an extensive infiltration of leucocytes and rows of muscle nuclei indicate the position of preëxisting fibers (Fig. 4). Some of the original muscle nuclei, displaced and distorted by the swelling of the fiber, are also found crowded on the sarcolemma. Later they undergo complete karyorrhexis and may disappear. The collapsed fibers often contain only granular debris and newly formed nuclei.

In the succeeding stage of this dystrophy, characterized clinically by an improvement in locomotion and lessening of the paralysis, there is already histologically a regeneration of part of the muscle fibers. Within an area filled with infiltrated leucocytes, connective tissue elements and debris, newly formed isolated fibers appear. In accordance with the description given by Forbus[11] of regenerating skeletal muscle, these fibers always arise in connection with the rows of muscle nuclei. Subsequently myo-fibrils develop between the nuclei and regenerated fibers with well defined cross and longitudinal striations appear. The nuclei stain lightly with hematoxylin and are at first centrally placed in the fiber.

Summary. The skeletal musculature of paralyzed young of E-low rats invariably shows a progressive degeneration which is correlated with the severity of the paralysis. In those cases where, as described in the preceding paper, a spontaneous recovery from the paralysis has occurred, a regeneration of the musculature can be observed to have taken place.

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Experimental Production of Arteriolonecrosis and Medionecrosis of Arteries by Means of Tyramine Injections.

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(Introduced by W. L. Holman.)

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It is the opinion of many workers that certain forms of hypertension are produced by means of a pressor substance elaborated in ischemic renal tissue. Wolf and Heinsen[1] have expressed the belief that tyramine is in fact the pressor substance responsible for the development of hypertension in animals rendered hypertensive by

[11] Forbus, W. D., *Arch. Path.*, 1926, **2**, 318.

[1] Wolf, H. J., and Heinsen, H. A., *Arch. f. exp. Path. u. Pharmakol.*, 1935, **179**, 15.

the establishment of renal ischemia. Some support is given to this hypothesis by the derivation of a pressor principle having many of the properties of tyramine from the digested saline extract of renal cortex.[2] Whether or not tyramine is concerned in human hypertension, it seemed of value to determine whether systemic injection of tyramine can produce vascular lesions since it is generally acknowledged that the arteriolar lesions found in association with arterial hypertension in man are of fundamental importance in relation to the disease.

In suitably controlled experiments lasting from 1 to 106 days, fresh 1% solutions of tyramine (Hoffman-La Roche) in sterile normal saline were injected daily into the ear veins of 10 rabbits under 6 months of age maintained on an adequate diet. In preliminary experiments initial doses of over 100 mg of tyramine had proved fatal so that a daily dose of from 50 to 100 mg was adopted for all except one rabbit in which the dose was gradually increased up to 190 mg without fatal results, indicating the development of a degree of tolerance. In all animals pupillary dilatation and hyperpnoea lasting up to 45 minutes followed the injections of tyramine. In 7 rabbits death eventually occurred in convulsions after an injection. The other experimental animals and the controls were killed with ether. Complete autopsies were done and thorough histological studies carried out in each case.

Although lesions of the arterial tree were not produced with regularity, 6 of the 10 rabbits receiving tyramine showed significant vascular lesions. Arteriolar lesions were present in 4 animals. In 2 of these and in 2 additional rabbits medionecrosis was seen in the aorta or in the large arteries, particularly the renals, or in both. In the aorta and large arteries pale anuclear areas of necrosis were present over large segments of their walls, spreading out from the center of the media to occupy the greater part of its thickness. Weigert stains revealed intact elastic fibers in these areas; calcification was lacking. These lesions differed in several respects from the familiar spontaneous medial lesions of the rabbit's aorta.

Arteriolar lesions, in the 4 animals showing them, were encountered in brain, kidney and heart, but all 3 organs were not always involved, nor were all the arterioles affected in any one organ. Thus, careful search was necessary to determine the presence of arteriolar lesions in the organs least affected. The slightest alterations were pyknosis, or swelling and fading of medial nuclei, followed by frag-

[2] Williams, J. R., Jr., Harrison, T. R., and Mason, M. F., *Am. J. M. Sc.*, 1938, **195**, 339.

mentation or entire disappearance of medial nuclei and of the elastica. The cells of the lining endothelium were intact but swollen. In some cases there was thickening of the vessel walls by the deposition of a deeply eosinophilic substance which spread apart the partially necrotic cells of the media. The most advanced changes consisted of complete necrosis of arterioles with glassy, homogeneous, hyaline swelling of their walls, accompanied by a more or less marked accumulation of pink-staining, homogeneous material in the adventitial tissues. In one animal in which extensive cerebral arteriolonecrosis was found, massive cerebral hemorrhage had resulted in death. It was not possible to establish a relationship between the occurrence or extent of the vascular lesions and the dosage of tyramine or the duration of the experiment. We are, therefore, endeavoring to discover what factors determine the development of vascular lesions.

Some of the experimental arteriolar lesions resembled very closely the arteriolonecrosis commonly associated with malignant hypertension in man, as well as the arteriolonecrosis occurring in dogs in which malignant hypertension has been produced by the establishment of severe renal ischemia (Goldblatt[3]). Although Rich and Duff[4] have produced local necrosis and hyalinization of vessels by the subcutaneous injection of trypsin, widespread hyaline arteriolonecrosis has not hitherto been produced, so far as we are aware, by the systemic injection of any substance.

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[3] Goldblatt, H., *J. Exp. Med.*, 1938, **67**, 809.

[4] Rich, A. R., and Duff, G. L., PROC. SOC. EXP. BIOL. AND MED., 1934, **31**, 470, and *Bull. Johns Hopkins Hosp.*, 1937, **61**, 63.