NASA TECHNICAL MEMORANDUM NASA TM 75073

DYNAMICS AND CERTAIN MECHANISMS IN THE CHANGES OF THE SKELETAL-MUSCULAR SYSTEM OF MAN UNDER BEDREST CONDITIONS

V. S. Oganov

(NASA-TM-75073) DYNAMICS AND CERTAIN MECHANISMS IN THE CHANGES OF THE SKELETAL-MUSCULAR SYSTEM OF MAN UNDER BEDREST CONDITIONS (National Aeronautics and Space Administration) 37 p HC A03/MF A01 N78-16608 Unclas G3/52 01887

Translation of "Dinameka i nekotoryye mekhanizmy izmeneniy v opornomyshechnoy sisteme cheloveka v usloviyakh postel'nogo rezhima", "Interkosmos" Council, Academy of Sciences U.S.S.R., and Directorate of Space Biology and Medicine, Ministry of Health, U.S.S.R., Moscow, Report, 1977, pp. 1-40.

NATIONAL AERONAUTICS AND SPACE ADMINISTRATION
WASHINGTON, D. C. 20546 DECEMBER 1977

STANDARD TITLE PAGE

1. Report No.	2. Government Accession No.	3. Recipient's Catalog No.
NASA TM 75073		

4. Title and Subtitle	5. Report Date
Dynamics and Certain Mechanisms of the Changes of the Skeletal Muscular System of Man under Bedrest Conditions	December, 1977
	6. Performing Organization Code
7. Author(s)	8. Performing Organization Report No.
V. G. Oganov	
	10. Work Unit No.
9. Performing Organization Name and Address	11. Contract or Grant No.
SCITRAN Box 5456 Santa Barbara, CA 93108	NASw-2791
	13. Type of Report and Period Covered
	Translation
12. Sponsoring Agency Name and Address	14. Sponsoring Agency Code
National Aeronautics and Space Administration Washington, D.C. 20546	

15. Supplementary Notes

Translation of "Dinamika i nekotoryye mekhanizmy izmeneniy v oporno-myshechnoy sisteme cheloveka v usloviyakh postel'nogo rezhima", "Interkosmos" Council, Academy of Sciences U.S.S.R. and Directorate of Space Biology and Medicine, Ministry of Health, U.S.S.R., Moscow, Report, 1977, pp. 1-40.

16. Abstract

A vast amount of literature has been dedicated to the study of the state of the human muscle-support system under conditions of hypokinesia. This report presents the results of reserach on the indicated topic which was mainly conducted in the Institute of Medical and Biological Problems with the participation of colleagues from other institutions.

17. Key Words (Selected by Author(s))	18. Distribution Statement
	Unclassified - Unlimited

19. Security Classif. (of this report)	20. Security Classif. (of this page)	21. No. of Pages	22. Price
Unclassified	Unclassified	38	

"INTERKOSMOS" COUNCIL OF USSR ACADEMY OF SCIENCES
ADMINISTRATION OF SPACE BIOLOGY AND MEDICINE
USSR MINISTRY OF PUBLIC HEALTH
[MOSCOW 1977, NO.10/77-1]

DYNAMICS AND CERTAIN MECHANISMS IN THE CHANGES IN THE HUMAN MUSCLE-SUPPORT SYSTEM UNDER BED REST CONDITIONS

A vast amount of literature has been dedicated to the study of the state /1* of the human muscle-support system under conditions of hypokinesia. This report presents the results of research on the indicated topic which was mainly conducted in the Institute of Medical and Biological Problems with the participation of colleagues from other institutions.

The bed rest conditions in the experiments had two variants: the longitudinal axis of the body perpendicular to the vector of gravitational forces (clinostatic hypokinesia--CH) and the cranial portion of the body inclined from the horizontal by -4° (antiorthostatic hypokinesia--AH). The duration of the bed rest fluctuated in various experiments from 30 to 182 days. The state of muscles and neuromuscular system was judged on the basis of the recording of various functional indices, as well as by certain results of morphological and biochemical studies and the data from study of the motor functions.

I. Functional Characteristic of the State of Skeletal Musculature

In order to evaluate the state and functional reserves of the skeletal muscles a study was made of the dynamics for the change in muscle mass and the

*Numbers in the margin indicate pagination in the original foreign text.

"hardness" of the muscle tissue, the strength indices and the endurance of individual muscle groups, the excitability and electromechanical efficacy of the muscles.

In the process of clinostatic hypokinesia there naturally was observed a reduction in the volume of muscles progressing with an increase in the duration of the bed rest. The pronounced nature of the changes in the perimeters was the /2 greatest in the crus and was 5-6 cm by the end of a 120-day bed rest pattern. The changes were viewed as a consequence of atrophic processes, more pronounced in the leg muscles. However, the more rapid, although not complete, restoration of perimeters in the crus after the end of the experiment permitted the hypothesis that either atrophy of the muscles was accompanied by a weakening of their function related to the guarantee of venous return, or, besides atrophy, a disorder occurred here in the regulation of the regional circulation [31].

Under conditions of antiorthostatic hypokinesia, the degree of change in muscle mass of the crus was also directly dependent on the duration of the experiment. By the end of the 182-day bed rest pattern the crus volume was reduced by 26% from the original level. The femur dimensions after the initial reduction had the opposite tendency. By the end of the 182-day experiment the volume of the femur was 33% greater than the norm. Here, apparently, are more clearly manifest the changes in circulation regulation and/or reduction in the operation of the "muscle pump", which to an equal degree can produce congestion in the vessels of the femur and small pelvis (fig. 1).

Study of the hardness of the muscle tissue, as one of the indirect indices of muscle tone, revealed its essentially similar reduction under the influence of both versions of bed rest. We must note the procedural imperfection in the study of muscle tone on the basis of evaluating "hardness" of the muscle tissue. Nevertheless, changes in the muscle dimensions and indices of "hardness" of muscle tissue in both variants of the bed rest pattern were expressed more in the muscles of the lower extremities.

Under conditions of antiorthostatic hypokinesia of varying duration progressive reduction in the maximum strength of the muscles was naturally noted. /3

After 182 days of AH the strength of the muscles in the crus and torso was reduced by 18.4% and 39.9% respectively, while the hypodynamics of the brachial muscles was expressed to a lesser degree (fig. 2). An analogous nature of changes was noted in the study of static and dynamic endurance (fig. 3), which testified to the reduction in the reserve possibilities of the skeletal musculature.

In the process of bed rest the dynamics was traced for excitability and lability of the musculus biceps brachii and musculus quadriceps femoris. Changes in the rheobase indicated a reduction in the direct excitability of the muscles which progressed with an increase in the duration of the experiment and reached the maximum at the end of the 182-day bed rest pattern (fig. 4). The frequency limits for assimilation of the rhythms of electrical stimulation were also lowered. The impairment in lability of the neuromuscular conduction was the most marked in the 7-8 week of the experiment. The degree of change in the studied parameters in the musculus quadriceps femoris was more pronounced than in the musculus biceps brachii (fig. 4).

It was established by investigating the electrical phenomena in the muscles that the mean amplitude of electromyograms at rest or during the test with maximum contraction has a tendency to drop under conditions of bed rest [32,33]. The most significant changes in the amplitude characteristics of the EMG were noted in the distal muscle groups and especially in the leg muscles.

Lengthy limiting of muscle activity was also accompanied by certain qualitative changes in the EMG. During hypokinesia of varying duration on the interference EMG (most often the musculus gastrocnemius) spontaneous outbursts of activity of an unusually rare frequency were observed, as well as individual /4 potentials of fasciculation (see also [1]). These phenomena are usually associated with an increase in excitability of the motor neurons and the development of conditions promoting synchronization.

In favor of this hypothesis were data from a study of the reflex activity of the spinal chord (N-reflexes) and the activity of individual motor units (MU).

ORIGINAL PAGE IS
OF POOR QUALITY

In the seventh week of clinostatic hypokinesia a reduction was established in the thresholds for summoning the N-reflexes in the musculus gastrocnemius, an increase in the ratio of N/M-responses and a decline in the duration of MU potentials.

Data on a reduction in the mean amplitude of EMG during hypokinesia to a certain extent contradicted the results of the EMG study after space flights. When the cosmonauts fulfilled adequate muscle work in the period of readaptation an increase was noted in the amplitude and a decrease in the frequency of EMG oscillations [21], which testified to the greater intensity of muscle contractions.

The effort to make the EMG a more informative index resulted in the development of a new method for functional diagnosis of the state of muscles on the basis of evaluating the bioelectric cost of their mechanical effects. The integral value of the electrical energy in the crus muscles was measured during random rhythmic plantar flexures of the foot under a standard load.

A statistically reliable, monotonous increase was established in the integral EMG during the 7-10 weeks of bed rest in the antiorthostatic position. This indicated, according to our concepts, the impairment in electromechanical efficacy (EME) of the given group of muscles. With longer periods of bed rest (to 182 days) the changes in EME were of a fluctuating nature (fig. 5). /5

Restoration of the EME after seven weeks of hypokinesia occurred in the course of three weeks of the readaptation period with the use of rehabilitation measures (fig. 6). Restoration of the studied function of the crus muscles after 182 days of bed rest took roughly 5-7 weeks according to preliminary data.

II. Morphological and Biochemical Studies

Studies were made on biopsy specimens taken from the musculus soleus of six subjects on the thirtieth [3] and forty-ninth [3] days of antiorthostatic hypokinesia. Biometrically it was shown that there was a statistically reliable reduction in the volume of red and white muscle fibers on the average by 33% and 22% respectively [42].

Electron microscopic data indicated that the bed rest (AH) was accompanied by marked structural changes in the contractile apparatus (separation of myofibrils, local lysis, thickening and destruction of Z-striae). Histochemical studies revealed shifts in the level of oxidizing metabolism.

After lengthy hypokinesia a decrease was noted in the content of sarcoplasmic and especially contractile proteins in the musculus soleus (table 1), which could be a manifestation of intensified catabolic processes. At the same time the activity of the aspartate aminotransferase and alanine aminotransferase was noticeably increased in the subjects after lengthy bed rest. Apparently, the intensification in catabolism on the feedback principle elicited activation of enzymes participating in synthetic processes [9].

Certain data of biochemical analysis of blood and urine were also viewed as /6 an indication of the intensification in catabolic processes in the muscle. This was shown by the increase in content of creatine phosphokinase in the blood [39], increased removal of nitrogen and phosphorous from the urine [12] and increased nitrogen creatinine in the urine [3].

It is appropriate here to cite certain results of morphological and biochemical analysis of muscles after space flight lasting 23 days (material from the autopsy of the"Salyut-1" crew). On the background of on the whole normal muscle structure of the crus and femur signs of atrophy were observed in individual muscle fibers and focal dystrophy. Fibers were found which were increased in volume, with homogeneous sarcoplasma; a reduction was noted in the diameter of certain fibers with a considerable increase in the number of nuclei extended into a chain, and losses in the transverse and longitudinal striation of individual fibers. In single fibers sections were found of coagulation necrosis, "marginal swelling" of the sarcoplasma (according to the data of V. V. Portugalov and co-workers).

Biochemical studies of the same material did not reveal gross signs of muscle atrophy. The quantity of general and sarcoplasmic proteins did not change in the deltoideus, gastrocnemius and quadriceps femoris musculi. At the same time there was an increase in proteins of the T fraction and a reduction in the contractile protein actomyosin. The described changes had a focal nature and indicated the initial signs of dystrophy, more pronounced in the lower extremities (according to the data of M. S. Gayevskaya and co-workers).

III. Neurological Status and Motor Functions

In the set of neurological disorders accompanying lengthy bed rest several characteristic symptom-complexes are usually distinguished which are classified as astheno-neurotic, hemodynamic, painful syndromes, syndromes of neuromuscular and statokinetic disorders. The last two are important for this report. Certain manifestations and the dynamics for the development of the syndrome of neuromuscular disorders in the process of seven-week bed rest in the antiorthostatic position are presented in fig. 7. Here attention is drawn to the reanimation of the tendon reflexes with signs of asymmetry and increase in the plantar reflexes with pathological signs. In longer periods of bed rest these symptoms were intermittent. They, in addition, agreed with the activation of the reflex activity of the spinal cord previously noted on the basis of recording the M- and N-responses. /7

The statokinetic disorders found in clinical observations were expressed in the disruption of stability and coordination of automated motor habits (locomotion) and preservation of the vertical pose.

On the whole the clinical observations permitted detection of greater markedness in the syndrome of hemodynamic disorders (all the way to cerebral symptomatology) under conditions of antiorthostatic hypokinesia in comparison with bed rest in a horizontal position.

Clinical signs of the statokinetic syndrome were confirmed in the study of motor functions with the help of quantitative methods of study. After hypokinesia in the majority of subjects a reduction was observed in the mean rate of movements due to a shortening in the length of the double step and an increase in the rate of walking [37, 41]. Simultaneously there was an increase in the scope of the coxofemoral, knee and talocrural joints, which indirectly indicated the uneconomical nature of the structure of walking. The described changes in the kinematics were noted in both types of hypokinesia, had an adaptive nature and permitted the subject under conditions of a disorder in movement coordination nevertheless to maintain a rate of advance close to the initial. The indicated changes in step were combined, according to data of movie film, with an increase in torso fluctuations in transverse and longitudinal directions [41]. /8

A reduction in the stability of the vertical pose in the early stages of bed rest in clinostatic and antiorthostatic positions was stabilographically established. At the same time the amplitude of oscillation of the common center of gravity in the body increased in comparison with the norm 1.5-2 times and more [15].

IV. Possible Mechanisms for the Change in Functional State of Skeletal Muscles

Analysis of the findings permits one to state that the stay of a man for a long time under bed rest conditions was accompanied by the development in the skeletal muscles and neuromuscular system of a set of changes which, in our opinion, are well defined by the term "functional atrophy" [48]. It is expressed in the reduced muscle mass and hardness of muscles; decrease in the strength of muscles and their endurance; drop in excitability and functional mobility; increase in the bioelectric "cost" of the mechanical effect. Also noted were certain morphological and biochemical signs of the development of the atrophic process in the muscles. All of this was accompanied by a disruption in movements at various levels of its organization.

The described picture agrees well with the changes in the functions of muscles in cosmonauts after space flights [2, 13, 14, 20, 21, 44, 46, 64]. This is fairly clearly manifest also in the preeminent reduction in the functional potentialities of muscles in the lower extremities and torso in comparison with the muscles in the shoulder girdle [2, 21, 64]. /9

Comparison of the effects of clinostatic and antiorthostatic positions did not reveal essential differences in the main functional indices. Some observed differences in the dynamics of the changes in perimeters of crus and femor were apparently governed by the fact that the antiorthostatic position is accompanied by a more pronounced development of weakness in the venous "muscle pump." This is possibly not only a secondary result of progressive muscular atrophy, but also a consequence of the reconstruction of regulatory mechanisms in the circulatory system.

Data of biochemical studies under conditions of bed rest mainly also correlate well with the results of space flight [12, 54, 68]. However, certain analogous studies did not find such significant changes either in the metabolism of the organism tissue [40] or in the structure and metabolism of muscles (analysis of autopsy material on "Salyut-1" crew, see above).

In this respect attention should be drawn to the opinion of Sandler [62] and many other researchers that flight experiments are not without known deficiencies: small number of targets of observation, differences in the conditions and tasks of flights, in the composition and volume of preventative measures significantly masking the true manifestations of changes, limited opportunities for studying the dynamics of the phenomena. Experiments on animals in space, which in particular, are not "protected" by anything from the effect of weightlessness, were free of some of these deficiencies.

The results of research on the biosatellites revealed that after the animals had been in space for 20-22 days ("Kosmos-605" and "Kosmos-690") certain /10 contractile functions and biochemical properties of the studied muscles (long extensor of the digits and soleus) underwent noticeable (statistically significant) changes; inhibition in the occurrence of single responses, losses of strength (fig. 8) and elasticity of muscles (fig. 9), reduction in functional mobility and resistance to fatigue. In the musculus soleus, besides a greater markedness of these changes, an acceleration was also noted in the development of tetanic isometric contraction (fig. 10). The main characteristics for the functional activity of muscles for the 26 days of the animals' stay on earth statistically did not differ from the level of control values, with the exception of indices for strength and elasticity [28, 29].

One of the main features of the study results consists of the fact that the noted changes are more pronounced in the musculus soleus, related, in all probability, to the morphofunctional differences between the studied muscles. The musculus soleus, as is known, consists primarily of "slow" fibers which are characterized by the slow development of the contractile process, aerobic type of metabolism and high resistance to fatigue. The long extensor of the digits belongs to the "fast" muscles. Its composition contains a small number of "slow" and "intermediate" fibers, however, fibers of the "fast" type predominate; they are characterized by a rapid rate of contraction, anaerobic type of metabolism and low resistance to fatigue [16, 47, 63].

One can consequently hypothesize that the slow musculus soleus which is adapted to the development and maintenance of lengthy stresses and functionally designed for doing work on earth against the force of gravity, under conditions of zero gravity to a greater degree is subject to inactivity than the "fast" muscle which mainly participates in the physical activity. This, apparently, also /11 governs the greater markedness in the musculus soleus of such changes as losses in weight and strength, increase in rigidity, which can be viewed as functional manifestations of atrophy from inactivity.

This is confirmed by the results of morphological investigations on parallel material and agrees with them. In the musculus soleus changes were histologically and histochemically found in many of its structural components which were more pronounced as compared to the "fast" muscle: reduction in the dimensions of fibers, presence of foci of dystrophic degeneration, active proliferation of connective tissue elements in the endomysium and adventitia of vessels [17].

The selective acceleration in the process of tetanic contraction of the musculus soleus, apparently, strengthens the viewpoint [67] according to which "unuse" make the muscles "faster". These results, in addition, correspond well with the data on the change in the musculus soleus under the influence of space flight of the spectrum of isoenzymes of lactate dehydrogenase, which is viewed as one of the manifestations of the reconstruction of metabolism in the muscle towards reduction in the activity of its inherent oxidizing processes and activation of the glycolytic path of metabolism [34].

An indication of the possibility of such reconstruction can be seen also in the results from study of the strength characteristics of muscles. It is known that each type of motor units corresponds to a specific level of ratio for the amplitude of tetanic (A_t) and solitary (A_o) responses, and the value of the ratio A_t/A_o is greater in the "slow" muscles [53, 61]. From this viewpoint the obtained data on reduction in the amount of A_t/A_o can be viewed as the result of transformation of a portion of the slow fibers of the musculus soleus into fast (fig. 8). /12

A definite role in the acceleration of the process of tetanic contraction can also be played by a reduction in the pliability of its elastic components [16, 45, 47], which agrees with the increase in rigidity of the musculus soleus (fig. 9) after space flight [29].

It is theoretically possible [50, 52] that the previously described deceleration in solitary isometric contractions can be related to an increase in the duration (or reduction in the intensity of development and drop) of the active state of muscular contractile apparatus. According to [69], the reduction in rate of unified tetanus of the muscles which was established in our studies can support this hypothesis. In that case this circumstance can indicate the known weakening in the power of the calcium pump and the mechanisms for it which determine the nature of development and the length of the active state [16, 45, 59].

The findings on skeletal muscles in model experiments with bed rest and experiments on biosatellites are summarized in table 2.

We will assume that the previously described changes in the skeletal muscles of man and animals are based on identical or mechanisms close in genesis. In that case it can be seen that many of the manifestations of "functional atrophy" of muscles observed under conditions of bed rest and space flight, as well as the metabolic reconstructions closely associated with them, are equal to the preset conditions and have an adaptive nature. In all probability, they are linked to changes in the regulating systems which have a varying degree of organizational complexity and varying time constants. Somehow or other, the cited data apparently confirm the opinion on the dynamic nature of the adaptation of muscles to a varying level of their functioning [49, 58, 65]. /13

As for the starting mechanisms of these processes, there are all the bases for the assumption that of them the strength discharge of the skeletal muscles and reduction in the percentage of tonal component of movements are important. This widespread opinion is confirmed by direct experimental data [22] on the nature of change in the muscular function ina situation which, without limiting the participation of muscles in the physical movements, significantly reduce or decrease the strength load on them (amputation model).

The above noted tendencies in the change of contractile properties of the skeletal muscles can, apparently, play a definite role also in the emergence of certain phenomena of disorganization of motor functions. This can be shown, for example, in the impaired structure of movements based on the interaction of muscles which differ in their anatomical-functional characteristics (slow and fast). A change in the function of muscles, in addition, can affect the adequate sensory provision of certain motor syngergies.

V. Study of the State of Osseous Tissue

It is known that in cosmonauts after fairly lengthy flights an increase is observed in the content of Ca in the blood and the separation of Ca and P with the urine, and a drop in the mineral saturation of certain bones of the skeleton [19, 5, 66, 56]. At the same time, careful study of the autopsy material form the Salyut-1 crew (histochemistry, x-ray structural analysis of crystalline lattice, evaluation of microhardness and biochemical analysis of correlation of protein and mineral fractions) did not reveal any changes in the osseous tissue which could be viewed as pathological [11]. /14

An investigation of this topic in situations with bed rest produces more unambiguous results. They were reviewed at the previous analogous meeting [62] and there is practically no doubt that limited muscular activity or load on the support apparatus is accompanied by an increase in the removal of calcium and phosphorous from the organism, which is related, in all probability, with an alteration in the balance between synthesis and resorption of the calcified tissues under the given conditions.

We can supplement this picture with the following data. The stay of a man in a bed rest pattern for two months (clinostatic position) was accompanied by demineralization mainly of the tubular bones and this process is expressed in a greater degree than could be expected according to the data of calcarinuria. The most pronounced changes were observed on the 15-30 days of the experiment, after which the intensity of demineralization had a tendency to drop [4]. In analogous conditions an increase to 40% was also established for the removal of calcium [36] and a reduction in the indices of densitometry in the calcaneus on the average by 11-12% [13, 24] and in the metaphysis of the first phalanx of the five fingers of the hand on the average by 7% [24]. Attempts to prevent these changes with the help of pharmacological drugs or physical excercises did not have a distinct effect.

Significant help in the further progress of studying this problem can be given, in our opinion, by research on animals in space and under simulated conditions.

We attempted to generalize some of the results from studies and presented them in the summary table 3. Analysis of it permits certain preliminary considerations to be stated.

It is theoretically possible that the thinning and reduction in density of the osseous tissue may be governed both by the deceleration in its regeneration and the acceleration in the processes of resorption, or the both simultaneously. The overall picture presented in the table has definite signs of a rise in the catabolic processes in bone. However, the impression is created that, with the exception of situations with very rigid fixation, the processes of deceleration /15 in regeneration of osseous tissue have a no less pronounced nature. It is possible that this refers to a greater extent to results obtained in experiments on biosatellites where the periods of observation are limited.

The set of phenomena known at present are apparently more successfully described by the term "osteopenia", in contrast, for example, to senile osteoporosis, where the processes of resorption clearly predominate [6]. The main questions emerging from this discussion appear to be how soon (at what periods of the space flight) does the dominance of breakdown processes possibly become decisive and how can they be prevented. It is necessary to note that until now results have not been obtained which basically solve this difficulty.

In the set of mechanical forces, which in accordance with Wolf's law determine the growth and development of skeletal bones, the decisive role, according to [51] belongs to the deforming loads which are governed by earth gravity. At the same time, analysis of the extensive experimental material results in the conclusion that muscular tone and mechanical forces created by the muscle stress more effectively prevent resorption of osseous tissue than a weight load [18, 62].

Analysis of the results presented in table 3 to a certain degree confirms /16
this viewpoint. In any case, the findings from biosatellites reveal that weightlessness only aggravates certain manifestations of disorganization in the bone metabolism which are noted in parallel experiments with partial immobilization of animals. It is not excluded that the expressed opinion is accurate only for experimental situations with animals where the elimination of the hydrostatic pressure and the redistribution of fluids in the organism which is linked to it is not so essential as in man. It is possible that in man this circumstance more actively stimulates the engagement of other, most likely neuroendocrine, mechanisms of regulation which can aggravate reconstruction of metabolism of the osseous tissue in weightlessness.

Comparison of the aforementioned results from study of the muscular system and osseous tissue in hypokinesia and under conditions of zero gravity, as well as comparison of columns 3 and 4 in table 3 permit one to hypothesize that the aggravating action of weightlessness on the osseous tissue to a greater extent is determined by the change in muscles under these conditions. Apparently, the lack of earth gravity is accompanied in animals by a lower reduction in load on the bone apparatus, and in particular on the vertebral column, than in man. At the same time, as follows from the examined material, the contractile properties, mainly of the antigravitational muscles, change so that they cannot develop lengthy and fairly large stresses. If one takes into consideration that the fast muscles also adaptively develop smaller stresses, then these circumstances, besides the lack of gravitational load on the skeleton, additionally strain the bone. Here, apparently, also should be directed the main efforts to find preventative measures which could have a differentiating effect on individual muscle or muscle groups. /17

As noted previously, as before we still know very little about the details of disorders in mineral and protein exchange in bones under conditions of zero gravity. For this purpose it is necessary to develop analytical studies on the state of the microstructures of the osseous tissue, crystalline lattice of bone and protein matrices and their link to the metabolic activity of certain endocrine glands, first of all, of the thyroid-parathyroid complex and others [6, 11]. Of no less importance is the further perfection of methods for intra vitam study and measurement of the composition of osseous tissue in man. From this viewpoint, the elaboration of a method for photon absorbsiometry or the equivalent mu-meson method of intra vitam analysis of the mineral composition of osseous tissue is encouraging. The latter was employed by the colleagues of our institute jointly with the Institute of Nuclear Studies in the experiment with lengthy (182 days) bed rest. Unfortunately, the findings are in the stage of processing and we are unable to present the results.

Conclusion

The informational and procedural value of experiments with bed rest for solving many basic tasks of space medicine at the present time, apparently, does not elicit doubts.

In this report we attempted to illustrate this thesis in the results of a study on the muscle-support system. It can be assumed that between "functional atrophy" of the skeletal muscles and "osteopenia" occurring under space flight conditions there exists a closer and seemingly, more complex bond. It can be thought that studies under conditions of a bed rest pattern will significantly promote further understanding of the essence of this bond, as well as of the mechanisms involved in the adaptation changes in individual physiological systems both neuromuscular and osseous. /18

One should favorably evaluate the perspective for conducting joint research to solve the indicated questions. From this viewpoint it is expedient to examine and discuss a number of questions of methodological and methodical nature in addition to those previously state [62]: objectivation and standardization of control over observance of bed rest (a better variant, apparently, would be the possibility of quantitative analysis of the degree or measure of "inactivity" of the muscle-support system); selection and standardization of the nature of bed rest (for example, clinostatic or antiorthostatic positions); standardization of the methods for selecting subjects and patterns of rehabilitation; selection and unification of methods for mathematical planning of experiments and processing of their results.

The advantages of cooperation in solving these so complicated problems are obvious.

TABLE 1 /19

EFFECT OF 49-DAY ANTIORTHOSTATIC HYPOKINESIA ON COMPOSITION OF PROTEIN FRACTIONS AND ENZYME ACTIVITY OF SARCOPLASMIC FUNCTION OF PROTEINS IN HUMAN MUSCULUS SOLEUS [9]

Indices		Stat. indic.	before	after
Sarcoplasmic proteins	1% of protein per wet weight of tissue	M	6.29	5.27
		±	0.47	0.41
		п	3	3
		p**		0.2
Actomyosin	1% of protein per wet weight of tissue	M	5.54	5.20
		±	0.35	0.41
		п	6	6
		p**		
Proteins of T fraction	1% of protein per wet weight of tissue	M	2.30-1.90	1.38
		±		0.10
		п	2	3
		p**		
AST	MKM of pyruvate per mg of protein per hour at 37°	M	20.79	26.15
		±	0.87	0.62
		п	3	3
		p*		0.002
		p**		0.001
ALT	MKM of pyruvate per mg of protein per hour at 37°	M	4.34	6.46
		±	0.09	0.10
		п	3	3
		p*		0.002
		p**		0.001

* Criterion of reliability for difference between data before and after experiment.

** Criterion of reliability for difference between mean original and amounts obtained after the experiment.

TABLE 2

COMPARATIVE DATA ON THE STRUCTURAL-FUNCTIONAL CHANGES [illegible] RECONSTRUCTIONS IN THE HUMAN SKELETAL MUSCLES UNDER CONDITIONS OF BED REST AND IN ANIMALS AFTER SPACE FLIGHT /20

Bed Rest in Man		:	Weightlessness and other factors [ ] in animals		
Metabolism	Structure	Function (and anthropometry)	Function	Structure	Metabolism
Drop in content of sarcoplasmic and especially myofibrillar proteins, 49 days [9]; Increase in activity of AST and ALT [9] ; In blood: wave-like changes in content of lactate and pyruvate with [illegible]	Drop in cross dimensions of fibers, signs of atrophy [42]; Focal dystrophy [42]; Histochemically: shift in carbohydrate exchange towards dominance of aerobic oxidation [42]	Drop in strength; reduction in volume and perimeter of muscles; Reduction in hardness of muscles; Reduction in strength impulse due to shortening of movement time;	Drop in amplitude of tetanic stresses per unit weight of muscle [29]; Losses in elasticity (increase in angle of slope for curve in relationship "length-stress" [29]; Shortening of time for development tetanic stress (normalized by amplitude) [28, 29]	Drop in cross dimensions of fibers, atrophy [17]; Proliferation of connective tissue elements in endomysium [17]; Disorganization of cross striation [17];	Losses in myofib. proteins [ ] Increase in activity of AST and ALT [10] Dominance of "muscular" fraction in LDG spectrum: LDG_4 and LDG_5 [34];

Continuation of table 2

/21

...tendency towards their reduction in second half; Signs of predominance of anaerobic breakdown of carbohydrates. Throughout entire experiment (49 days) content of cardiac fractions LDG increased [1,2]; gradual and sharp rise in LDG_5 at end of experiment [39]; Increase in creatine phosphokinase in blood [39] and nitrogen creatinin in total nitrogen of urine [3].	Increase in thresholds of direct electro-excitability; Reduction in rate of recruited rhythm of excitation; Increase in bioelectric "cost" of mechanical effect; Reduction in static and dynamic endurance;	Decrease in amount of ratio tetanus/twitch Reduction in rate of unified tetanus [29]; Drop in rate of solitary stresses [29]; Decrease in resistance to fatigue in rhythmic stimulations [29].

TABLE 3

COMPARATIVE DATA ON THE STRUCTURE AND METABOLISM OF OSSEOUS TISSUE IN MAN AND ANIMALS AFTER SPACE FLIGHT AND UNDER SIMULATED CONDITIONS

Lack of bearing load			Presence of bearing load
Reduction in muscle activity			Limited muscle (phase) activity
[ ]; tonal of muscles in lower extremities	Tonal - for all muscles		
Bed rest (man) (1)	Weightlessness (man) (2)	Weightlessness (animals) (3)	Hypokinesia (limited mobility) in animals (4)
Increase in content of [ ] in blood; Increase in separation of [ ] and P with urine; Reduction in mineral saturation of bones, [ ]ophotometrically [...4, 18, 24, 36];	Duration of flight 14-84 days. Increase in content of Ca in blood; Drop in mineral saturation of bones [5, 19, 56 66]; Increase in removal of Ca and P with urine [5,19,56,66]; Preserved structure of compact and spongy bone; Markedness of crystalline structures better than in cont. preparations	Moderate thinning of spongy osseous tissue of metaphyses (in $\frac{1}{2}$ of cases) expressed more than in synchronous contr. plans (in 1/3 of cases); Perilacunar osteolysis, more marked in comparison with synchr. control; Deceleration of periosteal osteogenesis; Deceleration in growth in length, femur and tibia [43];	Delay in growth of bones in extremities, disruption in exchange of Ca^{45}, P^{32}, glycine-$2C^{14}$ in bones and teeth; hypokinesia 60 and 100 days, rats [23, 25]; Small increase in conc. Ca in plasma of blood and reduction in total protein and inorganic phosphorous [7]; Phase changes in content of alkali and acid phosphatase in osseous tissue and alkali phosphatase in blood serum, increase in activity of both phosphatases by end of 3 months of hypokinesia; rats [26]; Decrease in density of bone (radiometr. method) and increase in removal of Ca with feces; primates, non-support content 35 days [55];

Continuation of table 3

Content of mineral fraction and its correlation to protein without essential differences; Microhardness--without essential deviations from norm; pathomorphological data "Salyut-1", duration of flight--23 days [11].	Reduction in periosteal osteogenesis; Drop in rate of maturation of osteocytes and linear rate of growth of bones (tibia) no reliable data on increased resorption (according to data of E. Kholton, D. Beylink). Reduction in strength of tibia and femur in flights as compared to synchr. contr. (according to data of G. Stupakov, V. Korolev). No pronounced changes found in content of Ca and P in calcified tissues in humerus and incisors; Drop in specific activity of calcium exchange, i.e. rate of restoration [35]; By EPR method no differences found in correlation of amorphous phosphates Ca and crystalline hydroxy appetites in osseous tissue [30].	Morphological signs of dystroph.process in comp. and spong. substance of tibia; dogs, limited movement 6 months [27]; Drastic disruption in structure, wearing down of trabecular base--with rigid fixation, primates [57]; Reduction in mineral saturation of tibia and lack of it in bones of forearm with parallel increase in PTG activity (max. in 3 weeks)--limited mobility 10 weeks [70]; Redistribution of Ca^{45} in different mineralized tissues:resorption from bones of rear extremities and increase in jaws and teeth [8].

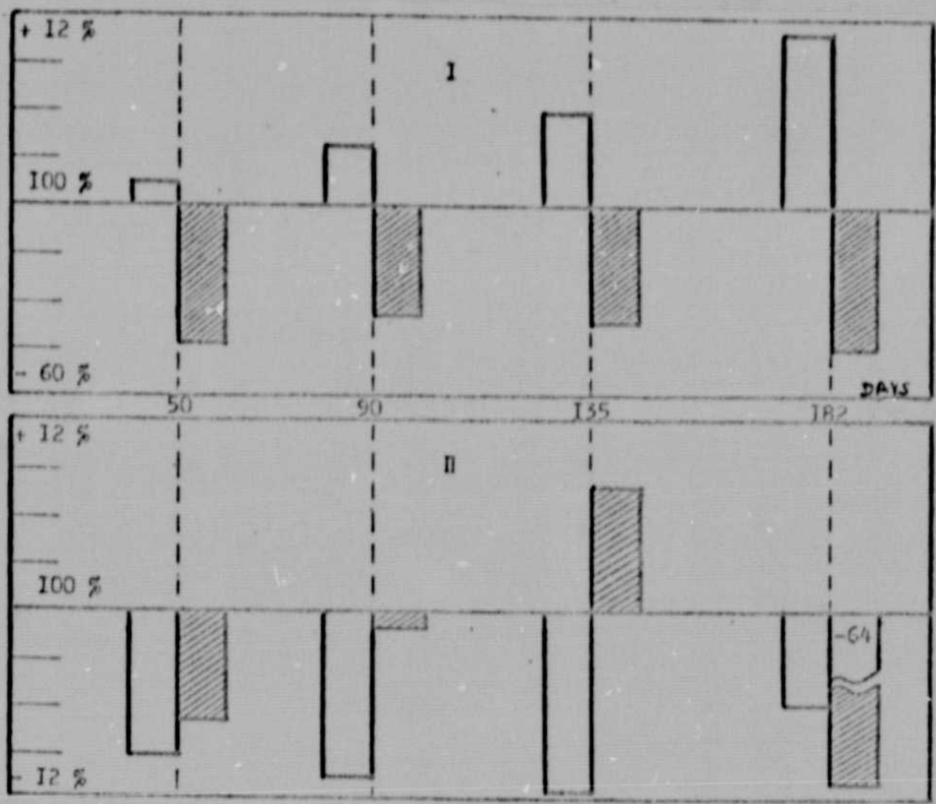


Figure 1. Dynamics of Amount of Volumes of Femur (I) and Crus (II) in Process of Antiorthostatic Hypokinesia (in percentages of initial level). Non-shaded columns--amount of volumes in prone position, hatched columns--difference in volumes measured in positions of standing--lying.

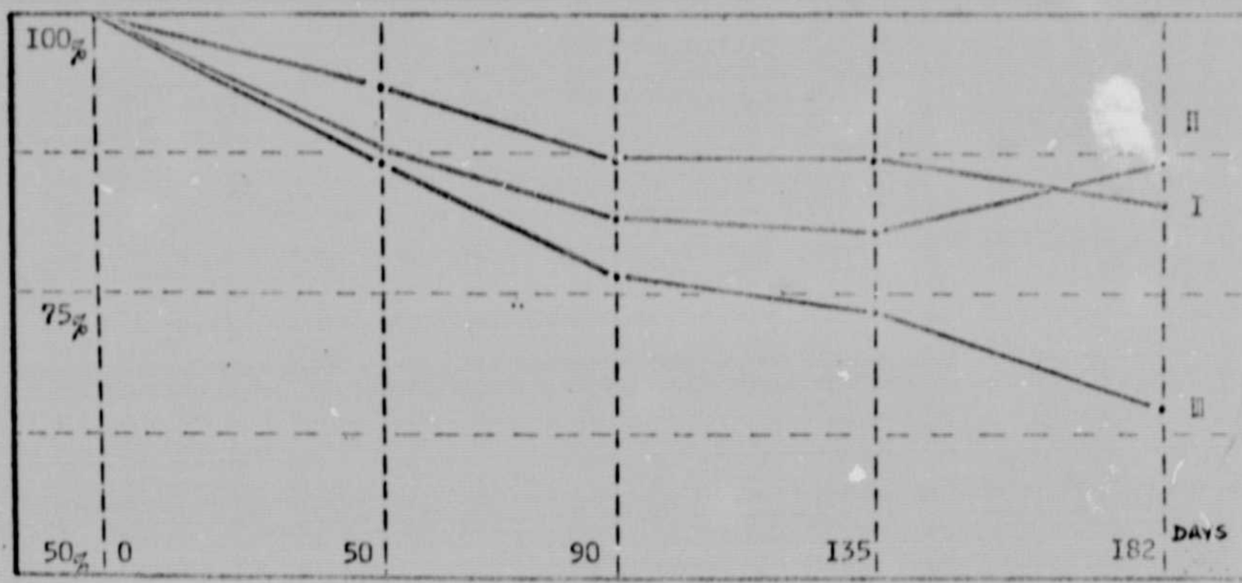


Figure 2. Dynamics of Amount of Maximum Strength of Muscles in the Posterior Group of Crus (II), Brachial Extensors (I) and Torso (III) in Process of Antiorthostatic Hypokinesia

ORIGINAL PAGE IS OF POOR QUALITY

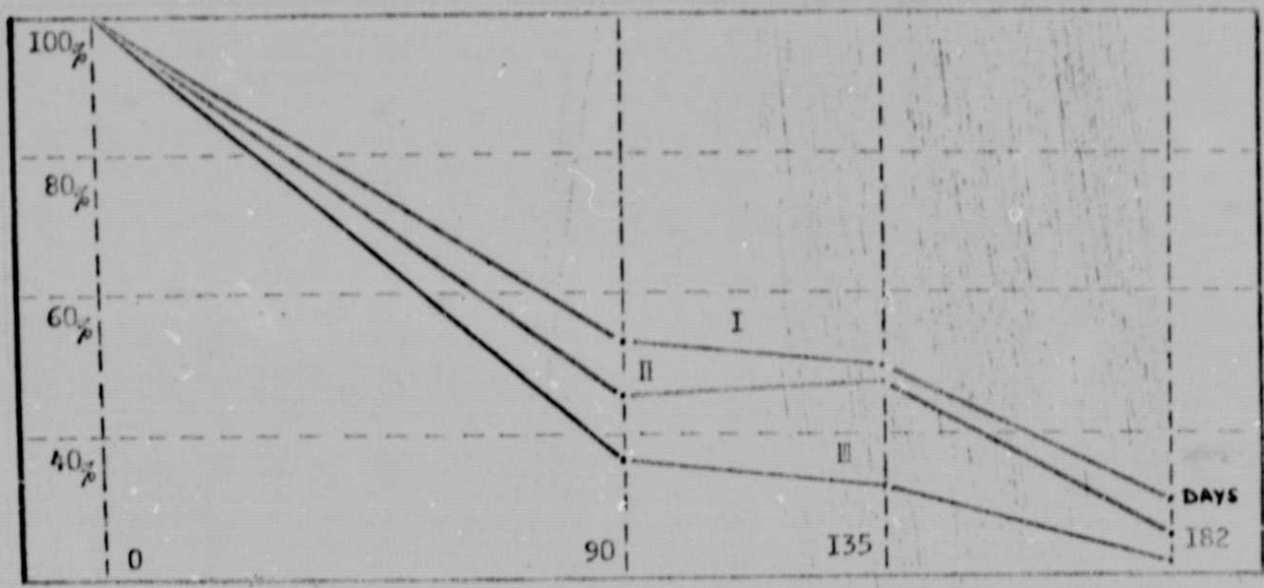


Figure 3. Dynamics of Static Endurance of Muscles in Posterior Group of Crus (I), Extensor (II) and Flexors (III) of Torso in Process of Antiorthostatic Hypokinesia

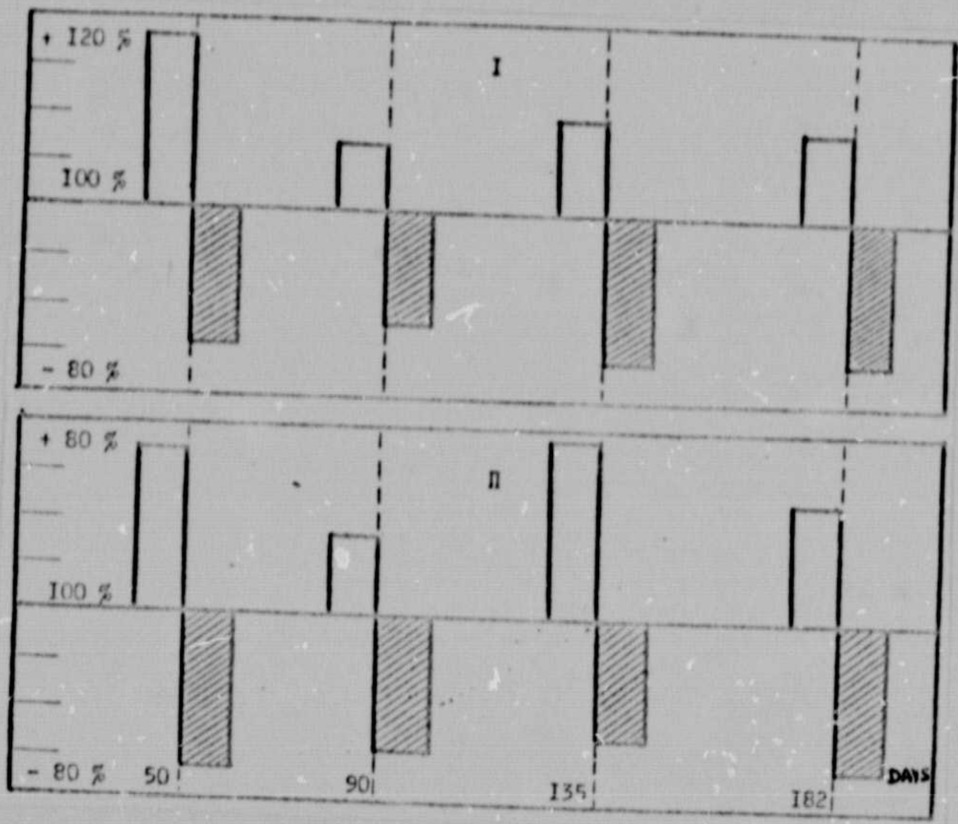


Figure 4. Dynamics of Indices for Excitability (non-shaded columns) and Lability (shaded columns) for Musculus Biceps Brachii (I) and Musculus Quadriceps Femoris (II) in Process of Antiorthostatic Hypokinesia

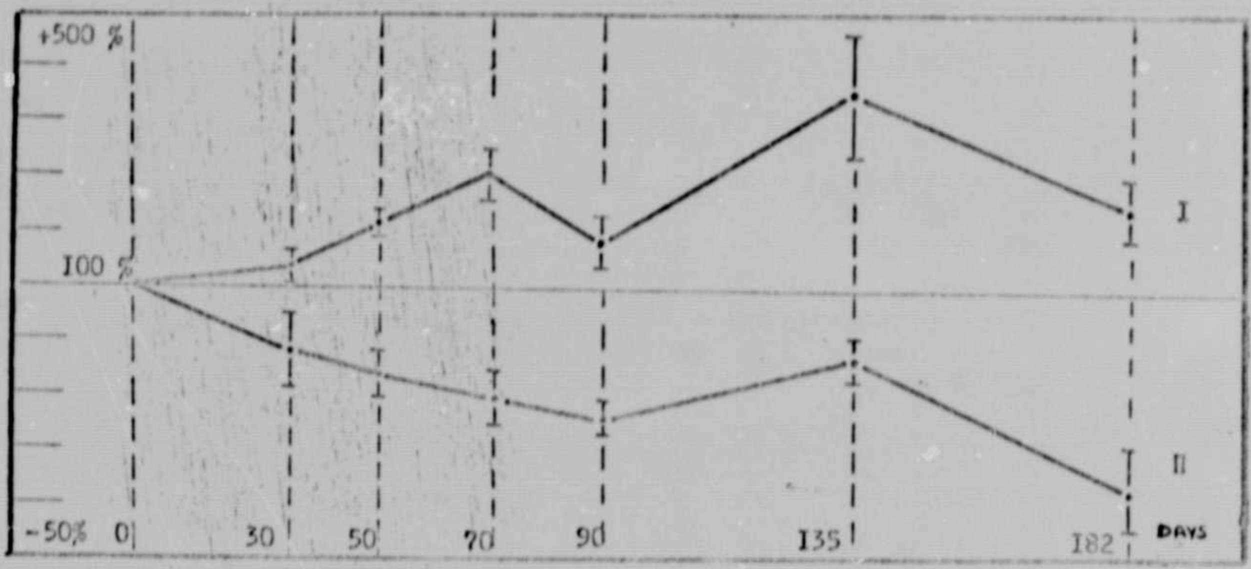
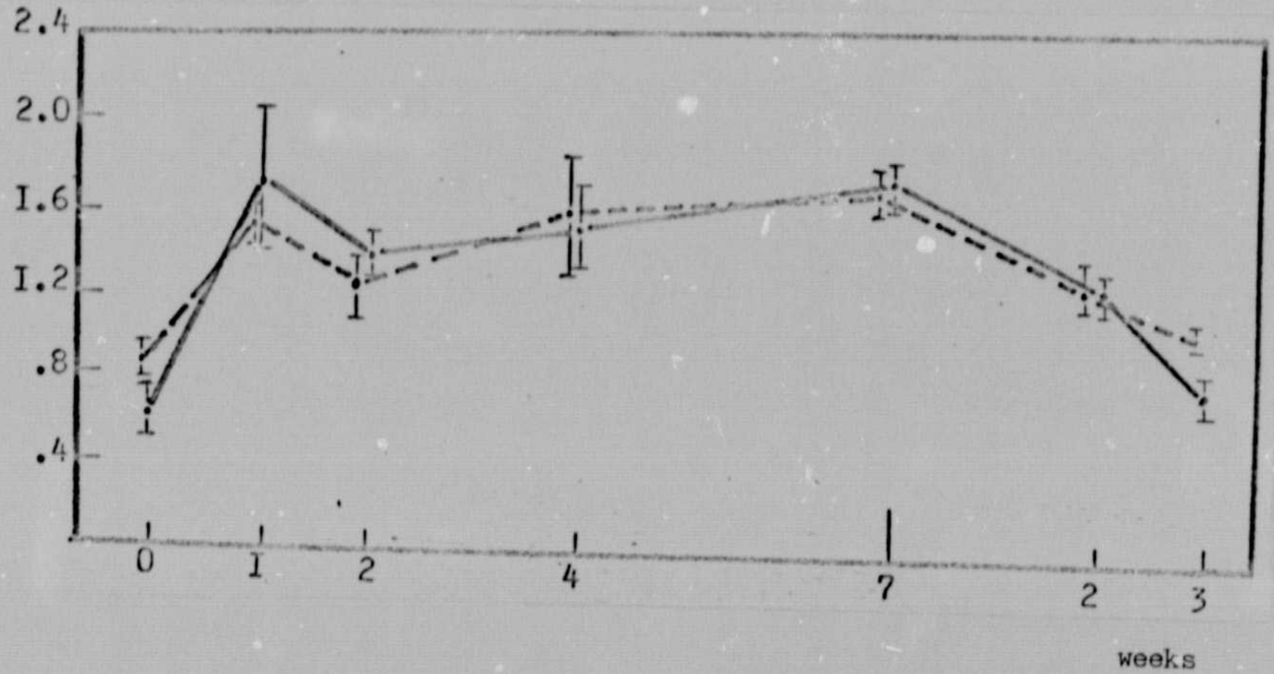


Figure 5. Dynamics of Integral Energy of EMT of Musculus Gastrocnemius with Standard Load (I) and Maximum Strength (II) in the Process of Anti-orthostatic Hypokinesia



/29

Figure 6. Dynamics of Amount of Electrical Energy (in conventional units) of Gastrocnemius (solid line) and Soleus (dotted line) Musculi in Process of Antiorthostatic Hypokinesia

/30

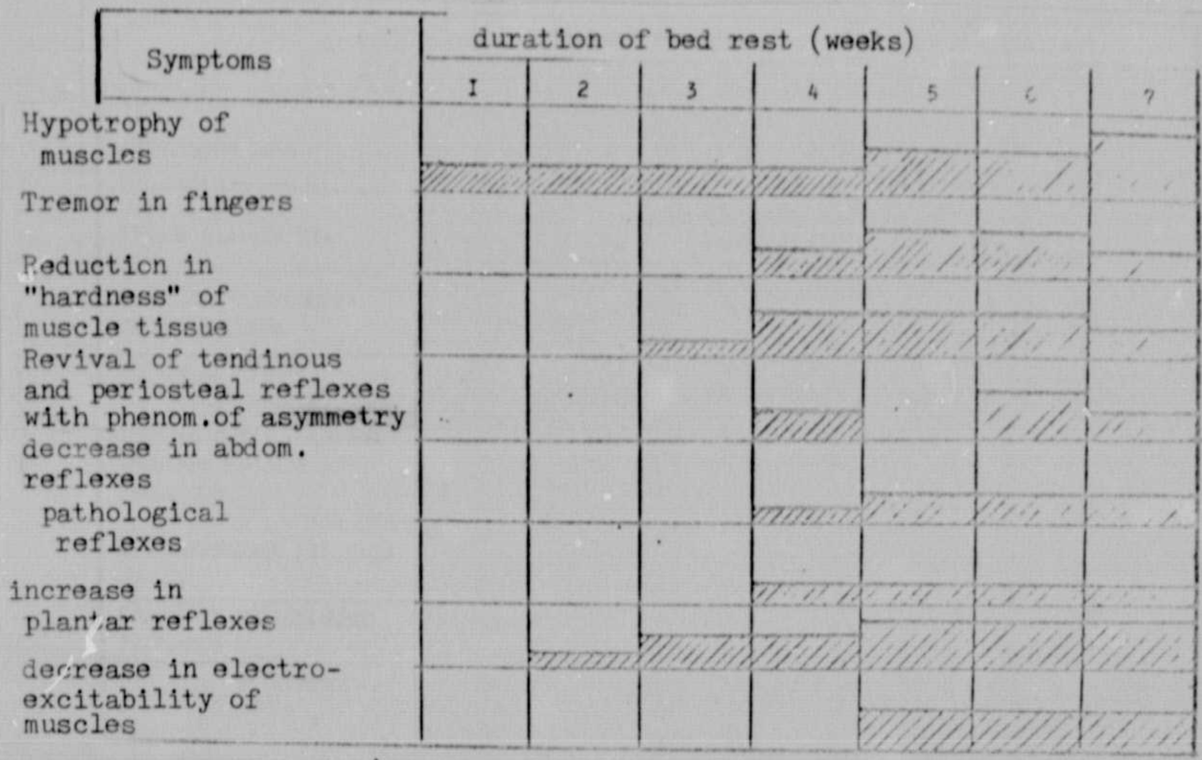


Figure 7. Development of Syndrome of Neuromuscular Disorders in Process of Antiorthostatic Hypokinesia

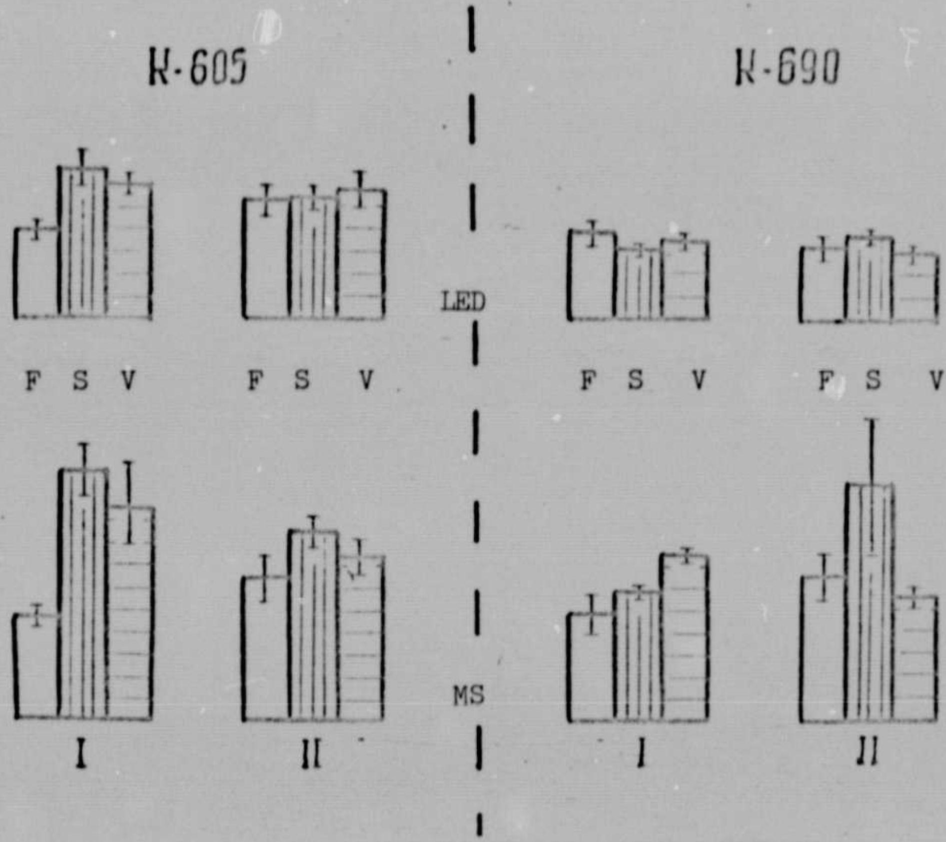


Figure 8. Ratio of Amplitude of Tetanic and Solitary Isometric Contractions of Musculus Soleus (MS) and Long Extensor of the Digits (LED) of White Rats on First (I) and Twenty-Sixth (II) Day after Flight in Biosatellites "Kosmos-605" and "Kosmos-690".
F--flight; S--synchronous control experiment; V--vivarium control.

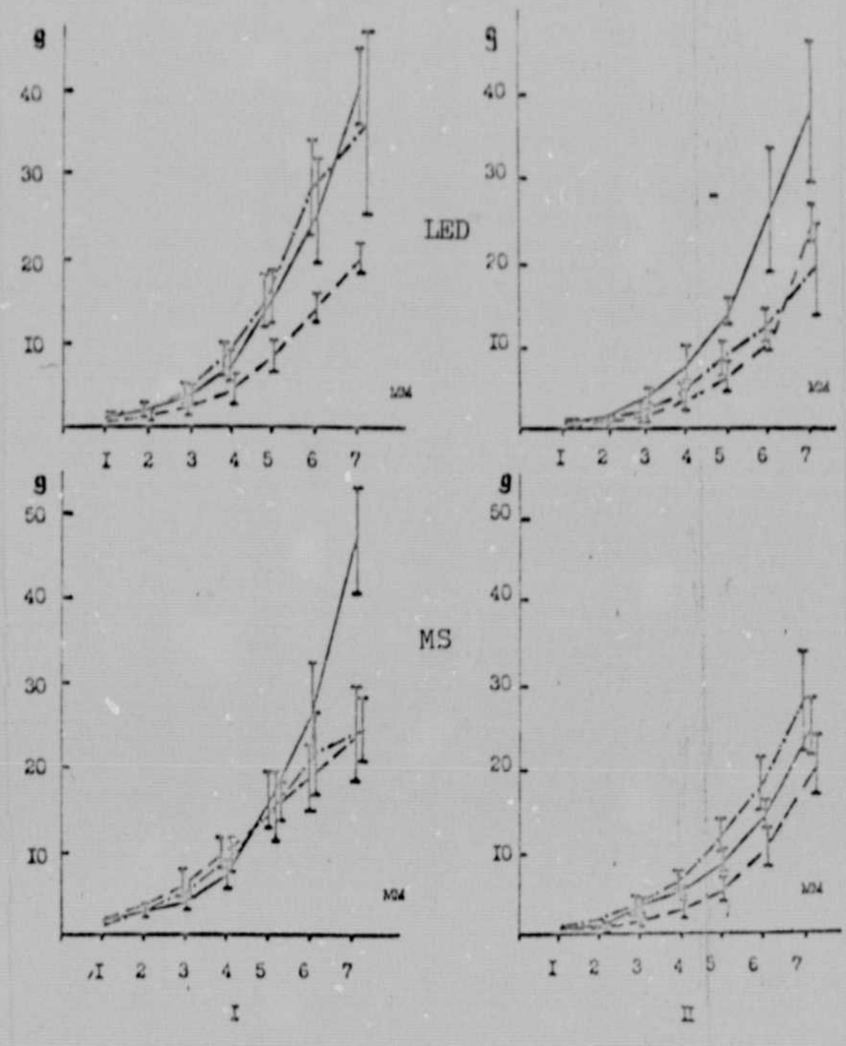


Figure 9.Relationship of "Length-Stress" in Skeletal Muscles of White Rats After Flight on Biosatellite "Kosmos-605". Solid line--flight; dotted line--synchronous control experiment; dash-dot-- vivarium control. Remaining designations the same as in fig. 8.

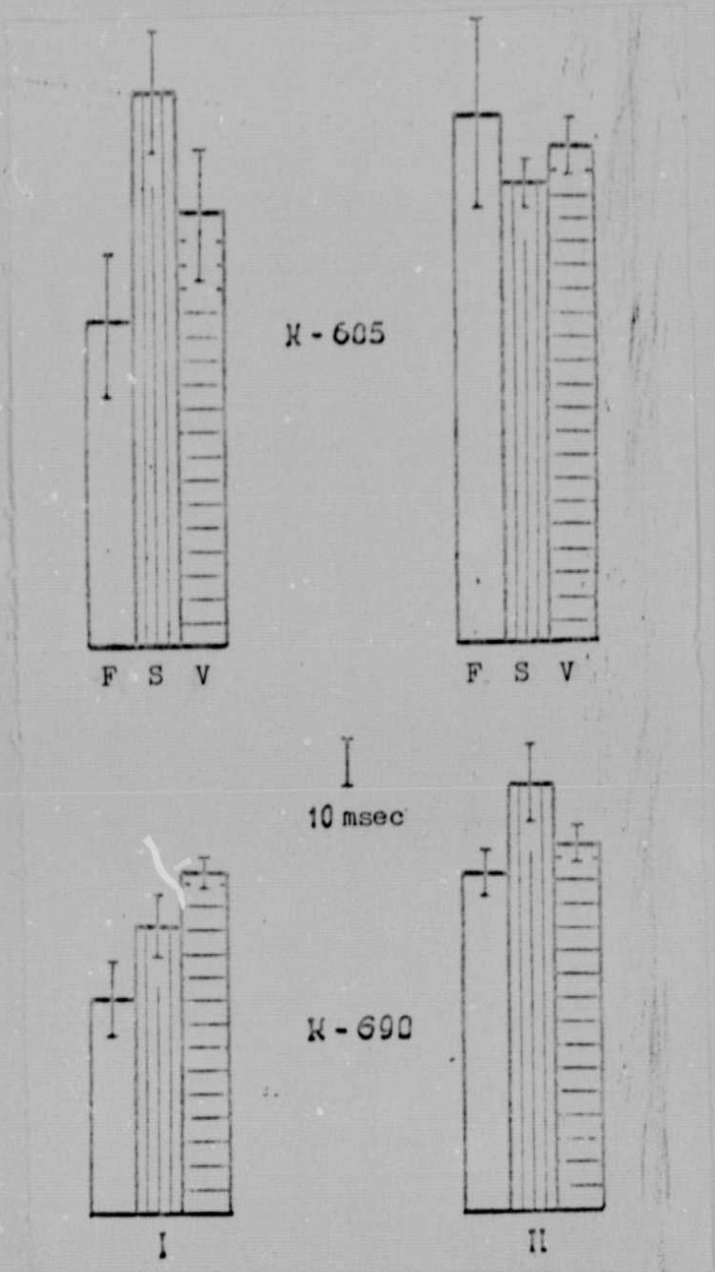


Figure 10. Duration of Development of Tetanic Conjugation (to ½ maximum) of Musculus Soleus in White Rats after Flight on Biosatellites "Kosmos-605" and "Kosmos-690". Designations the same as in fig. 8.

ORIGINAL PAGE IS
OF POOR QUALITY

References

/34

1. Belaya, N. A., R. Z. Amirov, et al., "Certain Peculiarities in the Bioelectric Activity of Muscles in Prolonged Hypokinesia," Vopr. Kurorotologii, No. 3 (1975), 238-241.

2. Bryanov, I. I., M. D. Yemel'yanov, et al.,"Peculiarities in Statokinetic Reactions," in Kosmicheskiye polety na korablyakh "Soyuz". Biomeditsinskiye issledovaniya [Space Flights on 'Soyuz' Crafts. Biomedical Studies"], Moscow: Nauka, 1976, 195-230.

3. Buznik, I. M. and S. A. Kamforina, "Removal of Creatinin with Urine in Prolonged Limited Movement," Kosm. biol., No. 4 (1973), 60-64.

4. Biryukov, Ye. N., Izmeneniye mineral'noy nasyshchennosti kostnoy tkani i kal'tsievogo balansa v usloviyakh eksperimental'noy gipokinezii i kosmicheskogo poleta ["Change in Mineral Saturation of Osseous Tissue and Calcium Balance under Conditions of Experimental Hypokinesia and Space Flight"], Diss. Cand. Med. Sci., Moscow, 1968.

5. Biryukov,Ye.N.and I. G. Krasnykh, "Change in Optical Density of Osseous Tissue and Metabolism of Calcium in Cosmonauts A. G. Nikolayev and V. I. V. I. Sevost'yanov," Kosm. biol., Vol. 4, No. 6 (1970), 42-45.

6. Briskin, A. I., A. I. Volozhin and V. S. Shashkov, "State of Osseous Tissue under Conditions of Hypokinesia and Weightlessness and Action of Tyro-Calcitonin," Kosm. biol., 10, 2 (1976), 17-22.

7. Volozhin, A. I., "Experimental Study of Calcium Exchange in Bones and Teeth during Limited Motor Activity," Pat. fiziol., No. 6 (1971), 65-69.

8. Volozhin, A. I., P. V. Vasil'yev, et al., "State of Calcium Exchange in Calcified Tissues of Rats during Prolonged Hypodynamics and Use of Tyrocalcitonin," Kosm. biol., No. 3 (1972), 10-15.

9. Gayevskaya, M. S., L. M. Kurkina, et al., "Change in Protein Fractions of Skeletal (Soleus) Muscle of Man under Influence of Hypokinesia and Possibility of Preventing these Changes with the Help of a Special Set of Excercises," Fiziologiya cheloveka, Vol. 2, No. 6 (1976), 997-1001.

10. Gayevskaya, M. S., A. S. Ushakov, et al., "Effect of 22-Day Space Flight on Metabolism of Tissue in Skeletal Muscles of Rats," Kosmich. biol. i aviakosmich. med., 10, No. 4 (1976), 25-30.

11. Gazenko, O. G., A. A. Prokhonchukov, et al., "State of Microscopic and Crystalline Structures, Microhardness and Mineral Saturation of Osseous Tissue of Man after Lengthy Space Flight," Kosm. biol., 11, 3 (1977), 11-20. /35

12. Grigor'yev, A. I., G. I. Kozyrevskaya, "Exchange-Endocrine Processes," in Kosm. polety na korablyakh "Soyuz". Biomed. issledovaniya, Moscow: Nauka, 1976, 266-304.

13. Gurovskiy, N. N., L. I. Kakurin, et al., "Certain Results of Medical Studies during and after Flight of Space Craft 'Soyuz-9'", Materialy simpoziuma po kosmicheskoy biologii i meditsine, Interkosmos ["Materials of Symposium on Space Biology and Medicine, Interkosmos"], Budapest, Sept.-Oct., 1970, p. 1-7.

14. Gurovskiy, N. N., A. V. Yeremin, et al., "Medical Studies during Flights of Space Crafts 'Soyuz-12', 'Soyuz-13', 'Soyuz-14' and Orbital Station 'Salyut-3'", Kosmich. biol. i aviakosm. med., No. 2 (1975), 48-54.

15. Gurfinkel', V. S., Ye. P. Pal'tsev, et al., "Changes in Certain Motor Functions of Man after Prolonged Hypodynamia," in Probl. kosm. biol., ["Probl. Space. Biol."], vol. 13 (1969), 148-160.

16. Zhukov, Ye. K., "Development of Contractile Function in Cross-Striated Muscles in Ontogenesis," in Razvitiye sokratitel'noy funktsii dvigatel'nogo apparata ["Development of Contractile Function of Motor Apparatus"], Leningrad: Nauka, 1974, 89-112.

17. Il'ina, [], Ye. I. Kakuyeva, et al., "Effect of Factors in Space Flight on Skeletal Musculature," Kosmich. biol., 11, 1 (1977), 20-25.

18. Kakurin, L. I., "Effect of Prolonged Limited Muscle Activity on Human Organism and Hypokinetic Component of Weightlessness," Kosmich. biol. i med., Vol. 2, No. 2 (1968), 59-63.

19. Kakurin, L. I. and Ye. N. Biryukov, "Problem of Decalcination during Hypodynamia of Man Applicable to Conditions of Prolonged Space Flight," in Probl. kosm. biol. i med., ["Probl. Space Biol. and Med."], Moscow, 1966, 187-188.

20. Kakurin, L. I., V. I. Pervushin, M. A. Cherepakhin, "State of Neuromuscular Apparatus in Members of Space Craft 'Soyuz-4' and 'Soyuz-5'", Kosm. biol. 4, No. 5 (1970), 64-67.

21. Kakurin, L. I., M. A. Cherepakhin, V. I. Pervushin, "Effect of Brief Space Flights on State of Human Neuromuscular Apparatus," Kosm. biol., 6 (1971) 53-56.

22. Katinas, G. S., V. S. Oganov, A. N.Potapov, "Hypodynamic and hypokinetic State of Skeletal Muscles," Fiziol. zh. SSSR, 60, 10 (1974), 1106-1608. /36

23. Kovalenko, Ye. A. and E. S. Mailyan, "Functions and Metabolism of Organism during Prolonged Hypokinesia in Complex Experiment," Uspekhi fiziol. nauk.,6, 3 (1975), 110-136.

24. Krasnykh, I.G., "Mineral Saturation of Osseous Tissue under Conditions of Lengthy Hypodynamia," in Probl. kosm. biol., vol. 13 (1969), 93-99.

25. Lobachik, V. I., Nekotoryye storony kal'tseyevogo obmena u krys v usloviyakh dlitel'noy gipokinezii [Certain Aspects of Calcium Exchange in Rats under

Conditions of Lengthy Hypokinesia"], Author's abstract of cand. diss., 1970.

26. Menendes, A., R. A. Zavalishina, A. A. Pokrovskiy, "Study of Activity of Phosphatase in Osseous Tissue and Blood Serum during 90-Day Hypokinesia," Kosmich. biol., i aviakosm. med., 10 (1976), 22-26.

27. Novikov, I. I. and V. B. Vlasov, "Morphology of Blood Channel of Elements of Soft Framework and Bones of Hind Extremities in Dogs during Lengthy Hypodynamia," in Vopr. struktur. organiz. i vzaimodeystviya elementov v systeme mikrotsirkulyatsii ["Topics in Structur. Organiz. and Interaction of Elements in System of Microcirculation"], Moscow, 1976, 37-40.

28. Oganov, V. S. and A. N. Potapov, "Comparative Study of Functions of Skeletal Muscles under Conditions of Weightlessness and Simulated Situations," in Aviakom. med., Tez. dokl. na V Vsesoyuzn. konf. ["Aerospace Med. Summ. of Rep. at Fifth All-Un. Conf."], Moscow-Kaluga, Vol. 2 (1975), 167-169.

29. Oganov, V. S. and A. N. Potapov, "On the Mechanisms of Changes in Skeletal Muscles in the Weightless Environment," Life Sci. and Space Research, XIV Berlin: Academic-Verlag, 1976, 137-143.

30. Ostrovskiy, K. A. Dzedzits-Gotslavska, V. Stakhovich, "Evaluation of the Degree of Crystallinity of the Mineral in Osseous Tissue in Rats after Stay under Zero Gravity by Method of Electron Paramagnetic Resonance," in Interkosmos, IX Simpos. po kosmich. biol. i med. ["Interkosmos. Ninth Sympos. on Space Biology and Medicine"], Summaries of reports, Budapest 1976, 42-43.

31. Parin, V. V., T. N. Krupina, et al., "Main Changes in Organism of Healthy Man in 120-Day Bed Rest," Kosm. biol., 4, 5 (1970), 59-64.

32. Panov, A. G., V. S. Lobzin, V. A. Belyankin, "Changes in Functions of Nervous and Muscular Systems under Influence of Prolonged Hypodynamia," in Probl. kosm. biol., Vol. 13 (1969), 133-147.

33. Petukhov, B. N. and Yu. N. Pyrakhin, "Electrical Activity of Muscles of the Crus in Standing after 120-day Bed Rest," Kosm. biol., 5, No. 3 (1971), 64-68.

34. Portugalov, V. V. and N. V. Petrova, "LDH Isoenzymes of Skeletal Muscles of Rats after Space Flight and Hypokinesia," Aviat. Space and Environ. Med., 47, 8 (1976), 834-838.

35. Prokhonchukov, A. A., R. A. Tigranyan, et al., "Content of Calcium, Phos- /37
phorous and Ca^{45} inclusion in Bones and Teeth of Rats after 22-day Orbital Space Flight on Satellite Craft 'Kosmos-605'", Kosm. biol., 11, 1 (1977), 26-30.

36. Seregin, M. S., I. G. Popov, et al., "Nutrition and Metabolism during Lengthy Hypodynamia," in Probl. kosm. biol. ["Probl. Space Biol."], Vol. 13 (1969), 78-92.

37. Skrypnyk, V. G., "Changes in Biomechanical Peculiarities of Walking under Influence of Hypodynamia according to Data of Ichnography," in Probl. kosm. biol., Vol. 13 (1969), 161-170.

39. Tigranyan, R. A., M. I. Belyakova, et al., "State of Processes of Metabolism under Conditions of Limited Motor Activity," in Aviakosm. med. Tez. dokl. V. Vsesoyuzn. konf. ["Aerospace Med. Summ. of Rep.of Fifth All-Union Conf."], Moscow-Kaluga, Vol. 11 (1975), 187-190.

40. Tigranyan, R. A., I. A. Popova, et al., "Results of Study on Processes of Metabolism in Crew Members of Second Expedition of Orbital Station 'Salyut-4'", Kosm. biol., 11, 2 (1977), 48-53.

41. Chekirda, I. F., A. V. Yeremin, et al., "Peculiarities in Human Walking after 30-day Hypokinesia," Kosm. biol. i med., No. 4 (1974), 48-51.

42. Cherepakhin, M. A., L. I. Kakurin, et al., "Evaluation of Efficacy of Electrostimulation of Muscles to Prevent Disorders Related to Lengthy Limited Motor Activity of Man," Kosm. biol. i med., No. 2 (1977), 64-68.

43. Yagodovskiy, V. S., L. A. Triftanidi, G. P. Gorokhova, "Effect of Space Flight on Skeletal Bones of Rats (Light-Optical and Electron Microscopic Study)," Kosm. biol., 11, 1 (1977), 14-20.

44. Baker, J. T., A. E. Nicogossian, et al., "Changes in the Achilles Tendon Reflexes following Skylab Missions," in Proc. Skylab Life Sci. Symp., 1 (1974), 297-305. /38

45. Bendall, J. R., Myshchtsy, molekuly i dvizheniye ["Muscles, Molecules and Motion"], Moscow: Mir, 1970.

46. Berry, Ch. A., "Weightlessness," in Bioastronautics, Data Book, NASA, Washington, chapt. 8, 1973, 349-415.

47. Close, R., "Dynamic Properties of Fast and Slow Skeletal Muscle of the Rat," J. Physiol., 173 (1964), 74-95.

48. Dietlein, L. F., "Skylab: A Beginning," in Proc. Skylab Life Sci. Symp., NASA,Houston, 11 (1974), 369-388.

49. Guth, L., "Regulation of Metabolic and Functional Properties of Muscle," Regulat. Organ and Tissue Growth, 1972, 61-75.

50. Hill, A. V., "The 'Instantaneous' Elasticity of Active Muscle," Proc. R. Soc. B., 141 (1953), 161-169.

51, Issekutz, B, J. J. Blizzard, et al., "Effect of Prolonged Bed Rest on Urinary Calcium Output," J. Appl. Physiol., 21 (1966), 1013-1020.

52. Jewell, B. R. and D. R. Wilkie, "Mechanical Properties of Relaxing Muscle," J. Physiol., 152 (1960), 30-36.

53. Lindquist, Ch., "Contraction Properties of Cat Facial Muscles," Acta Physiol., Scand., 89, 4 (1973), 482-490.

54. Leach, C. S. and P. C. Rambaut, "Biochemical Responses of the Skylab Crewmen," in Proc. Skylab Life Sci. Symp. NASA, Houston, 11 (1974), 427-454.

55. Mack, P. B., R. A. Hoffman, A. H. Alshawi, "Physiologic and Metabolic Changes in Macaca nemestrina on Two Types of Diets during Restraint and Nonrestraint: II. Bone Density Changes," Aerosp. Med., 39, 7 (1968), 698-704.

56. Mack, P. B. and P. L. La Chance, "Effect of Recumbency and Space Flight on Bone Density," Am. J. Clin. Nutrition, 20 (1967), 1194-1205.

57. McCally, H., L. Kasarian, von Gierkeh, "Cardiovascular and Metabolic Effects of Bed Rest and Immobilization Simulated Weightlessness," XXI Int. /39
Astronaut. Congr., 1970, 314-315.

58. Melichna, J. and E. Gutmann, "Stimulation and Immobilization Effects on Contractile and Histochemical Properties of Denervated Muscle," Pflügers Arch., 352(1974), 165-178.

59. Nicolet, M., "Le Controle Intracellulaire de la Contraction du Muscle Strie Squellettique: Rôle due Calcium," Bull. Fed. Soc. Hist. Natur., Franche-Comte, 74, 4 (1972), 90-103.

60. Palmer, H. E. and M. T. Karagianes, "Use of ^{85}Sr as an Indicator of Bone Mineral Replacement in Dogs after Disuse Demineralization," Aviat. Space and Environ. Med., 47 , 1 (1976), 17-19.

61. Proske, U. and P. M. E. Waite, "Properties of Types of Motor Units in the Medial Gastrocnemius Muscle of the Cat," Brain Res., 67, 1 (1974), 89-101.

62. Sandler, H., "Uses of Bed Rest Studies to Simulate the Problems of Human Existence in a Space Flight Environment," Doklad na 7-y vstreche sovetsko-amerikanskoy rab. gruppy po kosm. biol. i med. ["Report at Seventh Meeting of Soviet-American Work. Group on Space Biol. and Med."], USSR, Yerevan, 1976.

63. Stein, J. M. and H. A. Padycula, "Histochemical Classification of Individual Skeletal Muscle Fibers of the Rat," Amer. J. Anat., 110 (1962), 103-124.

64. Thornton, W. E. and J. A. Rummel, "Muscular Deconditioning and its Prevention in Space Flight," in Proc. Skylab Life Sci. Symp. NASA, Houston, 1 (1974), 407-414.

65. Van Der Meulen, J. P., P. H. Peckman, J. T. Mortimer, "Use and Disuse of Muscle," Ann. N. Y. Acad. Sci., 228 (1974), 177-188.

66. Vogel, L. D. and M. W. Whittle, "Bone Mineral Measurement--Experiment M078," in Proc. Skylab Life Sci. Symp., NASA, Houston, 1 (1974), 387-400.

67. Vrbova, G., "Changes in Motor Reflexes Produced by Tenotomy," J. Physiol., 166 (1963), 241-250.

68. Whedon, G. D., L. Lutwak et al., Experimental M071. Mineral Balance. Skylab 1/2 Preliminary Biomedical Report, NASA, JSC-98439, 1973, 162-176.

69. Yamamoto, Y., "Comparison of Histochemical and Physiological Characteristics of M. digastricus and M. semitendinosus of the Guinea Pig," Jap. J. Physiol., 23, 5 (1973), 509-528. /40

70. Young, D. R., R. R. Adachi, W. H. Howard, "Bone Mineral Losses during Hypokinesia in Primates (M. nemestrina)," Prepr. Annu. Sci. Meet., Aero-Space Med. Assoc., San Francisco, Calif., 1975, Washington, D. C., 185.