and "overloading" of the type II alveolocytes by phospholipids, the rate and pathways of synthesis of which are modified under the influence of colchicine, but evidently only to an insignificant degree. These results indicate both a varied role of the cytoplasmic microtubules in the migration and secretion of surfactant in different compartments of the cell, and also the important role of the microtubules in the release of secretion from the apical surface of the type II alveolocytes.

The results described above suggest that lung pathology connected with the action of factors inactivating the cytoplasmic microtubules is based on a disturbance of the character and level of secretion of surfactant by type II alveolocytes.

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MECHANISMS OF NEUROTROPHIC DISTURBANCES IN SKELETAL MUSCLES CAUSED BY BOTULINUS TOXIN

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In botulism, disturbances of the electrogenic properties of striated skeletal muscles arise without any structural or ultrastructural changes in the neuromuscular synapses [4, 7]. Meanwhile in the fibers of muscles paralyzed by botulinus toxin (BT), histological investigations have revealed an increase in the number of cell nuclei [3, 5]. It was decided to study whether any causal relationship exists between changes in electrogenesis of fibers of skeletal muscles paralyzed by BT and the increase in the number of their cell nuclei under these conditions.

EXPERIMENTAL METHODS

Experiments were carried out on 20 male Wistar rats weighing 120-130 g. Local botulinus paralysis was induced by intramuscular injection of a sublethal dose of type A BT (0.05 mg/100 g body weight; 1 mouse MLD = 0.00005 mg) into the right (experimental) leg. The animals' left limbs served as the control. Inhibition of DNA synthesis in the muscle tissue was produced by daily (starting 24 h before intramuscular injection of BT) intraperitoneal injections of fluouracil, which blocks DNA synthesis, into the rats in a dose of 50 mg/kg [2] starting the day before intramuscular injection of BT. The experimental animals were divided into two groups. Only

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TABLE 1. Synaptic Transmission from Nerve to Soleus Muscle and Electrical Constants of Cell Membranes of Soleus Muscle Fibers of Rats on 5th Day of Botulinus Paralysis and Administration of Fluouracil

Series of experiments	CNMST	d, μ	RMP, mV	R_{in}, MΩ	τ, msec	AB-AP
BT intramuscularly:						
experimental mice	0,12±0,03 (6)	28,63±1,09 (30)	66,45±1,75 (46)	0,47±0,03 (26)	2,48±0,09 (26)	96 (50)
control mice	0,91±0,02 (6)	30,20±1,54 (30)	76,14±2,24 (21)	0,41±0,04 (15)	2,20±0,19 (15)	5 (38)
P_{e-c}	>0,001	<0,2	>0,001	<0,5	<0,2	
BT intramuscularly + fluouracil intraperitoneally:						
experimental mice	0,28±0,07 (6)	28,93±0,99 (30)	74,63±2,26 (30)	0,43±0,04 (25)	2,37±0,06 (25)	10 (30)
control mice	0,89±0,02 (6)	28,96±1,14 (30)	75,54±2,13 (24)	0,39±0,04 (28)	2,36±0,09 (28)	4 (24)
P_{e-c}	>0,001	<0,5	<0,5	<0,5	<0,5	

Legend: 1. CNMST) Coefficient of neuromuscular synaptic transmission; d) diameter of muscle fibers; R_{in}) input resistance; τ) time constant of plasma membrane; AB-AP) percentage of muscle fibers tested giving anode-breaking AP. 2. Number of animals given in parentheses. e) Experiment, c) control.

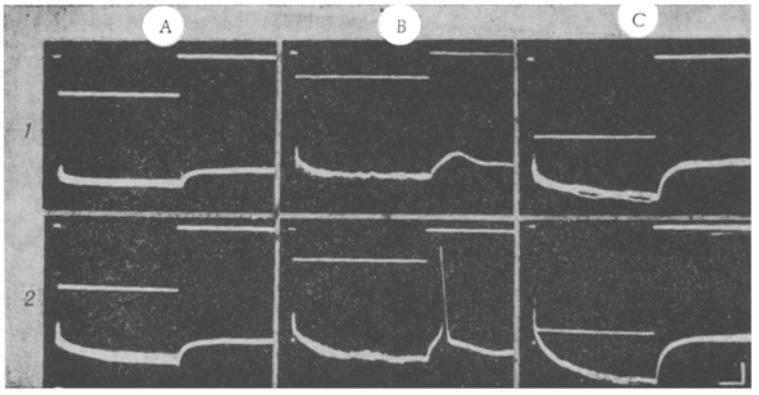

Fig. 1. Electrical activity of muscle fibers of rats in response to anodal intracellular polarization of increasing intensity. A) Muscle fiber of control limb; B) fiber of experimental limb, 5th day after intramuscular injection of BT; C) fiber of experimental limb, 5th day after intramuscular injection of BT+daily intraperitoneal injection of fluouracil. Calibration: 10 msec, 10 mV, 10 nA. Top beam records polarizing current (strength of which increases from 1 to 2), bottom beam records response of muscle fibers.

BT was injected into the animals of one group whereas the animals of the other group received, besides intramuscular injection of the corresponding dose of BT, intraperitoneal injection of fluouracil. On the 5th day after injection of BT the coefficient of neuromuscular synaptic transmission was investigated in the two groups of animals: This coefficient was calculated on the basis of the amplitudes of tetanic responses to direct and indirect stimulation. Resting membrane potentials (RMP) and electrical activity of the myocytes of the soleus muscles of the experimental (right) and control (left) limbs were recorded by microelectrode derivation with direct intracellular polarization. The diameter of the muscle fibers was measured with an ocular micrometer on sections stained with hematoxylin-eosin. The experimental results were subjected to statistical analysis.

EXPERIMENTAL RESULTS

Injection of a sublethal dose of BT into the right leg on the 5th day evoked a marked fall in RMP of the soleus muscle fibers (Table 1). At this stage atrophy of the muscle cells had not yet occurred and no changes had taken place in their input resistance or the time constant of the cytoplasmic membranes. Despite this, the electrogenic properties of the electrically excitable membranes were considerably disturbed. For instance, whereas in the control muscles anodal intracellular polarization was accompanied only by the appearance of anelectrotonic potentials of the membrane (Fig. 1A, 1, 2), polarization of the cells of the muscles paralyzed by BT evoked local responses and the generation of anodal breaking action potentials (AP; Fig. 1B, 1, 2). This occurred because disturbance of regenerative electrogenesis in the myocytes paralyzed by BT corresponded in type to that due to inactivation of the sodium channels of the electrically excitable membrane [1].

Inhibition of DNA synthesis in the muscle tissue by daily intraperitoneal injection of fluouracil into rats considerably prevented the appearance of disturbances of the electrogenic properties of myocytes of muscles paralyzed by BT. In that case, despite the identical degree of the neuromuscular block on the 5th day after injection of BT, the level of polarization of fibers of the paralyzed muscles was indistinguishable from that of the control limbs (Table 1), and against this background ability to generate local potentials and anode-breaking AP in the muscle cells disappeared (Fig. 1C, 1, 2).

It can be concluded from the results described above that in botulinus paralysis disturbances of the electrogenic properties of the skeletal muscle myocytes and the increase in the number of nuclei in the muscle cells are evidently interconnected. As regards the mechanism of the increase in the number of nuclei in the muscle cells, there is evidence that their source may be satellite-cells capable of mitotic division and of subsequent incorporation into muscle fibers [6].

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