STUDIES ON THE PHYSIOLOGY OF PLAIN MUSCLE.
The effect of alteration of initial length on the tension produced on contraction. By R. J. BROCKLEHURST.

(*From the Physiological Laboratory, St Bartholomew's Medical College, London.*)

THE energy set free by the isometric contraction of skeletal (1, 2, 3, 4, 5) or cardiac (6) muscle, depends upon the initial resting length of the muscle; the graph relating tension-increment on contraction to initial length shows that the energy set free first increases with increasing initial extension, and then declines with further extension (2, 4). The purpose of the present experiments was to find whether plain muscle exhibits similar properties.

A difficulty is met with owing to the fact that plain muscle cannot be said to have any definite "unloaded length," but exhibits very great variations in length on the application of minimal loads; this was circumvented by starting with the muscle always definitely extended so as to produce a very slight initial tension when at its shortest length. Fluctuations in tension due to variations of tonus were usually slight.

Method. The lower part of the cat's ileum was used throughout as a source of plain muscle. (Crane and Henderson (7) found that the ileum in the guinea-pig is much more sensitive to a stretching stimulus than is the upper part of the small intestine.) The cats were killed by bleeding immediately after the induction of complete ether anæsthesia. A portion of the ileum, measuring between 2·5 and 4·0 cm. in length, was removed immediately after death, washed thoroughly and placed with a minimum of manipulation in the recording apparatus; this consisted of a vessel of oxygenated Tyrode's fluid (without glucose) at 38° C., in which the intestine was suspended between a fixed isometric lever above (recording frontally on a slowly moving drum) and the hooked end of a glass tube below. The glass tube was led out of the bath and rigidly fixed into a Palmer stand; by means of a worm gear this could be raised or lowered, thus shortening or lengthening the gut.

After a preliminary rest of 10 minutes in the Tyrode bath, the lower attachment of the gut was adjusted so that the gut itself became just taut without producing any appreciable tension in the isometric lever;

at this point the effective "relaxed" length of the intestine was measured (to within 0·5 mm.). The muscle was then stimulated to give a maximal contraction by the addition of a solution of "Ergamine Acid Phosphate" (B.W.), to give a concentration of one part of histamine in 1,000,000.

The use of a drug such as histamine has certain advantages over electrical stimuli when dealing with plain muscle. It is more readily applicable and more certain in its results, a maximally effective dose of histamine always giving a satisfactory and uniform contraction.

The response of the gut to the addition of histamine was recorded on the drum as an immediate powerful contraction (after a short latent period), followed by a series of strong rhythmic contractions, usually at the rate of about seven or eight per minute; these rhythmic contractions were never as powerful as the first contraction, and they gradually decreased in force, the tension in the muscle once more approaching zero at the end of a minute or two. After the greatest contraction had been recorded, the bath was emptied and the histamine removed by three washings with fresh Tyrode at the required temperature.

The gut was then lengthened by means of the worm gear and the whole process was repeated at different initial lengths, first lengthening the gut through a definite range, and then allowing it to shorten by similar stages back to its original length. At the end of the experiment

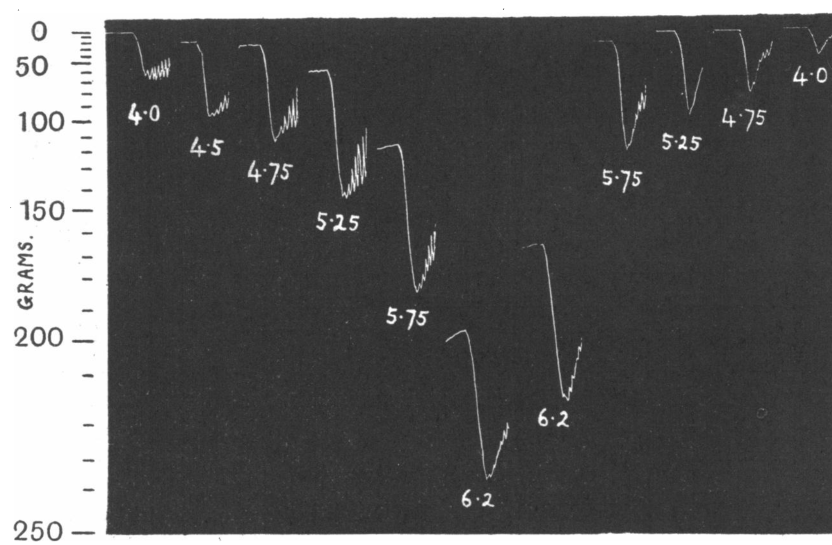

Fig. 1. The figures indicate the lengths in cm. at which the muscle was stimulated. Contraction downwards.

the recording apparatus was calibrated by adding 10-gm. weights to the isometric lever from the same point from which the gut had been suspended.

Fig. 1 shows portions of a typical record. The length of the contracted intestine was not more than 0·25 mm. shorter than when relaxed.

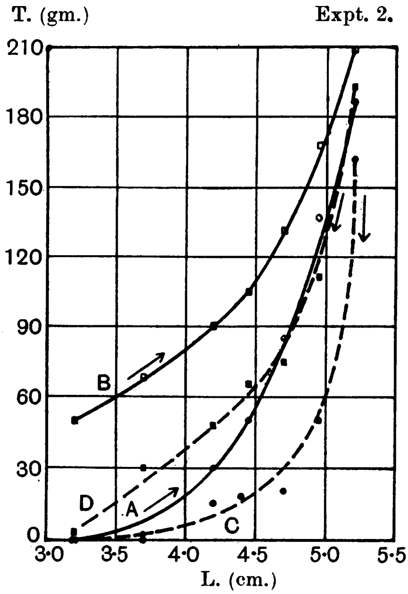

Fig. 2.

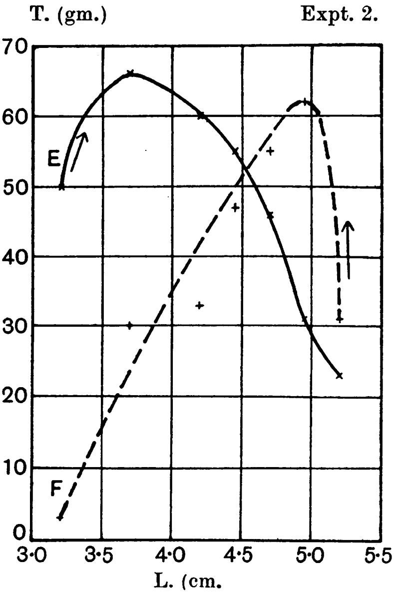

Fig. 3.

Fig. 2. A = tensions when uncontracted, B = total tensions on contraction, when lengthening the gut; C = resting tensions, D = tensions on contraction, when allowing gut to shorten. Ordinates, tension in gm.; abscissæ, length in cm.

Fig. 3. Drawn from data in Fig. 2. $E = B$ minus A, $F = D$ minus C. Ordinates, tension-increment in gm.; abscissæ, length in cm.

Fig. 2 represents graphically the results of a typical experiment of the series. The continuous curves show the effect of lengthening the gut by short stages; the broken curves represent the reverse procedure, viz. allowing it to shorten by stages to its original length. All the curves are of similar shape, differing only in degree. A and B are very similar to the corresponding curves obtainable with skeletal muscle; the writer has not seen any "shortening" curves (corresponding to C and D) in the case of skeletal muscle. Similar curves were obtained from all the experiments performed.

An obvious difference is seen between the tensions of the "lengthening" and the "shortening" curves; in every case the tensions on the latter are lower than on the former at similar lengths. The shapes of *A* and *B* are similar, also those of *C* and *D*. The "contracted" curves *B* and *D* are clearly dependent for their shapes on those of *A* and *C* respectively.

There are a number of factors which, singly or collectively, may account for the difference in appearance between *A* and *C*.

(1) The intestine can, for the purposes of this investigation, be considered as a mixture of contractile and non-contractile tissues, the latter including the serous coat, the mucous membrane and a certain amount of connective-tissue in the submucosa and in the muscle layers. The sharper rise of *A* as compared with *C* is undoubtedly due partly to the presence of these non-contractile elements of low elasticity. On relaxing the gut, the stretched connective-tissue exhibits little or no retraction except at the beginning, and this would account, in part at any rate, for the sharp fall of *C*. The differences in level between *B* and *A*, and between *D* and *C*, are of course due entirely to the tension exerted by the musculature on contraction.

To avoid this difficulty if possible, a few èxperiments were performed with the retractor penis (bull and dog), which is as free from non-contractile tissue as plain muscle from any other source. Unfortunately this muscle does not respond readily or in a regular way to histamine, relaxation being sometimes produced.

(2) *Viscosity.* On lengthening the muscle, there is a sudden increase in tension at the moment of lengthening, followed by a gradual decrease to a stable tension. It is obvious that only by stretching the muscle infinitely slowly can this factor be eliminated. On relaxation, the viscosity factor does not apparently alter the tensions appreciably; as the gut was allowed to shorten, it always assumed immediately a tension which did not vary thereafter. It would appear that whereas skeletal muscle can be compared to a thin rubber tube filled with a viscous mixture (8), plain muscle in this respect would more closely resemble a similar system with very little or no elastic component. It is not necessary to enter here into the possible explanations of "viscosity" in plain muscle, whether it is due to a molecular rearrangement within the fibres, an adjustment of liquid crystals disordered by the stretching (9), or to a movement of the fibres one over the other (10).

(3) *Damage.* In one or two instances a small degree of tearing at the ends of the gut was noticed at the end of the experiment, due to a partial rupture of the muscle coats by the thread used for ligaturing. This was obviated by fitting small flanged glass tubes into the ends of the gut and tying the gut over them. These tubes also served to keep

the ends of the gut open, thus allowing the free access of saline to its lumen; this enabled the gut to rid itself of metabolites, secretions of mucus, etc.

(4) *Any other irreversible effects produced by extension.* Under these experimental conditions there appeared to be no permanent stretching of the muscle; in one experiment (No. 3 in the table) the gut was subjected to a second lengthening, during which the tensions obtained were exactly similar to those during the first process.

The muscular contraction itself is best studied by means of tension-increment—length diagrams.

In Fig. 3, *E* represents the mechanical energy liberated (as measured by the tension-increment) with increasing initial length, and *F* the same with decreasing initial length; *E* bears a close resemblance to the corresponding curve for skeletal muscle shown by Evans and Hill(2). There is clearly a certain optimum length for maximum tension development, and this optimum is different in the two cases (*a*) of muscle which is being lengthened and (*b*) of the same muscle being shortened. A possible explanation of this difference is afforded by the behaviour of the non-contractile elements of the gut wall. On lengthening the gut, *E*, the lack of plasticity of these tissues shows itself as a rapidly increasing rise in the resting tensions, especially noticeable when it is considerably stretched; the effect of this is a falling off of the tension-increment. The optimum length in *F* occurs very soon after the shortening process begins, and is always greater for a given piece of gut than the optimum in *E*; in this case the tension-increment is not interfered with by a stretching of the non-plastic tissues which are here allowed to relax.

It may be noted in passing that the muscle of a small piece of intestine is capable of developing considerable tensions; in experiment 4, a piece of gut, 4·3 cm. long, exerted a maximum tension-increment of 168 gm.

Working with the gastrocnemius, Beck(4) found that the maximum tension developed on contraction occurred when the muscle was stretched to just beyond its greatest physiological length. A. V. Hill(11) has emphasised the unsuitability of the gastrocnemius for experiments of this kind owing to the presence of tendon, etc., and to the obliquity of some of the fibres; he uses, instead, the sartorius and other skeletal muscles with parallel fibres. The maximum physiological length of a given piece of plain muscle cannot easily be determined with any accuracy owing to the very indefinite range of movement of the "insertion" with respect to the "origin"; *e.g.* the circular and longitudinal muscle coats of the hollow viscera. There is no doubt that in the experiment summarised graphically above, and in many of the others, the muscle was stretched beyond its physiological limit, and the tensions obtained from it when being gradually shortened may have been disturbed thereby. As mentioned above, however, a second lengthening process in one experiment indicated no permanent stretching effect. A few experiments were carried out in which the gut was not stretched by more than 25 p.c. of its initial length; curves drawn from these were found to be similar to those already described, with the exception that in some cases the maximum tension-increment was not reached.

The following table gives a summary of a number of experiments performed under similar conditions:

		Optimum length-increase	
Expt.	Original length cm.	Up p.c.	Down p.c.
1.	4·0	10·25	38·7
2.	3·2	15·6	54·8
3.	(i) 3·3	30·3	56·0
	(ii) 3·3	30·3	
4.	4·3	19·8	29·1
5.	4·2	11·9	23·8
6.	3·5	9·3	14·6
7.	4·5	16·7	22·3
8.	4·0	25·0	50·0
9.	2·5	28·0	60·0
10.	3·8	52·6	60·5
11.	3·5	14·3	48·5
12.	2·5	4·0	8·0
13.	2·5	8·0	

There is clearly a great variation in the "optimum length-increase" when comparing several pieces of ileum under similar conditions. Thus, on lengthening the gut, this figure varies between 4·0 p.c. and 52·6 p.c.; on shortening, between 8·0 p.c. and 60·5 p.c. The cause of such extreme variation is difficult to explain; the only factor which could not be controlled was the tonus existing in the muscle itself, and changes in tonus may possibly account for it.

SUMMARY.

(1) Tension/Length curves obtained from plain muscle (cat's ileum) stimulated by histamine, are very similar to those obtained from skeletal muscle stimulated electrically. The muscle was first lengthened by stages and then allowed to shorten back to its original length. The resting curve in the latter case shows smaller tensions at the greater lengths than does the resting curve during the lengthening process.

This difference is explained as being due to the viscosity of the muscle and to the stretching of the non-muscular elements of the intestine.

(2) The total tensions developed on contraction appear to depend on the tensions obtaining in the relaxed condition at the various lengths.

(3) There is a definite optimum length at which the maximum tension is developed by the muscle investigated. This optimum length is less on lengthening than on shortening the same muscle.

(4) The optimum length varies considerably in different pieces of muscle from similar sources and under identical treatment. This appears to be due to unexplained differences of tonus.

I wish to acknowledge my indebtedness to Professor Lovatt Evans, F.R.S., for his frequent advice during this investigation.

REFERENCES.

1. Blix. Skand. Archiv f. Physiol. 5. p. 173. 1895.
2. Evans and Hill, A. V. This Journ. 49. p. 10. 1914.
3. Doi. Ibid. 54. p. 335. 1921.
4. Beck. Pflüger's Arch. 193. p. 495. 1922.
5. Fulton. Proc. Roy. Soc. B, 96. p. 475. 1924.
6. Starling. Linacre Lecture, "The Law of the Heart" (Longmans, Green). 1918.
7. Crane and Henderson. Amer. Journ. Physiol. 70. p. 22. 1924.
8. Gasser and Hill, A. V. Proc. Roy. Soc. B, 96. p. 398. 1924.
9. Garner. Proc. Roy. Soc. B, 99. p. 40. 1925.
10. Grützner. Ergeb. d. Physiol. 3(2). p. 12. 1904.
11. Hill, A. V. This Journ. 60. p. 237. 1925.