pairs.

Discussion. The results of these experiments indicate that when a large dose of mustard is given intraperitoneally it rapidly enters the blood stream in considerable quantity. Within 30 minutes, however, it has disappeared from the circulation. This confirms chemical determinations of mustard in the blood of poisoned dogs.[2]

The survival of the unpoisoned members of cross-circulated pairs when cross-circulation began 30-60 minutes after poisoning indicates that no large amount of any "secondary toxin" was present in the circulation after the original poison had disappeared from the blood. It should be emphasized that the dose of the poison was many times larger (80-100 mg/kg) than the LD_{50} dose. If production of a "secondary toxin" was proportional to the dose of the original agent, a relatively small exchange of blood between a poisoned and an unpoisoned animal should have caused death in the second animal. We must conclude, therefore, that death by acute mustard poisoning does not result from liberation of a "secondary toxin" which is freely diffusible into the blood stream.

When smaller doses of the poison are used death is delayed for several days. The cross-circulation technic is not suited to determining whether a "secondary toxin" is involved in such cases.

Summary. 1. A large intraperitoneal dose of di-β-chlorethyl sulfide was given one member of a cross-circulating pair of dogs. Death was produced in both animals, though it was much delayed in the second member. 2. Cross-circulation between 2 dogs was begun 30-60 minutes after poisoning one with a large intraperitoneal dose of mustard. In no case was death produced in the second, unpoisoned dog. 3. It is concluded that a "secondary toxin" is not responsible for death in acute mustard poisoning.

[2] Thomson, J. F., unpublished.

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Effect of Activity on the Visco-Elasticity of Normal and Iodoacetate Muscles.

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Gasser and Hill's studies[1] on the visco-elasticity of muscle by the damped vibrating spring method have been questioned in subsequent work.[2-4] The present research employs the spring technic, but criticisms of it have been largely overcome by eliminating slack of the muscle at all times, by holding constant the initial length of any muscle subjected to a series of tests, and by limiting visco-elastic comparisons to either states of contraction or rest as modified by previous activity.

Excised, Ringer's-equilibrated *Rana pipiens* sartorii were used throughout. The muscles (average excised length, 34.8 mm) were stretched 15% when attached to the undeflected spring, and a further 15% stretch occurred with the spring maximally deflected.

In the work reported below, each plotted value represents the average behavior of at least 3 different muscles, and, in general, the mean deviation for the viscosity coefficient

[1] Gasser, H. S., and Hill, A. V., *Proc. Roy. Soc., B*, 1924, **96**, 398.

[2] Hogben, L. T., and Pinhey, K. F., *Br. J. Exp. Biol.*, 1926, **4**, 196.

[3] Steinhausen, W., *Pflüg. Arch. f. d. ges. Physiol.*, 1926, **212**, 31.

[4] Schoepfle, G. M., and Gilson, A. S., Jr., *J. Cell. and Comp. Physiol.*, 1946, **27**, 105.

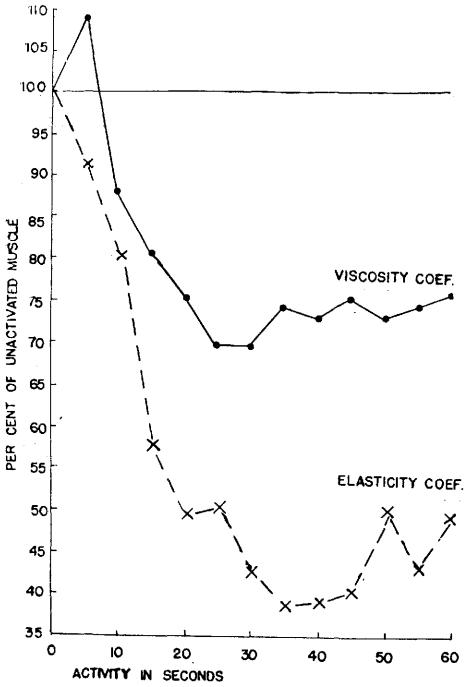

FIG. 1.
Normal muscle: intertetanic changes.

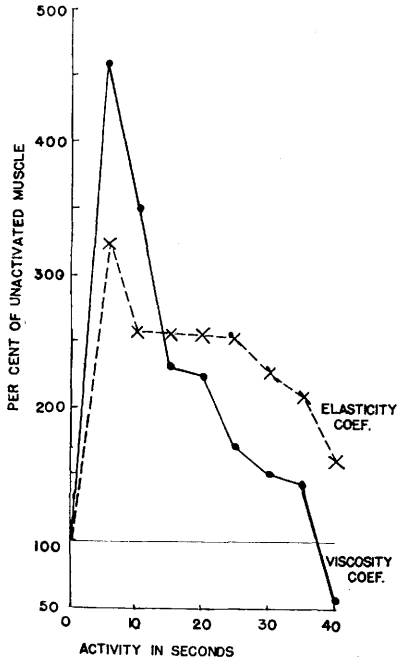

FIG. 2.
Normal muscle: intratetanic changes.

values is about $\pm 6\%$, and for the elasticity coefficient values, about $\pm 12\%$.

Fig. 1 shows the progressive relative effects of a series of 5 sec. maximum isometric tetani of the normal muscle (the spring acting as the isometric lever) when the visco-elastic determinations were made during 25-sec. rest periods interposed between the tetani. Apart from the initial rise in the viscosity coefficient, the progressive effect of the activity is to cause a general reduction in both the viscosity and elasticity of the resting, gradually fatiguing, muscle.

Fig. 2 presents the changes in the visco-elastic behavior when the determinations are made during each of the 5-sec. tetani of a tetanus series of a normal muscle. Here the viscosity and the elasticity become progressively reduced in the muscle as it becomes more and more fatigued. Thus, whatever the values of the viscosity and the elasticity coefficients in the normal muscle, initially at rest or during the first tetanus, the effect of the development of fatigue is to reduce these coefficients within each of the series of successive contracting or resting states, although, as comparison of Fig. 1 and 2 demonstrates, the course of the changes in the resting series is not paralleled in detail by that in the contracting one.

Fig. 3 and 4 summarize the results of experiments essentially like those above, except that the muscles involved had been treated with 1:80,000 iodoacetic acid (IAA). The intratetanic visco-elastic changes are similar to those of the normal muscles, though they develop with activity more rapidly. But in the IAA intertetanic series, viscosity and elasticity, after initially falling, as in the normal muscles, then show behavior different from that of the unpoisoned tissue in the sharp increases in both coefficients which occur after the first 10 to 15 sec. of activity, *i.e.* the period during which the IAA rigor develops.

The interpretation of these results is difficult for it is not even certain that the observed changes are attributable to alterations in the contractile material, since, as

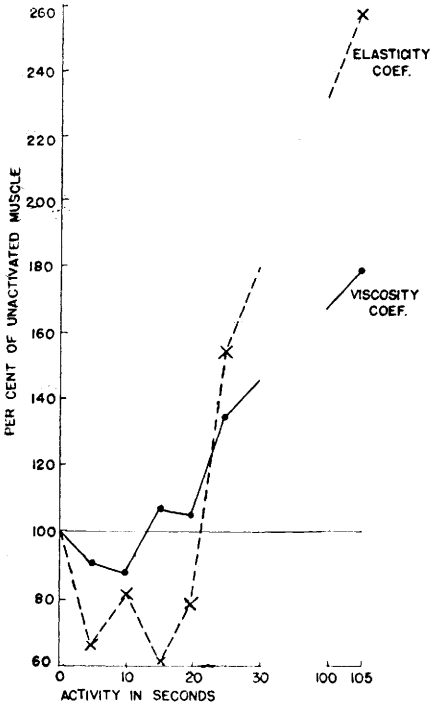

FIG. 3.
IAA muscle: intertetanic changes.

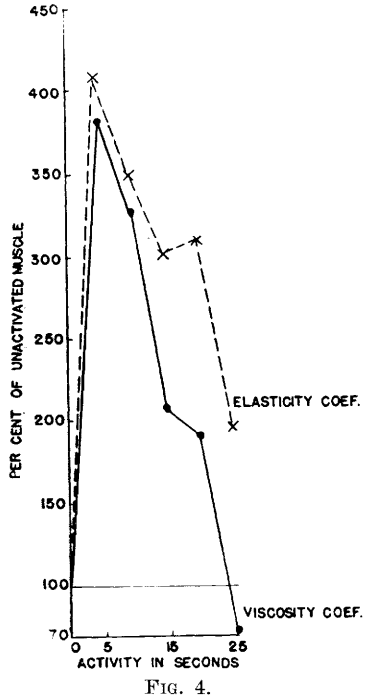

FIG. 4.
IAA muscle: intratetanic changes.

indicated by recent work,[4,5] important elastic properties are associated with the sarcolemma of the muscle fiber. However, the sarcolemma is quite inert and its elastic behavior should remain constant as a given muscle is altered, provided, as is the case in our experiments, the initial muscle length is held constant.[6] It is noteworthy that our method can reflect known changes in the myosin, for muscles treated with 2.5 M urea show a marked reduction in viscosity (and, incidentally, elasticity also)[7] like that found[8,9] after similar treatment of myosin solutions. Furthermore, our intertetanic results for the IAA muscle especially indicate that the observed visco-elastic changes are determined by modifications in the state of the contractile material, since these alterations show a certain correlation with the onset of the rigor that activity causes to appear in the contractile system poisoned with IAA.

Thus, it is possible that our results in general refer to changes in the properties of the contractile system under the influence of progressively developing fatigue. The recent work of the Engelhardt[10] and of the Szent-Györgyi[11] schools on the mechanical and enzymatic properties of muscle proteins shows that these systems, in consequence of their involvement in a variety of mechano-chemical coupling reactions, undergo marked visco-elastic changes. We cannot present here a detailed analysis of the relation between these changes and our observations. It is suggested, however, that evidence such as ours may be used to test the validity of contraction schemes based on the behavior of protein systems extracted from muscle.

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