

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 Meyerhof²) 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 depilation 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.

experiments. In the series reported 24 animals were used, the same number being inoculated intravenously as by the intra-articular route.

After intravenous injection, rabbits usually develop a positive blood culture. Daily blood cultures then show one of two things. The animal tends to recover and the daily blood culture shows fewer and fewer organisms, or the animal grows rapidly worse with more and more organisms per cc. of blood and soon dies. The rabbits surviving may or may not develop metastatic joint infections.

Rabbits inoculated into joints rarely develop a positive blood culture; only one animal in whole series did, and it died on the fourth day. Blood cultures, however, in rabbits inoculated by the intravenous route and which have recovered, as well as animals inoculated directly into a joint, usually become positive just before death of the animal when death is due to some intercurrent disease.

All animals, in both routes of inoculation become allergic after the fifth or sixth day. This allergy or sensitization can be roughly measured by the size of the reaction and is represented in this paper by numerals the value of which were arrived at by taking the measurement of the discolored area in cm. in 2 diameters and using the product of the numbers.

In animals which were given organisms by the intravenous route, the allergy tends to grow less and finally disappear unless the animal develops some metastatic focus. In the animals with infected joints, allergy was present as long as the infection persisted. Spontaneous recovery from a metastatic joint infection was accompanied by a diminution in the allergic state as manifested by the skin reaction. Surgical draining of a joint, whether infected by the metastatic route or by direct inoculation was accompanied by the same result.

A dissemination of organisms by the blood stream is not necessary for the development of the allergic state as rabbits inoculated directly into a joint become allergic without ever developing a positive blood culture.

The pathological changes found both at the site of the focus and through the animal body were studied and reported in previous articles. However, autopsies were done on half of the present series and sections of lung, heart muscle, aorta, skeletal muscle, liver, spleen, and kidney examined. The pathology was found to be the same in rabbits inoculated by both routes and the same in allergic and non-allergic animals.

This pathological change consisted of a proliferative perivascular infiltration which did not show multinuclear cells.