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THE PHYSIOLOGY AND BIOCHEMISTRY OF TOTAL BODY IMMOBILIZATION IN ANIMALS: A COMPENDIUM OF RESEARCH

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This compendium comprises the major studies that describe the physiology and biochemical mechanisms of total body immobilization in animals. Wherever possible a detailed annotation is provided under the subheadings: (a) purposes, (b) procedures and methods, (c) results, and (d) conclusions. The annotations cover material through December 1973. They are listed in alphabetical order by first author; author and subject indexes are provided. Additional references are provided in the selected bibliography.

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INTRODUCTION

This compendium comprises the major studies that describe the physiology and biochemical mechanisms of total body immobilization in animals. Wherever possible a detailed annotation is provided under the subheadings: (a) purpose, (b) procedures and methods, (c) results, and (d) conclusions. The annotations cover material through December 1973. They are listed in alphabetical order by first author; author and subject indexes are provided. Additional references are provided in the selected bibliography.

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1. Ader, R. Behavioral and physiological rhythms and the development of gastric erosions in the rat. *Psychosomatic Medicine* 29:345-353, 1967.

   Author's abstract: Rats immobilized at the peak as compared to the trough in the 24-hr activity cycle are more susceptible to gastric erosions. In a series of experiments designed to delineate some of the factors which may have contributed to this phenomenon, it was found that the 24-hr rhythm in plasma corticosterone levels is not correlated with activity and is not related to the development of erosions under 6-hr immobilization: plasma pepsinogen levels show a 24 hr rhythm which is synchronized with activity, but the magnitude of the daily fluctuations are not sufficient to account for the altered erosion susceptibility; and the increased susceptibility shown by animals immobilized during a period of maximum activity obtains even when one eliminates animals protected by the presence of food in the stomach.

2. Ader, R. Gastric erosions in the rat: Effects of immobilization at different points in the activity cycle. *Science* 145:406-407, 1964.

   Author's abstract: Predictable, cyclic patterns of activity were obtained from 30 male rats. Seventeen of these were subjected to physical immobilization just as they were approaching their period of peak activity, and 13 animals were restrained during the inactive phase of their cycle. Eight animals were found to have gastric erosions following the immobilization. All of these came from the group immobilized during the time they would have been in the active phase of their particular cycle.

3. Andrianova, L. A. Effect of hypokinesia on the hypothalamic-hypophyseal neurosecretary system in rats. *Kosmicheskaya Biologiya i Meditsina* 5:26-29, 1971.

   Author's abstract: Work was done on 70 rats to investigate the state of nuclei in the frontal hypothalamus and posterior lobe of the hypophysis during hypokinesia by a comparison of data from a morphological investigation and the results of determination of biological activity of extracts of the hypothalamus and blood plasma. Animals exposed to hypokinetic conditions exhibited an activation of the hypothalamic-hypophyseal neurosecretory system at early stages during exposure. The reaction was characterized by release of the neurosecretory substance from the hypophyseal posterior lobe and an increase in the antidiuretic hormone concentration in the blood. It can be postulated that during early times of hypokinesia the increased content of the antidiuretic hormone in the blood of rats does not exert any effect characteristic of normal conditions on kidney function. Changes in the neurosecretory function of the hypothalamic-hypophyseal system are evidently a compensatory-adaptive reaction directed to maintaining equilibrium between the body and the environment. The observed reaction can be characterized by two phases: first, an activation phase (from the 3rd through the 45th days) and, second, a normalization phase (on the 60th day).

4. Araszkiewicz, Z., L. Tomaszewska, S. Kozlowski, and H. Styszewska. Effect of immobilization on the calcium metabolism in rats. *Acta Physiologica Polonica* (*Warsaw*) 23:89-97, 1972.

   Authors' abstract: The study was aimed at elucidation whether immobilization affects the calcium loss from skeletal system as well as whether the calcium-enriched diet may affect the course of skeleton demineralization during hypokinesis. The experiments were carried out on 20 Wistar strain rats. Half of the animals were fed a standard diet containing 1000 mg of calcium in 100 gm of food and the other half, a standard diet enriched up to a content of 1458 mg of calcium in 100 gm of food. A three-week immobilization of the rats in specially constructed hypokinetic cages caused an increase of calcium excretion in urine and feces and of hydroxyproline in urine. The densitometric analysis of a caudal vertebra of rats showed a diminution of the bone density. In rats supplied with the calcium-enriched diet, the demineralization of bones was less marked and lasted a shorter time. Thus the immobilization caused an increased calcium loss from skeletal bones, and the calcium-enriched diet prevented to some degree the demineralization of the skeleton in conditions of immobilization.

5. Asymaolov, B. F. and A. D. Voskresenskiy. Effect of two-week hypokinesia on the cardiovascular response of dogs during orthostatic tests and exposure to transverse accelerations. *Kosmicheskaya Biologiya i Meditsina* 2:33-37, 1968.

Authors' abstract: Experiments were carried out on female dogs weighing from 6 to 12 kg after they had been immobilized by plaster dressings for two weeks. After the period, four dogs were examined for orthostatic tolerance and six animals were studied for their tolerance to transverse accelerations increasing at a rate of 1 g each 10 sec. Orthostatic tests demonstrated variations in the pulse rate and arterial pressure. However, this is not as yet suggestive of the disordered influx of venous blood to the heart. Exposure to accelerations was accompanied by higher tachycardia with a more pronounced inverse relation between changes in pulse rate and arterial pressure. A comparison of the magnitudes of acceleration which caused symptoms of damaged compensation does not help to establish regularities in acceleration tolerance. The absence of a distinct decrease in orthostatic tolerance and acceleration tolerance can be attributed to the fact that the immobilization does not involve a significant reduction in hydrostatic effects on hemodynamics and the cardiovascular system of dogs has certain anatomical and physiological peculiarities.

6. Baranski, S., Z. Edelwejn, and M. Wojtkowiak. Hemodynamic and bioelectric disturbances in striated muscles of rats subjected to accelerative forces after a period of hypokinesia. *Space Life Sciences* 2:400-403, 1970.

Purpose: To investigate the effect of a period of hypokinesia on the tolerance to accelerative forces applied for various durations.

Procedure and methods:

Male Wistar rats were divided into four groups: (1) control, (2) acceleration-centrifuged $+5G_Z$ for 15 min or 1, 2, or 3 hr, (3) hypokinetic immobilized for 2 months, and (4) hypokinetic-acceleration–(3) condition followed by (2) conditions.

The animals were given 50 microcuries per hundred grams body weight ^{131}I-albumin, after 1 hr, animals in group 2 and 4 were subjected to the acceleration profiles.

Electromyography was performed on all animals, and they were anesthetized and sacrificed by exsanguination.

Specimens of hind leg and foreleg muscles were taken for radioactivity measurements (impulses per milligram dry mass).

The distribution of the radionuclide was examined scyntigraphically in the control and experimental animals, supplemented by examination of animals frozen in liquid nitrogen during actual centrifugation.

Results:

Prolongation of the time of centrifugation resulted in increased radioactivity of the hind-leg samples.

Hemodynamic disturbances induced by acclerative forces appeared earlier and more pronounced in the immobilized group.

Immobilized animals demonstrated a markedly lower tolerance to acceleration, they survived only 22-37 min.

The percentage displacements of the radionuclide attained +62 percent.

Findings reflect an increase in permeability of vascular walls to albumin, but this increase is not sufficient to permit migration of globulin having greater molecular weight than albumin.

No differences were noted between control and experimental animals regarding swimming.

Markedly increased polyphasic potentials were observed.

A decrease in amplitude of the electromyographic record was noted after 8 weeks of immobilization.

Visible reduction in bioelectric activity of the muscle was observed in immobilized animals when subjected to acceleration forces.

Conclusions:

Measurements of radioactivity of ^{131}I-albumin in muscle shows that in animals subjected to acceleration forces ($+5G_Z$) for more than 1 hr a redistribution of albumin is seen.

Hemodynamic disturbances are earlier and more profound in animals subjected to the associated influences of hypokinesia and acceleration.

7. Baranski, S., K. Kwarecki, S. Szmigielski, and J. Rozynski. Histochemistry of skeletal muscle fibres in rats undergoing long-term experimental hypokinesia. *Folia Histochemica et Cytochemica* 9:381-386, 1971.

Purpose: To evaluate the morphochemical picture of skeletal muscle after a few weeks of experimental hypokinesia and to compare it with changes observed following muscle denervation (cutting of sensory and motor nerves).

Procedure and methods:

Mature male Wistar rats weighing 250 ±20 gm underwent long-term hypokinesia in special cages. The animals were fed ad libitum and kept in a constant temperature of 20° ±2°C. Control and experimental groups consisted of five animals each and both groups were observed during 6 weeks.

After the period of observation, the animals were decapitated and bled. Small pieces (about 1 gm of the central part of musculus quadriceps were taken for investigation. The muscle pieces were frozen at −160°C (isopentane in liquid nitrogen) and cut transversely into 10μ sections and stained with haematoxylin-eosin following fixation in cold (4°C) Baker solution; Masson technique, and PAS reaction (with control digestion with Take-diastase) were performed in sections fixed in the same way. In fresh, unfixed sections the following histochemical techniques were performed: cytochrome oxidase activity demonstration (Nadi technique with the use of DPDA as substrate) and lactic acid dehydrogenase activity demonstration (using L-lactic acid as substrate and Tetra-Nitro-BT as tetrazolium salt). The intensity of the reactions in the sections was evaluated subjectively (range 0 to +++).

Morphometric measurements of fiber diameter were also performed in the routine way (250 fibers were counted in each case) with the aim of finding a correlation between fiber diameter and enzyme activity.

Results:

Histological investigations showed a slight growth of connective tissue in between the muscle fibers following cutting of the sensory and motor nerves; this was not observed in animals undergoing hypokinesia.

About 35-40 percent of all muscle fibers of normal animals were type I fibers. Type I fibers were 25-40μ wide while type II fibers were 50-60μ.

Following sensory or motor nerve cutting and in animals undergoing hypokinesia, a diminished diameter of both types of muscle fibers was observed. These changes were pronounced to the highest degree after motor nerve cutting and to the lowest after sensory nerve cutting.

In normal muscles, PAS reaction was higher in type I fibers (++) than in type II fibers (+). After diastase digestion, no reaction was observed, except slight coloration of the connective tissue. Fibers were mostly stained diffusively, sometimes only in type I fibers a few large PAS-positive granules being seen. Following sensory nerve cutting, a diminished PAS reaction was observed, though some of the muscle fibers showed normal staining. After motor nerve cutting in degenerating fibers, small granules of PAS-positive material were seen and a generally reduced reaction. In muscles taken from animals undergoing hypokinesia, a very weak PAS reaction was observed without differences between type I and type II fibers.

Using Masson technique, in normal muscles only a very small amount of connective tissue was seen in between the fibers. After cutting the sensory and motor nerves, polychromatic staining was observed in the muscle fibers. Both stronger and weaker staining was seen as compared with normal muscle. In both these cases, much more connective tissue was seen. In muscles taken from animals undergoing hypokinesia, the same changes were observed, but expressed to the lower degree than after nerve cutting.

Using cytochrome oxidase in normal muscles, the enzyme activity was expressed as very small blue granules. In type I fibers many more granules were observed than in those of type II. Many fibers with intermediate enzyme activity were also seen.

After sensory nerve cutting, diminished enzyme activity was observed with differences between types I and II preserved. After motor nerve cutting a marked increase in enzyme activity was seen in type I fibers, while in those of type II the activity was similar to that observed in normal muscles. In muscles taken from animals undergoing hypokinesia, cytochrome oxidase activity was similar to that in animals with the sensory nerve cut. Differences between type I and type II fibers were also pronounced.

Using lactate dehydrogenase in normal muscles, the enzyme activity was expressed as diffuse staining with a few large granules in some fibers. In type I fibers the enzyme activity was much higher than in those of type II. Many fibers with intermediate enzyme activity were seen. After cutting of the sensory nerve a generally higher activity of lactate acid dehydrogenase was seen. These changes were expressed mostly in type I fibers, where strong diffuse staining and large granules were observed.

After motor nerve cutting, the enzyme activity was still higher than after sensory nerve cutting and in some type I fibers, very dark staining was observed. Type II fibers stained much weaker and did not differ very much from the intensity seen in normal muscle.

Conclusions: Cutting of the sensory and motor nerves causes marked changes in enzyme activity, particularly in "red" fibers. The fibers in these cases contain a lower concentration of glycogen and a higher activity of lactate acid dehydrogenase. Cytochrome oxidase activity is lower following cutting of the sensory nerve and higher following that of the motor nerve, as compared with normal muscle. Higher activity in the last case is probably due to muscle fiber degeneration as the result of a better penetration of the substrate into damaged mitochondria. Immobilization lasting 6 weeks resulted in changes in the morphochemical picture of muscle fibers. More connective tissue, reduced glycogen concentration, decreased cytochrome oxidase, and increased lactate dehydrogenase activities were observed. All the above mentioned changes were seen mainly in "red" fibers. Biochemical and functional changes in human and animal muscles caused by prolonged immobilization rapidly disappear after a return to the normal motor activity.

8. Bartlett, R. G., Jr. Stress adaptation and inhibition of restraint-induced (emotional) hypothermia. *Journal of Applied Physiology* 8:661-663, 1956.

Author's summary: From the data presented, three general conclusions may be drawn: (a) the rat is able to adapt to the dual stresses of cold and restraint; the rapidity of this adaptation suggests that a familiarity or emotional component may be involved in the process; (b) there is a fairly rapid loss of the adaptation if it is not reinforced by the application of the stress; (c) adaptation to stress may protect against the body temperature drop in this restraing-induced (emotional) hypothermia. This is suggested by the observation that repeated exposures of the rat to the stress of forced muscular activity as well as adaptation to cold and/or restraint inhibit his hypothermia.

9. Berendt, R. F. and T. D. Williams. The effect of restraint and position upon selected respiratory parameters of two species of Macaca. *Laboratory of Animal Science* 21:502-509, 1971.

Authors' abstract: The minute volumes, tidal volumes, and respiration rates of Macaca mulatta and Macaca fascicularis were measured at selected intervals after the monkeys were restrained in a plastic chair or strapped to a V-board in upright or supine positions. Restraint had a more pronounced effect upon both species than position. Monkeys confined to the plastic chair had high tidal volumes and low respiration rates; the reverse occurred with animals strapped to the V-board. Resting time caused a marked diminution of all parameters except the respiration of animals strapped to the board. Restraint and position do affect tidal volume and respiration rate, and the data obtained from these studies suggest that experimenters must be concerned with these variables as well as the duration of aerosol experiments. They must also be aware that differences in these respects may produce results that are difficult or impossible to interpret.

10. Besch, E. L., R. R. Burton, and A. H. Smith. Organ and body mass changes in restrained and fasted domestic fowl. *Proceedings of the Society for Experimental Biology and Medicine* 141:456-459, 1972.

Authors' summary: Organ and body mass changes in restrained adult, male domestic fowl were compared with tissue from control and fasted animals. Body mass loss rate in the restrained animals was 63.5 percent ($p < 0.001$) greater than in the fasted group, yet the two groups recovered at the same rate. Compared with controls and fasted animals, restrained fowl exhibited an increase in size of heart, lungs, kidneys, liver, and adrenals, but a greater loss of speen, superficial pectoral muscle, small intestine, and pancreas masses. The relative water content of organs generally increased in restrained and decreased in fasted animals. The data suggest that restraint – although accompanied by inanition – affects organ and body mass in the domestic fowl in a different way than does fasting.

11. Besch, E. L., A. H. Smith, R. R. Burton, and S. J. Sluka. Physiological limitations of animal restraint. *Aerospace Medicine* 38:1130-1134, 1967.

Authors' abstract: In the development of procedures which will sustain a mature domestic fowl for prolonged periods of time (i.e., 30 days), several types of restraint were investigated. The effect of restraint appears to be directly proportional to the duration of exposure and, uniformly, these animals show symptoms not unlike those incident to starvation syndrome in addition to a generalized dehydration. These results do not appear to be due to inanition per se since animals deprived completely of feed and water survive for significantly longer periods of time and have a weight loss rate greater than the restrained animals. The effects of restraint on white blood cells is similar to that following injection of ACTH and cortisone-acetate, indicating a state of acute stress. There was a relative and absolute lymphopenia, a relative and absolute rise in heterophils with no change in the absolute numbers of erythrocytes. It appears from the results of the experiments that the domestic fowl may be unable to adapt physiologically to chronic restraint since therapeutic modifications of the various restraint procedures caused little, if any, change in the lethality of the treatment. This inability to adapt to restraint may limit its usefulness as a research animal in a variety of studies. On the other hand, if

there is reason to believe that there is a relationship between restraint and enforced bedrest, and the chicken cannot survive chronic restraint necessary for physiological data collection, it may not be able to survive the weightless condition incident to space flight.

12. Burton, R. R. and J. R. Beljan. Animal restraint: Application in space (weightless) environment. *Aerospace Medicine* 41:1060-1065, 1970.

Authors' abstract: Chronic restraint was found to produce a typical environmental-type stress response in the adult male domestic fowl. This included a relative lymphopenia and loss of body mass resulting in death if continued for several days. Approximately 50 percent of the restrained animals were thus affected. Repeated restraint trials on the same birds indicated statistically (analysis of variance) that this stress response was an individual animal characteristic. A restraint method was developed and described for the domestic fowl which was apparently not physiologically stressful nor did it produce immobilization. The degree of restraint, however, was considered sufficient as an animal orientation aid for space (weightless) experimentation. These birds appeared to tolerate this form of chronic restraint for several months without significant changes in their hematology or several other determined physiological parameters.

13. Bykov, G. P., A. V. Novikov, and S. M. Ivanova. Morphology of the liver and skeletal muscles during hypokinesia and a protein deficit. *Kosmicheskaya Biologiya i Meditsina* 4:80-81, 1969.

Purpose: To determine the effects of immobilization and a protein-deficient diet on hepatic and skeletal muscle morphology.

Procedure and methods: Forty-four white male rats were divided into four groups: group 1 received a protein-deficient diet and were immobilized for 30 days; group 2, low protein; group 3, standard 18 percent protein diet and immobilization for 30 days; group 4, standard 18 percent diet. Immobilization was induced by restriction in individual cages.

Results:

Groups 1 and 2 had accumulated liver lipids with fatty cysts formation, most were located at the center of the lobes. Liver glycogen content was reduced. RNA content was unchanged. Ultraviolet microscopy showed a decrease in protein content at the center of the lobes. Succinic dehydrogenase and alkaline phosphatase were reduced in liver sections. Liver tissue changes were similar to those obtained on protein-deficient diets.

There were no detectable structural and histochemical changes of the livers of animals on a standard 18 percent protein diet and immobilized.

Muscular atrophic and dystrophic changes were observed in immobilized animals. Muscle glycogen content was reduced but there was no evidence of lipid accumulation.

Conclusions: A decrease in motor activity results in changes in protein metabolism of a reduced synthesis and dissolution of skeletal muscle during immobilization. Protein deficiency exacerbated immobilization changes favoring the process of muscle fiber degeneration.

14. Bykov, G. P. and V. P. Smirnov. Morphological changes in bone and muscle tissue during hypokinesia. *Kosmicheskaya Biologiya i Meditsina* 4:46-51, 1970.

Authors' abstract: A study was made of the bone and muscle tissues of rats kept for different time intervals in small cages and rabbits with cast-immobilized limbs, as well as biopsies of muscles of human subjects afflicted

with myasthenia. The investigated structures revealed changes with respect to the nature of hypodynamic conditions. Cast immobilization and myasthenia which rigidly block motor activity result in bone and muscle atrophy. Confinement of animals in small cages results in indistinct morphological changes, indicating limited functional activity.

15. Cockett, A. T. K., A. Elbadawi, R. Zemjanis, and W. Ross Adey. The effects of immobilization on spermatogenesis in subhuman primates. *Fertility and Sterlity* 21:610-614, 1970.

Authors' summary: Five animals were immobilized for periods ranging from 20-25 days. Testicular biopsies were obtained before and after couch restraint. Tissue section revealed spermatogenic arrest following restraint. One animal (P-470) was placed into orbital flight after 13 days of full restraint. Postflight biopsy revealed testicular alterations similar to the changes seen in the immobilized animals.

16. Cockett, A. T. K., R. Zemjanis, A. Elbadawl, and W. Ross Adey. Male infertility: histochemical changes in the subhuman primate testes after prolonged immobilization. *Fertility and Sterility* 22:565-572, 1971.

Authors' summary: Male Macaca nemistrina were used to study the histochemical alterations in the testicular sample obtained before and immediately after immobilization. Histochemical stains were modified and adapted for use in subhumam primate testicular tissues. Conventional histologic stains were also made to allow comparisons.

Fourteen days of immobilization results in spermatogenic arrest in the seminiferous tubules of subhuman primates. These enzymatic changes include lactic dehydrogenase, succinic dehydrogenase, and alkaline phosphatase. Histologic alterations are also demonstrated.

17. Corrodi, H., K. Fuxe, and T. Hokfelt. The effect of immobilization stress on the activity of central monoamine neurons. *Life Sciences* 7:107-112, 1968.

Purpose: To determine whether specific activation of various noradrenaline nerve terminal systems of the brain and spinal cord occurs under the influence of immobilization stress.

Procedure and methods: Male rats were immobilized in small wire cages by attaching their legs to metal wires which comprised the cage. Various inhibitor drugs were administered before or after immobilization to selectively allow various amine syntheses and clinical determinations of brain dopamine (DA), noradrenaline (NA), and 5-hydroxytryptomine (5-HT).

Results: With immobilization, slight decreases occurred in DA, NA, and 5 HT of the brain and spinal cord. The decreases in 5-HT were significant after 3 hr but not 16 hr. Depletion of NA was accelerated after 4 hr of immobilization but changes in DA were not certain. Histochemically amine depletion was evident in practically all of the various NA nerve terminals of the brain and spinal cord of skeletal rats. 5-HT changes did not occur.

Conclusions: Immobilization specifically increases the amine depletion in various nerve terminal systems of the brain and spinal cord obtained by treatment with chemical inhibitors. Central NA neurons, but not DA and 5-HT neurons, are activated under the influence of immobilization stress.

18. Curzon, G., M. H. Joseph, and P. J. Knott. Effects of immobilization and food deprivation on rat brain tryptophan metabolism. *Journal of Neurochemistry (London)* 19:1967-1974, 1972.

Authors' abstract: Withdrawal of food or immobilization both led to changes in rat brain tryptophan metabolism. Brain tryptophan and 5-hydroxyindolylacetic acid concentrations both increased while changes in

5-hydroxytryptamine were much smaller. Changes were greater upon withdrawal of food. The brain tryptophan change did not appear merely to reflect an overall increase of brain amino acid concentrations, brain tyrosine concentration being only slightly increased by food withdrawal and significantly decreased upon immobilization. Plasma tryptophan did not increase. The changes in brain indole metabolism were not abolished by adrenalectomy. Results suggest that 5-HT turnover is highly correlated with brain tryptophan concentration and that increase of the latter explains the maintenance of 5-HT concentration during the stress situation used even though breakdown to 5 HIAA is apparently elevated. It is possible that the associated increases of brain tryptophan and 5 HIAA upon deprivation or immobilization reflect a feedback control of 5 HT synthesis following its increased presynaptic release. Alternatively, the above stress situations might lead to increased brain tryptophan concentration by a mechanism not mediated by 5 HT release but nevertheless maintaining normal 5 HT concentrations. Defective control of brain tryptophan concentration could be of pathological significance, for example, in depressive illness in which there is some evidence of reduced brain 5 HT metabolism. Increased brain tryptophan concentration in stress is presumably due to increased influx of tryptophan from plasma although release of tryptophan in the brain from a bound form is not excluded. Increased influx is not explicable by a net increase of plasma tryptophan as this was not found. A final mechanism for the brain tryptophan changes on immobilization is that they might result from reduced plasma concentrations of other amino acids (e.g., tyrosine) which compete with tryptophan for transport to the brain.

19. Dolgun, Z. S. and S. P. Novikova. Dynamics of elimination of 5-oxyindoleacetic acid in rats during prolonged hypokinesia. *Kosmicheskaya Biologiya i Meditsina* 3:74-75, 1969.

Purpose: To study the effect of prolonged immobilization on the elimination of urinary 5-oxyindoleacetic acid (5-OIAA) in rats.

Procedure and methods: Male Wistar rats (170-180 gm) were individually immobilized in restricted activity cages. Feces and urine were collected separately. Urinary 5-OIAA was analyzed daily.

Results: The urine of rats contains a substance which, after processing, gives a color reaction similar to 5-OIAA. The content of this serotonin metabolite varied from 20-200 μg/day independent of urine volume. There were day-to-day variations but no seasonal changes. Immobilization resulted in increased 5-IOAA elimination; significant increases were noted on days 1, 3, and 13. After 3 weeks, 5-OIAA elimination decreased and after 7 weeks was near normal. Greatest body-weight losses occurred on days 13-15, followed by weight gains.

Conclusions: Immobilization procedures change in the elimination rates of urinary 5-OIAA and causes definite shifts in serotonin metabolism.

20. Fedorov, I. V. Intensity of tissue autolysis in animals during hypokinesia. *Kosmicheskaya Biologiya i Meditsina* 5:82-84, 1971.

Purpose: To determine the change in intensity of tissue protein synthesis during immobilization by the rate of tissue autolysis or decay.

Procedure and methods: Male rats (160-180 gm) were immobilized in plaster jackets and sacrificed after 15-22 and 51-59 days of hypokinesia. Autolysis intensity was judged from the increase in free amino acids in the tissue homogenate.

Results: After 15-22 days immobilization, the total content of free amino acids was similar to normal control animals. After 51-59 days immobilization, the free amino acid content showed a decrease ($p < 0.05$). Intensity of autolysis in all tissues other than muscle tissue was decreased after 2-3 weeks of immobilization.

In skeletal muscle, autolysis increased but not significantly ($p > 0.2$). After 8-9 weeks, autolysis showed a significant increase in all tissues except cardiac muscle.

Conclusions: During the first few weeks of immobilization, tissue decay decreases and the total reserve of free amino acids of the tissues is unchanged. The opposite findings occur after 8-9 weeks immobilization. The latter effect may be associated with a decrease of amino acids with food intake. The decay process may be due to a decrease in synthetic processes due to a decreased availability of amino acids.

21. Fedorov, I. V. Dynamics of changes in protein metabolism in rats during prolonged hypokinesia. *Kosmicheskaya Biologiya i Meditsina* 4:18-21, 1970.

Purpose: To study the changes in protein metabolism in immobilized rats.

Procedure and methods: Seventy-five rats were immobilized in plaster casts. Twenty-five were sacrificed after 15 days immobilization and 10 sacrificed after 60 days. The intensity of tissue protein synthesis was determined.

Results: Slower growth was noted during immobilization. After 15 days, body weight was 34 percent lower and after 60 days, 48 percent lower. Similarly, organ weights were reduced. Relative weight of the skeletal muscles decreased by 6 percent after 15 days, but after 60 days it was the same as in the controls. Nitrogen content of the skeletal muscle remained unchanged after 15 days immobilization but after 60 days, increased by 7 percent.

Labeled tryptophan-1-C-14 studies showed a reduced organ uptake after 15 days immobilization and remained at this low level after 60 days.

Conclusions: After 60 days immobilization, depressed protein metabolism did not show any indications of returning to normal. Tissue protein synthesis was also depressed but after 60 days there was also an increase in the intensity of their expenditure. Protealysis is increased as indicated by the increased serum transaminase activity. These factors lead to a marked suppression of growth. It is practically impossible for an animal to adapt to immobilization and normalize its metabolic processes.

22. Fedorov, I. V. Free amino acids in animal tissues during hypodynamia. *Kosmicheskaya Biologiya i Meditsina* 7:35-39, 1973.

Purpose: A determination of free amino acids in the tissues of animals at different times during hypodynamia.

Procedures and methods:

Male rats weighing 100-180 gm were immobilized by placing them in gypsum fitted "jackets."

The content of 11 free amino acids was determined by the method of one-dimensional descending paper chromotography, in the tissue of the liver, kidneys, heart, skeletal muscle, and brain of the healthy control animal and animals killed on the 15th-20th and 45th-60th days of hypodynamia.

Results:

The immobilization caused a lag in growth and a decrease in body weight.

During the first two or three weeks of hypodynamia, the total sum of the content of all free amino acids in the investigated tissues, excluding the heart, on the average was 10 percent higher than in the control animals.

During prolonged hypodynamia (45-60 days), the total sum of amino acids in all the tissues was reduced on the average by 20 percent of their level in the control animals.

In the cardiac and cerebral tissues, there is a considerable decrease in the quantity of alanine.

Conclusion: Experiments on rats revealed that the content of amino acids in tissues changes by the second to third week of hypokinesia: the content of some amino acids increases and that of others decreases. During the eighth to ninth weeks of hypokinesia, the content of amino acids and the level of individual amino acids decrease noticeably.

23. Fedorov, I. V. and L. A. Grishanina. Nitrogen metabolism in animals exposed to hypokinesia. *Kosmicheskaya Biologiya i Meditsina* 1:43-48, 1967.

Authors' abstract: Changes of metabolism were studied in rats exposed to experimental hypokinesia. Under these conditions, the animals exhibited a sharp increase of total nitrogen, urea, creatinine, and phosphorus released with the urine, as well as a stable negative equilibrium of nitrogen. Comparison of the changes of nitrogen metabolism in rats with the corresponding data in the literature on the change of nitrogen metabolism during human hypokinesia indicates an identical direction of these impairments in humans and animals. This circumstance makes it possible to recommend this model in carrying out further experiments in the study of metabolism in the organs and tissues of animals during hypokinesia and the influence of different pharmacological preparations on it.

24. Fedorov, I. V. and I. F. Shurova. Content of protein and nucleic acids in the tissues of animals during hypokinesia. *Kosmicheskaya Biologiya i Meditsina (Moskva)* 7:17-21, 1973.

Authors' abstract: The protein and nucleic acid content and weight of the gastrocnemius muscles were determined in rats in the organs and tissues on the 15th, 20th, 30th, and 60th days. It was established that the weight of the gastrocnemius muscles decreased by almost a factor of 2, the protein content in them decreased substantially, and the DNA and RNA quantity increased. The content of proteins also decreased in the tissues of the liver, kidneys, and heart; the DNA quantity did not change whereas the RNA quantity either did not change or in certain periods increased. It can be postulated that during hypodynamia there are impairments in individual links in protein synthesis, in particular, in the transcription stage, as a result of blockade of the corresponding operons. Under ordinary conditions, their depression occurs under the influence of impulses (nerve impulses or indirectly as hormonal actions) constantly arriving from the working muscles. With immobilization such impulsation is sharply restricted.

25. Fedorov, I. V., V. N. Vinogradov, Yu. I. Milov, and L. A. Grishanina. Synthesis of tissue proteins in animals during hypodynamia. *Kosmicheskaya Biologiya i Meditsina* 1:53-57, 1967.

Authors' abstract: A 10-to 15-day exposure of rats to hypodynamia caused a significant decrease in the rate of protein synthesis in their liver, kidneys, intestinal walls, heart, and skeletal muscle. The rate had not returned to its initial values by the sixth day after the 15-day exposure to hypodynamia. By this time, normalization of the peripheral blood picture had likewise not commenced nor had the glycogen level in the liver or weight of the adrenals begun to normalize.

26. Galaktinov, V. G. and A. S. Ushakov. Effect of hypokinesia on cellular and humoral indices of antibody formation in rats. *Kosmicheskaya Biologiya i Meditsina (Moskva)* 3:43-47, 1969.

Authors' abstract: The effect of hypokinesia on antibody formation in rats was studied. The number of antibody-producing cells in the spleen and hemolysin titers of test animals was dependent on exposure time. For example, 2- and 9-day exposures of rats prior to immunization resulted in an inhibition of antibody formation, that is, a decrease in cellular and humoral indices; a 45-day exposure improved the

antibody-producing function. A longer exposure (90 days) caused repeated inhibition of antibody production. The degree of expression of the antibody-producing function of rats subjected to hypokinesia is dependent on the duration of restricted mobility. The nature of manifestation of antibody formation during hypokinesia corresponds to the well-known model of development of the general adaptation syndrome.

27. Gayevskaya, M. S., L. M. Slez, and N. A. Ilyushko. Effect of hypokinesia on the protein composition of skeletal muscles. *Kosmicheskaya Biologiya i Meditsina* 4:25-29, 1969.

Authors' abstract: Experiments conducted on rats revealed that the animals did not develop hypokinesia immediately after their enclosure but only after extinction of the "freedom reflex." During the period of muscular activity preceding hypokinesia, the content of sarcoplasmic proteins decreased in the hind-limb muscles whereas the quantity of myofibrillar proteins increased. The period of hypokinesia which followed considerably reduced the content of myofibrillar proteins in skeletal muscles but caused no changes in the concentration and composition of sarcoplasmic proteins.

28. Gondos, B., R. Zemjanis, and A. T. K. Cockett. Ultrastructural alterations in the seminiferous epithelium of immobilized monkeys. *American Journal of Pathology* 61:497-518, 1970.

Purpose: To study the electron microscopic appearance of the seminiferous epithelium during immobilization and the significance of the cellular changes associated with spermatogenic inhibition.

Procedure and methods:

Four Macaca nemestrina monkeys were placed in specially designed suits and suspended in couchlike frames for 14 days, in an upright sitting position during the daytime and in a horizontal resting position at night.

Six testicular specimens were obtained: (1) initial, prior to immobilization; (b) after 7 days of immobilization; (c) after 10 days of immobilization; (d) after 14 days of immobilization; (e) 30 days after release; and (f) 60 days after release.

Initial biopsies were taken from the cranial surface of the right testis. Subsequent specimens were obtained from alternate testes and surfaces in sequence.

Tissue was prepared for electron microscopy by fixing finely minced fragments in ice-cold 1 percent osmium tetroxide with salt added for 1 hr, followed by dehydration in graded alcohol and imbedding in Araldite.

Sections cut with an LKB ultramicrotome were stained with uranyl acetate and Uad citrate and examined with a Hitachi HUIIC electron microscope.

Results:

Testicular biopsies taken after immobilization showed progressive degeneration and disappearance of spermatocytes and spermatids.

Variations in size and shape of the spermatid nuclei were commonly seen during immobilization. Multinucleation was a common finding during immobilization.

Autophagic vacuoles were occasionally seen in the cytoplasm of normal spermatocytes.

Changes in spermatogonia were of limited degree.

Sertoli cells were actively engaged in phagocytosis of degenerated cells.

Conclusions: The effect of immobilization on the seminiferous epithelium of Macaca nemestrina monkeys was studied with the electron microscope. The most severely affected cells were spermatocytes and spermatids, which underwent rapidly progressive degeneration. After 14 days of immobilization, only spermatogonia and Sertoli cells remained in the seminiferous tubules. The spermatogonia appeared normal, except for the presence of numerous lysosome-like bodies resembling those previously described in degenerating gonocytes. Sertoli cells exhibited active phagocytosis of degenerating germ cells and contained large accumulations of lipid droplets and dense bodies derived from breakdown of cellular material. Although their nuclei were markedly irregular, the Sertoli cells showed no signs of degeneration. Specimens obtained after release of the monkeys showed active and normal spermatogensis, indicating that the damage produced by immobilization was reversible.

29. Grinberg, L. N. Change in respiration of rat liver mitochondria during prolonged hypokinesis. *Voprosy Meditsinkoy Khimii* 16:387-390, 1970.

Purpose: To investigate mitochondrial respiration of mitochondria isolated from the livers of rats which were subjected to long-term limitation of the capacity for free movement.

Procedure and methods:

Sixty-eight mongrel rats weighing 160-190 gm were divided into two groups: experimental, which were placed in individual cells 20X5X7 cm; and control, in which four or five rats were kept in common cages.

Absorption of oxygen was investigated in a closed cell by the aid of a platinum electrode and values were recorded using PA-3 polarograph or N-373 recorder.

Results:

There was a change in the rate of respiration of mitochondria after 30 days of hypokinesia.

With 30-day-long hypokinesis, the weight of mitochondrial respiration in the fourth state exceeds by more than three times this value in the control with the use of succinate.

For the NAD-dependent substrate (α-ketoglutarate), respiration of mitochondria of hypokinetic animals is characterized by an increase in the rate of respiration in the fourth state and a decreased rate in the third state, in comparison with the control.

A decrease in the magnitude of respiratory control is particularly pronounced at the 30th day of hypokinesis while, by the 60th day, one detects a tendency toward an increase in its value.

Conclusion: It is necessary to note that succinate has the capacity to monopolize the respiratory chain and to provide an extremely high rate of electron transport in the formation of energy-rich compounds. It is possible that during hypokinesis the role of succinate as an oxidizing substrate increases, which is indicated by the extremely significant increase in mitochondrial respiration in the fourth state and by the absence of a decrease in the rate of respiration in the third state under the influence of hypokinesis (against a background of succinate but not against a background of α-ketoglutarate).

30. Guth, L. Effect of immobilization on sole-plate and background cholinesterase of rat skeletal muscle. *Experimental Neurology* 24:508-513, 1969.

Author's abstract: The observation that the cholinesterase activity (ChE) of muscle decreases more profoundly during denervation atrophy than during non-neurogenic (disuse) atrophy has led to the suggestion that the nerve specifically regulates muscle ChE. However, denervation results in a flaccid paralysis in which the muscles are not used; therefore, it is not justifiable to consider denervation and disuse atrophy as wholly separate entities. The present study was undertaken to investigate separately the changes in sole-plate and background ChE during disuse and denervation atrophy to determine whether the nerve specifically influences ChE at either of these sites. Disuse atrophy of the rat's soleus muscle was produced by internal fixation of the knee and ankle joints and denervation atrophy by transection of the sciatic nerve. With regard to protein loss, immobilization plus denervation produced greater atrophy (31.7 percent) than did immobilization alone (19.9 percent). The decrease in background ChE after each of these operations (35.6 and 22.4 percent, respectively) was not significantly different from the loss in protein. Sole-plate ChE, on the other hand, exhibited a large decrease (53.4 percent) in response to denervation plus immobilization, but was little altered by immobilization alone (8.7 percent decrease). Although the question of the specificity of the neural influence on background ChE remains unresolved by these results, it is concluded that the nerve specifically regulates ChE at the sole-plate.

31. Hänninen, O. and K. Hartiala. The induction of liver tyrosine 2-oxoglutarate transaminase in rats by immobilization. *Acta Endocrinologica* 54:85-90, 1967.

Authors' abstract: The immobilization of unfasted young female rats caused a linear increase in liver tyrosine 2-oxoglutarate transaminase activity reaching a four-fold level within 12 hr. This was followed by a decrease. No gastric lesions were observed macroscopically in 26 hr, but in many cases these appeared after immobilization of at least 40 hr. The enzyme activity in the liver of rats with macroscopic gastric lesions was double or more than double the activity in immobilized rats with no lesions or in non-immobilized control animals. The increase was partially inhibited by pretreating the animals 30 min before immobilization with a subcutaneous injection of actinomycin D. Adrenalectomized rats showed no increase in enzyme activity during immobilization.

32. Hoffman, R. A., E. A. Dozier, P. B. Mack, W. N. Hood, and M. W. Parrott. Physiologic and metabolic changes in Macaca nemestrina on two types of diets during restraint and non-restraint: I. Body weight changes, food consumption and urinary excretion of nitrogen, creatine and creatinine. *Aerospace Medicine* 39:693-698, 1968.

Authors' abstract: Four groups of male Macaca nemestrina ranging in weight from 7.4 to 8.4 kg were used in this investigation. The primates were fed two diets which were similar in provision of calories, but which differed in content of major nutrients. Diet A surpassed diet B in protein, but was exceeded by diet B in fat, carbohydrate, and major minerals. Calcium was approximately three times as high in the second diet. Two groups of animals were put on the respective diets and were placed in restraint on couches for 35 days followed by 35 days of reconditioning. One group of animals on each diet was nonrestrained throughout the study. All primates, restrained and nonrestrained, were exposed to a Biosatellite simulated reentry profile with centrifugation to 12-G on the 35th day of the study. The diet A restrained primates lost a higher percentage of weight during restraint and exposure to the reentry profile than did the diet B animals, although the two groups consumed approximately the same quantity of food and the same amount of energy based on initial body weights of the primates. The four groups of animals differed in urinary excretion of nitrogen, creatine, and creatinine.

33. Hoffman, R. A., P. B. Mack, and W. N. Hood. Comparison of calcium and phosphorus excretion with bone density changes during restraint in immature Macaca nemestrina primates. *Aerospace Medicine* 43:376-383, 1972.

Authors' abstract: Calcium and phosphorus balance data on Macaca nemestrina monkeys during immobilization are presented and correlated with x-ray bone densitometry findings. A positive mineral balance

was maintained during the immobilized period. A reduced bone density was observed in most skeletal sites examined with increased density observed in epiphyseal regions. Migration of mineral from one site to another is suggested as a possible explanation for the findings.

34. Hrubes, V. and V. Benes. The time course of metabolic changes during prolonged stress in rats. *Journal of Psychosomatic Research* 13:327-331, 1969.

Authors' summary: Two types of prolonged immobilization as the stress factors were applied in rats for the study of metabolic responses. The immobilized animals showed a marked rise in serum NEFA in both groups. The values of NEFA were almost regularly higher after 18 hr than after 24-hr immobilization. Dopamine and norepinephrine in the brain of experimental animals decreased and a similar trend was observed also in the adrenal epinephrine. All experiments were made in comparison with the control animals. The results and reciprocal metabolic relationships are discussed.

35. Khruleva, L. N. Effect of hypokinesia on conditioned reflex activity of white rats. *Kosmicheskaya Biologiya i Meditsina* 3:75-76, 1969.

Purpose: To study the changes in conditioned reflex activity before and after immobilization.

Procedure and methods: Twenty-seven white rats received conditioned reflex tests for 3-1/2 months using unconditioned reinforcement. Motor activity and reflex time were observed. Nine rats acted as controls. All animals were fed ordinary diets. Conditioned reflexes were tested on days 6, 16, 23, and 30 of the 30-day immobilization period and for 35 days after.

Results: Body weight loss of 52 gm was noted early after immobilization. Several animals were hypothermic (3.5°-8° below normal). Conditioned reflexes showed a gradual depression as latent periods were increased significantly. Control animals were 102 gm heavier than immobilized animals after 30 days.

After return to ordinary environment, the animals showed aggression and paid no attention to food. After 2 days the animals manifested increased motor activity. By the 34th day, they reached body weight of the control animals. By 20 days, the conditioned reflexes and response times were normal.

Conclusions: Immobilization produces considerable neural stress which is characterized by altered reflex times, and prolonged recovery time is necessary to restore initial functions.

36. Kogan, A. B., G. I. Sil'Chenko, and I. G. Arnautova. Effect of long-term physical restriction of an animal on some body functions. *Kosmicheskaya Biologiya i Meditsina* 3:52-54, 1969.

Purpose: To determine the effects of immobilization on body functions of the cat.

Procedure and methods: Three cats were immobilized for 20-30 days in a specialized rig. They were fed ad libitum and kept in a soundproof underground room. Electrodes were implanted in the brain for registration of potentials and subcutaneous electrodes for electrocardiogram recording.

Results:

There was a reduction in the mean amplitude of basic activity waves of the electroencephalogram (EEG) which was restored upon release of the animals. The waves were reduced when exposed to acoustic irritation (siren). After 3 weeks immobilization in response to the siren, large slow waves were seen.

There was a marked reduction in motor reactions which continued for 1 month after release. Also, after

release there was a decrease in walking rate, stride length, and overall disruption of normal locomotion. Various impairments and irregularities in cardiac activity were observed during and after immobilization.

Conclusions: Long-term immobilization causes a considerable change in nervous and cardiac activity. It is suggested that cats may be exceptional cases because of their species and the effects of immobilization may be multiplied in these animals.

37. Kolpakov, M. G., V. P. Tarasevich, and A. L. Markel'. Effect of aldosterone on hemodynamics under conditions of restricted motor activity of dogs. *Kosmicheskaya Biologiya i Meditsina* 4:52-56, 1970.

Purpose: To investigate the effect of aldosterone on the hemodynamic indices of dogs under conditions of restricted motor activity.

Procedure and methods:

Thirty-two dogs of both sexes ages 2 to 6 yr weighing from 12 to 25 kg were divided into two groups: control and those subjected to hypokinesia for 2 weeks.

After 2 weeks of immobilization, a course of aldosterone administration was initiated in doses of 100 μg/kg/day for 6 days.

Hemodynamics of the experimental animals was investigated under chloralose narcosis two times: 2 weeks after placement in the close cages, after which administration of aldosterone began at once, and then 6 days after commencement of aldosterone administration or 3 weeks after presence in close cages.

The ECG was registered synchronously in three standard leads: a phonocardiogram and curves for the central anal peripheral pulse were registered at the same time.

Curves of dilution of the indicator (T-1824) were registered using a photoelectric pickup.

Arterial pressure was measured by an electric manometer in the femoral artery.

Results:

The principal indices of hemodynamics for animals with restricted motor activity differed substantially from the control group: (a) There was a decrease in cardiac minute volume stroke index and a marked decrease in the mean rate of blood expulsion from the left ventricle; (b) the mass of the circulating blood was reduced; and (c) there was evidence of a decrease in vascular tone, a decrease in pulse wave propagation velocity, and as a result, a decrease in systemic arterial pressure.

A significant quickening of the rhythm of cardiac contractions was accompanied by a well-expressed shortening of the period of blood expulsion from the left venticle.

There was a decrease in the duration of the stress phase due to a shortening of both asynchronous and isometric contractions.

The introduction of aldosterone under hypokinetic conditions leads to a marked intensification of cardiac operation: (a) The minute volume becomes considerably higher than in control; (b) arterial pressure remains low; (c) peripheral resistance is not reduced and even has a tendency to increase; and (d) vascular tone is reduced.

A dynamic comparison of the phase indices before and after the introduction of aldosterone reveals a phase "load of volumes" syndrome including: (a) lengthening of the expulsion phase, total and mechanical systole; (b) a decrease in the index of myocardial stress; and (c) an increase in the intrasystolic index.

Despite the increase in blood mass, the time required for its total circulation has a tendency to decrease.

Conclusions:

Hypokinesia is accompanied by characteristic shifts in activity of the cardiovascular system which are expressed in a decrease in cardiac minute volume and a decrease in systemic pressure.

The cardiotonic effect of aldosterone is associated not only with the transport of electrolytes, but also with the hormonal effect on the energy balance of the myocardial cell.

38. Kovalenko, Ye. A., V. L. Popkov, E. S. Mailyan, Yu. S. Galushko, N. V. Gordeycheva, Yu. I. Kondrat'yev, N. A. Ilyushko, A. N. Poptapov, L. N. Grinberg, and M. A. Seydametov. Effect of hypodynamia on gas exchange in animals. *Kosmicheskaya Biologiya i Meditsina* 5:3-8, 1971.

Authors' abstract: This paper reports on investigations of the pathogenesis of prolonged hypokinesia (up to 100 days), including total gas exchange, gas homeostasis in tissues, rate of *in vivo* oxygen consumption in muscles (polarographic method), tissue respiration and oxidative phosphorylation in the skeletal muscles, myocardium, brain and liver, as well as oxidative processes in liver mitochondria. The weight of the animals and individual skeletal muscles of the limbs was also examined. On the 120th day of hypokinesia, functional (static and dynamic) tests were performed to determine work capacity and acute hypoxia tolerance of animals. During an exposure to 60-day hypokinesia, the dogs showed a decrease in gas exchange which was most clearly pronounced by the 30th day. By the end of the experiment, gas exchange increased and immediately returned to a normal level after the experiment. Rats exposed to a longer hypokinesia exhibited no noticeable changes in total gas exchange at early stages of the experiment and a distinct acceleration of gas exchange and regional oxygen consumption in muscles by the 90th-100th day. Changes in the oxidative processes in tissues were found during the 30th-60th day of hypokinesia. The rats also revealed substantial weight losses due to a decrease in muscle mass. They also experienced a noticeable loss in their capacity for performing active muscular work. Their tolerance to an altitude test remained unchanged.

39. Krasnykh, I. G. and L. A. Tyutin. Motor-evacuation function of the gastrointestinal tract in dogs during prolonged hypodynamia. *Kosmicheskaya Biologiya i Meditsina* 7:40-45, 1973.

Authors' abstract: The hypodynamic effect of the motor-evacuation function in the gastrointestinal tract was studied in dogs. In the first experimental series, 10 dogs were exposed to 15-day hypokinesia, in the second experimental series 10 dogs were exposed to 30-day hypokinesia; in the third experimental series 9 dogs were exposed to 60-day hypokinesia. The hypodynamic effect was brought about by confining the animals in cages of variable volume. The motor-evacuation function in the gastrointestinal tract was investigated by serial radiography. Exposure to 15-day hypokinesia delayed bowel evacuation of these dogs by an average of 1.4 hr (in this case and in all other cases the difference is statistically significant); 6 of the dogs exhibited pyloric spasms. On the average, the bowel evacuation of these dogs ended 30 hr later than prior to exposure to hypodynamia. With an increase in exposure the gastrointestinal changes progressed. During 60-day hypokinesia, the duration of the pyloric spasm increased to 2-4 hr. The duration of bowel evacuation exceeded the pretest data by a factor of 2; for the large intestine, by a factor of 4. The functional changes are attributable to disturbances of the motor-visceral influences on the gastrointestinal tract due to hypokinesia.

40. Kravchuk, L. A. Soporific and toxic effect of amobarbital sodium during 33-day hypokinesia and isolation of mice. *Kosmicheskaya Biologiya i Meditsina* 5:87-89, 1971.

Purpose: To study the effects of immobilization on the soporific and toxic effects of amobarbital.

Procedure and methods: Three groups of 30 male white mice (17-19 gm) per group were test animals. One group acted as a control, one was placed in isolation, and one underwent immobilization. All animals were tested after 30 days in the following way. Amobarbital sodium (producing brief sleep) was injected intraperitonically (IP) on the 31st day and a toxic dose administered on the 34th day.

Results: Immobilized mice showed a lag in body weight. A slight hypothermia of 1.5°-2.0° was evident in all mice. Some control animals (3 percent) died for no apparent reason while 26.6 percent of immobilized animals died. Amobarbital sodium (AS) exerted its soporific effect at a lower dose and more rapidly in immobilized animals. Also, the duration of sleep was greater. ID_{50} was less in immobilized than control animals.

Conclusions: After 30 days confinement, immobilized animals are more sensitive to the soporific and toxic effects of amobarbital sodium.

41. Kravchuk, L. A. and V. G. Ovechkin. Effect of amobarbital sodium and the somatotrophic syndrome on mice during prolonged hypokinesia. *Kosmicheskaya Biologiya i Meditsina* 2:7-12, 1968.

Authors' abstract: A 35-day experiment conducted on mice exposed to hypokinesia and isolation showed that test animals differed from controls in their weight changes, mortality rate, orthostatic tolerance, and sensitivity to isobarbital sodium (as judged by the mean effective dose, time of onset, and duration of sleep). The preliminary administration of somatotrophic hormone resulted in the prolongation of sleep induced by amobarbital sodium by three or four times, the ED_{50} of the latter remaining unchanged. The results of our experiments give basis for assuming that the use of the somatotrophic hormone together with sleep-inducing drugs can result in clinical practice in a deepening and broadening of the effect of these drugs. On the other hand, the use of amobarbital after exposure to hypokinesia and isolation can delay the onset of sleep and shorten it. However, further investigations are required for additional clarification of the collected facts and drawing final conclusions.

42. Krotov, V. P. Study of water-mineral metabolism during restricted motor activity. *Kosmicheskaya Biologiya i Meditsina* 6:66-74, 1972.

Author's abstract: The hypokinetic effect on the pattern of changes in fluid and electrolyte metabolism was studied in rabbits. On the first day of hypokinesia, plasma liquefaction was noted, accompanied by a decrease in the hemotocritic index and the hemoglobin concentration. The plasma volume as calculated by the Strauss method was found to increase by 5.1 percent. During the three subsequent weeks of hypokinesia, fluid redistributions occurred between the plasma and red blood cells. The potassium and sodium concentration in the plasma decreased with lengthening of hypokinesia. The pattern of changes in the plasma calcium concentration correlated with the variations in total blood serum protein. These changes seem to be one of the factors responsible for the pronounced disturbances in the plasma calcium concentration in hypokinetic animals. The potassium and sodium content in various myocardial parts of the experimental rabbits varied in different ways. A study of variations in potassium and sodium content in the femur extensor and the back long muscle revealed no significant discrepancies in the changes in electrolyte content. This may be attributable to a generalized pattern of the electrolyte metabolism disturbances. The fluid-redistribution in rabbits exposed to hypokinesia was studied by the indicator dilution method. The data obtained show the lack of dehydration of animals during their exposure to hypokinesia.

43. Kustov, V. V., B. I. Abidin, V. I. Belkin, and L. T. Poddubnaya. Effect of preliminary exposure to carbon monoxide on development of hypokinetic disorders in white rats. *Kosmicheskaya Biologiya i Meditsina* 6:18-21, 1972.

Authors' abstract: The experiments demonstrated physiologically and biochemically that preliminary exposure to carbon monoxide with a concentration of 0.6 ±0.02 mg/liter (10 exposures) insignificantly enhanced the development of hypokinetic disturbances. The effect of preliminary chronic exposure to carbon monoxide on the development of hypokinetic disorders was studied using 90 growing albino male rats weightin 130-150 gm. Effect of 10-day exposure to carbon monoxide increase, oxygen consumption, some peripheral blood indices, and tissue enzymes in the rats was investigated.

44. Kustov, V. V., V. I. Belkin, B. I. Abidin, T. A. Lekareva, L. T. Poddubnaya, and O. F. Ostapenko. Effect of restricted mobility of animals on the intensity and excretion of some gaseous products of vital functions. *Kosmicheskaya Biologiya i Meditsina* 5:14-17, 1971.

Authors' abstract: Male white rats weighing 200 gm were used to study the effect of relative hypokinesia on the intensity of formation and body elimination of some end products of its vital functioning. It was demonstrated that 15-day reduced activity of male white rats has an insignificant effect on the elimination of ketones and aldehydes and accelerates the elimination of carbon monoxide and ammonia.

45. Kvetnansky, R., G. P. Gewirtz, V. K. Weise, and I. J. Kopin. Effect of hypophysectomy on immobilization-induced elevation of tyrosine hydroxylase and phenylethanolamine-N-methyl transferase in the rat adrenal. *Endocrinology* 87:1323-1329, 1970.

Authors' abstract: The depletion of adrenal epinephrine observed after immobilization stress in normal rats is even greater in hypophysectomized rats. The activities of adrenal tyrosine hydroxylase (TH) and phenylethanolamine-N-methyl transferase (PNMT), enzymes in the epinephrine biosynthetic pathway, are decreased following hypophysectomy. After repeated immobilization, TH levels in hypophysectomized rats increase significantly but do not reach control levels. In hypophysectomized rats, PNMT levels remain markedly decreased with repeated immobilization. When ACTH is administered to hypophysectomized rats before each period of immobilization there is less depletion of adrenal epinephrine and levels of TH and PNMT approach those found in sham-hypophysectomized immobilized rats. When dexamethasone is given prior to immobilization, there is again less depletion of adrenal epinephrine and an increase in PNMT levels but no change in TH levels. Thyroxine does not increase epinephrine or enzyme levels in hypophysectomized immobilized rats. Adrenal denervation completely blocks the immobilization-induced increase in TH in hypophysectomized rats. When ACTH is given before immobilization there is a marked increase in TH activity in the intact adrenal and a small but significant increase in TH in the denervated gland. PNMT levels increase in intact and denervated adrenals of hypophysectomized rats given ACTH prior to immobilization. Increases in TH levels induced by immobilization stress require both intact neuronal and pituitary-adrenal systems. PNMT levels appear to be controlled by both systems, but the pituitary-adrenocortical system appears to be more important.

46. Kvetnansky, R., G. P. Gewirtz, V. K. Weise, and I. J. Kopin. Enhanced synthesis of adrenal dopamine β-hydroxylase induced by repeated immobilization in rats. *Molecular Pharmacology* 7:81-86, 1971.

Authors' abstract: Repeated immobilization of rats results in a striking increase in adrenal medullary dopamine β-hydroxylase activity. After six periods of immobilization, the levels are highest preceding the next immobilization, decrease during the immobilization, and increase upon termination of the immobilization. Six hours after the immobilization, the activities return nearly to the pre-immobilization levels. Denervation of the adrenal markedly diminishes the increase in dopamine β-hydroxylase activity that occurs with repeated immobilization. Prior treatment with hexamethonium prevents the decrease in activity during the immobilization interval, whereas the protein synthesis inhibitors actinomycin D and cycloheximide prevent the increase in enzyme activity seen after termination if immobilization. These observations support the view that dopamine β-hydroxylase is released as a result of neural stimulation during immobilization and suggest that its increase following cessation of immobilization is a consequence of accelerated synthesis of the enzyme.

47. Kvetnansky, R. and L. Mikulaj. Adrenal and urinary catecholamines in rats during adaptation to repeated immobilization stress. *Endocrinology* 87:738-743, 1970.

Authors' abstract: Adrenal and urinary catecholamine levels were measured in rats subjected to one immobilization stress or during adaptation to daily repeated immobilization. A decrease in adrenal epinephrine was apparent after 90 min of the first immobilization and persisted for 24 hr after the immobilization was terminated. Adrenal norepinephrine was not affected. Urinary epinephrine and norepinephrine (24-hr excretion) were increased by one immobilization; most of these catecholamines were excreted during the interval of immobilization. After daily repeated immobilization for 2.5 hr, "adaptation" of the adrenal medulla appeared to occur. Immediately after the ninth immobilization, adrenal epinephrine was still decreased, but 24 hr later it was at the control level. After 40-350 times repeated immobilization, adrenal epinephrine was not decreased and adrenal norepinephrine was increased. Urinary excretion of epinephrine was greater in rats subjected to repeated immobilization than in unstressed or once-immobilized rats. These results suggest that the "adaptation" of the adrenal medulla in repeated immobilization stress in rats is the result of an enhanced ability to replace the released catecholamine rather than to a diminished catecholamine release after repetition of the stress.

48. Kvetnansky, R., S. Silbergeld, V. K. Weise, and I. J. Kopin. Effects of restraint on rat adrenomedullary response to 2-deoxy-D-glucose. *Psychopharmacologia (Berlin)* 20:22-31, 1971.

Authors' abstract: Male rats immobilized for 2-1/2 hr daily for 7 or 40 consecutive days were compared to control animals. Urines were collected for two consecutive 24-hr intervals, starting with the beginning of the last 2-1/2 hr restraint interval. Four days after the last restraint interval, all rats received a single injection of 2-deoxy-D-glucose (2DG) (500 mg/kg). Immediately afterward, urine specimens were collected for another 24-hr period. The 24-hr urinary epinephrine (E) of the initial period was markedly increased after 7 immobilizations and 40 immobilizations. The increase in E was significant during the second day of collection after 7 immobilizations, but not after 40 immobilizations. The urinary E during the period after 2DG administration was increased for all immobilized rats; the E levels after 40 immobilizations were greater than after 7 immobilizations.

For evaluating adrenal changes, animals were immobilized daily and given 2DG daily. Six hours after one immobilization followed by 2DG, there was a marked lowering of adrenal epinephrine and a small increase in adrenal tyrosine hydroxylase (TH) and phenylethanolamine-N-methyl transferase. Those animals immobilized and treated with 2DG daily for 1 week showed marked lowering of adrenal E and an increase in adrenal TH and dopamine-B-hydroxylase.

49. Kvetnansky, R., V. K. Weise, G. P. Gewirtz, and I. J. Kopin. Synthesis of adrenal catecholamines in rats during and after immobilization stress. *Endocrinology* 89:46-49, 1971.

Authors' abstract: Repeated intervals of immobilization previously have been found to cause elevation of levels of tyrosine hydroxylase in the adrenals of rats. In the present study it was found that the increased levels of enzymes result in enhanced synthesis of epinephrine-^{14}C from tyrosine-^{14}C but not from dopa-^{3}H. During immobilization, conversion of tyrosine-^{14}C to catecholamines is further increased and may exceed the cpaacity of even the elevated levels of dopamine-β-hydroxylase to convert dopamine to norepinephrine. Thus, while tyrosine hydroxylase is normally rate-limiting, dopamine-β-hydroxylation may become rate-limiting when dopamine formation is markedly accelerated.

50. Kvetnansky, R., V. K. Weise, and I. J. Kopin. Elevation of adrenal tyrosine hydroxylase and phenylethanolamine-N-methyl transferase by repeated immobilization of rats. *Endocrinology* 87:744-749, 1970.

Authors' abstract: Repeated daily immobilization of rats results in a neuronally dependent elevation of tyrosine hydroxylase in the adrenal medulla. Phenylethanolamine-N-methyl transferase levels are also increased. After cessation of immobilization intervals, tyrosine hydroxylase levels decrease toward preimmobilization levels with a half-life of about 3 days.

51. Lenskaya, G. N. Blood supply to the skeletal muscles of rats during hypokinesia. *Kosmicheskaya Biologiya i Meditsina* 7:14-17, 1973.

Author's abstract: Quantitative changes in capillary blood flow were studied in vivo in M. semimembranosus and M. soleus of rats exposed to 5-, 15- and 30-day hypokinesia using intravascular injections of india ink and gelatin mixtures. Blood flow was determined with respect to the number of capillaries per unit area and per one muscle fiber as well as with respect to the total surface of capillaries from the total surface of muscle fibers. The skeletal muscles of rats differing with respect to their morphological and functional properties exhibited certain differences in their hypokinesia-induced adaptive changes. M. semimembranosus exhibited a significant increase in the mean radius of the muscle fibers and capillaries. Due to considerable weight losses during the early hypokinetic stages, the relative number of capillaries per unit area increased. M. soleus exhibited a significant decrease in the number of capillaries per unit area (by 14-16 percent) and per muscle fiber. Thus, in the skeletal muscles of rats differing in their morphofunctional properties, there were some differences in the nature of the adaptive changes to conditions of hypokinesia. The differences were evidently caused by the peculiarities of metabolic processes in the investigated muscles.

52. Lobova, T. M. Blood and tissue lipids in hypodynamic rats. *Kosmicheskaya Biologiya i Meditsina* 7:32-35, 1973.

Author's abstract: The effect of hypodynamic exposures of different duration on the level of cholesterol, β-lipoproteins, and total lipids in the serum, skeletal muscles, heart, liver, and brain of rats was studied. These investigations revealed that a hypodynamic exposure was followed by an increase in the level of cholesterol and β-lipoproteins in the serum. The cholesterol content in tissues, especially in the skeletal muscles, increased. The total quantity of lipids in the skeletal muscles, liver, and to a lesser extent, in the heart, decreased.

53. Mack, P. B., R. A. Hoffman, and A. N. Al-Shawi. Physiologic and metabolic changes in Macaca nemestrina on two types of diets during restraint and non-restraint: II. Bone density changes. *Aerospace Medicine* 39:698-704, 1968.

Authors' abstract: Four groups of Macaca nemestrina were fed two diets which differed in content of major nutrients, with diet A higher in protein and diet B higher in fat, carbohydrate, and major minerals. Animals on each diet were held in restraint on couches for 35 days, with exposure to a Biosatellite simulated reentry profile involving centrifugation at 12-G on the day that the restraint period ended. The period of restraint was followed by 35 days of reconditioning of the formerly restrained animals in cages, with the same diets continued. Two groups of unrestrained primates were placed on the respective diets and were kept in cages for 70 days of the experiment except for exposure to the reentry profile on the same day that the restrained primates were exposed. Bone mass was measured periodically in all primates by the method of radiographic bone densitometry, with 17 anatomic sites in the skeletal system evaluated. Bone density was improved significantly in most skeletal sites when the diet containing the higher levels of calcium and phosphorus was the sole experimental factor changed. Restraint had the opposite effect, with loss in skeletal mass found in both dietary groups when this factor was applied. The special diet had a greater effect on improving bone density during the reconditioning period which followed restraint than during the restraint period itself.

54. Mason, J. W. Corticosteroid response to chair restraint in the monkey. *American Journal of Physiology* 222:1291-1294. 1972.

Author's abstract: Mean urinary 17-OHCS levels show about a threefold elevation (1.7 mg/day vs. baseline of 0.5 mg/day) in monkeys during the first 3 days after placement in a restraining chair. While the major part of the 17-OHCS response usually occurs during the first week, the duration of response varies between different animals and also apparently in relation to prerestraining housing conditions. There were no significant differences in 17-OHCS levels in the same animals during cage housing as compared to the second month in the chair, indicating no appreciable chronic effects of chair restraint upon the pituitary-adrenal cortical system.

55. Mason, J. W. and E. H. Mougey. Thyroid (plasma BEI) response to chair restraint in the monkey. *Psychosomatic Medicine* 34:441-448, 1972.

Authors' abstract: Study of a series of 26 rhesus monkeys revealed significant elevations of plasma butanol extractable iodine (BEI) levels persisting through a 6-day period of chair restraint. There was a mean BEI increase from a control baseline of 3.2 μg percent to a peak of 5.1 μg percent on the third day of chair restraint. Study of 14 of these monkeys throughout a longer period of 8 weeks of chair restraint indicated that, although duration of response varied considerably between monkeys, mean BEI levels remained significantly elevated through the third week. BEI levels during the second month of chair restraint do not differ significantly from those levels observed in the same monkeys while housed in cages prior to chair restraint. This evidence of thyroid response to an unconditioned emotional stimulus supports findings in previous work with a conditioned emotional stimulus, indicating that acute emotional arousal elicits stimulation of the pituitary-thyroid system in the rhesus monkey.

56. Mason, J. W., E. H. Mougey, and C. C. Kenion. Urinary epinephrine and norepinephrine responses to chair restraint in the monkey. *Physiology and Behavior* 10:801-804, 1973.

Authors' abstract: Mean urinary epinephrine levels show a greater than threefold increase (8.2 μg/day vs. baseline of 2.2 μg/day) in monkeys during the first 3 days after placement in a restraining chair. Epinephrine levels remain significantly elevated, however, only during the first week in a total 8-week period of restraint. Although there also was a tendency for slight initial increases in urinary norepinephrine levels to occur, the changes were not statistically significant. There were no significant differences in either epinephrine or norepinephrine levels in monkeys during cage housing as compared to the second month of chair restraint.

57. Mateeff, D., N. Bodourov, K. Binev, D. Yonkov, L. Cheresharov, R. Radomirov, and S. Toshkova. Certain changes in the skeleton of immobilized and training albino rats. *Izvestiia na Instituta po Fiziologiia (Sofiia)* 13:139-144, 1970.

Authors' abstract: Comparative roentgenological investigations were carried out with three experimental groups of rats—controls, immobilized, and training animals, the aim being to ascertain the influence of movement on the compactness and structure of the bones. The results of the investigations indicate that the movement of the rats of the training group has a favorable effect on the quantitative accumulations in the bones, potassium and phosphorus salts in the first place, and is roentgenologically expressed in the more marked compactness of the individual bones. The compactness of the bones of the animals belonging to the immobilized group is the lowest, that of the rats in the control group being on a medium level or rather close to that of the immobilized animals, while that of the training animals is the highest.

58. Mateeff, D., Y. Tsacheva, D. Yonkov, S. Toshkova, L. Cheresharov, and R. Radomirov. Regeneration capacities of the skin in trained and immobilized albino rats. *Izvestiia na Instituta po Fiziologiia (Sofiia)* 13:145-152, 1970.

Authors' abstract: A study was made of the conditions of functional loading with physical work and of immobilization on the reparative regeneration processes of the skin after experimental lesions caused on albino rats. The process of healing has been followed by taking measurements of the wounds and by histological

examinations at certain interval of time. The functionally loaded animals showed accelerated decrease of the wound surface, the highest percentage of very early healing of the wounds, and cases of most rapid re-epithelization.

Immobilization results in a relatively delayed decrease of the wound surface. The histological investigations carried out established delays and irregularities in the differentiation of the granulation tissue in the wound upon the formation of the cicatrice, as well as reduced formation of keratin in the regenerated epidermis.

59. Mateeff, D., D. Yonkov, M. Hristova, L. Cheresharov, S. Toshkova, and R. Radomirov. On certain physiological and morphological changes in immobilized and training albino rats. *Izvestiia na Instituta po Fiziologiia (Sofiia)* 13:131-138, 1970.

Authors' abstract: The aim of the present work is to clarify more fully the influence of functional loading on the development of the organism. The investigation covered the specific water weight of the entire body, the specific weight of the bones of the limbs, the specific weight of certain internal organs, as well as their histochemical and morphological changes. The investigations were carried out on three groups of aging albino rats – training systematically on a treadcourse, immobilized, and control animals.

Physiological, morphological, and histochemical data have indicated that functional loading, even at the stage of aging, causes the appearance of processes of structural perfection under the form of working hypertrophy and increases the storage of energy in the organism. Immobilization, on the contrary, accelerates the processes of senile involution and atrophy.

60. Mikaleva, N. P., I. I. Ivanov, I. V. Federov, and E. M. Amdiy. Study of the fractional composition of skeletal muscle proteins during hypokinesia. *Kosmicheskaya Biologiya i Meditsina* 4:42-45, 1970.

Authors' abstract: Changes were detected in the fractional composition of skeletal muscle proteins in white rats exposed to hypokinesia for 15, 22, and 30 days. During the three experimental series, the content of actomyosin proteins decreased significantly whereas the content of the T fraction and stroma proteins increased. Muscles of the control and experimental animals differed insignificantly with respect to total nitrogen concentration. The weight of the experimental animals decreased reliably by an average of 19 percent. The water content in the skeletal muscles remained unchanged during the 15- and 22-day experiments and increased by 1 percent during the 30-day experiment in comparison with the controls. The ATP concentration decreased significantly during the 15- and 22-day experiments but returned to the normal level by the 30th day. The substantial decrease in the weight of the experimental animals undoubtedly is associated with a decrease in the total mass of organic substances (proteins) in the tissue, primarily the skeletal muscles; this evidently must be attributed to a decrease in intensity of synthesis of tissue proteins.

61. Orimo, H., T. Fujita, M. Yoshikawa, K. Hayano, and T. Sakurada. Effect of estrogen on immobilization osetoporosis in rat. *Endocrinology* 88:102-105, 1971.

Authors' abstract: The inhibitory effect of estrogens on the development of immobilization osteoporosis in the rat was studied through the analysis of calcium and hydroxyproline content of the femur and tibiae, and the measurement of cortical thickness of the femurs. A marked decrease in the calcium content of the right tibiae of rats in which the right-hand limb was immobilized through the application of a plaster cast was significantly inhibited by the simultaneous oral administration of 100 μg of conjugated estrogens. Furthermore, administration of conjugated estrogens significantly protected against the decrease in the bone density and the cortical thickness of the femurs of the immobilized limbs of rats. It is concluded that conjugated estrogens diminish the effect of immobilization in the development of osteoporosis, possibly through the inhibition of bone resorption.

62. Paul, M. I., R. Kvetnansky, H. Cramer, S. Silbergeld, and I. J. Kopin. Immobilization stress induced changes in adrenocortical and medullary cyclic AMP content in the rat. *Endocrinology* 88:338-344, 1971.

Authors' abstract: The levels of adrenal cyclic AMP in adrenal cortex and medulla have been examined during immobilization stress under varying conditions. After 30 min of immobilization, there was a highly significant rise in whole adrenal cyclic AMP, returning to baseline levels after 150 min. Theophylline pretreatment shifted the maximal cyclic AMP increase after immobilization to 10 min, with return to almost baseline values at 30 min. Hypophysectomy blocked the rise in adrenal cyclic AMP and, in fact, there was a small but significant decrease after 10 or 30 min of immobilization. Denervation of the adrenal gland did not alter the level of cyclic AMP in unstressed animals but reduced the elevation of cyclic AMP to about 50 percent of the response observed in the intact adrenals of stressed animals. There was no increase in cyclic AMP in the adrenal medulla after stress although the medullary component of cyclic AMP was 50 percent of the total. There was a highly significant cortical increase in cyclic AMP after immobilization. Finally, a significant increase was observed in adrenocortical cyclic AMP in denervated adrenals of stressed animals but not in the medulla. Thus, either the splanchnic nerve or the adrenal medulla via the nerve may be releasing a factor which takes part in the regulation of adrenocortical cyclic AMP.

63. Pfeiffer, C. G. The physiologic effects of restricted activity in the rat: Stress effects of chronic restraint. *Experimental Medicine and Surgery* 25:201-217, 1967.

Author's summary: The stress effect of chronic (5 week) but light restraint on the rat has been appraised. It is apparent that the maintenance of animals in cages which greatly prohibit exercise and normal freedom of movement constitutes a slight stress. The physiologic responses to this environmental stress are manifest, in part, by depressed growth, adrenal histopathology (cortical lipid depletion, hypertrophy, etc.), and slight thymic involution. The physiologic responses of the rat to this type of confinement stress are much less severe than those resulting from starvation stress (5-day fast, water ad libitum), and the magnitude of these responses is more exaggerated in immature rats than in adult animals. Rats do not develop gastric lesions either during the early or late stages of chronic, light restraint as they do following the psychogenic stress of total immobilization. It is suggested from these experiments that the above factors warrant consideration in the interpretation of physiologic data gathered from animals subjected to any degree of chronic restricted movement or restraint. Furthermore, although the environmental components leading to psychogenic stress in the rat are not necessarily extrapolative to human situations, the metabolic changes due to restraint and affecting growth and development may be phylogenetically similar.

64. Popkov, V. L., E. S. Mailyan, Yu. S. Galushko, Ye. A. Kovalenko, Ye. I. Zaytseva, I. A. Nitochkina, L. V. Smulova, and A. V. Ryazhskiy. Changes in the gas metabolism, gas homeostasis and tissue respiration in the rat during prolonged hypokinesis. *Fiziologichnoy Zhurnal SSSR im. I. M. Sechenova* 56:1808-1812, 1970.

Purpose: To study overall gas metabolism, intratissue gas homeostasis, and the intensity of tissue respiration in white rats kept in a condition of long-term (60-day) hypokinesis.

Procedure and methods:

Forty-eight test rats, each placed in special restricting cages and 30 control rats, housed 10 per 45X45X35 cm cage were used to study overall gas metabolism.

After the rats were placed for 1 hr in a sealed chamber, the average sum consumption of oxygen, liberated carbon dioxide gas, and the respiratory coefficient were determined according to the final chemical composition of the air.

The percentage composition of the gaseous mixture was calculated for oxygen tension (pCO_2) in mm

Hg, with calculation of common atmospheric pressure, the vapor pressure of water (pH_2O), and the temperature of the gaseous medium mixture in the depot were determined.

Intensity of tissue respiration was determined at the 45th and 60th days of hypokinesis in sections of tissue of the cerebral cortex, the heart, the liver, and the skeletal muscles (quadriceps muscle of the hip).

At the end of the 60-day-long experiment, in both the test and control animals, determination was made of the maximum physical working capacity tested by maximum swimming time of rats under a load equal to 15 percent of the animals weight (maximum dynamic work), and according to maximum time the animal could stay in a vertical seat with transverse straps (maximum static work).

The relationship of free and phosphorylation oxidation was studied.

Results:

No significant differences in oxygen consumption in the course of the experiment were found among the test and control rats.

The absolute values of pO_2 and pCO_2 in the subcutaneous gas depots during hypokinesis did not significantly change.

The consumption of O_2 in slides of the liver at the 45th day of hypokinesis increased. By the 60th day, this increase in respiration became less pronounced.

In the myocardium, after only 45 days, a tendency toward a decrease in absorption of O_2 was detected, and on the 60th day there was a significant, statistically reliable weakening of respiration.

After 45 and 60 days from the onset of hypokinesis, there were no clearcut changes in the intensity of respiration in the brain tissue and tissues of the skeletal muscles.

No differences were found in the percentage relationship of amytal-resistant and amytal-sensitive respiration at the 60th day of hypokinesis.

The relationship of free and phosphorylation oxidation in the test animals remain the same as in the control.

The weight of the test rats constantly lags behind the weight of the control.

After 60 days of hypokinesis, there was a sharp decrease in the animals' physical endurance.

Conclusions:

A 60-day-long period of hypokinesis does not have a significant influence on the general gas metabolism and intratissue gas homeostasis.

Long-term hypokinesis causes changes in the intensity of tissue respiration: an increase of respiration in the liver and a decrease in the myocardium (at the 45th and 60th days).

Physical working capacity of the animals after a 60-day-long period of hypokinesis decreases several times.

A 60-day-long period of hypokinesis causes a significant retardation in the increase in the animals' weight.

65. Portugalov, V. V., O. G. Gazenko, Ye. I. Il'Ina-Kakuyeva, V. B. Malkin, T. V. Artyukhina, I. A. Bukayeva, V. Ya. Gotlib, K. D. Rokhlenko, N. A. Roshchina, and B. I. Starostin. Some effects developing during hypokinesia (Experiments on mice). *Kosmicheskaya Biologiya i Meditsina* 1:18-25, 1967.

Authors' abstract: The effect of reduced motor activity (hypokinesia) on mice was studied during 30-day experiments by physiological, cytochemical, electron microscope, and histological techniques. It was found that during the first days of hypokinesia, most test animals exhibited stress reactions. In the course of further confinement, this type of response became less marked. By the 15th day, changes caused by hypokinesia itself (atrophy of skeletal muscles, etc.) were manifested. By the 30th day, the changes were less distinct than during earlier stages in the experiment. While attributing great significance to the general stress reaction during the initial period of the hypokinesia syndrome, we find it impossible to suggest complete correlation between the two. It is quite probable that many of the manifestations of hypokinesia, for example, atrophy of the voluntary muscles, dyskinesia of the intestine, etc., are based on entirely different mechanisms.

66. Portugalov, V. V. and K. D. Rokhlenko. Changes in striated muscle fibers of mice under restrained conditions. *Kosmicheskaya Biologiya i Meditsina* 3:45-52, 1969.

Authors' abstract: The quandriceps muscle of mice kept for 15 days under restrained conditions was investigated by electron microscopy. It was found that the myofibrillar apparatus, mitochondria, and sarcoplasm of muscle fibers developed changes which appeared to be reversible. It is assumed that the changes serve as the material substrate underlying the muscular deconditioning and atrophy observed during hypokinesia.

67. Potapov, A. M. Some indices of the growth of rats and their skeletal muscles during prolonged restriction of mobility. *Kosmicheskaya Biologiya i Meditsina* 6:16-20, 1972.

Author's Abstract: The exposure of rats to prolonged hypokinesia for 4 months resulted in the delayed growth of animals, their corpses, and skeletal muscles. The inhibitory effect of hypokinesia on the development of the animals and their muscles was most distinct during the second experimental month. The exposure produced a greater effect on the growth of the flexors in the ankle joint than on the extensors. In the lag in growth of the skeletal muscles during restricted mobility, an important role is played not only by stress factors, but evidently also by changes in the muscles caused by their "nonuse" as a result of a decrease in motor activity. According to data published by L. I. Sazanovich, the motor activity of rats was reduced to the greatest degree by hypokinesia and continued to decrease at a slower rate during the second and third months. It is known that "nonuse" exerts different effects on rapid and slow muscle fibers (acting primarily on the rapid fibers). This probably can, in part, explain the differences in the dynamics of development of slow (soleus muscle) and rapid (plantaris and long extensor of the fingers) muscles. The dissimilar course of development of the flexors and extensors evidently was probably caused by peculiarities in reflex activity of these muscles under hypokinetic conditions rather than by aspecific stress factors.

68. Prokhaska, I., I. V. Khavkina, and Z. I. Barbashova. Effect of prolonged hypokinesia on the heart muscle of rats. *Fiziologicheskiy Zhurnal SSSR* 59:1237-1241, 1973.

Authors' summary: Male white Wistar rats, weighing 220-270 gm, were used to study the effect of hypokinesia in the myocardium, its efficiency, resistance to the stress effect of anoxia, and anaerobic metabolism. Thirty-to-forty-day hypokinesia leads to a sharp reduction in body weight and heart weight, especially its right ventricle, in experimental animals. A weakening of the contractile power of the myocardium and its resistance to the stress effect of anoxia were found. In this case, a reduction in the rate of anaerobic metabolism was found in the right ventricle, of glycolysis and glycogenolysis and in the left, of glycogenolysis. The glycogen content in the heart muscles of rats after 30-40-day hypokinesia was unchanged.

69. Pyke, R. E., P. B. Mack, R. A. Hoffman, W. W. Gilchrist, W. N. Hood, and G. P. George. Physiologic and metabolic changes in Macaca nemestrina on two types of diets during restraint and non-restraint: III. Excretion of calcium and phosphorus. *Aerospace Medicine* 39:704-708, 1968.

Authors' abstract: Studies on body-weight changes, food consumption, urinary excretion of nitrogen, creatine, and creatinine, and bone densitometry as reported in two previous papers of this series have been supplemented by analyses of urinary and fecal excretion of calcium and phosphorus with the results outlined in this report. Although the change to the special diet which provided a higher level of calcium and phosphorus effected an increase in bone density in the majority of the skeletal sites tested, with the imposition of restraint tending to cause a loss in bone density regardless of which diet was fed, urinary calcium excretion did not always follow in a direction opposite from that of the bone density. When the diet change and restraint acted jointly, these antagonistic factors induced no net change in urinary calcium, although the diet change and restraint increased calcium excretion in the feces and phosphorus excretion in both urinary and fecal phosphorus.

70. Rassolova, N. P., A. N. Potapov, I. M. Sapelkina, and I. I. Grebennikova. Effect of prolonged hypokinesia on some indices of energy metabolism in the skeletal muscles and in some internal organs. *Kosmicheskaya Biologiya i Meditsina* 7:26-33, 1973.

Authors' abstract: Metabolic changes in the skeletal muscles, the heart, and liver of rats exposed to 120-day hypokinesia were investigated. As the exposure continued, oxidative phosphorylation decreased and anaerobic oxidation increased. This was very clear in the skeletal muscles and less distinct in the myocardium and liver. The muscles also showed morphological signs of atrophy. These changes can be attributed to the cumulative effect of hypokinesia as such and chronic stress.

71. Reklewska, B., L. Tomaszewska, H. Kaciuba-Uscilko, and S. Kozlowski. Changes in the thyroid and adrenal glands during prolonged immobilization of rats. *Bulletin de L'Academie Polonaise des Sciences* 20:685-689, 1972.

Purpose: To elucidate whether the increase of adrenaline excretion and the decrease of noradrenaline excretion and blood thyroxine during immobilization are associated with alterations in activity and morphological structure of the thyroid and adrenal glands.

Procedure and methods:

Forty-eight albino rats weighing 203-255 gm, were divided into two groups: control and experimental. The control animals were kept in individual, metabolic cages, while the experimental ones were placed into special plastic cages which restricted partly their physical activity. All the animals were given food and water ad libitum. On the 10th, 21st, 42nd, and 56th days, 6 rats from each group were weighed and injected intraperitoneally with 1μCi of ^{131}I. Three hours after the injection, the rats were killed by decapitation. Both lobes of their thyroids were removed, weighed, and their total radioactivity was measured by means of a scintillation probe connected with an LL-1 counter.

Immediately after the measurements, the left lobe of the thyroid was fixed in Boun's fluid for histological examination. The 7-μ-thick histological slices were stained either with hematoxylin and eosin or using the periodic-acid-Schiff method.

The uptake of ^{131}I by the thyroid gland was expressed as a percentage of the injected dose and then calculated per 1 mg of the thyroid tissue.

Both adrenals of the rats from the control and the experimental groups were removed immediately after

decapitation of the animals, weighed, and fixed in 10 percent formaline solution. The 7-μ-thick histological sections were stained with HE.

The Duncan test was used to determine the differences between the two groups studied.

Results:

The restriction of physical activity of rats caused a decrease of absolute weight of their thyroid glands. Differences between the control and experimental animals were statistically significant on the 21st ($p = 0.01$), 42nd ($p = 0.05$), and 56th ($p = 0.01$) days of immobilization. However, when the weight of the thyroid glands was calculated per 100 gm of body weight, the differences between the two groups disappeared.

Absolute weight of the adrenal glands of the immobilized rats increased during the first 10 days of immobilization. The difference between the experimental and control groups was statistically significant after 10 days of immobilization.

Relative weights (per 100 gm of body weight) of adrenal glands of the immobilized rats were much higher in comparison with the control values. The differences were statistically significant on the 10th ($p = 0.01$), 21st ($p = 0.01$), and 56th days of immobilization ($p = 0.01$).

The uptake of ^{131}I by the thyroid glands of the immobilized rats was lower than that in the controls. Statistically significant differences between the two groups were noted on the 21st, 42nd, and 56th days of the experimental period. The uptake of ^{131}I by 1 mg of thyroid tissue of the immobilized animals was also lower than that in the controls.

Histological observations of thyroids of the rats immobilized for 10 or 21 days did not show any distinct changes in morphological structure in comparison with the control animals.

In some rats immobilized for longer periods (42 or 56 days), larger follicles, low epithelial cells, and deeply stained, unvacuolized colloid were noted.

In a few cases, degeneration of follicular structure and an increased number of "C" cells, disposed irregularly in the thyroid parenchyma were observed.

Morphological structure of adrenal glands of the immobilized rats changed markedly in comparison with the control animals.

An increase of the zona fasciculata in the adrenal cortex and an increased number of granules within the cells of the adrenal medulla were observed after 10 days of immobilization of the rats.

Progressive morphological transformation was observed in adrenals of the rats within 42 days of immobilization. In the external zona fasciculata, "balloon" cells with a light cytoplasm, irregularly distributed within the zone were found.

The adrenal medulla cells of the experimental rats increased in size and nearly all the cells were filled with secretory granules.

After 56 days of immobilization, regressive transformation was observed in the adrenal cortex of some rats. The borderline between the zona fasciculata and zona reticularis was not so distinct as in the control glands, which suggests the migration of cells to the outer zone of the adrenal cortex.

In the adrenal medulla cells, a number of the secretory granules was still noted.

Conclusions:

Reduced thyroidal ^{131}I uptake values in the immobilized rats in comparison with the controls and changes in morphological structure of the thyroids in most rats immobilized for longer periods of time seem to suggest that the restriction of physical activity causes a depression of the thyroid function.

Microscopic observations of the adrenal glands indicate that within the first 6 weeks of immobilization, stimulation of the adrenal cortex as well as the adrenal medulla is manifested. During the following weeks of immobilization in some rats, symptoms of decreased activity of the adrenal cortex were observed. However, the average relative weight of adrenals of the rats immobilized for 8 weeks was markedly higher than that of the controls as well as that of the rats immobilized for 6 weeks. Activation of the adrenal cortex in the immobilized rats seems to suggest an increase of ACTH secretion. ACTH is known to reduce TSH secretion and consequently the thyroid activity.

The histological investigations seem to suggest that an increase of biosynthesis of adrenaline occurs in the rats during immobilization. Thus, the marked increase of adrenaline excretion in the urine of the experimetal rats may be due to the activation of the adrenal medulla.

72. Rokotova, N. A., I. D. Bogina, O. P. Bolotina, T. M. Kucherenko, Ye. S. Rogovenko, and R. L. Shevkin. The effect of prolonged limitation of motor activity on the activity of monkeys. *Problems of Space Biology* 2:424-434, 1962.

Purpose: To determine the effects of immobilization on the activity and behavior of monkeys.

Procedure and methods: Three macaques, one hamadryad, and one capuchin were immobilized for 10 days. Two monkeys were immobilized for 3.5 months.

Results:

Ten-day immobilization did not produce any changes in physiological function or activity. Prolonged immobilization showed that the animals health, behavior, and activity were not markedly changed during the first 20-30 days. Food intake was slightly reduced during the later period of immobilization. One animal lost 41 percent of its body weight, another lost 19 percent in 41 days.

Muscle rigidity and definite weakness of the hind limbs were observed upon release from immobilization. These symptoms only lasted for a day or so and disappeared. After 3.5 months immobilization, several days were required before the animals regained normal activity. Orientation was more pronounced after immobilization.

Conclusions: Prolonged immobilization did not produce any unfavorable effects on physiological functions, on animal behavior, or functional condition of the nervous system.

73. Sabayev, V. V., V. S. Shashkov, P. V. Sergeyev, V. A. Chistyakov, and M. A. Seydametov. Effect of radioprotectants on the functional state of histo-hematic barriers in restricted animals. *Kosmicheskaya Biologiya i Meditsina* 6:7-10, 1972.

Authors' abstract: The effect of mexamine and cystamine on the permeability of histohematic barriers in intact and restricted animals was studied. During the experiments, rats were kept under hypokinetic conditions for 10 days. Intraperitoneal injections of radioprotectants increased substantially the I^{131}-albumin permeability of tissue barriers in most organs and tissues. In response to an injection of radioprotectants during the 10-day hypokinetic experiment, the label transfer through the hemato-encephalic barrier and tissue barriers of the femur and back muscles, thymus, and adrenals increased to a lesser extent.

74. Serova, L. V. Change in resistance of animal tissues during prolonged restriction of motor activity. *Kosmicheskaya Biologiya i Meditsina* 5:82-83, 1971.

Purpose: To determine the effect of a decrease in tissue resistance resulting from immobilization on overall body resistance.

Procedure and methods: Adult male rats (250 gm) were immobilized in small cages. Tissue resistance was determined from the uptake of neutral red dye by the diaphragm muscles.

Results: After 30-day immobilization, there was a 27 percent increase in dye uptake by the diaphragm muscle, indicating a decrease in the resistance of the muscle tissue. Uptake is inversely proportional to resistance. After 45 days, dye uptake was twice as great as controls. After 60 days, dye uptake was only 65 percent greater, indicating a normalization of tissue resistance.

Conclusions: The decrease in overall body resistance during prolonged immobilization is accompanied by a change in tissue resistance. There may be a decrease in physiochemical strength of protein complexes. In most instances, increased dye uptake was accompanied by an increased cytoplasmic viscosity, probably associated with its dehydration. Cellular dehydration may be one of the vital links in overall body water balance during hypokinetic conditions.

75. Simonov, Ye. Ye. and I. V. Fedorov. Activity of some enzymes in the blood serum of rats during prolonged immobilization. *Kosmicheskaya Biologiya i Meditsina* 4:16-18, 1970.

Purpose: To study the dynamics of some enzymes in the blood serum during 60 days immobilization.

Procedure and methods: Thirty-nine albino male rats (150 ±20 gm) were immobilized in small cages. Forty animals acted as controls. Animals were sacrificed after 1, 15, and 60 days immobilization. Blood was collected and the serum was separated from the formed clot.

Results: After 15 days, the following enzymes showed increased activity: glutamate-aspartate (GA), glutamate-alanin-aminotransferase (GAA), ketose-1-phosphate aldolase (KPA), lactate dehydrogenase (LDH), and nonspecific cholinesterase (NCE). After 60 days, GA and GAA activity continued to increase while KPA, LDH, and NCE decreased.

Conclusions: Continued increase of GA and GAA activity evidently reflects and increases entry into the blood stream while the others showed reduced entry. The latter change is due to a reduced tissue formation of KPA, LDH, and NCE. The "critical" interval between 15 and 60 days indicates a suppression of tissue protein synthesis; GA and GAA changes suggest a continuing increase in atrophic and dystrophic processes.

76. Sobocinska, J. The effect of prolonged immobilization on diuresis and water intake in rats. *Space Life Sciences* 4:200-203, 1973.

Author's abstract: Diuresis and water intake was determined in 20 male albino rats during 8 weeks of immobilization and in 10 rats in post-immobilization recovery phase. Increase of diuresis and water intake during the immobilization period has been observed. Neither changes in sodium and potassium excretion nor in Na/K ratio were found. As the immobilization of the rats did not cause any changes of their natural body position in relation to the direction of gravity forces, the effect of immobilization on diuresis and water intake could not be related to an orthostatic shift of blood or inhibition of the hypothalamo-hypophyseal antidiuretic system. In conclusion, these experiments have demonstrated that diuresis and water intake increase in rats during immobilization periods. It seems that the increase of diuresis appears earlier than the increase of water intake. A cause in the increase of diuresis in the immobilized animals is still unknown.

77. Stroganova, Ye. A. Effect of prolonged hypodynamia on rat biology. *Kosmicheskaya Biologiya i Meditsina (Moskva)* 6:38-43, 1972.

Author's abstract: The effect of hypodynamia on the growth and development of offspring was studied in experiments on 36 rats. The test animals were housed in small cages for 62 days before mating. During this period the test animals lagged greatly behind the controls in their weight gain. Following exposure to hypodynamia the test animals changed their sexual behavior. During the first 2 days in the mating period, the females were very aggressive toward the males. This accounted for the fact that the test females littered two or three days later than the controls. It can be concluded that hypodynamia caused not only regular and functional changes in the animal body, but also later determines the appearance of biological shifts, in particular, a decrease in the activity of sexual behavior in the animals during the posthypodynamic period and a lag in weight of offspring.

78. Stroganova, Ye. A. and A. I. Volozhin. State of skeletal bones in ratlets born from females exposed to prolonged hypodynamia. *Kosmicheskaya Biologiya i Meditsina* 7:28-32, 1973.

Authors' abstract: Nine male and 9 female rats were exposed to 60-day hypokinesia. Eight male and 8 female rats which served as controls were kept in normal cages. After the exposure to hypodynamia, the test animals were mated simultaneously with the controls. In comparison with the controls, the test rats delivered their young later and in a smaller number. These young rats opened their eyes and became hair-covered at a later time. During the first 30-40 days, their weight and size lagged behind the parameters of the controls. At later stages the difference in these parameters disappeared. During the development test, young rats exhibited a higher degree of mineralization and Ca^{45} incorporation in bone and tooth tissues. This seems to be a manifestation of compensatory mechanisms aimed at restoration of metabolic processes in calcified tissues during the postembryonal period.

79. Tiavokin, V. V. Experimental atherosclerosis in rabbits with motility restriction. *Cor et Vasa (Praha)* 9:68-76, 1967.

Author's summary: The author made two series of experiments. The aim of the first series was to assess how soon changes in the aorta and myocardium develop when the movement in rabbits fed exogenous cholesterol is restricted. The purpose of the second series of experiments was to produce atherosclerosis by mere restriction of exercise without administration of cholesterol. The experiments were carried out on 11 experimental and 7 control animals. The restriction of movement was effectuated by placing the rabbits into special cages designed by the author. The results of the first series of experiments revealed that restriction of movement promotes the genesis and development of experimental cholesterol atherosclerosis, whereby myocardial changes are more marked than atherosclerotic changes on the coronary arteries. In the second series of experiments, it actually proved possible to produce experimental atherosclerosis without administration of exogenous cholesterol. Atherosclerotic changes in the aorta were similarly as in the first experimental series associated with myocardial changes, manifested on the ECG by signs of coronary insufficiency.

80. Tomaszewska, L., H. Kaciuba-Uscilko, B. Reklewska, J. Sobocinska, and S. Kozlowski. Effect of immobilization on urinary catecholamine excretion and blood-thyroxine level in rats. *Space Life Sciences* 3:174-176, 1971.

Purpose: To investigate the possibility of change in the adrenergic system and thyroid gland activity occurring during prolonged immobilization of rats.

Procedure and methods:

Twenty-four-hour urinary catecholamine excretion was determined daily in 30 albino rats immobilized for a period up to 10 weeks and 20 control rats kept separately for the same period of time.

Urine collected before and during the experiment was analyzed for free adrenaline and noradrenaline.

Thyroxine level in the blood serum was estimated in rats immobilized for 10 days and 3, 6, and 8 weeks as well as in control animals.

Results:

Within approximately 2 weeks of immobilization, the amount of noradrenaline excretion stabilized after decreasing slowly, at a much lower level than before immobilization, also much lower than that of the control rats.

Considerable variation in adrenaline excretion was observed between individual rats during the first few days of immobilization.

Adrenaline excretion increased gradually from the end of the first week of immobilization.

The level of thyroxine in the blood of immobilized rats was lower than in controls after 10 days of immobilization.

Marked decline of thyroxine level in comparison with control rats was observed after 6 and 8 weeks immobilization.

Conclusion: The low level of thyroxine would indicate that inactivity caused an inhibition of the release of thyroxine from the thyroid gland. The low level of thyroxine may also be caused by increased degradation of the hormone in the liver and its faster excretion with urine and feces. The authors' preliminary observations on T 1/2 of thyroxine in the blood seems to confirm such a possibility, as this was found to be much shorter in the immobilized rats than on control ones.

81. Tyavokin, V. V. Effect of limitation of muscular activity (hypodynamia) on the blood serum protein concentration. *Byulleten' Eksperimental'noi Biologii i Meditsiny* 74:55-56, 1972.

Author's abstract: A decrease in the albumin concentration and an increase in the globulin concentration were found in the blood serum of rabbits kept for 7 and 14 days in a state of hypodynamia. There was a particularly marked increase in the β-globulin concentration. The total protein concentration was unchanged. These indices remained practically unchanged in control rabbits throughout the period of observation. The changes in the concentrations of the blood protein factors discovered in the experimental animals are similar to those which occur in man during atherosclerosis.

82. Vasil'yev, P. V., N. N. Uglova, A. I. Volozhin, and V. Ye. Potkin. Investigation of some blood indices in white rats exposed to sixty-day hypokinesia. *Kosmicheskaya Biologiya i Meditsina* 7:13-17, 1973.

Authors' abstract: The effect of 5, 10, 20, 40, and 60 days of hypokinesia on circulating plasma volume, red blood cell count, hemoglobin content, and hematocrit index was studied using 100 white rats. Under the influence of prolonged hypokinesia, the experimental animals developed insignificant changes in the total volume of circulating plasma and blood (which, however, increased if calculated per 100 gm of body weight), a distinct increase in the hematocrit, red blood cell count and hemoglobin, and weight losses. The fact that the circulating plasma volume of hypokinetic animals remained unaltered suggests that the horizontal position of animals, which is normal for them, excludes the possibility of activating the Henry-Gauer reflex as the triggering mechanism bringing about a decrease in the circulating plasma volume.

83. Vikhert, A. M., V. I. Metelitsa, V. D. Baranova, and I. Ye. Galakhov. Morphological and biochemical changes in rabbits subjected to considerable limitation of mobility. *Kardiologiya* 12:143-146, 1972.

Purpose: To determine the nature and etiology of changes in the aorta, coronary arteries, and myocardium following immobilization.

Procedure and methods: Male rabbits (2.5 kg) of the chinchilla strain were immobilized individually. Ten animals acted as controls and 20 were immobilized. All animals received a normal diet. Blood samples obtained on days 10, 20, and 30 were analyzed for total cholesterol, lipoproteins, triglycerides, and total lipeds. Fifteen of the experimental animals died at verious stages due to symptoms of cardiac and cardiopulmonary insufficiency. Five rabbits were killed on days 19, 20, 23, 29, and 30 after immobilization.

Results:

Experimental animals lost 500 gm of body weight over 30 days while controls gained weight.

No changes were observed in lipid matabolic parameters at the end of the experiment. Cholesterol was slightly but not significantly increased on day 10. Control animals did not show any significant changes in lipoprotein fraction.

Autopsy of all the dead animals indicated a plethora of the parenchymatous organs; the hearts of the experimental animals were flaccid. One showed hydropericarditis, one pyothorax, and five pneumonia.

The aorta showed the following pathological changes: roughness of the intima, pits, depressions, and aneurisms. Pathological changes were noted in the middle layer of the aorta.

Myocardial changes included tissue splitting and edema of the walls of the fine intramural arteries and constriction of the arterial lumina. The myocardium also contained capillary stasis, fatty dystrophy, necrobiosis, and necrosis of small groups of muscle fibers.

Conclusions: Prolonged limitation of mobility in rabbits causes the development of changes of medionecrotic type in the aorta, with subsequent mediocalcinosis and the formation of aneurisms of various sizes. The myocardium is subjected to the development of fatty and protein dystrophy, necrobiosis, and necrosis of small groups of muscle fibers with further development of fine-focal cardiosclerosis. The etiology of these changes has not been solved.

84. Vinogradov, V. N., V. G. Petrukhin, and I. V. Fedorov. Morphological changes produced in animal organs by prolonged hypodynamia and subsequent physical exertion. *Byulleten' Eksperimental'noi Biologii i Meditsiny* 65:96-99, 1968.

Authors' abstract: Restriction of mobility of rats for 15 days leads to atrophy of skeletal muscles, an increase in weight of the adrenals, a decrease in the glycogen reserves of the body, an increase in succinate dehydrogenase activity, and a decrease in alkaline phosphatase activity in the liver. The resistance of animals to physical exertion (swimming, radial acceleration) is lowered in animals after hypodynamia, and more marked morphological changes are found in the myocardium, lungs, and liver than in animals under normal conditions.

85. Volozhin, A. I. Effect of hypoxic hypoxia and hypercapnia on calcium, inorganic phosphorus, and total protein in the blood of rats during hypodynamia. *Kosmicheskaya Biologiya i Meditsina* 5:17-22, 1971.

Author's abstract: The effect of adaptation to hypoxic hypoxia (7000 m) and hypercapnia (5 percent CO_2) on the content of calcium, inorganic phosphorus, and total protein in the blood of rats performing normal and diminished activity was studied. The hypodynamic animals exhibited an increased calcium concentration and a decreased content of inorganic phosphorus and total protein. Hypoxic hypoxia used as a factor for increasing animal tolerance produced no normalization of these three parmaeters in hypodynamic rats. The experiments

indicated that hypercapnia improved these parameters: the level of inorganic phosphorus and protein in rats exposed to hypodynamia and hypercapnia was higher than in rats exposed to hypodynamia alone.

86. Volozhin, A. I., P. V. Vasil'yev, N. N. Uglova, and V. Ye. Potkin. Status of calcium metabolism in the calcified tissues of rats during prolonged hypodynamia and thyrocalcitonin administration. *Kosmicheskaya Biologiya i Meditsina* 6:10-15, 1972.

Authors' abstract: The influence of 5-, 10-, 20-, 40- and 60-day hypodynamia and thyrocalcitonin administration on the resorption rate of Ca^{45} given 70 days before the exposure was investigated in experiments on 180 albino rats. In comparison with the controls, the hypolinetic exposure decreased the increment in the weight of skeletal bones to a considerable extent. The mineral content decreased in the hindleg, scapular and mandibular bones, increased in the parietal and maxillary bones, and remained unchanged in the shoulder bones. This exposure considerably reduced the rate of Ca^{45} resorption from the molars and the nonreadily exchangeable bone fraction. Daily injections of 5 μg of thyrocalcitonin in combination with polyvinyl pyrrolidone to nonrestrained rats also caused a decrease in the Ca^{45} level in their calcified tissues. Injections of the drug to restrained animals exerted an opposite effect: the renovation rate of the nonreadily exchangeable fraction increased in comparison with that in animals exposed to hypodynamia alone. The drug exerted an insignificant effect on the growth rate of skeletal bones in restrained rats.

87. Weinstein, H. and J. W. Driscoll. Immobilization-produced gastric pathology in wild rats (Rattus norvegicus). *Physiology and Behavior* 9:39-41, 1972.

Authors' abstract: Seven groups of wild rats (Rattus norvegicus) were deprived of food and immobilized in wire-mesh cocoons for varying periods of time. Following immobilization, they were examined for gastric ulcers. Minimum immobilization necessary to produce ulcers given that pre-immobilization food deprivation was sufficiently long appeared to be between 12 and 24 hr. When compared to results obtained by other investigators using similar procedures with the laboratory rat, wild rats appear to be more resistant to immobilization-produced gastric pathology than laboratory rats, especially in the length of pre-immobilization food deprivation required.

88. Yegorov, B. B., V. I. Lobachik, and L. N. Kleymenova. Changes in calcium metabolism in rats during hypokinesia. *Kosmicheskaya Biologiya i Meditsina* 3:55-58, 1969.

Authors' abstract: Calcium metabolism in rats kept for 30 and 60 days under restrained conditions was analyzed using the radioactive isotope ^{45}Ca. The investigations covered the skeletal system of the animals. A significant increase in ^{45}Ca incorporation into the bone tissue of restrained animals was noted. It reached the maximum value in the epiphyseal parts of the femur bones. The rate of ^{45}Ca elimination from the bone tissue of the test animals was greater than in the controls. These changes in calcium metabolism in bone formations, which during the experiment were subjected to different functional loads, make it possible to conclude that impairments in the processes of incorporation and elimination of ^{45}Ca under the given experimental conditions have a systemic generalized character. This is evidence that a functional "underload" is not the only cause of development of a generalized decalcination of the bone system under conditions of hypokinesia.

89. Yurgens, I. L. and O. I. Kirillov. Mitotic activity of adrenal cortical cells in rats during prolonged hypokinesia. *Byulleten Eksperimental'noi Biologii i Meditsiny* 74:98-101, 1972.

Authors' abstract: Male Wistar rats weighing 95-100 gm were placed in small containers restricting their movements. Experimental and control rats were sacrificed in groups after 1 and 12 hr and 2, 5, 9, 14, and 19 days. Mitotic division in the adrenal cortex was sharply inhibited after 1 hr. Subsequently (from 12 hr to 9 days), the mitotic index in the zona glomerulosa returned to the control level, but in the outer zona fasciculata it was considerably higher than in the control. After 14 and 10 days, when signs of exhaustion of the animals had developed and hypertrophy of the adrenals was less marked, the mitotic index in both zones was again

reduced. The presence of a phase of stimulation in mitosis in the outer zona fasciculata indicates that adrenal hypertrophy under stress conditions takes place not only through hypertrophy of the cells, as is usually considered, but also on account of stimulation of mitotic division.

90. Yurgens, I. L. and O. I. Kirillov. Morphological changes in the suprarenals of rats during hypokinesia. *Kosmicheskaya Biologiya i Meditsina* 6:3-6, 1972.

Authors' abstract: Male rats of the Wistar strain weighing 95-100 gm were kept in boxes. Control and experimental animals were killed 12 hr and 2, 5, 9, 14, and 19 days after their enclosure. Under hypokinetic conditions, the weight of the suprarenals increased due to an enlargement of the fascicular zone. At later experimental times, hypertrophy of the suprarenals decreased whereas dystrophy developed. The size of the nuclei increased in all zones in the experimental rats. This was very distinct in animals killed 12 hr and 2 days after the beginning of the experiment. As dystrophy increased, hypertrophy of the nuclei decreased, the dropoff being greater in the inner than in the outer parts.

91. Zemjanis, R., B. Gondos, W. R. Adey, and A. T. K. Cockett. Testicular degeneration in Macaca nemistrina induced by immobilization. *Fertility and Sterility* 21:335-340, 1970.

Authors' summary: Four M. nemestrina males were immobilized for 14 days. Testicular biopsies were taken prior to immobilization and on days 7, 10, and 14 of immobilization. Follow-up biopsies were obtained 30 and 60 days after release of the monkeys. Early degenerative changes were apparent already on day 7 of immobilization. Only Sertoli's cells and spermatogonia A, most of which were degenerating, lined the seminiferous tubules after 14 days of immobilization. Regeneration of the seminiferous epithelium was apparent 30 days after release of the monkeys. Complete recovery of the seminiferous epithelium was observed 60 days following release. It is suggested that stress-induced, central nervous system, pituitary, adrenal gonadal interaction might be involved.

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