sistent change in threshold to induction shocks or short condenser charges could be found.

Shocks were then produced by means of a double condenser stimulator[3] having a *k* value of 2 and a time to maximum voltage of 0.018 seconds. With such shocks, the absolutely refractory period was shortened during periods of vagus inhibition but for a given S-I time as above, the voltage required to stimulate the atrium was invariably increased. These results were to be expected in the light of published time-intensity curves plotted from results obtained with normal and vagus inhibited hearts under conditions of controlled rate.[4]

Such findings offer another example of the need for considering not only the intensity but also the time functions of electrical stimuli used in determining tissue excitabilities. Specifically, we would point out that when measurements are made by use of induction shocks only, there may be seen only an apparent quickened recovery of the vagus inhibited tissue following a previous systole. On the other hand, with the longer shocks which were selected to approach pararesonance with the tissue, there is demonstrable both the shortened absolute refractory period which is probably correlated with the shortened period of mechanical systole, and a later prolonged period of depression. The data obtained by the use of such long duration shocks seem to be in closer accord with the observed functional changes than are data obtained by the use of induction shocks alone.

7975 P

Fate of Hexosemonophosphate During Aerobic Recovery of Frog Muscle.*

A. H. HEGNAUER, R. E. FISHER, G. T. CORI, AND C. F. CORI.

From the Department of Pharmacology, Washington University School of Medicine, St. Louis.

An accumulation of hexosephosphate was produced in thin frog muscles (sartorius, ileofibularis, etc.) by keeping them anaerobically

---

[3] Monnier, A. M., *L'excitation électrique des tissues,* Paris. 1934, 115 ff.

[4] Ashman, R., and Garrey, W. E., *Am. J. Physiol.,* 1931, **98**, 109.

* Aided by a grant from the Rockefeller Foundation to Washington University for research in science.

for 2 hours in phosphate-Ringer's solution (pH 7.2) containing epinephrine in a concentration of 1 :10^7. As shown previously,[1] the hexosephosphate so formed disappears when the muscles are transferred to oxygenated Ringer's solution containing no epinephrine. In the present experiments the O_2 consumption was measured in a Warburg apparatus during the disappearance of hexosephosphate. Matched muscles were used, one group being analyzed for hexosephosphate and lactic acid at the beginning and the other at the end of the aerobic period. The O_2 consumption was markedly increased in the first 20 minutes and then returned slowly to a steady rate, which was assumed to represent the basal O_2 consumption. The total period of O_2 measurement was between 1.5 and 2 hours. In one group of experiments the muscles were poisoned with iodoacetate (1 :10,000) during the last half hour of the anaerobic period in order to investigate the disappearance of hexosephosphate in muscles with inhibited lactic acid formation.

The following results (in mg. per 100 gm. muscle) were obtained (average of 4 experiments each).

TABLE I.

	Decrease in		Carbohydrate equivalent of	
	Hexose-phosphate	Lactic acid	Total O_2 consumption	Extra O_2 consumption
Without	41	7	16	7
With iodoacetate	42	4	14	2

It may be seen that hexosemonophosphate disappears aerobically at the same rate whether or not the path to lactic acid is blocked by iodoacetate. In either case the total O_2 consumption is insufficient to account for the disappearance of hexosephosphate and the extra O_2 consumption accounts for only 1/6 to 1/20 of the amount which disappears. This seemed to indicate that hexosephosphate is disposed of in some other way and suggested the possibility that it might be reconverted to glycogen.

The following experiments were performed on summer frogs because of their low glycogen content. An increase in hexosephosphate was produced by tetanic stimulation through the pelvic nerves. Small muscles of the right and left side were dissected immediately after stimulation. When the muscles of the 2 sides were analyzed at once, the differences in glycogen were: +40, +24, —26, +30, —11, —38, average +3 mg. %. When the muscles of one side were analyzed at once and those of the other side after 2

---

[1] Cori, G. T., and Cori, C. F., *J. Biol. Chem.*, 1934, **107**, 5.

hours of recovery in O_2, the increases in glycogen were: +125, +110, —60, +154, +75, +66, +77, +42, +71, average +73 mg. %. The average amount of lactic acid which disappeared during 2 hours of recovery in O_2 was 38 mg. %, hence more glycogen was resynthesized than could have come from lactic acid. Assuming that ¼ of the lactic acid which disappeared was oxidized, while the rest was reconverted to glycogen, there remain $73 - 29 = 44$ mg. % of glycogen which could have been formed from hexosephosphate. The amount of hexosephosphate which disappeared during 2 hours of recovery in O_2 was more than sufficient to account for this increase in glycogen.

In order to determine the disappearance of hexosephosphate after iodoacetate poisoning, previously pithed frogs were first tetanized through the pelvic nerves and were then given an intravenous injection of iodoacetate.[†] During 1 hour of recovery in O_2 the muscles poisoned with iodoacetate lost on an average, 46 mg. % hexosephosphate, as compared to 50 mg. % for unpoisoned muscle. The fact that hexosephosphate disappears from muscle poisoned with iodoacetate suggests that resynthesis to glycogen occurs directly and not by way of lactic acid.[‡]

Summary. More hexosemonophosphate disappears during aerobic recovery of frog muscle, either unpoisoned or poisoned with iodoacetate, than is accounted for by the total oxygen consumption. Glycogen determinations show that hexosemonophosphate is resynthesized to glycogen.

[†] Control experiments showed that muscles removed 5 minutes after injection were poisoned completely, since no lactic acid was formed during rigor. Hexosemonophosphate and diphosphate do not accumulate to an appreciable extent in muscles poisoned with iodoacetate until rigor begins to develop. In the above experiments, the muscles were analyzed before the onset of rigor.

[‡] The first step in the resynthesis to glycogen is presumably the splitting off of the phosphoric acid group. The fermentable sugar content of muscle was found to increase when previously stimulated muscle was allowed to recover in O_2.