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PATHOGENESIS OF WEIGHTLESSNESS SYNDROME

Ye. A. Kovalenko and P. V. Vasil'yev

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PATHOGENESIS OF WEIGHTLESSNESS SYNDROME

Ye. A. Kovalenko and P. V. Vasil'yev

ABSTRACT: Under conditions of a prolonged spaceflight a reorganization of many physiological systems of the organism such as: the analyzers, blood circulation organs, respiration, the stato-kinetic apparatus, various kinds of metabolism etc. takes place.

The peculiarities of the character of the organsim's reaction to the action of weightlessness permit discerning five stages: I – transition from super gravitational stress to weightlessness: II – partial adaption to weightlessness; III – gradual increase (cumulation) of the unfavorable effects of weightlessness influence; IV – transition from weightlessness to super gravitational stress and terrestrial gravitation; V – residual effects of the weightlessness influence and adaption to terrestrial gravitation.

The basic pathegenetic links of the disturbances arising in connection with the influence of weightlessness on the system of analyzers, hydrostatic pressure of the fluids stato-kinetic appartus, the organism's energetics and metabolism are considered.

Of the several factors which exert a constant effect on the living organism in spaceflight, weightlessness is the most important. This factor takes on a particular importance under the conditions of prolonged (long duration) flight. In their great majority, the data available in the special literature indicate that as the duration of the flight increases, weightlessness begins to exert an ever more distinctly unfavorable effect on the organism. The practical tasks that lie ahead and the need for further purposeful research in this area make necessary the summarizing of the information already available to us and, on this basis, an attempt at generalizing and formulating at least an approximate general model of the pathogenesis of the zero-gravity effect. /356*

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

There is no question but that the development at the present time of a mechanism rigorously defensible scientifically in all of its aspects is an extremely arduous task, and any variant of such a model will inevitably be to some degree hypothetical and subject to objection.

In the course of the evolutionary development of the biological world, weightlessness has played a definite role. The development of life, it will be recalled, began in the universal ocean. In conformity with Archimedes' law, the weight of the majority of the inhabitants of the seas and oceans is held in an almost complete balance by the salt water medium. Under these conditions, the effect of gravity basically reduces to the stratification and settling of the smallest organisms over an extended period of time. Consequently, that titanic evolutionary stage of living matter — the ascent from the simplest single-celled organisms to the fish — occurred in a state characterized by the partial loss of weight. A qualitatively new step in the development of the living world was heralded by the exodus from the ocean onto the dry land. New and higher energy expenditures were demanded, and essential improvements were made in the means of oxygen delivery. Suffice it to say, with the transition to a terrestrial mode of life the gaseous exchange of the amphibians increased four-fold (Korzhuyev, 1964). With the development of the animal kingdom in the form of larger and taller specimens with vertical locomotion and a higher hydrostatic liquid pressure within their organisms, terrestrial gravitation began to acquire an increasingly important significance among the environmental factors.

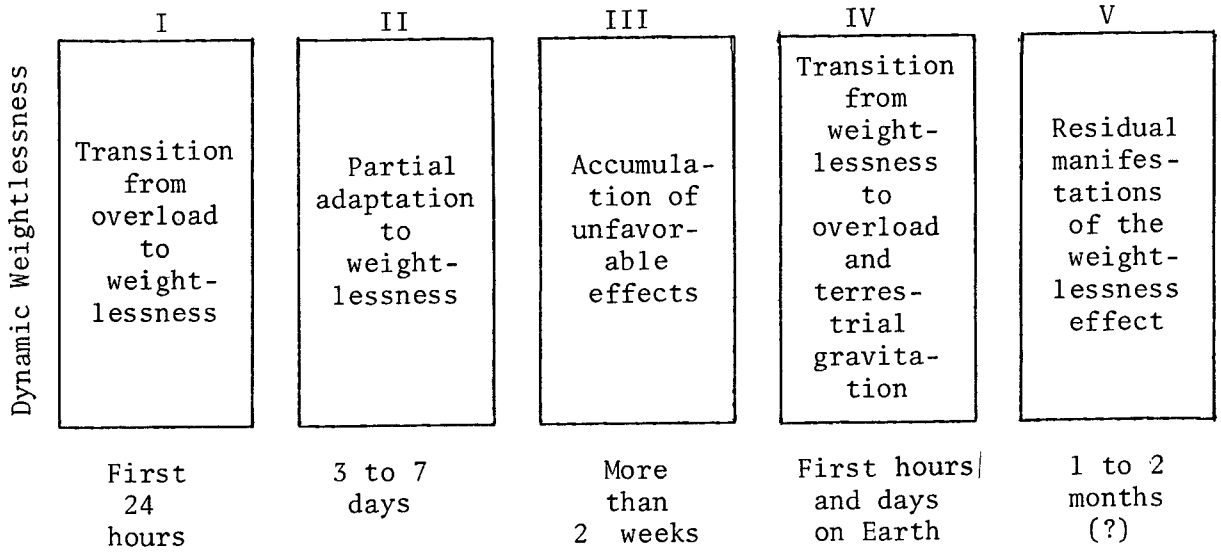
The logic of the biogenetic law points to the need that a second, no less important aspect of the problem also be considered — the ontogenetic aspect. During their ontogenesis, man and most mammals spend several months in a state of partial weightlessness and hypodynamia during the period of intrauterine development. What is remarkable is that the fragile and imperfect organism of the developing animal and human creature is protected not only against a host of other environmental factors, but is also to a significant degree spared the effect of the ubiquitous and powerful action of the Earth's gravity. Under these conditions the organism's energy requirements are substantially lower

than during the subsequent period of extrauterine life. A gradual advancement and overcoming of the forces of terrestrial gravity can be seen in the development of the human child, who first only lies, then crawls and rises uncertainly to his feet, until finally his walking is more and more perfected and he becomes capable of splendidly vanquishing the force of gravity whether in the form of 100-meter dashes in 9 to 10 seconds or 2-meter high jumps. This entire pattern of development is a vivid demonstration of the evolution of aggregate systems of the organism engaged in a struggle with terrestrial gravity. What is important here is that concommitantly with this there are also perfected all those systems which supply the organism with energy and, above all, the transport of oxygen and the maintenance of its partial pressure in the tissues at a level sufficiently high to ensure the required intensity of biological oxidation. In our opinion, it is absolutely imperative that, even now, the nexus between these two interrelated problems be taken into account and that they be considered in parallel: the development of the capacity to overcome the forces of gravity and the perfecting of the energy cycle which makes that capacity possible. This is particularly essential to further discussions of, and searches for, possible pathological disorders.

A consideration of the phylogenetic and ontogenetic aspects indicates that the organism has already encountered conditions approximating weightlessness and has travelled an evolutionary path whose ultimate end is, in a certain sense, to surmount these conditions.

In our inquiry into the problem of the possibility of a protracted sojourn in the weightless state we must, above all, know what will happen to the organism if it is deprived of its antigravitational mechanisms. This is one of the possible investigatory approaches, but one which has by no means been as yet thoroughly exploited. A significantly more broad-based and, evidently, more effective approach is provided by the method of simulating the individual effects of weightlessness under laboratory conditions: either by prolonged confinement to bed with greatly curtailed motor activity, immersion-media testing, Kepler--parabola flights, and the like. However, only actual spaceflight can furnish a complete picture of the "weightlessness syndrome".

The effect of weightlessness on the organism in protracted flight can be divided into five stages:



I — the transitional process from the launch overload g-forces to weightlessness, the "first encounter with weightlessness", as it were. This period lasts until approximately the end of the first twenty-four hours. During this time there may be observed marked vestibular and vegetative disorders, illusions of inverted position, and a sense of discomfort. These disorders were observed /358 in the case of cosmonauts G. Titov, V. Tereshkova, B. Yegorov, K. Feoktistov, and others (Sisakyan, 1965; Gazenko, Gyurdzhian, 1965 a, b; Kas'yan, Kopanev, 1967, et al.).

II — partial adaptation to weightlessness. As a rule, this period is characterized by a gradual reduction in the severity of the organic dysfunctions originally encountered. The duration of this period is approximately three to seven days.

III — the protracted and gradual accumulation of unfavorable effects of weightlessness on certain functions and systems of the organism. At the present time, this crucial period, of major concern to us, remains to a considerable degree obscure. We can only suppose that the effect of weightlessness on the organism is a "time function" of its action (Figure 1). Evidently, pivotal significance here may attach to the unconditioning ("detonification") of the

cardiovascular and muscular systems, the disruption in the interaction of the regulatory systems, and the imbalance in the energy and metabolic constellation of functions aimed at the organism's ability to counteract the forces of terrestrial gravity. A unique paradox occurs: the organism adapts itself to weightlessness, but in the sense of conventional life on Earth it becomes readapted, that is, the organism becomes unconditioned and its adaptational capabilities are curtailed. Simultaneously, there may be a sharp drop in the general and immunobiological reactiveness of the body and in its resistance, resulting in inadequate reactions to a number of external stimuli (Vasil'yev, 1968) and the occurrence of diseases with an unusual pattern of development.

For the moment it is still not entirely clear whether this cumulative process of unfavorable effects remains at some new functional level with respect to the organism's physiological systems, indicated by point X in Figure 2, or whether it proceeds further. Quite obviously, it is precisely the search for this hypothetical point X that will constitute one of the primary goals of future research into the effect of weightlessness on the organism.

IV – the effect of overload (g-forces), following protracted weightless flight, during deceleration of the spacecraft and reentry into the dense layers of the atmosphere. This stage is accompanied by the distinct danger of serious disorders in general and regional blood circulation: cerebral anemia, severe general oxygen starvation, fainting, and other disorders may ensue. An important task in this connection is the determination of the period of time in the weightless state during which the organism retains its capability of withstanding descent-related stress, as opposed to that period after which its adaptational capacities, without supplementary and auxiliary techniques of prophylaxis and protection, will be inadequate. In the diagram (Figure 2) the limit of this period of exposure has been marked by point Y. Consequently, the determination of point Y is the second important task to be resolved in forthcoming physiological and pathophysiological research. /359

V – residual manifestations of the effect of protracted weightlessness and adaptation to conditions of terrestrial gravity. On the basis of data already available, G. Cooper exhibited aftereffects for 18 hours following a

34-hour exposure to weightlessness (1963), and for more than 30 hours following his 8-day flight (in 1965). However, according to Berry (Berry, 1966), following their 14-day flight on "Gemini 7" astronauts F. Borman and D. Lovell exhibited no appreciable difference in orthostatic stability in comparison with their colleagues following their 8-day flight on "Gemini 5". US specialists have revealed that astronaut W. Shirra, following his comparatively short flight, was affected for an extended period of time with a loss of tone in the vessels of his legs. The peripheral surface veins were very distended and the skin on his feet and near them showed a dark violet-red discoloration, quite certainly attesting to a venous congestion of the blood. Also noted was orthostatic instability, despite the fact that the astronaut had been exposed to weightlessness for only a little more than 9 hours (Ditlein, 1964).

Significant stress by the physiological systems of the organism on orthostatic load and reduced pressure applied to the lower half of the body was clearly observed during the postflight period in the crews of "Apollo 7" and "Apollo 8", which remained in orbit 11 and 7 days, respectively (Berry, 1969).

Only two specialists have gone on record in the technical literature with a definite opinion as to the limiting duration of safe human exposure to the conditions of orbital flight. Gerathewohl (Gerathewohl, 1964) believes that this period will not exceed two weeks, while Berry concedes the possibility of flights of as much as 30 days. The question then arises: what should be the next step — the gradual extension of the duration of manned flight, building up little by little the possible cumulative effect of weightlessness and in this manner probing the limit of probable pathological conditions, or the application of experimentation with animals placed in orbit for avowedly protracted periods (more than a month) for the purpose of discovering the basic directivity and biological significance of the alterations occurring in the organism under these circumstances. It would appear that this second approach should precede the slower and certainly more cautious technique of experimentation through manned flight.

Let us turn now to our consideration of the proposed general model of the mechanism underlying the effect of weightlessness on the human organism (Figure 3).

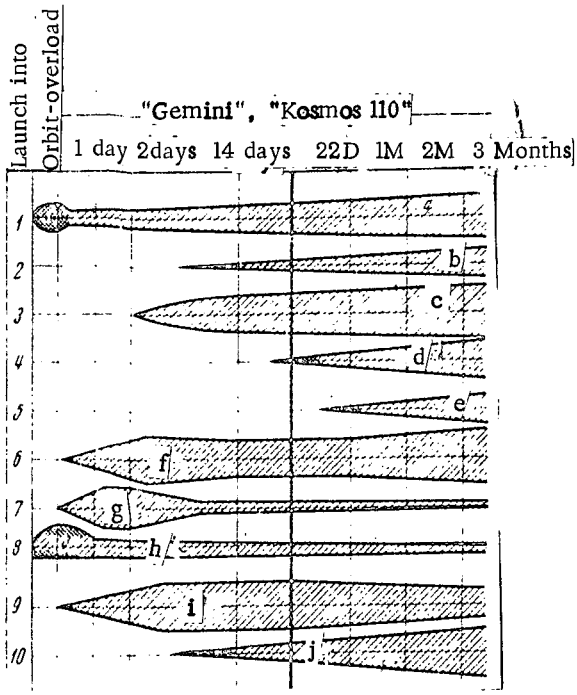


Figure 1. Presumptive Pattern of Disorders in Organic Functions with Protracted Exposure to Weightlessness (Further Development of the Scheme Proposed by L. E. Ditlein, 1964): a, cardiovascular system dysfunctions; b, muscle atrophy; c, water-salt exchange disorders, dehydration; d, calcium exchange dysfunction, bone demineralization; e, hemopoiesis disorder; f, digestive disorders; g, vestibular disorders (nausea, vertigo); h, basic exchange level; i, gas-energy exchange disorder; j, sleep and variation of diurnal regime; k, general asthenia caused by a complex of flight-related factors (weightlessness, hypokenesia, monotony of surroundings and habitational environment). D=days; M=months.

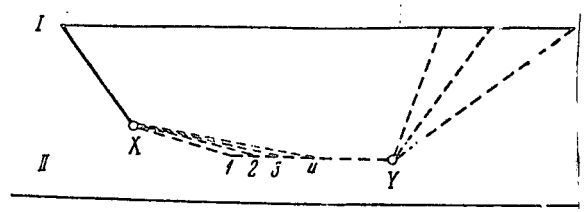


Figure 2. Variations in the Functional Levels of Certain Organic Systems in Extended Spaceflight (Hypothetical Model): functional level on Earth (I); in weightlessness (II).

This effect is primarily manifested /360 in the disruption of the analyzer interaction functions which are normal under terrestrial conditions, the limitation or distortion of afferent information, the disturbance of the established stereotype of spatial orientation, vegetative disorders (vertigo, nausea, illusions of inverted position, etc.).

It has been assumed that because of the weight loss the otoliths cease performing their function as stimuli of the peripheral nerve instruments of the vestibular apparatus, and since there exists between the otoliths and the cupuloendolymphatic system a functional relation expressed in the inhibition of the semicircular canals, the latter, once "freed" of the inhibiting effects of the otoliths, become more sensitive to adequate stimuli (Komendantov, Kopanev, 1962; Graybiel et al., 1964 a, b; Schock, 1961; Graybiel, 1968, and others). Another point of view has been put forward by Ye. M. Yuganov and his colleagues (1963), who hold

that weightlessness is not accompanied by any functional disengagement of the otolith apparatus, but that an unusual "minus-stimulus" originates for the otoliths.

A number of investigators (Margaria, Gualtierotti, 1962; Margaria, 1963; Gualtierotti, Margaria, 1963) assert that vestibular disorders in dynamic weightlessness depend not on any absence of sensorial organ stimulation, since spontaneous electrical activity by the labyrinth continues the while, while, on the other hand, cutting the vestibular nerve and destroying the vestibular apparatus and nerve centers does not produce the same symptoms that are observed in weightlessness. In fact, G. S. Titov experienced none of the serious muscular coordination disorders which are typical of persons with a disturbed labyrinth. During the first hours of their six-day flight on "Apollo 8" Borman, Lovell, and Anders suffered vestibular-vegetative reactions in the form of sensations of nausea, vomiting, and general discomfort (Berry, 1969).

It is worthwhile noting that (according to both US and Soviet sources) in certain individuals, during a protracted exposure to weightlessness, there occurs a gradual reduction in the vegetative disorders caused by vestibular disturbances. The subject becomes accustomed to the effect of weightlessness and experiences the reduction, and in some instances the complete disappearance, of vegetative disturbances (Ditlein, 1964). Thus, according to Berry (1966), one day into their mission Borman and Lovell no longer experienced the illusion of finding themselves in an inverted position.

The next fundamental factor in the effect of weightlessness is the disappearance of hydrostatic pressure by the liquids of the organism. This factor gives rise to distinct alterations, primarily in the cardiovascular system. Figure 4 indicates the nature of the changes, in these circumstances, of blood circulatory conditions within the organism. Under normal terrestrial conditions, in the lower half of the body in the blood channel in addition to the pressure created by the activity of the heart there is added the weight of the blood column, that is, the hydrostatic pressure. If with the average human height of 175 cm the distance from the heart to the foot is 130 cm, and from the heart to the brain 40 cm, then it can be easily shown by simple calculation that at

foot level the blood pressure will be approximately 100 mm Hg greater (spec. /362
weight of Hg is 13.6) and in the brain approximately 30 to 31 mm Hg less than at heart level. The elastic walls of the arterial channel of the legs create a corresponding counterpressure, and these walls are not particularly distended.

In the venous portion of the channel, where there is normally contained an almost four-times greater amount of blood, the situation develops in a somewhat more complicated fashion: in effect, the hydrostatic pressure of the column of venous blood is directed against the heart-bound stream. This latter circumstance must always be well compensated by the tone of the vein walls, the muscles compressing the veins, the presence of venous valves, the sucking action of the thorax, and the slight residual surge of the blood which has passed through the capillaries.

In the upper portion of the body, conversely, the limited value of the hydrostatic blood column creates a force promoting the return of the blood to the upper vein and toward the heart.

Imagine a situation in which terrestrial gravity has disappeared. As a model for a state of this kind we might consider the transition of a human being from a vertical to a horizontal position, which is known to very closely approximate the pattern of hemodynamic alterations associated with weightlessness and which has long been employed as a convenient device for studying this state under terrestrial conditions. In the horizontal attitude the hydrostatic pressure factor disappears almost entirely since all the important basic vessels are located along the body's vertical axis. The amount of blood in the legs under these conditions drops by almost 15%, the pressure on the vessels in the lower half of the body is reduced, while the blood supply to the brain increases by almost 20% (Ditlein, 1965). It is interesting to note that during the missions of Soviet cosmonauts on the "Soyuz 4, 5, 6, 7 and 8" spacecraft the crews experienced the sensation of a rushing of blood to the head similar to that experienced by a person assuming a head-down position (Vorob'yev and colleagues, 1969, 1970). There is an appreciable increase in the quantity of blood flowing toward the heart from the lower portion of the body since the hydrostatic pressure counteracting venous return now disappears.

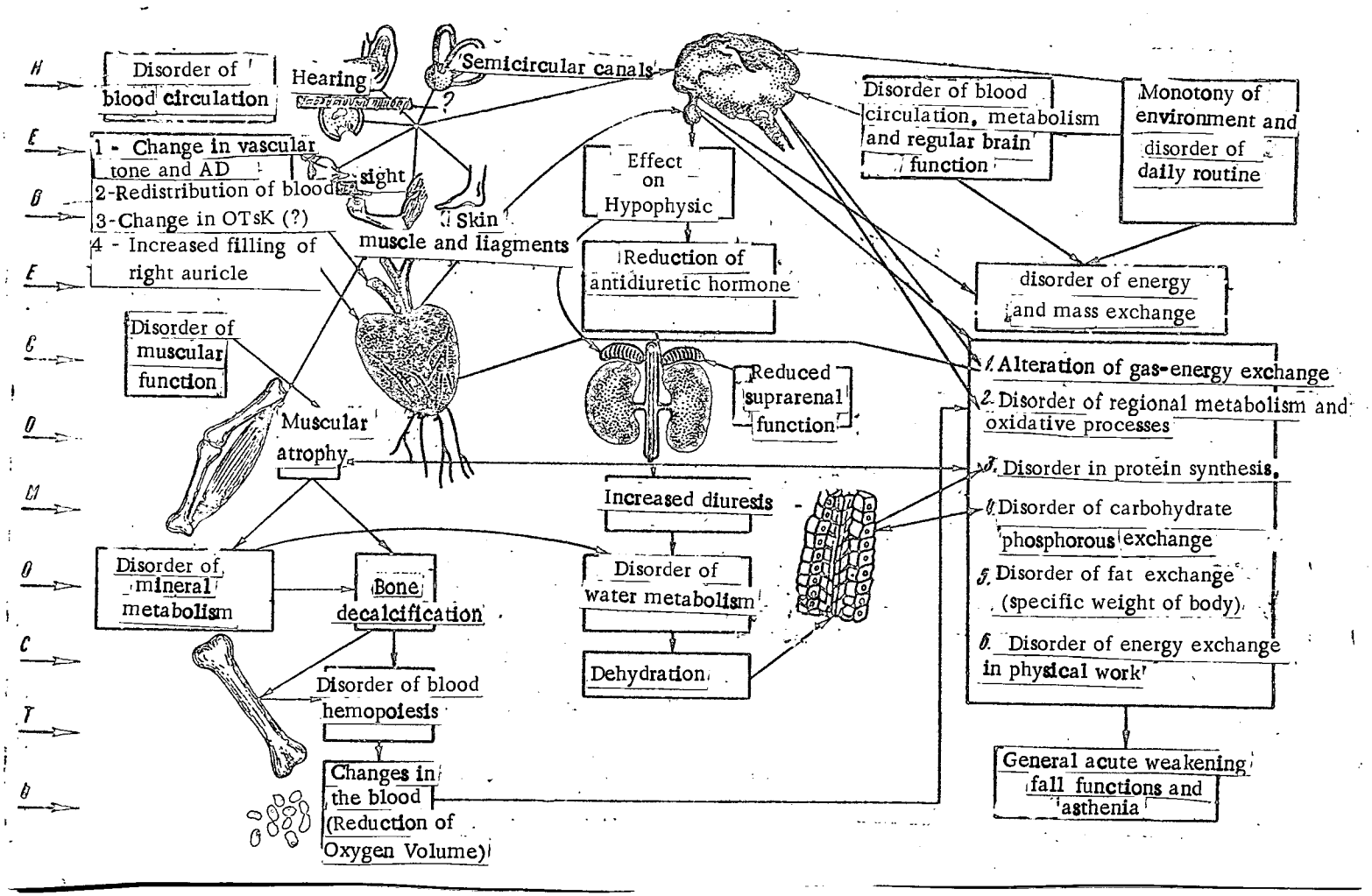


Figure 3. Model of the Mechanism of the Effect of Prolonged Weightlessness on the Human Organism.

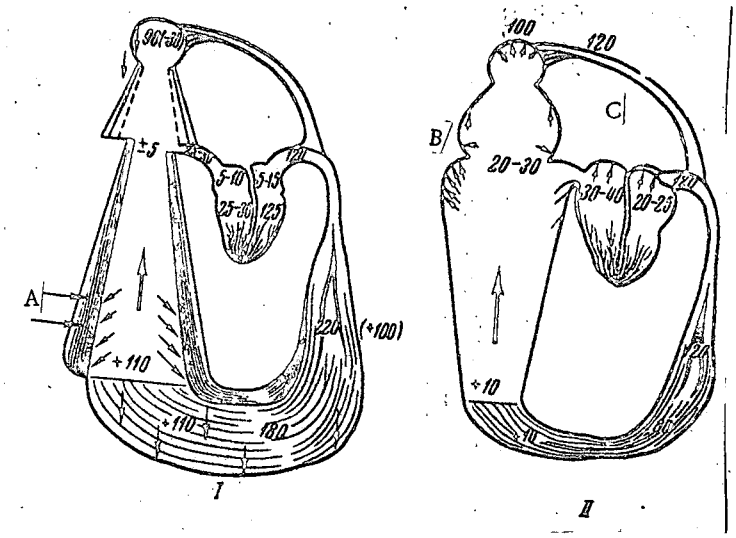


Figure 4. The Effect of Hydrostatic Pressure on Blood Circulation Under Conditions of Varied Gravitation: I, hydrostatic pressure; A, with orthostatic collapse; II, weightlessness; B, Bainbridge reflex; C, Henry-Hauer reflex.

According to Lamb (1964), /363 in the transition from a vertical to a horizontal position cardiac volume per minute increases from 4 to 5 and more liters. There is a substantial increase in the amount of blood present in the upper half of the body and in the venous return of blood to the heart. Lamb (1964) holds that in certain cases the blood flow in the legs in the lying position may decrease by almost 50%. Naturally, these conditions are accompanied by a severe drop in the permanently present load on the vascular channel of the legs and lower half of the body. If this state continued for an extended period of time, then, in the opinion of a number of authors, a large and extremely capacious segment of the vascular channel will lose its conditioning. As a rule, following reversion from weightlessness, even when the time spent in that state has been comparatively brief, or after an extended period in the horizontal position, orthostatic hypotension develops (Figure 5) as a consequence of the displacement of the blood to the lower half of the body and to the vascular channel which has now lost its normal conditioning and tone (Busby, 1968; Goldman, 1965; Cally D. Graveline, 1963). Once it has been disturbed, the fine regulatory alignment of the cardiovascular system is unable to immediately correct the regional blood flow. The result is cerebral anemia, loss of consciousness, and other manifestations typical of orthostatic collapse.

At the same time, it is also worthwhile noting the interesting observations of I. D. Pestov (1968), who, using a plethysmometry method, established that under the effect of a 70-day bed regime the vessels of the lower extremeties become relatively more rigid, with their extensibility and contractability

reduced, in what is regarded by the author as a biologically justified reaction of the organism aimed at enhancing its stability in the face of orthostatic influences. Consequently, the mechanism of the organism's reduced adaptability to the effect of heightened gravitation in the direction of the body's longitudinal axis following bed regime and spaceflight has not yet been completely explained and requires further study.

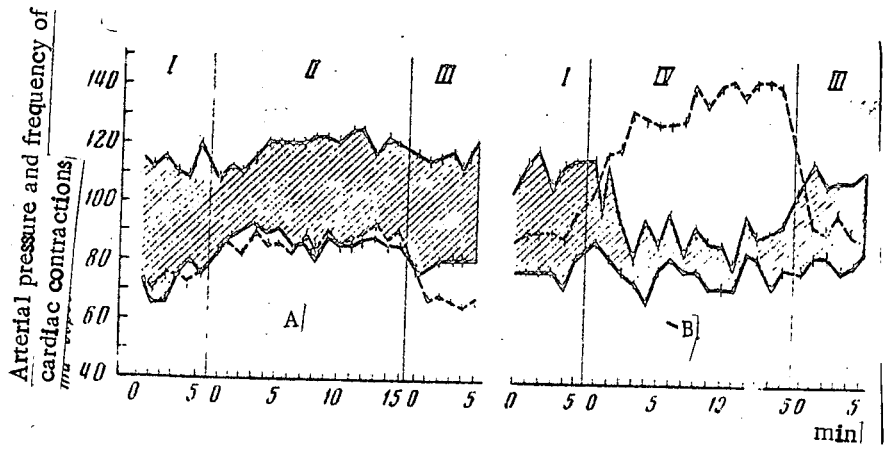


Figure 5. Reaction of Arterial Pressure and Frequency Variation of Cardiac Contractions to Orthostatic Load (70° — 15 min). For Astronaut McDivitt before and after 2 hours of orbital flight. The broken line indicates the frequency of cardiac contractions; the shaded zone indicates the pulse pressure. I, prior to orthostasis; II, during orthostasis; III, after orthostasis (after Ch. A. Berry; 1966); A, before space flight (11/4/1965); B, after space flight (12/18/1965).

The redistribution of the blood which occurs in weightlessness, along with the intensified blood supply to the venae cavae, the right atrium, the vessels of the small circle, and the left atrium, may seriously disrupt the normally well-balanced interaction of cardiac and vascular reflexes. Specifically, with /364 the venae cavae overfilled, a serious increase in the significance of the Báinbridge reflex component may occur in the general alliance of afferent influences from the vascular channel. Not excluded is the possibility of an alteration in the classic reflex from the sinocarotid zones by virtue of the unusual and protracted effect of the blood redistribution in the upper half of the body on the baroreceptors of this zone.

At the same time it is perfectly obvious that in the weightlessness state there may arise a stimulation of the volumoreceptors, leading to an increase in diuresis. Regrettably, there is thus far a lack of experimental data regarding the precise location of these formations in the organism. The supposition has been advanced that they are located in the wall of the veins, the arteries, within the brain, that is, in the upper portions of the body (Ginetsinskiy, 1963).

The excess blood supply to the atria, the inhibited production of the antidiuretic hormone (Henry-Hauer reflex), increased urination — all this may lead to a disruption of the water exchange and to dehydration of the organism. This latter fact was revealed in experiments on the "Gemini 7" spacecraft and was established in a particularly explicit fashion with dogs following the "Kosmos 110" flight (Gurovskiy and associates, 1968). Dehydration results in an increase in the hematocrit. In the case of astronaut W. Shirra, after 9 hours of weightlessness, the hematocrit increased from 44 to 47%, and in the case of G. Cooper, after 34 hours of weightlessness, from 43 to 49%.

Under the conditions of weightlessness and hypodynamia a reduction in the mass of circulating blood is observed. This was clearly indicated in simulation tests conducted with 12 subjects confined to a strict bed regime for a period of one month. After two or three days in the prone position the total volume of circulating blood decreased from 2,000 to 1,300 ml (by an average of 750 ml); the average reduction in plasma volume was 550 ml, and in erythrocytic mass, 180 ml (Giovanni, Birkhead, 1964). We have observed similar results with test subjects in complex investigations involving a bed regime of 70 to 100 days (Pekshev, 1969).

As is evident from the foregoing, the mechanism of the disturbances caused by the effect of weightlessness — or by conditions approximating it — involves a vicious circle. Disturbances in the redistribution of the blood lead to a reflex dehydration of the organism, and this in turn reduces the volume of circulating blood, resulting in an even further aggravation of the hemodynamic disturbance. With the release of considerable quantities of liquid and the disruption of the electrolytic balance, there is added to the chain of arising

disorders a lowering of aldosterone production. It has been already established that aldosterone effects the ability of sodium and potassium to pass through the cellular membranes. It converts the sodium and potassium ions, more accurately, their hydrated form, to a fat-solvent compound, and it is only after this that the sodium ions are able to penetrate the membrane.

Given a controlled intake of food and water, aldosterone secretion decreases in a human being in the prone position, and increases in the standing position (Liddle, 1966; Vagnucci, 1966). Protracted bed confinement leads to a reduction in the volume of extracellular fluid (Stevens et al., 1966). Immersion in water also results in a loss of Na^+ and water (Ditlein, 1966). This phenomenon is analogous to that of the loss of Na^+ and water by astronauts in the weightless state.

The prone position, it will be recalled, is accompanied by a redistribution of the blood in the form of its increase in the intrathoracic sections, leading to a stimulation of the volume receptors of the cardiovascular system (Henry--Hauer reflex and others). It is altogether reasonable to suppose that as a result there occurs a reflex inhibition of vasopressin secretion. However, with diuresis caused by extension of the left atrium no blockage of vasopressin secretion takes place (Ledsome et al., 1961).

Nevertheless, there is some basis for the assumption that, in the weightless state, diuresis and sodium diuresis are the consequence of the effect of vasopressin, with the endogen mineral-corticoid level absent or lowered. Clearly, still other factors are also involved in the regulation of diuresis. The effect of aldosterone secretion on the Na^+ loss and orthostasis is influenced /365
by the renin-angiotensive system (Carno et al., 1966). Antidiuresis in the standing position has been compared (Status van Eps et al., 1962) with the antidiuretic effect of angiotensin in the case of human water diuresis. For these reasons, further study is required into the interaction of vasopressin, the adrenocortical hormones, and angiotensin. Another point to be kept in mind is the fact that the vasopressin secretion level is controlled by the hypothalamus.

Such are a few of the intimate, deep-seated processes in this important link in the regulation of the water-salt balance. How this system will behave under conditions of prolonged weightlessness is not yet clear.

There is still one further noteworthy circumstance, to which normally the investigators of this problem pay very little attention. As we know, hydrostatic pressure assists in the filtration of liquid from the vessels into the tissue. With the hydrostatic factor eliminated in the weightless environment, the oncotic pressure of the blood will to a greater degree retain the liquid in the blood channel. Initially this results in hydremia of the blood, but subsequently, mechanisms may be triggered which operate to counter an excessive liquifaction of the blood and, again, should these originally defensive mechanisms be overemployed, the result may be the reinitiation of a new cycle of hyperadaptational disorder.

With 16 test subjects exposed to a 6-hour simulation of weightlessness by prolonged immersion in warm (33°) water, there was a four-fold increase in diuresis. In the view of Goodall (Goodall et al., 1964) this fact constitutes a convincing proof of the acute intensification of organic dehydration when the hydrostatic pressure is cancelled by the counterpressure of the water against the body.

We have thus considered merely a few of the possible complex interactions of various links of the pathogenesis which may be associated with the conditions described.

The next important pathogenetic link in weightlessness is an acute reduction in muscle function, motor activity, and the decreased expenditure of energy occasioned by the absence of weight.

It is quite clear that in the weightless state there is a considerable lessening of the load on the support-motor apparatus. Under the conditions of weightlessness that entire mass of muscles which was formerly engaged in countering the force of terrestrial gravitation is quiescent. Ye. M. Yuganov and his associates (1963) have shown that weightlessness is accompanied by a sharp reduction in the oscillation voltage and even a pattern of "bioelectrical silence on the part of the antigravitational musculature". It must be recalled

that this reduction of muscular activity may be intensified by the astronaut's spacesuit as well as by the spatial limitations within the spacecraft cabin. All this leads to acute hypokinesia. Under normal conditions, resistance to the force of gravity creates a tonic stress in the muscles of the lower extremeties and the tonic extensor apparatus of the trunk and neck.

The problem of the unfavorable effect on the human organism of a sharply curtailed muscular function has been rather extensively discussed in the literature. After four healthy men had spent six weeks in plaster casts, Deitrick and his associates (Deitrick et al., 1948) observed muscular atrophy and a disruption of nitrogen metabolism. These cases are usually accompanied by a reduction in the transverse dimension of the heart. Reduction of muscle tone results in venous congestion and in an even further aggravation of the hemohynamic disorder. In a weightlessness simulation by prolonged presence in a horizontal position (Birkhead et al., 1964; Mueller, 1963), an excess release of nitrogen was discovered in the urine, attesting to a loss of albumin with normal consumption. A human being who has for a long time been deprived of support may experience a breakdown in his most essential locomotive functions, central to which is the combined effect of a number of static reactions, tonic support phenomena, and static adaptation reflexes (Gurfinkel' and associates, 1969; Skrypnik, 1969 et al.). The nature of the variation of the biomechanics of movements in a ship and in unsupported space, when the inertia of the mass remains but there is no weight, is part of a problem area still awaiting solution.

An appreciable reduction in ability to work was observed in US astronauts /366
following the 14-day "Gemini 7" mission and the 11- and 6-day flights of "Apollo 7 and 8" (Berry, 1969).

The reduction of muscular activity and gravitational load on the osseous apparatus causes serious alterations in the bone metabolism. There is a breakdown in the albuminous bone marrow, a reduction in the osteoclast function, a washing away of calcium, and apparently, a progressive destructive process in the bones. Just how far this process will advance is not known.

An increase in calcium in the urine was detected in the case of Borman and Lovell following their 14-day flight and also in the crews of "Apollo 7 and Apollo 8". Densitometric tests revealed a loss of bone mass in the heel bone and final phalanx of the fifth finger of the right hand due to a separation of calcium (Berry, 1966, 1969). Similar findings were recorded with animals following a 22-day flight on "Kosmos 110" and also in tests involving 70- and 100-day hypodynamia with humans (Krasnykh, 1969).

Prolonged curtailment of muscular acitivity also leads to a reduction of adrenaline and especially noradrenaline production. Moreover, it should be remembered that the pressor activity of the katecholamines as depolarizing substances suffers when the electrolytic ratio becomes unbalanced, as may occur in flight. All this may result in a reduction of pressor reactions. It is essential to note that the ingestion during this period of certain pharmacological stimulators which normally increase arterial pressure and raise the impact and per-minute volume of the heart either has no effect or results in a distorted reaction (Figure 6) (Vasil'yev, Lapinskaya, 1969). Thus, there originates one more vicious circle which eventuates in a prolonged loss of vascular tone and hemodynamic disruption.

Perhaps one of the most vital and as yet least studies questions is that /367
concerning the alteration of gas-energy metabolism under the conditions of weightlessness. This problem involves, as it were, the two fundamental contradictions which may arise whenever there is a prolonged absence of terrestrial gravitation.

As we have already noted above, during the long evolution following the emergence of living creatures from the world ocean to the dry land and with the steadily increasing significance of the factor of the Earth's gravitational pull, the entire energetics of life underwent a radical change. This restructuring of the energy basis in living matter was guided by the need to satisfy the more demanding energy requirements of the organism. There ensued the development of effective oxygen-supply systems in the form of the evolution of the lungs, the appearance of the bone marrow, a more advanced system of blood circulation, and a sharp increase in the capillarization of the tissues. These

requirements for increased energy consumption rose in a particularly marked fashion with the performance of various kinds of physical labor.

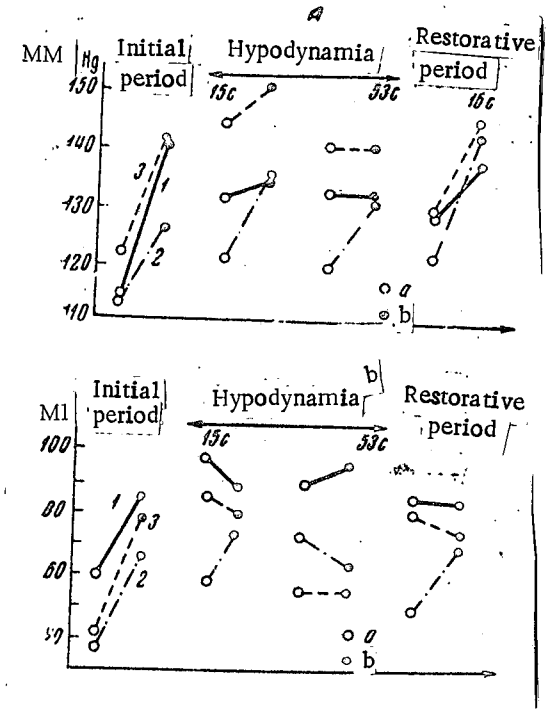


Figure 6. Effect of a Pharmacological Complex (Caffeine + Securinine + Phenamine) on Maximum Blood Pressure (A) and Cardiac Impact Volume (B) during Hypodynamia in Test Subjects B-go (1), B-you (2) and G-go (3); a - before taking; b - one hour after taking the preparation.

Under the conditions of weightlessness certain kinds of work, primarily those associated on the Earth with the overcoming of the forces of gravity, will be accompanied by reduced energy expenditure and lowered oxygen consumption. This applies specifically to working operations aimed at support of the body, the movement of the arms and legs, in some measure to the work of the heart, the movement of the thorax and diaphragm, etc. Consequently, we are confronted by new requirements for energy expenditure, with the production of energy in the organism and the systems which provide for its creation now aligned to a higher level. In this context, a reappraisal of the caloric value of the existing ration is indicated.

Stated differently, in the weightless environment we are faced with a new organic energy structure, whose precise definition will certainly constitute a major task in the research effort that lies ahead.

During the first stages of prolonged weightlessness the general detoning and weakening of a number of systems may be compensated by the reduced expenditure of energy. However, this in turn leads to a subsequent reduction in the functions of the organism and a further mutual weakening of both processes. Again, there may arise a kind of vicious circle unless certain measures are taken to break it by different techniques and means.

The purely theoretical assertions which have been advanced regarding the gas-energy exchange still lack supportive factual verification.

Studies of human energy consumption in a training device designed to simulate a gravity value of 1/4, 1/6 and 1/8 that of the Earth's gravitational pull, and involving pacing on a treadmill, in outer garments, at a speed of 6.4 km/hour revealed a reduction of energy expenditures of 48, 56, and 60%, respectively, from the initial value under normal terrestrial gravitation. In a paper by A. V. Yeremin and his associates (1970), who conducted low-weight testing (1/6 the weight of the body), energy consumption in walking at a speed of 4 to 4.5 km/hour were found to be 24% lower and in running (9 to 9.5 km/hour) — — 28% lower. It is evident that these changes are very significant, and as the force of gravity decreases the energy consumption falls. Obviously, even on the moon, where the force of gravity is still 1/6 that of the Earth, there may be a considerable reduction in energy consumption.

These data are in agreement with the opinion of Margaria and Covagna (1964), who also believe that metabolism must experience a reduction under conditions of reduced gravity.

The first data on the gaseous exchange under the conditions of actual spaceflight were obtained for P. I. Belyayev and A. A. Leonov (Kas'yan, Kopanev, 1967). It was found that A. A. Leonov's consumption increased by 206 ml/min, which is altogether understandable in view of the great emotional strain and the fact that he performed a number of work-related operations involving extravehicular activity. Belyayev's oxygen consumption declined by 72 ml/min in /368
comparison with initial data covering a period of many years. This latter fact substantiates previously expressed suppositions. Unfortunately, these unique data are still extremely scant, and final conclusions will require the findings of further observations involving the use of more sophisticated equipment.

We understand, of course, that the considerations we have expressed in this paper regarding the pathogenesis of the "weightlessness syndrome" will necessarily require refinement and correction as new facts are accumulated. We have also, in this article, not discussed in sufficient depth the role of the nervous

and endocrine systems as they relate to this problem. Our principal attention Has been directed to the primary, "trigger" mechanisms, with little effort made at tracking the further links in the genesis of the general weakening and alteration of the organism's reactive capacity, where, undoubtedly, paramount importance attacheds to the coordinating and integrating role of the nervous and endocrine systems. However, the analysis of these problems requires the implementation of a more broadly based experimental research program, both on the laboratory level and during actual space testing.

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