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Morphologic Effects of Acute Inanition on Motor End Plates.*

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The significance of the pathologic effects of acute inanition of rats upon motor nerve plates is unknown. Sokoloff[1] stated that the nerve endings were enlarged in fasting summer frogs and Woollard,[2] that a similar change occurred in the motor nerve plates in the fasting albino rat. Jackson[3] demonstrated that the muscles lost weight almost 10 times faster than the morphologically resistant nervous system and that the spinal cord actually gained weight in his acute inanition series of the albino rats. He did not study the microscopic changes in the motor nerve plates nor the functional fibrillation of skeletal muscle following acute starvation. Speidel[4] observed the swelling of the growing sensory terminals in the tadpole after starvation. The purpose of this paper is to record the morphologic changes in the terminals of motor nerves following acute inanition in the albino rat.

Methods. Seventy well-nourished albino rats between 200 and 300 g had been fed oats, corn, meats and vegetables for 3 weeks before starvation began. They were kept in cages with wire net bottoms and allowed to drink freely of water. Four animals were killed with chloroform every 24 hours up to 15 days. Ten animals were used as controls. The modified gold method, Carey,[5] of teased intercostal muscle is preferred for demonstrating the continuity of the medullated nerve, end plate, and skeletal muscle fiber. The Bielchowsky silver and the intravitam methylene blue methods were used also. In 10-15-day starved, skinned rats under nembutal anesthesia (25 mg/kilo in 25% aqueous solution, injected intra-

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1 Sokoloff, A. A., *Jahresb. d. Anat.*, 1876, **11**, 161.

2 Woollard, H. H., *J. Anat.*, 1927, **61**, 283.

3 Jackson, C. M., *Am. J. Anat.*, 1915, **18**, 75.

4 Speidel, C. C., *J. Comp. Neur.*, 1942, **76**, 57; *Proc. Am. Philo. Soc.*, 1942, **86**, 168.

5 Carey, E. J., *Anat. Rec.*, 1941, **81**, 393; PROC. SOC. EXP. BIOL. AND MED., 1941, **47**, 67; *Am. J. Path.*, 1942, **18**, 237.

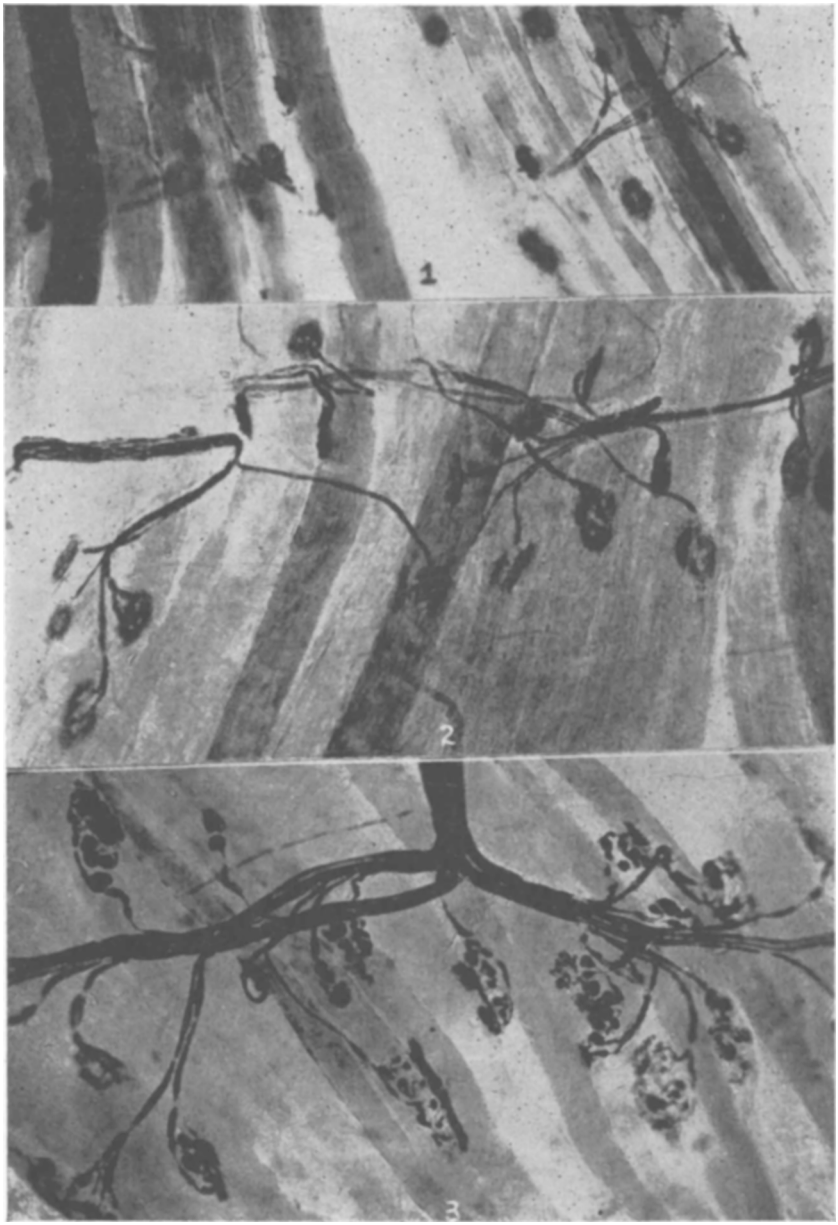
peritoneally) functional fibrillation of intact, living muscle, characterized by slow spontaneous, incoördinated, ceaseless twitchings of 2 to 8 per second, was observed with a hand lens in reflected light and was studied with an oscillograph in the intact animal. The complete study of this functional fibrillation of skeletal muscle following acute inanition is reserved for a future communication.

Results. The normal motor end plates (Fig. 1), in 5000 measurements, varied from 24 to 55 microns in diameter, measured in the longitudinal direction of intercostal muscle fibers. During the first 72 hours of starvation the motor end plates (Fig. 2), in 3509 out of 5000 measurements, were enlarged and varied from 55 to 95 microns in diameter. During the first 72 hours of acute inanition the respirations in contrast to the normal of 30 to 60 per minute, varied from 30 to 100 per minute. Between the 4th and the 15th day there was a gradual decline in the respiratory rate to that of 10 to 40 per minute. The hyposarcolemmal axons underwent progressive retraction, loss of granular sole plate of Kühne, and an uprooting from the atrophic muscle fibers, from the 4th to 15th day of acute inanition. During the same period there was an enormous acute dilatation of the episarcolemmal axons and also of the exuberant axonic branches found between the muscle fibers (Fig. 3). The multiple branches of the episarcolemmal axons had periodic dilatations and constrictions. The dilatations formed large reservoirs, 20 to 40 microns in diameter (Figs. 4, 5, and 6). The axons of the motor nerves were evidently highly resistant to acute inanition and were stained deeply by gold chloride. The muscles, however, underwent progressive atrophy, close aggregation of cross striations alternating with those widely spaced, increased visibility of longitudinal striations, orientation of hyposarcolemmal nuclei, and finally degeneration of many fibers. From the 8th to the 15th day about 20% of the motor nerves ended freely in bulbous expansions found between the muscle fibers, which expansions were devoid of hypolemmal ramifications within the muscle fiber. This morphologic evidence pointed to a progressive denervation or uprooting of motor nerves in skeletal muscle following acute inanition. Differential fiber types due to fractional contraction in normal muscle (Fig. 1) became progressively less definite during inanition atrophy (Fig. 3). This confirmed the observations and reviews of Cobb,[6] Needham,[7] Hines,[8]

[6] Cobb, S., *Physiol. Rev.*, 1925, **5**, 518.

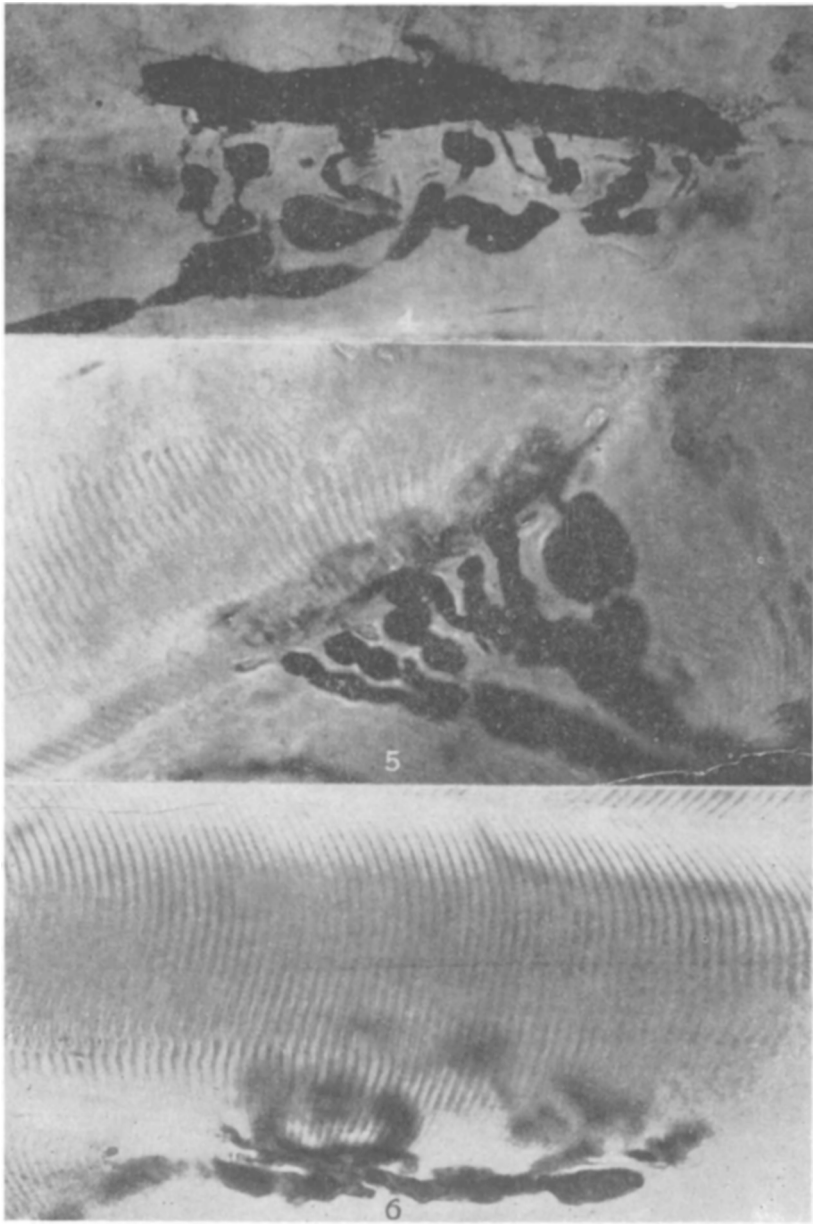
[7] Needham, D. M., *Physiol. Rev.*, 1926, **6**, 1.

[8] Hines, M., *Quart. Rev. Biol.*, 1927, **2**, 149.



FIGS 1, 2 AND 3.

Photomicrographs of teased normal intercostal muscle fibers and end plates of the white rat, Fig. 1; 72 hours inanition, showing enlargement of the end plates, Fig. 2; 8 days inanition, Fig. 3, showing dilated epilemmal axons outside of muscle fibers and different degrees of retraction of hypolemmal terminals of end plates within muscle fibers (gold chloride, × 150).



FIGS. 4, 5 AND 6.

Photomicrographs of motor end plates, profile view, in intercostal muscle eight days acute inanition, showing various degrees of dilatation of the epilemmal axons external to muscle fibers and progressive retraction of the hypolemmal terminals of the end plate within the muscle fibers. The granular sole plate of Kühne undergoes progressive dissolution during acute inanition (gold chloride, × 750).

Denny-Brown,[9] Hinsey,[10] Hines and Knowlton,[11] Tower,[12] and many others.

Summary. Starvation of the albino rat is fatal within 8 to 15 days and produces a structural detachment of about 20% of the motor nerves in skeletal muscle, morphologically manifested by: (1) progressive retraction and eventual uprooting of the hypolemmal end plate from within the atrophic muscle fiber and loss of the granular sole plate of Kühne, and (2) enormous distention of the epilemmal axons which stain very intensely with gold chloride.

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Age Factor in Responsiveness of Pituitary and Adrenals to Folliculoids.

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Several early investigators reported hypophyseal and adrenal enlargement following treatment with impure folliculoid preparations and Hohlweg[1] showed for the pituitary and Selye, *et al.*,[2] for both pituitary and adrenals that even crystalline estrone elicits these effects in the rat. Selye, *et al.*,[2] expressed the view that the adrenal enlargement is due to an increased secretion of the corticotropic hormone of the pituitary since it could not be obtained after hypophysectomy. Adrenocortical enlargement is a characteristic symptom of the alarm reaction and hence can be elicited by any nonspecific damaging agent. Histologically the cortical enlargement caused by folliculoids resembles that which appears during the alarm reaction,[3] yet it can hardly be regarded merely as a response to nonspecific damage as it is elicited by comparatively small doses of folliculoids which are not very damaging.

The observation that folliculoids enlarge the hypophysis and ad-

9 Denny-Brown, D., *Proc. Roy. Soc. B*, 1929, **104**, 371.

10 Hinsey, J. C., *Physiol. Rev.*, 1934, **14**, 514.

11 Hines, H. M., and Knowlton, G. C., *J. Physiol.*, 1939, **128**, 97.

12 Tower, S. S., *Physiol. Rev.*, 1939, **19**, 1; *Arch. Neurol. Psychiat.*, 1939, **42**, 219; *J. Neurophysiol.*, 1941, **4**, 398.

1 Hohlweg, W., *Klin. Wschr.*, 1934, **13**, 92.

2 Selye, H., Collip, J. B., and Thomson, D. L., PROC. SOC. EXP. BIOL. AND MED., 1935, **32**, 1377.

3 Selye, H., Harlow, C. M., and Collip, J. B., *Endokrinologie*, 1936, **18**, 81.