The subjects were able to remain in the hot and humid room without any discomfort for the period of 3 hours and could have remained there for longer periods without any real discomfort. The observers were unable to remain in the room for more than a few minutes at a time during the periods of observation without experiencing marked discomfort.

Comment. The data indicate that an individual resting in a hot and humid atmosphere can be made comfortable and many of his physiologic processes kept at a level for a comfortable environment by cooling a localized portion of the body. When only a small portion of the body is cooled, such as forearm and hand, the effects are definite, but not as effective as when larger areas are cooled. Cooling a localized portion of the body inhibits the accumulation of body heat. The forearm and hand represent about 5.5% of the total surface of the body,[5,6] while the lower two-thirds of the trunk of the body and upper two-thirds of the thighs represent about 50% of the total surface area. Obviously, since heat exchange between the environment and the body is a physical one, the larger the area of body cooled, the greater the loss of heat. However, the relatively great vascularity of the hand and fingers increases its capacity for heat transfer and thus tends to compensate for the smaller area cooled.

It is well to remember that when the parts are submerged in a cool water bath or enclosed in a cooled chair, the parts are not only sites for heat loss from the body, but also, in being isolated from the hot and humid environment, reduce the surface area exposed to the hot, humid atmosphere to absorb heat.

Since interruption of the blood supply to the cooled part with its nervous system intact failed to inhibit the production of physiologic changes by the hot and humid room, the effects of cooling the isolated part must result mainly from the maintenance of the normal body temperature and not to any significant neurogenic influences.

We wish to express our appreciation to Mr. G. Morgavi, Jr., who constructed the apparatus and participated in the studies.

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14515

Sudden Destruction of Motor End Plates by Lactic Acid.*

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The morphologic effects of lactic acid, in concentrations (0.05-0.3%) found in rigor mortis[1] of muscle, upon the labile structure of motor end plates are unknown. During postmortem rigidity of muscle in man, monkey, and mouse there is a sudden or gradual disappearance of the end plates dependent upon the time of onset of rigor: extreme exhaustion induced by either physical activity or acute infections immediately prior to the death of the experimental animal produces both rapid onset of rigor and rapid dissolution of the end plates.[2] Experimental morphologic studies of the motor end plates must be made therefore before the onset of rigor and preferably from muscles excised from the living animal and processed immediately by the gold method.

Methods. Kocher collar incisions were made through the shaved skin on the ventral aspect of the neck in adult white rats, *Mus norvegicus* (250-280 g), under anesthesia by intraperitoneal injection of nembutal, 25 mg

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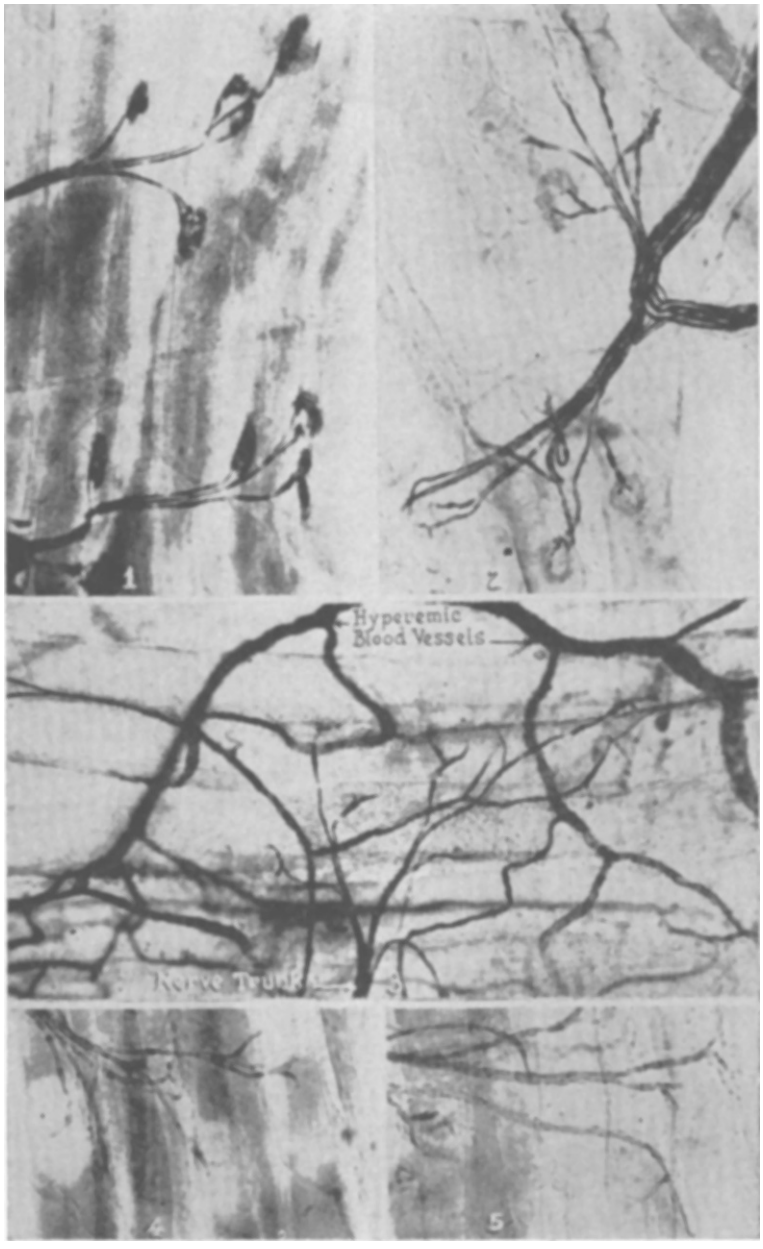

FIGS. 1 TO 5.

Photomicrographs, normal innervation, sterno-mastoid muscle, white rat, Fig. 1; motor end plates either expanded, Fig. 2, or destroyed and accompanied by hyperemic blood vessels, Fig. 3, and depletion of epilemmal axons, Figs. 4 and 5, of auriphilous substances, by lactic acid. × 100.

per kilo. Both sternomastoid muscles were exposed. The local zone of innervation was about 1 mm wide and more opaque than the rest of the muscle; it extended transversely mesiad to laterad and was about midway between origin and insertion. The right muscles were removed, with bleeding controlled, run through gold technique[3] and other

[3] Carey, E. J., *Am. J. Path.*, 1942, **18**, 237.

histologic methods, and used as control muscles. Into the opaque zone of the exposed innervation of the left muscle, 0.1 cc of 0.05% lactic acid was injected in 10 rats: 0.1 cc of 0.10% lactic acid into the muscle of 10 rats; and 0.1 cc of 0.30% lactic acid into the muscle of 10 rats. Five rats in each series were killed within 30 seconds and the remaining 5 in each series at 25-minute intervals. The above experiments on the same number of rats were duplicated, with the same concentrations as those used in the lactic acid series, by the injection of acetic, phosphoric, betaoxybutyric, and hydrochloric acids. Although the histologic results herein reported were those obtained with lactic acid, the increase of the hydrogen ion concentration effected by the other acids produced similar morphologic results. The muscles injected with lactic acid were excised, subjected to the gold technic previously described,[3] and the innervations teased out. Over 1500 gold preparations of the normal and abnormal innervations of the sternomastoid muscles in the white rat were used in this study.

Results. The normal end plates, Fig. 1, in the sternomastoid muscle of the white rat varied from 14 to 25 μ in length in the retracted state with related Kühne's granules, and from 25 to 48 μ in the expanded state with a diminution in the amount of the surrounding Kühne's granules. Immediately after the multiple injections of lactic acid into the zone of innervation the muscle grossly became opaque and shortened in a state of continuous isotonic spasm or rigor. The muscle, completely paralyzed by lactic acid, failed to respond to an electric stimulus of the spinal accessory nerve. Lactic acid, 0.05%, produced within 30 seconds retraction of many of the end plates with increased staining capacity for gold and dilatation of the epilemmal axons. This was quickly followed (30 seconds to 25 minutes) by abnormal expansion, Fig. 2, and a decrease in the quantity of Kühne's granules and in the staining capacity of the end plates with gold. The expanded hypolemmal axons were fragmented into discrete globules of various sizes progressively undergoing dissolution. The expanded end plates, continuous with dilated and beaded epilemmal axons, were found in 1825 of 2213 end plates counted. They varied from 35 to 65 μ, measured in the longitudinal axis of the muscle fiber. About 10% of the end plates had disappeared. Lactic acid, 0.10%, destroyed 814 end plates within 30 seconds, and within 25 minutes 2946 end plates of the 3119 epilemmal axons counted were destroyed. Lactic acid, 0.3%, destroyed 972 end plates within 30 seconds, and within 25 minutes 3891 end plates of the 4000 epilemmal axons counted were destroyed. The ends of the epilemmal axons were frequently divided dichotomously and denuded, Fig. 3, of their hypolemmal end plates within 30 seconds by 0.3% of lactic acid. Close to the zones of the injected lactic acid the intramuscular blood vessels, Fig. 3, were greatly enlarged and congested with agglutinated red blood cells within 30 seconds to 25 minutes. Many muscle fibers had the characteristics of so-called Zenker's waxy degeneration. There was irregular clumping of the protoplasm and loss of the regular periodicity of the cross striations in some muscle fibers. Likewise, in many muscle fibers, there were clear oval spaces of liquefaction, Fig. 4, indicated by the terminals of the epilemmal axons denuded of their hypolemmal end plates. The sudden destruction of the end plates by lactic acid altered the local structure of the striped muscle fiber. Within 25 minutes 0.3% lactic acid not only produced dissolution of the majority of the end plates but progressive depletion or exhaustion, Figs. 4 and 5, of the gold staining substance or substances in the epilemmal axons. These exhausted epilemmal axons, Fig. 5, had ghost-like outlines. Some of the nuclei of the muscle fibers were more clearly defined than normally and were either rounded and pyknotic or enlarged by 0.3% lactic acid within 25 minutes. In local spots within the muscle there was a beginning perivascular infiltration of polymorphonuclear leucocytes within 2 hours after injection of the lactic acid.

Comments. Observations had shown that the intravascular injection of alkaline solutions in animals and of defibrinated blood in a decapitated criminal removed rigor and re-established muscle irritability;[4] that indirect overstimulation of muscle through its

nerve supply led to Wedensky's inhibition of transmission of the nerve impulse at the motor end plates;[5] that lactic acid caused Zenker's waxy degeneration of muscle;[6] that the time of onset of rigor was influenced by the intact peripheral nerves;[7] that occlusion of circulation and muscle activity produced pain and "explosive" changes in the electric potential of the hyperexcitable sensory spindles;[8] that increased hydrogen ion concentration in muscle resulted in the discharge of augmented amounts of acetylcholine at the motor end plates;[9] and that nerve cell proteolysis was produced by lactic acid.[10]

The observations in this paper suggest that the abnormal accumulation of acid metabolites of muscle activity first increase the permeability of the end plates to the gold staining axonic substance, and that with increasing hydrogen ion concentration the end plates undergo complete liquefaction and act like chemical safety fuses.

Summary. Lactic acid in concentrations of 0.05 to 0.3% injected into the exposed zone of innervation of the sternomastoid muscle in the white rat produced sudden destruction of most of the motor end plates within 30 seconds to 25 minutes dependent upon the concentration of the acid. This liquefaction of the hypolemmal axons of the end plates was preceded by a first phase of retraction and a second phase of expansion and fragmentation. Lactic acid caused a progressive depletion, in both the hypolemmal and the epilemmal axons, of auriphilous substances. The blood vessels were enlarged, hyperemic, and contained clumps of agglutinated red blood cells in the rigorous muscle paralyzed by lactic acid. It is suggested that the acid metabolites which accumulate during rigor mortis of muscle are responsible for the destruction of the end plates and that during life certain processes that result in the intramuscular accumulation of acid, such as vascular congestion and anoxia, likewise may result in the destruction of the motor end plates.

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Excretion of Metabolic Products of Sulfapyridine in the Dog.

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It was suggested that, following the oral administration of sulfapyridine in man, water-soluble detoxication products of the drug appeared in the urine.[1] Later it was reported that administration of the drug caused a marked increase in the urinary glucuronides, and the glucuronic acid output paralleled the sulfapyridine levels.[2] The isolation of a hydroxysulfapyridine and a water-soluble hydroxysulfapyridine glucuronide was announced.[3] Details of this work are presented here.

Experimental. Daily doses of 0.5 g per kg body weight of sulfapyridine were fed to dogs and urine samples, collected from time to time, were worked up as follows:

Isolation of the hydroxysulfapyridine: 2400 cc of urine containing 18.0 g of sulfa-

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