"homeokinesis". The results obtained are in good agreement with Halberg's ideas about the chronome [5] as a genetically determined system of rhythmic changes of different frequency manifested at all levels of cognition of living matter.

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MORPHOLOGY AND PATHOMORPHOLOGY

Effect of Weightlessness on the Early Posttraumatic Regeneration of the Soleus Muscle in Rats

L. L. Babakova, M. S. Demorzhi, and O. M. Pozdnyakov

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Gaining information on how reparative processes proceed under conditions of weightlessness is an important objective of research in space biology and medicine, and such information is of both theoretical and practical interest. In skeletal muscles, regeneration in weightlessness occurs in the presence of atrophic and degenerative changes [3,5,6,8,9], as well as of local and general metabolic disturbances, and it is therefore likely that the regenerative process is modified by weightlessness.

Laboratory for Experimental Pathomorphology; Institute of General Pathology and Pathophysiology, Russian Academy of Medical Sciences, Moscow. (Presented by O. M. Pozdnyakov, Member of the Russian Academy of Medical Sciences)

In this ultrastructural study, we examined the course of posttraumatic regeneration in muscles of rats that had been exposed to weightlessness.

MATERIAL AND METHODS

For the ultrastructural study we used soleus muscles from 5 male Wistar rats that had spent 14 days on board the Kosmos-2044 biosatellite and from 5 rats each of three control groups: a vivarium control group (control group 1), one for which all flight conditions except weightlessness had been simulated (control group 2), and one in which the rats had been suspended by the tail in an antiorthostatic position (control group 3). Two

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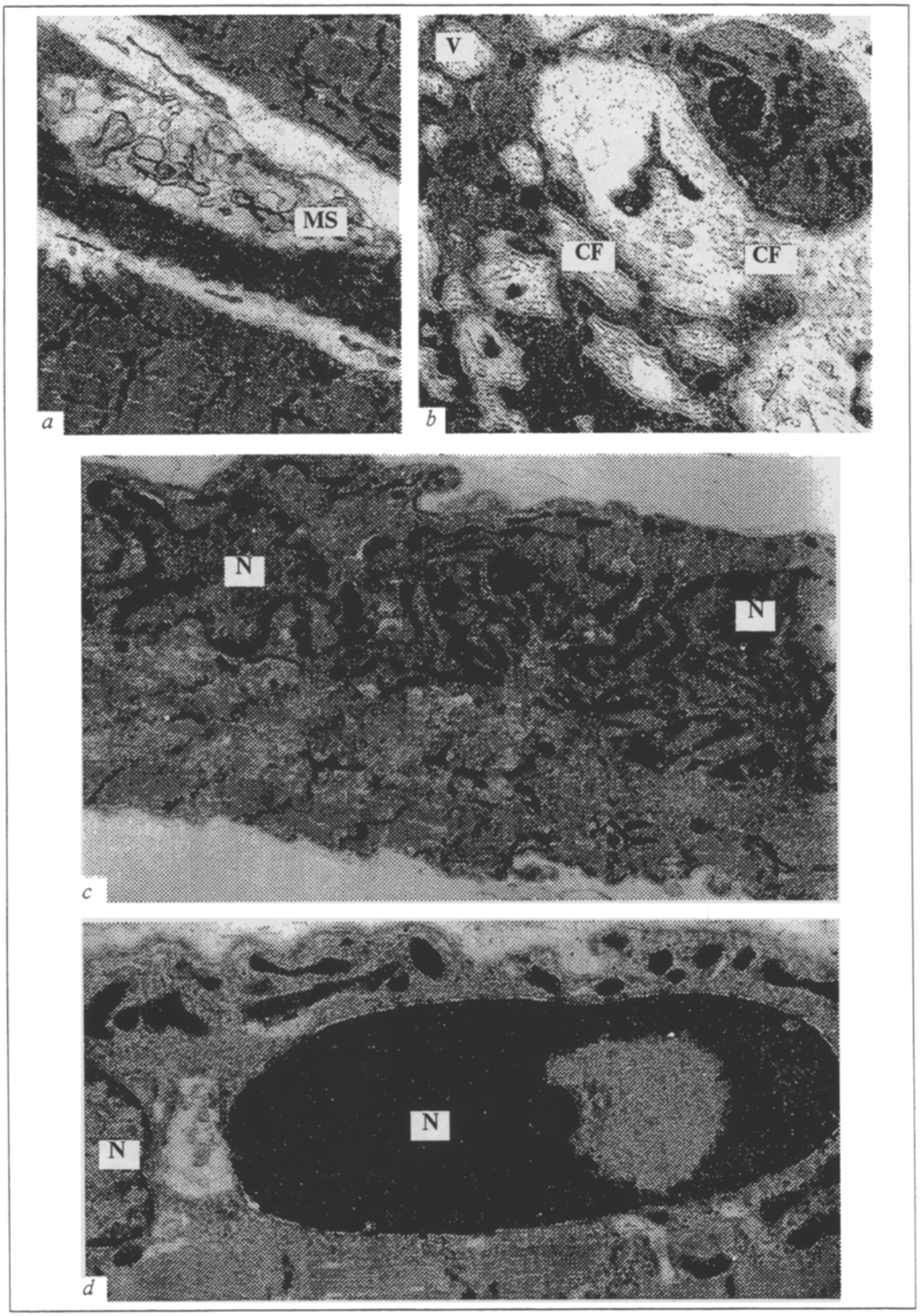

Fig. 1. Degenerative and atrophic changes in muscle fibers of rat soleus muscle after space flight. *a*) The muscle fiber has a reduced diameter, its myofibrils undergo lysis and breakdown and myelinlike structures are present (13,000×); *b*) muscle fiber in the process of vacuolar degeneration (25,000×); *c*) nuclei proliferate and migrate into muscle fiber; *d*) nucleus rich in heterochromatin; there is activation of the nuclear pores (25,000×).N: nucleus; CF: collagen fibrils; MS: myelinlike structures; V: vacuole.

days before the flight and the terrestrial tests, the soleus muscle in all rats was compressed with hemostatic forceps distal to its midpoint; 4 to 7 h after the landing, i.e. on day 17 after the start of the experiment, the rats were decapitated, and pieces of tissue taken from the damaged areas and synaptic region of the soleus muscle were sequentially fixed in a cooled formol-sucrose solution and a 1% osmium tetroxide solution and embedded in araldite. The prepared ultrathin sections were counterstained with uranyl acetate and lead citrate after Reynolds and examined under a JEM-7A electron microscope.

RESULTS

As shown by electron microscopy, the posttraumatic regeneration in *m. soleus* fibers passed through its usual phases in both the space-flight group and all three control groups. In the space-flight group, however, the ultrastructural characteristics of the regenerative process had distinctive qualitative features that suggested its possible subsequent modification. The combination of at least two injurious factors - trauma and disuse of the muscle - led to an intensification and wider distribution of destructive and degenerative processes in the muscle fibers from rats of this group. As a result, the first, destructive, phase that involved breakdown and resorption of the damaged muscle fibers, was not completed by day 17. In some fibers, areas with coagulation-necrotic and vacuolar-degenerative changes were present along with slight to moderate structural alterations suggestive of denervation (Fig. 1, *a* and *b*). Splitting of muscle fibers into fragments was seen. The area of damage contained large numbers of macrophages phagocytizing the destroyed structures. The widened interstitial spaces were filled with numerous fibroblasts of variable size, shape, and electron density and with unidentified electron-dense cells and a network of fibers composed of collagen filaments.

The destructive process induced all potential sources of regeneration. The most strongly marked changes were observed in nuclei. These were seen to proliferate and migrate toward the center of the muscle fiber; the nuclear envelope was invaginated (Fig. 1, *c*). Most of the nuclei were rich in heterochromatin which occupied the entire area in some nuclei (Fig. 1, *d*). A predominance of heterochromatin over euchromatin has been interpreted as a sign of adaptation [1,7]. The numbers of separated satellite cells and of segregated nuclear-sarcoplasmic areas were higher than in the control groups. For satellite cells it was possible to trace all stages of their transformation and their differentiation into free myoblasts, many of which had a large electron-dense nucleus and a narrow osmiophilic cytoplasmic rim (Fig. 2, *a*). Muscle tubules of a more complex structure than the myoblasts were also seen. They contained one or two nuclei with diffusely arranged chromatin and a lumpy nucleolus. Their cytoplasm was rich in organelles, including ribosomes, polysomes, and small electron-dense mitochondria, and it also contained peripherally situated individual myofibrils that in places were organized into sarcomeres (Fig. 2, *b*). Fine immature muscle fibers and myoblasts attached to muscle tubules (Fig. 2, *c*) were also noted.

Although the muscles of the space-flight and control groups were in the same stage of the regenerative process, the former muscles showed several features indicating that this process was inhibited. Thus, the muscles of control group 1 (vivarium control) contained, in the main, structurally mature muscle tubules and young muscle fibers, whereas myoblasts predominated in the muscles from the space-flight group. Also, signs of destruction (vacuoles and myelinlike structures) were seen both in individual myoblasts and in muscle tubules and young muscle fibers of the latter muscles; as a consequence, these muscles contained degenerating forms (Fig. 2, *d*) that were absent in muscles of control groups 1 and 2.

Muscle tubules and muscle fibers may be underdeveloped or die for various reasons. The outcome of regeneration depends in large measure on the state of the supplying blood vessels and nerves [1,2,4]. In the space-flight group, the endothelial cells of most microvessels exhibited degenerative changes indicative of impaired permeability of their walls. *De novo* formation of capillaries was delayed - in contrast to the vivarium control group, where many new capillaries were emerging. A further feature of regeneration in the space-flight group was the presence of innervated muscle-fiber fragments with signs of an active denervation-reinnervation process. These viable specialized islets appear to be necessary at this regenerative stage in order to exert neurotrophic influences during muscle repair. No formation of neuromuscular synapses could be detected in this group.

An important prerequisite for successful regeneration is the tension of skeletal muscles. An indirect indication that muscular tension was preserved in weightlessness was provided by the observation that numerous acellular and cellular elements (including myoblasts) were oriented along the muscle fiber axes.

Degeneration and death of muscle tubules may be one of the reasons for a reduced thickness and

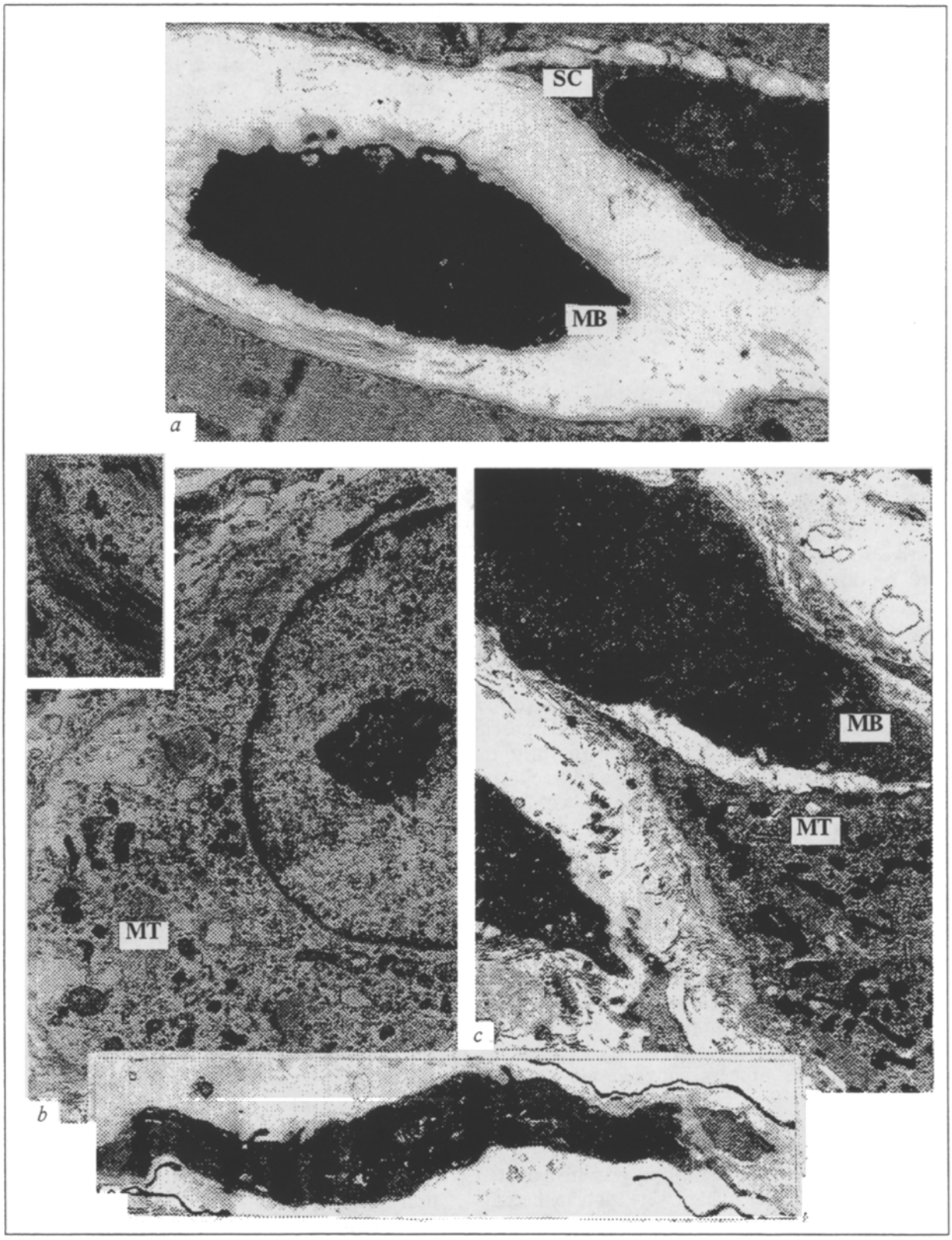

Fig. 2. Posttraumatic regeneration of muscle fibers in rat soleus muscle after space flight. *a*) a satellite cell has separated from the muscle fiber; a free myoblast can be seen in the interstitium (30,000×); *b*) fragment of a muscle tubule showing a large cleared central nucleus and a large nucleolus; the cytoplasm contains small mitochondria, glycogen granules, ribosomes, and myofibrils that are organizing into sarcomeres; there are signs of degeneration: vacuoles are present and the Z bands are disorganized (inset) (13,000×); *c*) myoblast has attached to the muscle tubule (13,000×); *d*) degenerative changes in an immature muscle fiber (16,000×). SC: satellite cell; MB: myoblast; MT: muscle tubule.

number of forming young muscle fibers, as is suggested, in particular, by a 2- to 3-fold decrease in the size of the reparative field noted in rats at the light-microscopic level [3].

The general conclusion from this study is that weightlessness prolongs the early regenerative process without substantially affecting the sequence of its phases. Presumably, the action of factors inhibiting this process will be eliminated subsequently in the course of restitution of the normal blood supply and trophic influences. Also, it should be borne in mind that the rate of regeneration is altered when the functional load is reduced.

Since, as indicated by this study (data not shown), the time course of atrophy and regeneration in the space-flight group has several features in common with that in control group 3 (the one in which the rats were suspended by the tail in the antiorthostatic position), the latter model may be used to study the further course of posttraumatic regeneration.

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Inhalation Injury in Burn Patients and Reparative Regeneration in Tracheobronchial Mucosa

T. S. Ustinova, N. V. Panova, E. V. Glushchenko, A. A. Alekseev, and Sh. A. Kurbanov

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Until just recently flame burn was the most common cause of death in burn patients (90%). In 85% of cases concomitant injuries were typical such, as skin burns with inhalation traumas of the respiratory pathways. These patients died within 20 days following injury, about half of them succumbing within the first 8 days. During recent years inhalation injury as a separate entity has been the focus of in-depth investigation by a number of workers in different fields [3]. The major aspects attracting interest include pathological changes in the bronchopulmonary system resulting from exposure to chemical toxins contained in smoke coupled with extensive tracheobronchial injuries and marked impairment of the pulmonary microcirculation [3,4]. Polymorphonuclear leukocytes causing pulmonary disturbances are thought to play the main role in the mechanism involved in inhalation injury [5].

Department of Pathological Anatomy and Burn Center, A. V. Vishnevskii Institute of Surgery, Russian Academy of Medical Sciences, Moscow. (Presented by D. S. Sarkisov, Member of the Russian Academy of Medical Sciences)

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