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Lactic Acid Increase in Muscle Under the Influence of Anesthetics.

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The increase of lactic acid in resting muscle under the influence of narcotics is a familiar phenomenon with high concentrations of chloroform, and was observed by Meyerhof[1] for alcohol and urethanes in concentrations about 10 times those sufficient for general anesthesia. It has now been found that the lactic acid content of isolated whole muscle of green frogs is increased on the average 20 to 50% by ether, nitrous oxide and ethylene at tensions sufficient for general mammalian anesthesia (0.028 atmospheres ether vapor, 0.85 atmospheres ethylene, 1 atmosphere nitrous oxide). This increase is comparable to that produced by chloroform at an equivalent tension (0.01 atmospheres). The lactic acid increase is greater with higher tensions of these anesthetics, being 75 to 105% when 5 to 8 times the anesthetic tension is used. These increases occur with ½–2 hours exposure to the anesthetic, and do not seem to be greater with the longer exposures. They are measured by comparing the total lactic acid content of several small muscles (one of each of several pairs) exposed to narcotics, with the lactic acid content of the mates to these muscles not so exposed but otherwise similarly treated.

The possibility that the increased lactic acid content is caused wholly by narcotic interference with the oxidative removal of lactic acid is eliminated by the fact that the increase under the influence of narcotics, especially in high concentrations, is very much greater than the increase when all oxidations are prevented by cyanide; and by the second fact that treating both sets of muscles with cyanide before application of narcotic to one of them, or keeping them in an atmosphere of nitrogen throughout the experiment, seems not to decrease the difference between the amounts of lactic acid in the two sets.

These results suggest that the lactic acidemia of general anesthesia may not be due entirely to narcotic interference with oxidations, as is generally supposed, but may be due at least in part to the direct lactic-acid-producing action of the anesthetic on the muscle. The fact that the rate of fall of blood pH and of increase

[1] Meyerhof, *Pfl. Arch. f. Physiol.*, 1921, clxxxviii, 150; *ibid.*, 1921, cxci, 138.

of blood lactic acid is maximal during the first part of a prolonged anesthesia may possibly be correlated with the experimental finding that the amount of lactic acid produced in isolated muscles in contact with narcotics does not seem to be much greater in 2 hours than in half an hour.

The explanation of the increase of muscle lactic acid under the influence of narcotics seems to involve the structure of the muscle (it is not observed in muscle extract according to Meyerhof[2]) and may be formulated in terms of displacement by the narcotic of adsorbed lactic acid precursor or enzyme, with resultant freer contact between the 2 participants in the lactic-acid-producing reaction; or in terms of narcotic increase of membrane permeability, with the same result.

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Studies of Experimental Arthritis. III. Behavior of Skin Tests.

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The purpose of this study was to observe the behavior of skin tests under the conditions of experimental arthritis. One of the questions which a clinical study of chronic rheumatism presents is whether a joint once infected can in itself be a focus from which further exacerbations of the disease may arise. Accordingly, in arranging the experimental conditions under which the subject of bacterial allergy was to be studied, arthritis was produced not only by inoculating animals intravenously but also by inoculating small amounts of bacteria into the joints. The organism used was a laboratory strain of hemolytic streptococcus, preserved by freezing and desiccating the culture. Skin tests were made on the backs of the rabbits, after the hair had been clipped and removed with sodium sulfide. This depilatation was carried out 2 to 3 days before the skin tests were made. The toxic filtrate used was prepared by seeding a 24-hour broth culture of the organisms into about 100 cc. of Harley's toxin media. This was incubated for 5 days, centrifugalized and filtered through a Berkefeld candle. Normal rabbits were found to give no skin reaction following the intradermal injection of 1/10 cc. of these filtrates. Animals so tested were used in these

[2] Meyerhof, *Biochem. Z.*, 1926, clxxviii, 489.