The large veins were also greatly dilated.

Discussion. These few preliminary observations indicate that following hemorrhage the circulatory effects of pentothal sodium are unpredictable. In 14 of 19 experiments they were rapidly deleterious.

These observations on laboratory animals suggest that due consideration should be given the occurrence of recent hemorrhage when pentothal is to be used intravenously for anesthesia. There is a tendency from previous experimental work[1] to consider barbiturates desirable during traumatic operations. However, the impression that pentothal is safe and even beneficial in "shocked" cases[2,3,4] is not established and should be tempered.[5,6]

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Studies on Muscle and Nerve in Biotin-Deficient Rats.*

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Several investigators have reported that rats reared on biotin-deficient diets develop a motor syndrome which is characterized by abnormality of locomotion, varying degrees of paralysis and spasticity. Nielsen and Elvehjem[1] have shown that this condition can be prevented and cured by crystalline biotin. Shaw and Phillips[2] reported that the skeletal muscles of biotin-deficient rats showed histologic evidence of atrophy but the spinal cord and peripheral nerves appeared quite normal. This report is concerned with a study of the functional state of muscles and nerves of biotin-deficient animals and includes observations on the rate of neuromuscular regeneration in such a deficiency.

Methods. Albino rats were reared from weaning on the basal egg-white ration of Nielsen and Elvehjem.[1] After symptoms characteristic of biotin deficiency appeared, studies were carried out on the gastrocnemius muscles and tibial nerves. In a number of animals the tibial nerve of one limb was crushed and the rate and extent of neuromuscular regeneration compared to that of control animals on an adequate diet. In the regeneration experiments the unoperated tissues of the contralateral limb served as controls. The strength of the muscles was determined by measuring the maximum isometric tension which developed in response to volleys of adequate stimuli applied directly to the muscle and to its motor nerve. The technics that were employed for denervation and strength measurements have been described in detail elsewhere.[3] In addition, observations were made concerning muscle and body weight ratios, creatine, chloride, and water concentration in the muscles.

Results. Because of an unpredictable survival time, the regeneration studies were conducted on animals which possessed the characteristic biotin deficiency symptoms but had not yet reached the terminal spastic condition. The muscles and nerves of such animals (Table I) were found to regenerate at rates compar-

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[2] Shaw, J. H., and Phillips, P. H., PROC. SOC. EXP. BIOL. AND MED., 1942, **51**, 406.

[3] Hines, H. M., Thomson, J. D., and Lazere, B., *Am. J. Physiol.*, 1942, **137**, 527.

TABLE I.
Average Values for Muscles of Control and Biotin-Deficient Rats.

Diet	No. rats	Time after lesion, days	Relative weight of denervated muscle*	Relative strength of denervated muscle* when activated through		Tension/g control muscle g
				Nerve	Muscle	
Control	14	21	68.3	40.1	51.6	1542
Biotin-defic.	8	21	71.4	39.4	42.7	1649
Control	14	28	78.9	65.9	68.8	1639
Biotin-defic.	5	28	85.9	58.8	73.6	1653

* Expressed in % of that in unoperated contralateral control.

able to those found for the tissues of control animals. If biotin is essential for neuromuscular regeneration, the requirements must be below that afforded by the prevailing dietary conditions. At the above mentioned stage of biotin deficiency, the strength per unit weight of the non-denervated gastrocnemii was not significantly different from that of control animals (Table I). Furthermore, the ratio of the muscle tension elicited through nerve stimulation to that resulting from direct muscle stimulation was not significantly altered, being 91.7% for the control animals and 93.4% for the biotin-deficient group. These deficient animals also exhibited normal creatine concentrations as well as normal values for the ratios of the gastrocnemius muscle weight to body weight.

Additional studies were made upon a second group of 18 rats which had reached the terminal stage of biotin deficiency characterized by a loss of body weight and an abnormal spastic gait. The creatine concentration (mg/100 g muscle) averaged 505 for the deficient and 452 for control animals of a comparable age; thus confirming the finding of Nielsen and Elvehjem[1] that there is a rise in the creatine concentration during the terminal stages of biotin deficiency. The chlorides averaged 1.36 mM/100 g wet muscle for the control group and 1.49 mM for the deficient animals, while the water content was normal. These findings indicate that the increased muscle creatine did not result from a decreased connective tissue phase. The muscles of this group showed a 24% reduction in strength per unit weight when compared to the muscles of control animals in good nutritional state. However, there was no significant deviation from normal in the ratio of the tension developed as a result of direct muscle stimulation to that developed upon stimulation of the motor nerve.

Our findings of normal muscle strength, creatine concentration, and neuromuscular relationships for the animals in the pre-spastic condition indicate that there are no functional muscle abnormalities at this stage of deficiency. With respect to the group of animals in the later deficiency states our observation of unimpaired neuromuscular relationships together with the absence of neural lesions as indicated by the studies of Shaw and Phillips[2] afford no explanation for the disturbance of locomotion seen in these rats. The fact that such animals are sensitive to handling suggests that the reflex effects of painful stimuli upon the motor behavior in this condition should be evaluated. Although the somewhat reduced muscle strength might conceivably indicate a specific effect of extreme biotin deficiency on the functional capacity of skeletal muscle, the loss in body weight and increased creatine concentration accompanied by a loss of muscle strength are data more suggestive of the conditions encountered during certain stages of non-specific inanition atrophy.

Summary. At no stage of biotin deficiency was the capacity of the motor nerve to elicit tension in its muscle found to be impaired. Only in the case of animals which were allowed to approach terminal states was there a reduction in the strength of the skeletal muscle. The rates of neuromuscular regeneration following denervation by nerve crush were not significantly different from those found for control animals on adequate diets.