, how can it be amply available for the one but nearly inaccessible for the other? If, on the other hand, the two have distinct energy supplies, why does the performance of the one affect the other? One thing is certain: that the energy supply is not necessarily derived from the breakdown of glycogen. Soaking a muscle in Ringer's fluid containing glucose does not augment the stretch response and, as recorded earlier, it exists undiminished in muscles poisoned with iodoacetic acid. One may suspect that the energy supply concerned is related to the phosphagen complex. The high initial rate of breakdown of phosphagen under anaerobic conditions is consistent with the great diminution suffered by the stretch response as a consequence of 50 twitches. The failure of oxidative recovery of the stretch response, following stimulation in nitrogen, of muscles poisoned with iodoacetic acid, is in keeping with the absence of phosphagen resynthesis in that case. Possibly a certain high level of phosphagen concentration is requisite for the conspicuous manifestation of the stretch response, and it is tempting to suggest that the different aptitudes for this response shown by three species of frogs might have a basis in their relative contents of phosphagen, or more likely perhaps in its state of combination.

The alternative possibility that the performance of contraction might change the condition of the muscle, so as to diminish its stretch response, is not readily confirmed. An increased acidity might perhaps be suggested, particularly in view of the diminishing effect of CO_2 on the stretch response. In a muscle, however, poisoned with iodoacetic acid, stimulation causes increased alkalinity, not acidity, and according to Lipmann and Meyerhof [1930] a normal muscle, when stimulated, first becomes more alkaline, coincident with the preponderant breakdown of phosphagen, and then later more acid. No reversal of the effect of stimulation on the stretch response, when stimulation is further continued, has been found. A change of *p*H therefore can scarcely be the cause of the effect of stimulation.

SUMMARY.

1. The resting metabolism of a muscle increases when it is stretched, the greater the stretch the more the increase. The phenomenon has been demonstrated, both by heat and by oxygen consumption measurements. It is referred to as the "stretch response."

2. The increment of resting heat rate due to a given stretch is about twice as great in oxygen as in nitrogen. Stretching a muscle in nitrogen causes an extra oxygen debt which can be detected in the form of a greater recovery heat when oxygen is admitted.

3. In a muscle in nitrogen the stretch response diminishes progressively with increasing amount of previous activity: 50 twitches often decrease it by one-half or more. After recovery in oxygen the stretch response is completely restored.

4. The stretch response exists undiminished in muscles poisoned with iodoacetic acid, but once diminished or abolished by stimulation in nitrogen it cannot recover in oxygen.

5. A great difference exists between the three species of frogs studied, in respect of the prominence of the stretch response. It is manifested most conspicuously by English *R. temporaria*, considerably less by Dutch *R. esculenta*, and only to a slight degree—often not at all—by Hungarian *R. esculenta.*

6. It is possible that a certain high level of the phosphagen content is requisite for a clear manifestation of the stretch response.

I wish here to express my sincere thanks to Prof. A. V. Hill for his encouragement and advice; to Mr A. C. Downing I owe my gratitude for instruction in managing his galvanometer, and to Mr J. H. Trendall for making the chambers used in the oxygen consumption measurements. To Mr J. L. Parkinson I am indebted for much assistance and advice during the course of this work.

REFERENCES.

Eddy, N. B. and Downs, A. W. (1921*a*). *Amer. J. Physiol.* **56**, 182.
Eddy, N. B. and Downs, A. W. (1921*b*). *Amer. J. Physiol.* **56**, 188.
Hill, A. V. (1925). *J. Physiol.* **60**, 237.
Hill, A. V. and Hartree, W. (1920). *Phil. Trans. Roy. Soc.* **210**, 153.
Lipmann, F. and Meyerhof, O. (1930). *Biochem. Z.* **227**, 84.
Meyerstein and Thiry (1863). *Z. rat. Med.* **20**, 67.
Schmulewitch, I. (1867). *Zbl. med. Wiss.* **5**, 81.
Westermann, H. (1868). *Ein Beitrag zur Physik des Muskels*, Dorpat. (Quoted from Wölisch, E. and Clamann, H. G. (1931). *Z. Biol.* **91**, 399.)