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Effect of Atropine upon Atrophy and Neuromuscular Regeneration.*

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The following is a report concerning the effects of atropine upon denervated skeletal muscle and neuromuscular regeneration. Levine *et al.*[1] have reported that large doses of atropine decreased the rate of atrophy of denervated skeletal muscle of the rat. Fischer[2] found that large doses of atropine did not retard the diminution of power and birefringence in denervated gastrocnemius-solei of rats and pointed out that the retardation of atrophy was apparent rather than real inasmuch as the non-denervated contralateral control muscles lost appreciable amounts of weight during the experimental periods.

Methods. The studies were made on the gastrocnemius-soleus muscles and tibial nerves of 3- to 5-months-old rats. The experimental and control animals were matched as to age, sex, and stock. In some animals a section of the tibial nerve was removed in order to exclude reinnervation. In other animals the tibial nerve of one limb was crushed and allowed to regenerate. The muscles and nerve of the unoperated contralateral limb served as controls. The groups of treated animals received daily injections of atropine sulfate in doses of 10 to 15 mg per 100 g of body weight. Studies were made on the muscles at 2 or 3 weeks after denervation. These included measurements of the capacity of the muscles to develop isometric tension in response to stimuli applied directly to the muscles and to the nerves according to methods described in detail in a previous report.[3] Additional studies included determinations of muscle weight, creatine concentration and measurements of oxygen consumption by muscle strips in Barcroft-Warburg manometers.

Table I summarizes the results of the various experiments. Atropine was without significant effect upon the creatine concentration and the *in vitro* oxygen consumption of normal and denervated muscle. The daily administration of this drug for a period of 2 weeks had no effect upon the strength per weight unit of denervated and control muscle. The tension per g of the regenerating and control muscles of animals receiving atropine for 21 days was somewhat lower than in comparable muscles of non-treated control animals. The average amount of tension developed by non-denervated muscles per g of body weight was lower in atropine-treated animals than in the non-treated groups. The cause of the low muscle to body weight ratios in the non-denervated muscles of atropine-treated animals is not clear. Fischer[2] suggested that this was due to the effects of a cachectic inanition resulting from anorexia. In our experiments there was no correlation between the amounts of body weight loss and the decrease in the muscle-body weight ratios in the different animals. However, it was noted that the atropine-treated animals lost weight in the early days of treatment and tended to regain weight during the later days of treatment. It is probable that total body weight was regained relatively faster than muscle weight in the periods following inanition. However, a specific wasting effect of atropine on skeletal muscle may also be involved. When the extent of atrophy or amount of regeneration is estimated solely from the terminal differences in weights of denervated and non-denervated muscles it can be calculated that the muscles of atropine-treated animals exhibited a slower rate of denervation atrophy and faster regeneration than those of non-treated controls. The unreliability of employing such a calculation for estimating the rate of atrophy

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1 Levine, R., Goodfriend, J., and Soskin, S., *Am. J. Physiol.*, 1942, **135**, 747.

2 Fischer, E., Proc. Soc. Exp. Biol. and Med., 1942, **51**, 208.

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

TABLE 1.

Average Values on the Gastrocnemius and Soleus Muscles of rats. D indicates denervated muscle and C signifies non-denervated contralateral control muscle. The *in vitro* O_2 consumption was measured on the solei. All other values refer to gastrocnemii.

Condition	No. of rats	Nerve lesion: Type	Nerve lesion: Days	Body wt, g: Initial	Body wt, g: Final	Gms tension per g muscle: D	Gms tension per g muscle: C	Muscle wt* / Final body wt: D	Muscle wt* / Final body wt: C	Muscle tension (g) / Final body wt (g) stimulated through Muscle: D	Muscle tension (g) / Final body wt (g) stimulated through Muscle: C	Muscle tension (g) / Final body wt (g) stimulated through Nerve: D	Muscle tension (g) / Final body wt (g) stimulated through Nerve: C	Muscle creatine mg/100 g: D	Muscle creatine mg/100 g: C	QO_2: D	QO_2: C	% atrophy†
Control	13	cut	14	183	188	965	1857	.358	.588	3.34	10.62			344	453	2.7	2.5	39.1
Atropine	10	cut	14	186	181	957	1879	.342	.533	3.25	9.37			321	459	2.5	2.4	35.2
Control	7	crush	21	255	243	1269	1830	.378	.595	4.22	10.82	2.35	10.75	392	483			36.3
Atropine	5	crush	21	230	198	1078	1557	.354	.528	3.82	8.27	2.23	7.89	383	469			32.4

* × 100.

† Calculated from the differences in weight between denervated and non-denervated control muscle.

or degree of regeneration under conditions in which control muscle undergoes appreciable changes in weight during the period of experimentation is obvious.

Summary. The daily administration of large doses of atropine to rats failed to retard the rate of atrophy of denervated muscle and did not enhance the rate of neuromuscular regeneration. Atropine did not significantly affect the creatine concentration and *in vitro* oxygen utilization of denervated and control muscle. When expressed as a fraction of the final body weight the strength and weight of the control muscles of the atropine-treated rats were found to be inferior to those of untreated control muscles. The change in weight of the contralateral control muscle following atropine administration invalidates any estimation of the extent and rate of atrophy or regeneration based solely on the differences between the terminal weights of the control and experimental muscle.

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Reproduction of Bacteria from the Large Bodies of *Streptobacillus moniliformis.**†

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In most strains of *Streptobacillus moniliformis* the bacteria develop by gradual swelling into large round forms. These forms transplanted under appropriate conditions germinate by the growth of small soft granules and diphtheroid-like forms and produce a pleuropneumonia-like, L1, colony.[1] Similar enlargement of bacteria and development to pleuropneumonia-like colonies was observed in the cultures of *B. funduliformis, B. coli,* and *B. influenzæ.*[1] In a culture of *B. coli*[2] and in the cultures of several strains of

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1 Dienes, L., *T. Bact.*, 1942, **44**, 37.

2 Dienes, L., PROC. SOC. EXP. BIOL. AND MED., 1939, **42**, 773.

3 Dienes, L., and Smith, W. E., PROC. SOC. EXP. BIOL. AND MED., 1942, **51**, 297.