comprehensive study has been started to determine, if possible, the reason for this variation.

Summary: Alterations in urinary pH have a definite effect on the vitamin C content of the urine. The amount found is less when the reaction is in the alkaline range.

8565 P

Enhancement of Muscle Contraction after Tetanus.

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(Introduced by H. S. Liddell.)

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The contractions of sciatic-gastrocnemius preparations of *Rana pipiens* were recorded isotonically by means of a free-weighted lever loaded with 20 or 30 gm. The preparations were repeatedly stimulated with maximal break shocks at intervals of one second. At one-half minute intervals a tetanising current (10 per second) was applied for 5 seconds. The following changes in amplitude of contraction after tetanus, as compared with the amplitude before tetanus, appeared:

1. *Normal Muscle.* A. *Indirect Stimulation.* In a fatiguing muscle an increase in amplitude occurred and the percent increase became greater (up to 800%) as fatigue progressed. No change was observed in unfatigued muscle, and tetanus during this time diminished the increase to be expected in fatigue. The enhancement of contractions in a fatigued muscle was greater after tetanus (for 5 seconds) than after a rest period of similar duration, and the enhancement persisted for a greater number of stimulations.

B. *Direct Stimulation.* Fine copper wires, inserted into the belly of the gastrocnemius, were employed. No increases appeared in most of the experiments. It is concluded that in those fatigued preparations in which enhancement occurred after each tetanus some muscle fibers were being stimulated indirectly. This has been proved by the studies on curarised preparations.

2. *Curarised Muscle.* There was no enhancement after tetanus during direct stimulation of the gastrocnemius. It is therefore

concluded that the enhancement phenomenon occurs in the myoneural junction. With simultaneous tetanising of the sciatic nerve and direct stimulation of the muscle at one per second no change in the height of contractions was observed. Since in these experiments curarisation had progressed just to the point where muscle gave no response to stimulation of the motor nerve, it is assumed that autonomic nerves, if present, were not curarised. Therefore, it is highly probable that the autonomic fibers are not responsible for the enhancement phenomenon since they are much less sensitive to curare than are the motor nerves. Thus, the enhancement is not due to an Orbeli phenomenon; *i. e.,* stimulation through the sympathetic fibers in the sciatic.

3. *Lactic Acid.* Indirect stimulation of muscles treated with one percent lactic acid-Ringer's for longer than 5 minutes gave very few contractions. As the concentration or periods of immersion were reduced so that the muscle was enabled to respond to stimuli for a longer period, enhancement appeared. Such increases after tetanus were, in general, less than those exhibited by a normal muscle in about the same state of fatigue. Lactic acid apparently affects the enhancement phenomenon only by limiting the number of contractions. Therefore, lactic acid is probably not related to this phenomenon.

4. *Iodoacetic Acid.* Preparations subjected to iodoacetic acid (0.02 gm. injected into the dorsal lymph sac) and stimulated indirectly responded for only a few (30-40) contractions. Tetanus during the very brief fatigue hastened fatigue but produced no enhancement.

5. *Isometric Lever.* When the preparation was stimulated indirectly and a crude isometric lever was employed no enhancement was observed after tetanus if the initial tension on the muscle exceeded 100 gm.

The enhancement phenomenon was observed equally well in normal preparations subjected to maximal break, super-maximal make and break, and supermaximal summated stimulations.

Contracture always followed tetanus and thus caused the first 3 or 4 contractions to be reduced in amplitude as compared with those directly preceding tetanus. The following 10-15 contractions exhibited the enhancement phenomenon.

It seems probable that some mediator is quantaly produced, in excess, at the myoneural junction during tetanus and remains to increase the contractions until it is gradually dissipated. The effect

of this excess is evident only in fatigued muscle. It seems unlikely that the effect is due to decreased viscosity resulting from the increased temperature which occurs in tetanus or that there is a more rapid regeneration of phosphagen during tetanus.

Work is in progress to ascertain the chemical nature of the mediator and to investigate fatigue phenomena in the single fiber preparation.

8566 C

Amino Nitrogen of Nephritic Transudates.

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It is obvious that low plasma protein is one of the factors contributing to the production of edema. Possible mechanisms responsible for the hypoproteinemia of nephritis must therefore be given careful consideration. Besides the factor of proteinuria, a leak of protein through capillary walls should seem significant. Determinations have, however, not shown a great increase in the protein content of edema fluid.

It seemed possible, though, that significant amounts of protein might be lost through capillaries and then rapidly broken down by extravascular proteolysis. This question was studied by making simultaneous determinations of amino nitrogen, by the method of Folin,[1] of serum and transudates of patients with nephritis. (These determinations were not made in the postab-

TABLE I.
Amino Acid Nitrogen, mg. % in Serum and Transudates.

Nephritic Peritoneal fluid				Nephritic Pleural fluid		Non-nephritic Transudates	
Serum	Fluid	Serum	Fluid	Serum	Fluid	Serum	Fluid
4.4	5.6	4.5	4.5	4.1	5.2	4.5	5.2
7.4	5.3	5.3	4.7	4.4	5.8	4.1	3.1
9.1	6.2	5.5	5.2	5.9	5.2	3.9	2.9
6.8	4.2	5.8	5.0	7.9	5.5	5.2	5.8
7.7	4.4	5.9	4.2	7.6	5.0	5.3	5.2
4.9	4.5	6.0	5.0			5.7	4.4
		6.2	4.6				
		Ave. 6.1	4.9	Ave. 6.0	5.3	Ave. 5.0	4.6

[1] Danielson, Irvin G., *J. Biol. Chem.*, 1933, **101**, 505.