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Chapter 8

WEIGHTLESSNESS[1]

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The development of astronautics poses many new problems both scientific and practical to physiology and medicine, which are due mainly to astronauts having to live in space under specific conditions of weightlessness.

The well-known gravitational, inertial, and external forces which determine kinetic and dynamic conditions producing weight, subgravity (or reduced weight), and weightlessness [109, 225] will be defined only briefly in this context. The weight of a body is determined by a given mass subjected to a given force and on the dynamic conditions of the body. The acceleration which acts on a body is conveniently expressed as a multiple of the standard acceleration of terrestrial gravity (g_0), and the force acting on a body as a multiple of the body's standard weight. This is equivalent to establishing a system of units in which the unit of acceleration equals 1 g and the unit of force equals 1 G. Weight in this denotation means that a given mass is subject to a given gravitational force. Since the actual force on a body (due to acceleration) equals the weight of the body, the symbol G is used in bioastronautics to indicate force and weight. The unit of acceleration in this system is always a true constant, i.e., 9.81 m/s^2, whereas the unit of force differs for bodies of different mass [109].

In all freely moving bodies, the force of inertia compensates the gravitational force at any point of their trajectory, thereby creating the so-called "gravity-free" state. However, this is not an accurate designation, since the body is always under the influence of gravitation, whether from the Earth or another celestial body. This state has therefore been described as "appressionless" or as the "zero-G" or "null-G" condition, since the resultant force exerted on the body due to gravity and inertia actually is zero [92].

Weightlessness, on the other hand, has been widely used to describe an individual's subjective experience in the unappressed or zero-G state. Other states of reduced appression, such as water immersion, suspension, or conditions of reduced friction, simulate the weightless state more or less accurately. In order to simulate the weightless condition and its effects on the human

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body, these techniques and bed rest have been used in experiments. The effects are based on associated hypokinesis and hypodynamia, but by definition they are not identical to those of weightlessness. At zero-G, the body is completely unsupported, weightless, and floats freely in space. Because of the physical characteristics of the zero-G state, its biological effects should be the same whether they occur inside or outside the Earth's gravitational field. However, it has been hypothesized that the inhomogeneity of the field forces may give rise to intermolecular forces within a body, which may produce different effects depending on the distance from its primary. While the investigation of this subject may be of scientific interest on the various levels of biological interactions, exploration of the health aspects of weightlessness is of paramount importance for future space flights and lunar and planetary excursions.

FIGURE 1.—Astronaut Edward H. White, II, floating freely in space during Gemini 4 extravehicular activity.

WEIGHTLESSNESS AS A UNIQUE AND EXTREME SPACEFLIGHT FACTOR

Significance of Gravitational Forces in Regulating Homeostasis

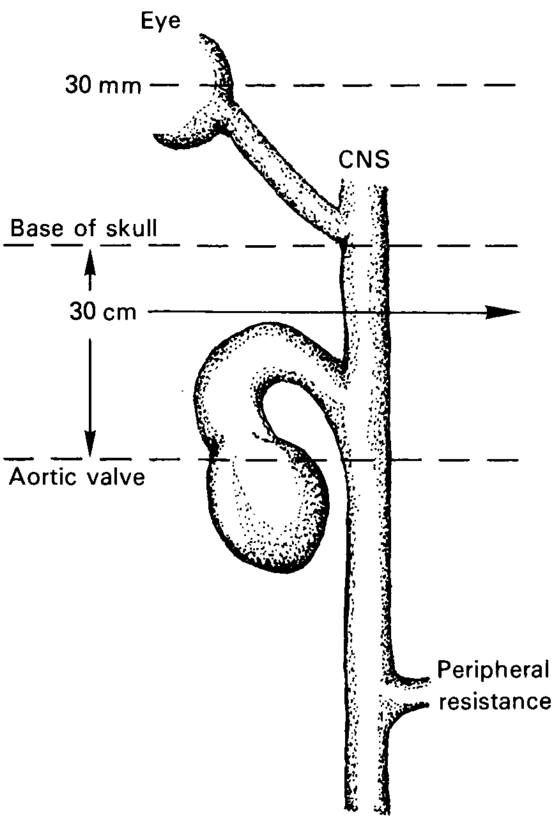
Life has evolved within the virtually constant gravitational field at the surface of the Earth, it is generally assumed. The bodies of all vertebrates, including man, consist mainly of cells, extracellular fluid, and rigid substances. The evolution of this entity as a fluid-bone-body continuum depended greatly on the development of physiological homeostasis, a constant first-order body system composed of blood and extracellular fluid, and a supporting second-order musculoskeletal system to cope with the gravitational effects of the environment. The musculoskeletal system is also the storage system for mineral ions in the bones [239].

The evolutionary process of life may have traversed the three stages of matter, starting in the liquid medium and spreading into the atmosphere and on the solid ground. Life in the liquid state and that immersed in water regulated by weight effects differ from those on land. However, many species of animals are well-equipped physiologically to adjust to land, sea, and air. Since muscle tissue is approximately the same in all animals, the total force produced by a muscle is *proportional to the square of the* muscle size. By and large, the total work performed by a contracting muscle is proportional to the cube of the size of the animal and approximately to that of its weight. The physical and gravitational weight-force relationship appears to hold for all organisms, even for living cells as small as 10 μm diam. [206].

Adaptability to gravitational changes of support was as important to survival of the species during the evolutionary process as homeostatic ability [76]. In mammals that have returned to an aquatic medium, the relative weight of the skeleton (in percent body weight) is less than that of terrestrial mammals, which is probably related to the lower weightload on the supporting structures in water immersion. Similar conditions have been observed in these animals in relative weight of bone marrow, which is important in hemoglobin synthesis [147].

Certain basic life processes apparently depend on the presence of gravity; included are growth and transport functions in certain types of cells, fluid exchanges in tissues and vessels, free convection of gases, and sedimentation processes of solids which affect cell metabolism. For example, geotropism demonstrates such gravity-dependency. On the other hand, many types of cells have active water and ion transport mechanisms, and some vertebrates remain relatively unaffected by changes in gravity. In man, for example, the carotid sinus reflex is one of many neural mechanisms equalizing differences in blood pressure due to hydrostatic changes; some blood pressure differences due to gravity changes are shown in Figure 2 [6].

The gravitational or weight effects on the body are removed in the weightless condition. Since the human body is semirigid, consisting of materials of different densities, external forces tend to change its form unless counteracted by other forces. Stresses involved in this process vary from point to point within the body and can produce functional changes. By and large, the living organism is capable of functioning properly under certain amounts of physical load; the mechanical stress of terrestrial gravitation is accepted as the normal physical and psychophysiologic zero state of the human body. Only if acceleration or gravitational stress exceeds the usual value does it become noticeable and, if exceeded, to an intolerable amount, can it cause permanent damage. The lungs are particularly sensitive to acceleration due to great differences in specific gravity between blood and gases on opposite sides of the thin, fragile alveolar membrane. In humans and animals, pulmonary function, circulation, and integrity of the lungs



	Earth	Mars	Moon	Weightlessness
	1 g	0.38 g	0.17 g	0 g
30 mm	66/26	81/41	86/46	90/50
Base of skull	96/56	111/71	116/76	120/80
30 cm	24 mm Hg	9 mm	4 mm	0 mm
Aortic valve	120/80	120/80	120/80	120/80

FIGURE 2.—Levels of systolic and diastolic blood pressure in man and their alteration under various subgravity conditions [6].

are very susceptible to changes in the direction and magnitude of the force environment [269].

Animals show chronic responses in an acceleration environment higher than 1 G for longer periods. Anatomical effects were observed as well as functional effects, the latter subsiding after return to normal gravity [124]. Both increased and decreased weight produced stress conditions resulting in reduced lymphocyte counts, increase of muscle and bone mass under increased weight and loss under decreased weight, and development of severe disorientation symptoms. Generally, tolerance to altered weight was a function of body mass [36].

In considering neuromuscular and sensory effects of moderate gravitational changes, functions of the central nervous system (CNS) seem quite adaptable. Neuromuscular responses normally depend on the body's position relative to the force of gravity. Ontogenetically, animals and man acquire and maintain posture and body orientation by means of kinesthetic, visual, vestibular, and statokinetic stimuli, interpreting and reacting to such signals by developing an appropriate gravity-dependent sensorimotor program. The proprioceptive system includes mechanoreceptors within the body which are normally tuned and calibrated to the terrestrial weight-force relationship, and gravity/acceleration sensitive vestibular organs, specifically the otoconia. These organs are important in the control of the sensorimotor activity and under certain conditions, modulate or override the input of other sense organs including that of the eye. However, if vestibular information is excluded, a stable visual reference can be established independently of gravitational input. The process appears to be conditioning through learning, experience, and conscious control. Since the individual becomes adapted to a wider range of perceptions with each increment of new experience, realistic exposure to changing gravitational conditions is useful in preparing the astronauts for missions in space and on the Moon [162].

The force of gravity has a significant effect on the regulation of homeostasis, and there is good reason to expect a number of functional and morphological changes under conditions of weightlessness. Although most life forms have adjusted well to the various Earth environmental conditions, prolonged effects of zero-gravity have not been encountered in the stages of evolution. Therefore, specific mechanisms have not developed for compensating the effects of lack of gravity or weight; general susceptibility to their effects is manifested in disuse or atrophy. This kind of "adaptation" is associated with a narrowing of the functional capacity of the organism and loss of resistance to gravitational and other external stimuli. If it is assumed that, theoretically, mankind is capable not only of adapting but also of adjusting to weightlessness on a homeostasis basis, he would be able to survive on other planets and in zero gravity without extinction. This would lead eventually to genetic specification and include such fundamentals as new characteristics of the musculoskeletal, cardiovascular, endocrine, and central nervous systems. Implications of these possibilities will be discussed in subsequent sections of this chapter.

Investigation of Effects of Weightlessness on the Human Organism

Subgravity and weightlessness, the major novelties in the space environment, have been the subjects of many speculative and empirical studies. Tsiolkovskiy, in 1895, described the peculiar condition that would be encountered by man in space:

> We shall not have weight, only mass. We can hold any mass in our hands without experiencing the slightest weight. . . . Man does not press himself against anything and nothing presses against him. . . . There is not top or bottom.

Tsiolkovskiy predicted changes or loss of spatial orientation and motor and sensory functions in space, differences in blood distribution, and anatomical changes in the human body. Although he assumed that man would eventually adapt to weightlessness, he suggested rotation of spaceships to artificially produce gravity [236].

Later, Oberth discussed the effects of zero-G on man during interplanetary flights.

> If the prolonged state of lack of appression should have undesirable consequences, which seems doubtful, however, two such vehicles could be connected by cables a few kilometers long and rotated about each other [186].

He recognized the possible adverse effect of Coriolis forces produced by artificial gravity in rotating spacecraft. The first experimental studies of the effects of weightlessness on the mammalian organism were made with rocket flights concomitantly in the US and the USSR after World War II. Scientists in both countries monitored the major physiologic and behavioral functions in small animals; in particular, heart and respiration rates, blood pressure, body temperature, sensory and motor activities, reflex and CNS behavior, and related functions during changing accelerations and short periods of weightlessness. While some animals were lost due to equipment failure, results obtained from recovered animals indicated that stresses associated with rocket flight, including episodes of weightlessness, were within range of biological tolerance in the mammalian organism [38, 113, 118, 241]. This conclusion was later confirmed by more extensive experiments and studies conducted in orbiting spacecraft [1, 47, 78, 99, 192, 276].

Brief periods of weightlessness were also produced in aircraft flights along a Keplerian trajectory [110]; these parabolic flights were conducted primarily to study perceptual, motor, CNS, autonomic-vegetative and related reactions in higher animals and man. Exposures from a few seconds to about 1 min did not produce deleterious effects on functions and performance when common-sense preventive measures were taken, and it was apparent that man could be safely exposed to periods of weightlessness produced in spacecraft available at that time [6, 11, 43, 94, 140, 159].

Suborbital and orbital flights of astronauts opened a new chapter of bioastronautical research. With successive increase in flight duration from several minutes to several weeks, extended biomedical experiments were conducted in space and on the ground [21, 104, 107, 219, 260]. This included pre- and postflight tests, examination of astronauts, in-flight monitoring, measuring and telemetering of physiologic and psychologic functions, and evaluation of various parameters in the spacecraft and on the ground. Astronauts, cosmonauts, and physicians participated in these studies as test subjects and experimenters [24, 70, 133, 190, 217, 218, 256].

Factors that characterize the health and working capacity of astronauts under prolonged influence of weightlessness were of the greatest interest, which included:

- state of the important vital functions, susceptibility to illness, resistance to stress effects during and after flight;
- simple and complex motor reactions, coordination of movement, possibility of carrying out work operations (including those in emergency situations), ability to perform scientific observations and evaluate their results in flight; and
- adaptability of spacecraft for man's life, work, and rest in the state of weightlessness.

Information from these studies was used to improve selection and training of astronauts and the design of spacecraft and their subsystems, also to develop means of preventing unfavorable effects on the human organism from prolonged weightlessness.

Since there is true weightlessness only in flight conditions involving many operational problems which are not readily available for systematic studies, various simulation techniques have been developed. These techniques include body immersion in water, partial body-support systems, air bearings and other friction-reducing devices, bed rest, devices to reduce pressure in the lower body parts, and various sensory deprivations [5, 35, 64, 83, 91, 97, 199, 264, 270, 275].

Experiments were conducted with complete water immersion up to 7 d, and 120 d bed rest, to determine the effects of simulated weightlessness on the body's weight-bearing structure, internal intravascular hydrostatic pressure, metabolism, fluid and water balance, mineral exchange, cardiovascular and respiratory functions, and related parameters [25, 40, 86, 101, 175, 195, 203, 235, 254]. Body position and restraints, work space and equipment handling, and other performance variables were also studied in the submerged state. The purpose of these studies was to determine the effects of simulated weightlessness and establish principles, methods, and means to remedy their long-term implications. The efficacy of various preventive actions such as astronaut selection, conditioning, and training, in-flight exercise, dietary programs, and use of drugs was empirically determined. Other experiments concerned the effects of hypokinesia on cellular level, muscle tissue and bone structure, metabolic processes, fluid and water balance, resistance to infectious or degenerative diseases, and other stress-producing factors [49, 74, 137, 138, 151, 157, 166, 202, 207, 214, 234, 238, 271, 282].

In conjunction with accumulation of experimental data directly related to protection of man in space, a number of more general scientific problems were investigated.

> Theories on biodynamic and biogravic effects of changing accelerations and systematic treatises of biological problems in space, including comparative and methodologic aspects of space physiology and medicine as related to weightlessness [76, 90, 191, 193, 244];
> Processes and mechanisms of deconditioning, adaptation, homeostasis and biological rhythms in zero-G [3, 12, 37, 55, 72, 111];
> Specific effects and interaction of various sensory and neural analyzers or systems [22, 140, 143, 257, 278]; and
> Hormonal, immunologic, regenerative and hematogenic functions [2, 3, 7, 20, 222];
> Mathematical modeling and statistical treatment of medical and human factor problems associated with subgravity and weightlessness [132, 153, 190, 249, 262].

With careful selection and application of results from the theoretical and empirical approaches, major biomedical problems during early phases of space flight were solved. The wealth of information from this effort is being applied not only to the man in space, but also for worldwide benefit of mankind.

State of Reduced Weight (Subgravity)

Locomotion and work on lunar or planetary surfaces follow principles of mechanics quite different from those on Earth. While the magnitude of terrestrial gravitation (g_0) is constant and defined as 1, and acceleration smaller than g_0 produces a state of subgravity, on the Moon it is about $\frac{1}{6}$ this value. Accordingly, weight is reduced on the surface of the Moon.

In order to prepare astronauts for the lunar environment, numerous theoretical studies and simulation experiments were conducted. The critical parameters studied included oxygen consumption and carbon dioxide balance, food and water metabolism, work capacity, limb movement and locomotion, and muscular and sensorimotor performance under lunar gravity conditions. Nonlocomotor tasks were performed with and without inflation of space suits. In a simulation experiment where the subject had only one hand available for steady support, reciprocating tasks required about 20% more oxygen than under 1-G conditions [159a, 208, 211]. Suit inflation added considerably to the energy requirements for specific tasks. The energetics of locomotion in $\frac{1}{6}$ G is a complex problem still under investigation [215]. Factors such as gait, traction, and limb velocity were simulated with apparently sufficient fidelity in experiments on Earth [232].

One simulation technique used reduced traction. As the level of simulated gravity was decreased, less energy was expended. Figure 3 shows the relationship between energy consumption and gravitational forces and the rate of movement both in a space suit and in ordinary clothing [31].

Studies at NASA Langley Research Center, Hampton, Va., carried out on a simulator equipped with an inclined plane, showed that a reduction in the force of adhesion resulted in humans' walking and running being slowed approximately 40% compared with the activities under terrestrial conditions [115]. As the rate of movement increased, the inclination of the trunk

TABLE 1.—*Influence of Pressure in a Space Suit Under Reduced Weight on Various Forms of Motor Activity in Man* (According to Hewes [115])

Energy expenditure in locomotion in a space suit without pressure, kcal/h

a.

		1/6 G	1 G	Ref. source [115]
Speed	3.2 km/h	142	205	[270]
	6.4 km/h	187	430	[270]
	6.4 km/h on surface sloping at 10° angle	329	709	[137]

b.

Gravity	Pressure in space suit, mm Hg	Maximum speed of forward movement, m/s	Maximum height of jumping in air, cm	Long-distance jump on horiz., cm
1 G	0	3.44	52.0	164.0
	180	2.8	30.5	100.0
1/6 G	0	1.64	234.0	366.0
	180	1.22	140.0	214.0

forward increased to a greater degree under lunar gravitation [31, 115] than under terrestrial conditions (Fig. 4).

In general, subjects reported that sensation and effort in the lunar simulator were similar to those in short-term parabolic flights at equivalent levels of subgravity. It was concluded that an astronaut wearing a pressurized suit should, with practice, be able to walk, run, and work on the lunar surface, if the terrain is relatively firm and smooth. The explorer would probably be able to carry backpack loads up to about 225 kg while at rest and in motion, provided that bulk and constraint of the pressure suit impose no severe penalties [31, 118].

Lunar Surface Activities

The effects of actual lunar gravity on man were evaluated for the Apollo 14 and 15 flights [14, 15]. Metabolic rates during lunar surface activities were determined by a number of methods, the best of which proved to be monitoring the inlet and outlet temperatures of the liquid-cooling undergarment. The average hourly lunar-surface energy production ranged between 900 and 1200 Btus.[2]

During the Apollo 14 mission, two crewmen, the commander (CDR), and the lunar module pilot (LMP) spent about 34 h on the Moon, which included about 9 h moderate to strenuous physical work, while the command module pilot (CMP) stayed in orbit. Their energy expenditure averaged 220–300 kcal/h, about the same as walking without any equipment under terrestrial conditions. A comparison of postflight medical data showed that the CMP, who did not experience $\frac{1}{6}$ G, was physically less fit than the other two crewmembers (Table 2, [15]). His weight loss was considerable, orthostatic tolerance more reduced, red cell mass decrease more pronounced, work capacity lower, and he showed greater loss in all body fluid volumes. However, the results in Table 2 must be interpreted with great caution. Such variables as increased fluid intake for the CDR and LMP during the return voyage and lunar exercise loads must be taken into account. Even with these reservations, the Apollo 14 results indicate that moderate work under partial gravity conditions may have a positive therapeutic effect.

The workloads imposed on Apollo crews were carefully calculated preflight; especially careful prelaunch estimates were made for lunar surface activities. In general, these correlated well

[2] To convert to joules, 1 Btu = 1054.8 J (absolute).

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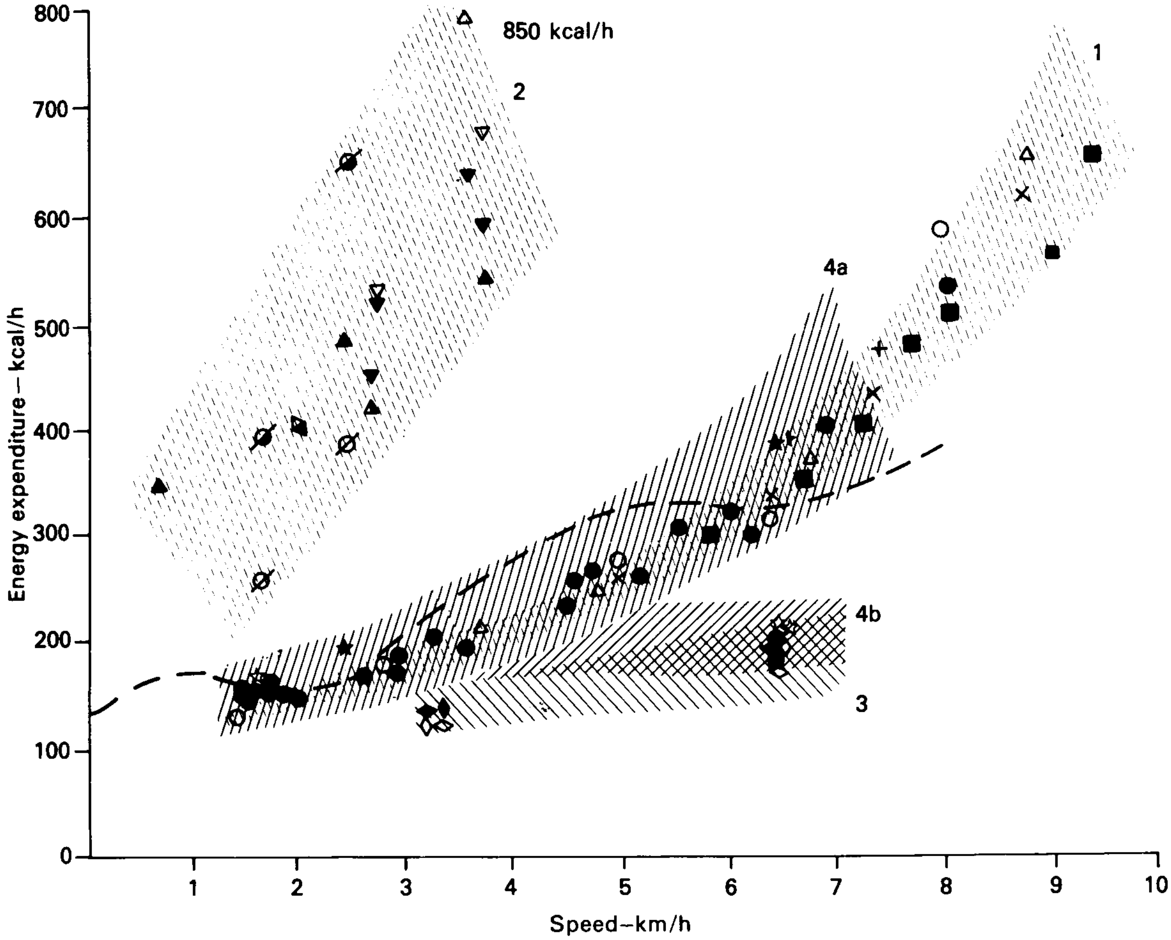

Terrestrial gravitation
1. Ordinary clothing (according to Passmore and Durnin, 1965)
● Atzler and Herbst, 1927, 1928
△ Benedicht and Murschnauser, 1915
■ Brezina and Kolmer, 1912
× Douglas and Haldane, 1912
○ Margaria, 1938
+ Morehouse and Miller, 1948 (according to Roth, 1966)
2. Space suit at ground level:
▲ Wortz (according to Roth 1966)
▼ Wortz et al, 1967
▼ Seminara and Shavelson, 1967
∅ Flexible space suit material or
∅ Rigid material (according to Robertson and Wortz, 1968)[206]
▽ At altitude in a pressure chamber: Wortz et al, 1967
▲ Seminara and Shavelson, 1967
◧ Harrington et al, 1965

Lunar gravitation
3. Ordinary clothing, vertical suspension:
◆ By the shoulders, Wortz and Prescott, 1966
◇ On a universal joint. Wortz and Prescott, 1966, inclined suspension:
♦ Flexible straps, Sanborn and Wortz, 1967
◊ Straps with frame, Sanborn and Wortz, 1967
4. Space suit
Kuehnegger and Martell, 1967
-- Robertson and Wortz, 1968:
a. Vertical suspension by a frame
☆ Flexible space suit material
⊤ Rigid material
b. Inclined suspension:
★ Soft space suit material
⊤ Rigid material

FIGURE 3.—Influence of lunar gravitation and a space suit with excess pressure on energy expenditure while walking on a flat surface [31]. Shaded area: approximate regions of standard deviation.

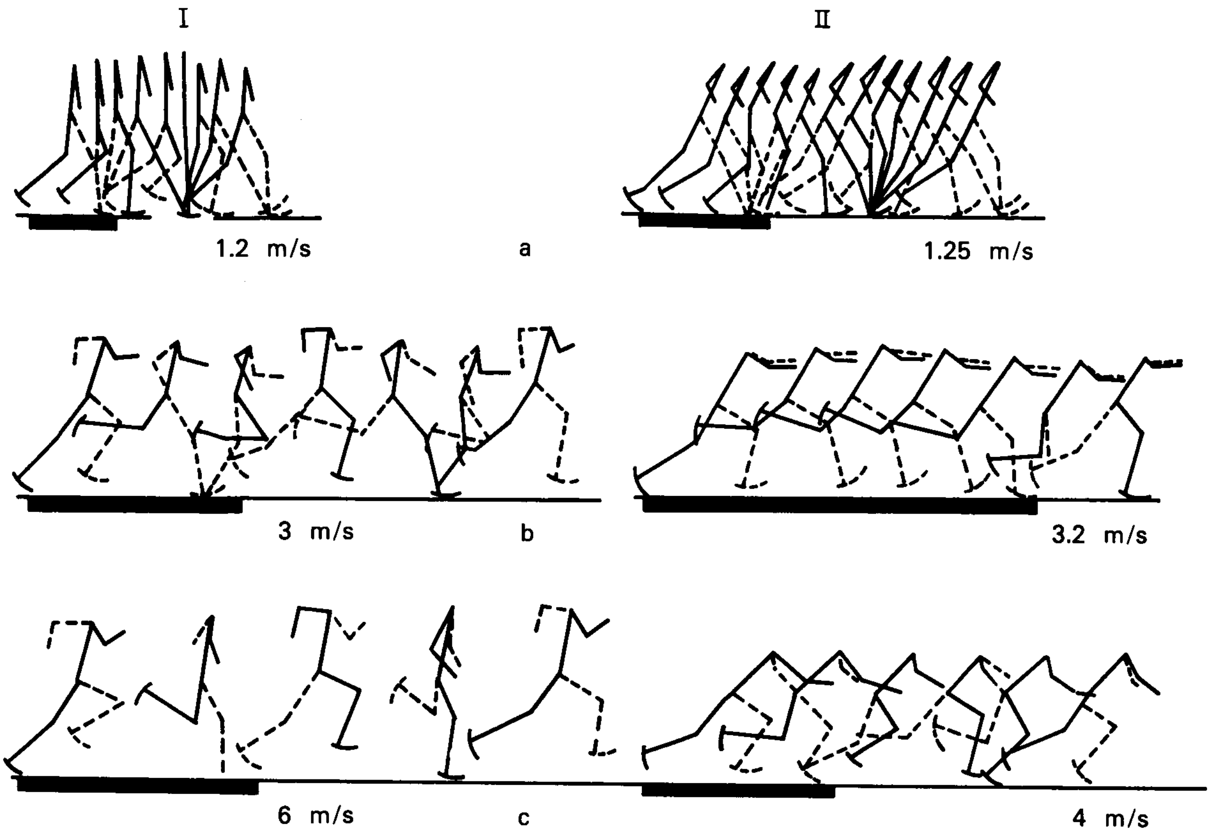

FIGURE 4.—Change in body kinematics during locomotion under lunar and terrestrial gravitation conditions. (After Spady [31]) Heavy line is length of stride; distance between figures 0.16 s. a, walking; b, running and jumping; c, running. I, terrestrial gravitation; II, lunar gravitation.

with the metabolic expenditures telemetered from lunar surface crews. Table 3 shows the average metabolic cost in kJ/h and Btu/h for the Apollo 17 lunar surface crew and a comparison of the figures with prelaunch predictions for lunar surface activities. Actual metabolic rates tended to be only slightly higher than those predicted. Lunar surface workloads were considered excessive only for the Apollo 15 crew; the mission was strenuous. In addition to heavy workloads, the crew was excessively fatigued as a result of sleep difficulties. Because of these problems and others, postflight responses of this crew differ from those of other crews in virtually all dimensions. Apollo 15 crew responses stand out as an anomaly.

Heart rates recorded during Apollo 15 lunar surface activities gave no early clues on the extent to which the crew was drawing on its physiological reserves. During some activities, heart rates reached nearly 160 beats/min. While this heart rate is relatively high compared to that of most lunar surface activities, it is not excessive; similar heart rates were recorded for Apollo 11, 12, and 14 crewmen. The first clue to an overload of work was indicated by cardiac arrhythmia in both crewmen on the lunar surface which recurred during the return flight to Earth. After splashdown, the crew had marked difficulty in physiologic readjustment to Earth gravity. Recovery of preflight work performance values was retarded. One crewman reported postflight dizziness, which he considered a sign of vestibular disturbance; it was, in fact, more likely related to cardiovascular dysfunction. This distinction is very important. The crew also showed marked potassium deficiency which undoubtedly contributed to their physiological

TABLE 2.—*Pre- and Postflight Data on Apollo 14 Crewmembers Constantly Exposed to Weightlessness or Subjected to Effects of 1/6 G* [15].

Medical data	Weightlessness	1/6 G	
	Command module pilot	Commander	Lunar module pilot
Weight loss	−5.4 kg	+0.45 kg	−0.45 kg
Pulse rate (decrease in orthostatic stability)	Significant increase	Minimal changes	Minimal changes
Erythrocyte mass	−9%	−4%	−2%
Plasma volume	−10%	+1%	No change
Total fluid in organism	−18%	−2%	−2%
Intracellular fluid	−27%	−3%	−3%
Working capacity (based on data on oxygen consumption and systolic blood pressure)	Considerable decrease	No change	Slight decrease

problems. The findings led to modification of the work/rest schedules and diets for Apollo 16 and 17 crews which successfully prevented recurrence of the difficulties experienced by the previous crew [19].

Biomedical Effects of Weightlessness, Adaptation to Zero-G, and Readaptation to Terrestrial Gravity

Considerable experimental data collected so far characterize the diverse phenomena of processes involved in living organisms adapting to the state of weightlessness and readaptation to terrestrial conditions. References in this section represent only a small part of those cited in the literature; additional information can be found in other surveys and thematic publications [21, 37, 128, 161, 166, 191, 193, 211, 217, 272].

Before the first studies were performed during space flights, it was felt that the effect of prolonged weightlessness could cause disruption of vital functions in the mammalian organism. Analysis of the results from several hundred studies of weightlessness effects shows that a number of *operative behavioral* changes enable the astronaut to cope successfully with the weightless condition. Of primary concern are *adaptive biological* changes within the various body systems, the medical consequences of which have not been unequivocally established. Nevertheless, data available at present provide evidence of the effect of zero-G on major body systems and their functions.

Table 4 summarizes some of the most general phenomena involved in the processes of adaptation to weightlessness and readaptation to terrestrial conditions.

Nervous System

Transition from the 1 G to zero-G state and early phases of weightléssness are often associated with disturbances of body orientation, illusory sensations, and symptoms of motion sickness, such as vertigo, nausea, and vomiting. Motion sickness symptoms are considered to be caused by disturbance of functional interactions of the sensory analyzers [143, 273]. Vision, hearing, touch, smell, and taste sensations generally were normal; there were no mental disturbances or hallucinations. Sensorimotor and pointing tests, caloric and other vestibular studies, and retinal photography revealed no significant changes from preflight data [88].

However, both neuromuscular and sensorimotor coordinations show various effects of weightlessness, such as changes in reflex excitability, subjective sensations of stress, and certain motor insufficiencies [48]. The latter probably are correlates of deficits in the musculoskeletal system.

In general, functions of the CNS, motor and neuromuscular coordination, diurnal periodicity of the organism, and neuropsychological proc-

TABLE 3.—*Metabolic Assessment Summary During All Surface Extravehicular Activity in Apollo 17* [19]

Activity	Commander				Lunar module pilot			
	Actual		Prelaunch prediction		Actual		Prelaunch prediction	
	kJ/h	Btu/h	kJ/h	Btu/h	kJ/h	Btu/h	kJ/h	Btu/h
Lunar roving vehicle traverse	505.4	479	580.3	550	471.6	447	580.3	550
Geological station activities	1092.9	1036	1002.3	950	1254.4	1189	1002.3	950
Overhead	1266.0	1200	1107.8	1050	1192.2	1130	1107.8	1050
Apollo lunar surface experiments package activities	1191.1	1129	1107.8	1050	1164.7	1104	1107.8	1050
All activities	998.0	946	941.1	892	1002.3	950	941.1	892

esses of the astronauts in flight did not show essential disturbances. Locomotion actually is facilitated in the weightless environment. Fortunately, there were no decapacitations due to malfunction of the vestibular organs [14, 22].

Some states of neuro-emotional tension and disconcerting states of fatigue experienced by several astronauts may not be directly related to weightlessness, but may have been brought about by other spaceflight stresses. By and large, they did not impair completion of the missions. This was particularly evident during the nearly disastrous Apollo 13 flight, which was successfully terminated despite exceptional emotional stress.

Cardiovascular System

Although the cardiovascular functions have been recorded in animals and men from earliest experiments to lunar excursions, the picture is still not entirely clear. Many variables contribute to the problem of assessing cardiovascular changes during complex interactions among various systems of the weightless body [125, 132]. Deconditioning of the cardiovascular system is clearly demonstrated by the disproportional increases in heart and respiratory rates during reentry accelerations and the orthostatic intolerance after return to Earth. Reduction in size of the cardiac x-ray image is definite [21]. Analysis of the phase structure of the cardiac cycle, electrocardiographic indices, and hemodynamic characteristics, especially in the immediate postflight period, clearly showed that myocardial activity had deteriorated temporarily to a certain degree [125]. It appeared that the longer the space flight, the more stressful the readaptation to normal gravity. Work capacity and physical competence were also reduced to levels observed after corresponding periods of bed rest, or to an even greater extent.

Increased ventilation rates and oxygen consumption postflight were closely related to deconditioning effects observed. Shortly after landing, even the sitting position caused significant elevations of heart rate and disproportionate reductions of workloads for heart rates. Reduced oxygen consumption was proportional to the workload. However, like blood pressure, pulmonary functions have not proved reliable indicators of weightlessness effects; more systematic investigations are needed [9, 125]. For example, striking differences between lunar landing crews and the men spending time in orbit around the Moon have added uncertainties about cardiovascular effects of weightlessness and subgravity, which must be resolved by further studies [125].

Metabolism

Exposure to weightlessness affects fluid balance, and protein, fat, carbohydrate and mineral metabolism as well as certain endocrine functions and electrolyte responses [7, 18, 21, 69, 259]. Almost all men lost weight during flight; most, but not all, regained normal weight within a few days. While most of this deficit is due to loss of body water and electrolytes, there is also loss

TABLE 4.—*Reactions of Man and Animals to Effects of Weightlessness* [19]

Reactions	Conditions and objects of observations [1]	Sources in literature (Ref)	Notes
1	2	3	4
Sensations of an unsupported position, floating, falling, spinning, turning, flow of blood to head, deterioration of orientation in space, predominance of visual information role in evaluating position of body in space	Man (TW, KP, SF)	[14, 15, 92, 93, 94, 140, 180, 211, 217, 244, 259, 260, 273, 275, 281]	Emotional coloring of sensations (fear, joy, etc.) depends on experience and training of subjects; in orbital flight-adaptation
Displacement of successive visual image during G-forces—downward (oculogravic illusion), and upward during weightlessness (oculoagravic illusion): illusions are characteristic of initial periods in weightlessness	Man (KP, SF)	[92, 93, 141, 211, 260]	Actual position of visual targets during G-forces—above the successive image, and below it during weightlessness; with gaze fixed on a target, the successive image coincides with it
Slowing down of speed and accuracy of movements; errors in trying to hit center of a target (deviation of hits upward)	Man (KP, SF)	[92, 94, 184, 211, 217, 244, 259, 260]	Only in initial phase of SF, then adaptation
Deterioration of ability to carry out measured muscular efforts and evaluate differences in mass of objects not fastened down	Man (KP)	[93, 211, 281]	
Pulse frequency: slowing of normalization following action of G-forces; subsequent tendency toward slowing, increase in variability (possible arrhythmias of the bigeminal type); in final stage of long SF, slight increase	Man, animals (SF)	[9, 17, 21, 60, 78, 94, 129, 134, 211, 217, 218, 249, 260]	With PBR following initial decrease in frequency of pulse, increase in frequency (lack of training)
Arterial pressure: moderate decrease, followed by stabilization, tendency toward decrease in pulse pressure	Man (SF)	[7, 17, 76, 133, 134, 136, 211, 256, 258]	In PBR, initial decrease followed by increase (sympathetic effect)
Heart: decrease in size (according to data from x-ray studies); symptoms of decrease in the contractile ability (according to electrocardiographic and seismocardiographic data and results of phase analysis of cardiac cycle)	Man (SF, R)	[21, 125, 190, 217, 258, 266]	Descriptions of cases of increased mechanical activity of heart during flight
Bone tissue: demineralization (according to the data from x-ray photometry) due to loss of Ca^{++}	Man, animals (R)	[14, 17, 18, 21, 26, 112, 196, 211, 260]	No changes observed when using method of photon absorption
Muscles: decrease in volume and strength	Man, animals (SF, R)	[21, 45, 94, 204, 258, 260]	Primarily atrophy of antigravitational musculature
Dehydration (decrease in plasma volume, followed by loss of intracellular fluid)	Man, animals (R)	[14, 15, 16, 18, 125, 196, 260]	Decrease in plasma volume develops on 1st or 2nd (Henry-Gauer reflex); recovery possible later

[1] See footnote at end of table.

TABLE 4.—*Reactions of Man and Animals to Effects of Weightlessness* [19]—Continued

Reactions	Conditions and objects of observations [1]	Sources in literature (Ref)	Notes
1	2	3	4
Decrease in weight (mass) of the body by 2–5% of original value	Man, animals (R)	[14, 21, 88, 125, 180, 184, 258, 259, 260]	Stay on moon in individual cases decreased body weight loss; following flight, weight rapidly returned to normal (exception: 18-d flight of Soyuz–9)
Protein metabolism: increase in blood urea content, increased excretion of creatinine with urine, negative nitrogen balance	Man, animals (SF, R)	[7, 16, 20, 69, 76, 77, 88, 161, 196, 217, 218, 258]	Similar changes in PBR
Lipid metabolism: increase in the cholesterol, lecithin, and nonesterified fatty acid content of blood	Man, animals (SF, R)	[76, 77, 88, 161, 196, 211, 217, 218, 219, 258]	Changes not constant, depending also on nature of diet
Decrease in excretion of Na^+, Cl^-, K^+ electrolytes with urine	Man, animals (R)	[15, 16, 18, 20, 21, 196, 260]	Related to previous losses of electrolytes during weightlessness
Reduced excretion of 17-oxycorticosteroids in flight, increase in excretion following flight	Man (SF, R)	[18, 20, 21, 69, 125, 180, 217, 218, 258]	Similar relationship in experiments with simulation of weightlessness
Increase in concentration of antidiuretic hormone, aldosterone, and renin	Man (R)	[15, 18, 20, 125]	Increase in aldosterone also noticed in SF
Blood: neutrophilic leukocytosis, lymphopenia, or lymphocytosis, eosinopenia, increase in ROE [?], changes in coagulatory and anticoagulatory systems of blood; thrombocytes—decrease or absence of changes	Man, animals (SF, R)	[4, 7, 18, 21, 69, 88, 134, 161, 180, 196, 217, 218, 219, 258]	Similar changes in experiments with PBR
Delay in excretion of water from organism in test with waterload	Man (R)	[7, 77, 259, 260]	Not noticed after 18-d flight of Soyuz–9
Deterioration of tolerance to transverse G-forces during launch	Man (SF)	[217, 244, 245]	Not on all flights
Sensation of heaviness of body, rapid fatigue, difficulty in walking, muscular pains	Man (R)	[45, 129, 180, 204, 217, 260]	Primarily after long-duration flights without preventive measures
Changes in postural, oculomotor reflexes and behavior	Animals (TW, KP)	[91, 282]	Changes less in delabyrinthized animals than in normals
Decrease in oculomotor activity, asymmetry of nystagmoid movements	Man (SF)	[217]	
Development of pain during movement or individual symptoms of it (dizziness, discomfort in stomach, nausea, vomiting)	Man (KP, SF)	[18, 21, 88, 91, 140, 143, 180, 256, 257, 261, 273, 278, 281]	Participation of both vestibular and extralabyrinthic mechanisms suggested, as well as change in interaction of afferent systems
Frequency of respiration and pulmonary ventilation: increase during flight along the KP; various changes in SF; increase in postflight period	Man (KP, SF, R)	[78, 133, 218, 244, 258]	Changes in flight depend on previous action of G-forces or nature of the work

[1] See footnote at end of table.

TABLE 4.—*Reactions of Man and Animals to Effects of Weightlessness* [19]—Continued

Reactions	Conditions and objects of observations [1]	Sources in literature (Ref)	Notes
1	2	3	4
Gas exchange: increase during flight along a KP; decrease (according to data from analysis of regenerative substance) during the SF; increase during post-flight period	Man (KP, SF, R)	[21, 23, 76, 133, 135, 244, 258, 261]	Based on an analysis of samples of expired air, collected during the SF, both a decrease and an increase were noted; decrease in the PBR
Decrease in food consumption	MAN (SF)	[18, 21, 217, 260]	Not observed on all flights; characteristic of PBR
Orthostatic instability	Man (R)	[16, 17, 21, 23, 58, 77, 94, 130, 161, 211, 219, 258, 260]	Develops also under conditions of terrestrial experiments involving simulation of weightlessness
Decrease in physical working capacity	Man (R)	[14, 18, 20, 21, 129, 258]	Consequence of hypodynamia
Decreased immunity	Man, animals (R)	[2, 196, 260]	Increased danger of infectious diseases during and after flight
Increase in recovery period on long compared with short flights	Man (R)	[94, 129, 180, 260]	Improved living conditions and preventive measures shorten recovery period

[1] TW—tower of weightlessness; KP—Keplerian parabola; SF—space flight; R—readaptation period; PBR—prolonged bed rest.

of intracellular fluid. Simultaneous decreases have also been noted in potassium, sodium, and chloride levels. Lost potassium was readsorbed shortly postflight in US astronauts when increased adrenalin, renin, and aldosterone levels should produce potassium diuresis, and postflight total body potassium deficit occurred. Moreover, a moderate decrease in red blood cell mass was observed after Apollo missions, probably due to increased oxygen concentration in the spacecraft atmosphere.

Musculoskeletal System

Reduction of external forces acting on the weight-bearing structure of the body results in loss of calcium and other minerals important to bone integrity [26, 112, 164]. Slight muscle atrophy and weakness of limbs were observed after long exposures to zero-G [16].

Muscle tone and strength as well as circumference of the legs were diminished [45, 180]. Changes in nitrogen balance were detected by US and Soviet scientists in animals and men after exposure to weightlessness, indicating increased composition of muscle protein [69, 196, 217, 234]. Physiologic changes and their interrelationships observed during weightlessness are schematically displayed in Figure 5. In this figure, the small arrows immediately adjacent to a body function or element indicate an increase or decrease in the measured value of this function when pre- and postflight measurements were compared on the same crewman. The larger or longer arrows which connect body functions or systems show the interrelationships of changes in one area with those in another [266].

Despite weightlessness and inactivity effects on the musculoskeletal system, such effects do not prohibit long space missions. First, countermeasures such as in-flight physical exercise, preparatory training, special diets, drugs, and artificial gravity, have been used effectively to keep the organism fit and intact. Second, some deficits observed after space flight may not be actually caused by weightlessness per se, but by other factors and stresses associated with specific flight conditions. Although the rate of change and end points of degradation of the body systems due to zero-G have not yet been determined, it appears that man will be able to adapt to this condition at some physiological cost.

It is also clear from this discussion that one of the foremost objectives in the investigation of weightlessness is the determination of adaptive trends, the adaptation level and the means necessary to maintain it. There is proof that man can live and work in zero-G up to 3 mo and that certain adaptive processes establish a new homeostasis. A schematic of the hypothesis concerning various major processes involved in adaptation is shown in Table 5 [15]. In essence, it is theorized that the circulating blood volume is distributed in accordance with the new force field upon entering the weightless state. This triggers the hormonal responses which restore the disturbed physiological balance. Cardiac, respiration, and metabolic activities are rearranged to comply with reduced physical load. It seems reasonable to assume that the functions will stabilize at a new, probably somewhat lower level of activity. The course of events is shown schematically in Figure 6 [159a].

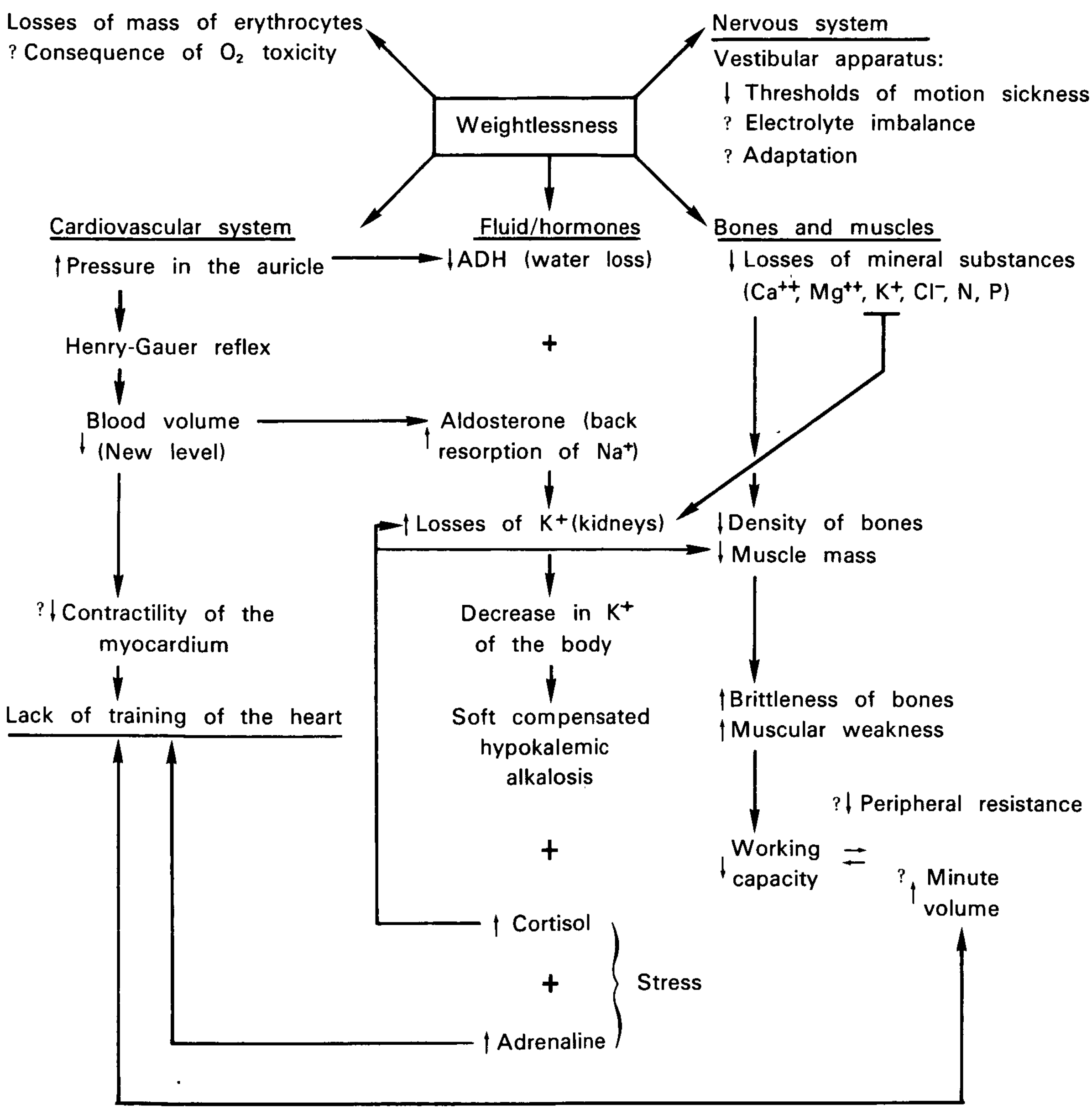

FIGURE 5.—Effects of the influence of weightlessness on man. (Working hypothesis adopted from [266])

The second major objective at this point is developing means to protect the organism against the adverse effects of zero-G. Musculoskeletal decay and cardiac deconditioning must be recognized as warning signs. Work was undertaken to find remedies, which included experiments with animals and men. It was recently reported that animals can be trained to accept an increased G-level as physiologically tolerable or "normal," and that gravity as a stimulus can affect mammalian behavior [168]. The minimum G-force, at which the motor functions and the bioelectric potentials of the muscles are normalized, is about 0.3 G [279]. It should be noted, that providing artificial gravity to man in space is a controversial subject and needs further study. The advantages and disadvantages of this concept must be carefully weighed, particularly in regard to functioning of the vestibular organs [79]. Preventive and therapeutic measures prior to and subsequent to the entry of man into different gravitational environments must be established.

MECHANISMS OF FUNCTIONAL CHANGES IN THE WEIGHTLESS CONDITION AND IN LABORATORY SIMULATION

Reactions Caused Primarily by Changes in the Afferent Nervous System

Experiments with animals and humans during parabolic and space flights showed that certain functions of the nervous system were disturbed by weightlessness. However, most of the consciously controlled processes, such as psychomotor performance, muscular activities, CNS functions, communication, and work proficiency remained intact. Examples of subjective, perceptual, and sensorimotor effects experienced by subjects while floating in large aircraft during Keplerian trajectories are in previously published papers [89, 90, 140, 211, 281]. By and large, these sensations and experiences were also reported by astronauts while floating in spacecraft and, to some degree, while suspended in free space during extravehicular activity (EVA).

Data are also available on other intra- and extravehicular activities in weightlessness and in zero-G simulators; for example, on suit donning, handholds, torquing, and handtool use, orbital and lunar work, walking techniques and aids, self-propelling dynamics, tethering and retrieval methods, as well as maneuvering devices in space and on the Moon [146, 193, 211, 224]. The function of the vestibular analyzer system is still of concern; cerebral control and nervous cross-coupling must also be considered.

Transition from 1 G into the weightless state increases the susceptibility to motion sickness in some persons [13, 89, 140, 143, 278]. In orbital flight, it would appear that the two components of the unusual force field—absence of gravitational stimulation on the otolith organs and possible stimulation of the semicircular canals by movements of the head and body—may bring about the abnormal reactions observed [277]. The otolith organs respond to acceleration changes during zero-G [90]; after initial increased activity during the transition period, they adjust to zero-G and fire at a lower rate [107]. Experiments in parabolic flights indicated that nausea and vomiting responses appear to require a functional labyrinth [103]. Coriolis effects are usually experienced in normal, but not in labyrinthine-defective subjects [51]. Experience of the "inversion illusion" also requires a functional labyrinth [66].

Illusion and motion sickness symptoms experienced by Apollo astronauts are summarized in Table 6 [19]. The entries show that almost all Apollo astronauts had motion sickness in land, air, or sea vehicles, four had no episodes, and only three (of 27) vomited in space (not necessarily due to zero-G). Otherwise, the existing relationship between motion sickness history and motion sickness symptoms displayed in space flight is rather unclear. The unfavorable reactions experienced equally by Soviet cosmonauts probably could have been caused by unexpected afferent impulses, in the absence of gravity, producing illusions of rocking and tumbling as well as episodes of stomach awareness, vertigo, and nausea. The hydromechanical processes in the semicircular canals may also contribute to spatial illusions, particularly sensations of rotation and inversion [66, 220].

Proper vestibular functioning is undoubtedly associated in several ways with proper functioning of other body systems. Circulation is profoundly affected by prolonged periods of immobilization and weightlessness [9, 55, 190, 240]. Under conditions of zero-G, there is occasionally a preponderance of vagal influence which results in bradycardia and gastrointestinal disturbances. This may produce nausea and a sensation of uneasiness, which could easily be mistaken for the autonomic manifestation of vestibular sickness. Such symptoms actually can be caused by cardiovascular inadequacy, secondary to diversion of circulating blood to the muscles in response to a threatened need for muscular action on the basis of inadequately perceived inertial and dynamic environments [226, 230].

With increasing duration of space flights and the associated zero-G condition which affects the afferent nervous system, the states of the blood circulation receptors and neuromuscular apparatus can substantially change the internal state of the mammalian organism and, in certain conditions, cause functional disorders. Their origin, it appears, can be traced back to single sources or their synergistic interaction, to inactivity of neurohumoral and neuroreflexic mechanisms of regulation due to absence of or impoverished sensory input, irregularity of neurophysiologic reactions due to inadequate or unusual sensory input, and failure or breakdown of neurophysiologic functions due to overloading or conflict of the specific organ system.

Two major questions must still be answered in regard to extended weightlessness exposure.

1. To what degree will the sensoriperceptual inputs and motor responses be altered?
2. Will the functional state of the organism be changed so much that it will be difficult, or even dangerous, to readapt to terrestrial gravity?

Basically, this means whether it is really desired that the organism adapt fully to the condition of zero-gravity. In order to solve this problem, it is necessary to better understand the intricate neurophysiologic adaptation processes and, as a secondary step, to determine the compensatory capabilities of the organism. The information presently available suffices to predict the reactivity of the mammalian organism during relatively moderate periods of zero-G. However, definite conclusions are not supported in regard to preventing disturbances of the afferent nervous system, associated sensory illusions, and motion sickness attacks and, finally, the desirability of man's complete adaptation to the weightless state.

Reactions Caused Primarily by Lack of Hydrostatic Blood Pressure

Redistribution of fluid in a system of elastic reservoirs is determined by the laws of hydrostatics. The hydrostatic pressure, whose level is

TABLE 5.—*Overview of Current Hypothesis Concerning Processes Involved in Man's Adaptation to Zero Gravity* [15]

Event		Response of body
Entry into zero gravity; redistribution of circulating blood volume	⇨	Body attempts to reduce volume; ADH decreases, aldosterone production decreases
	⬃	
Loss of water, sodium, potassium (loss of body weight)	⇨	Decrease in plasma volume; aldosterone increases (secondary aldosteronism)
	⬃	
Increased sodium retention; potassium loss continues; cell: acidotic—extracellular fluid: alkalotic	⇨	Intracellular exchange of potassium and hydrogen ions; decrease in bone density, muscle cell potassium, and muscle mass—possibly including cardiac muscle
	⬃	
Respiratory and renal compensation; halt to weight loss trend	⇨	Stabilizes with new effective circulating blood volume; new body fluid and electrolyte balance or "set"

proportional to the height of a column of fluid and its specific gravity, acting on the walls of the reservoir, causes their distension and corresponding movement of the fluid downward. This type of relationship also exists in the distribution of biologic fluids (mainly blood) in man and animals under terrestrial conditions. Remaining in a vertical position is accompanied by deposition of a certain volume of blood in the lower half of the body, decrease in venous return to the heart, systolic ejection, and a number of corresponding compensatory reactions. Distribution of a fluid medium in the organism is considered by some to be the most important biological reaction to gravitation [100]. Walking, running, jumping, changing the position of the body in space, change the magnitude and direction of gravitational shifting of blood in man. Hence, the organism is in a state of constant read-

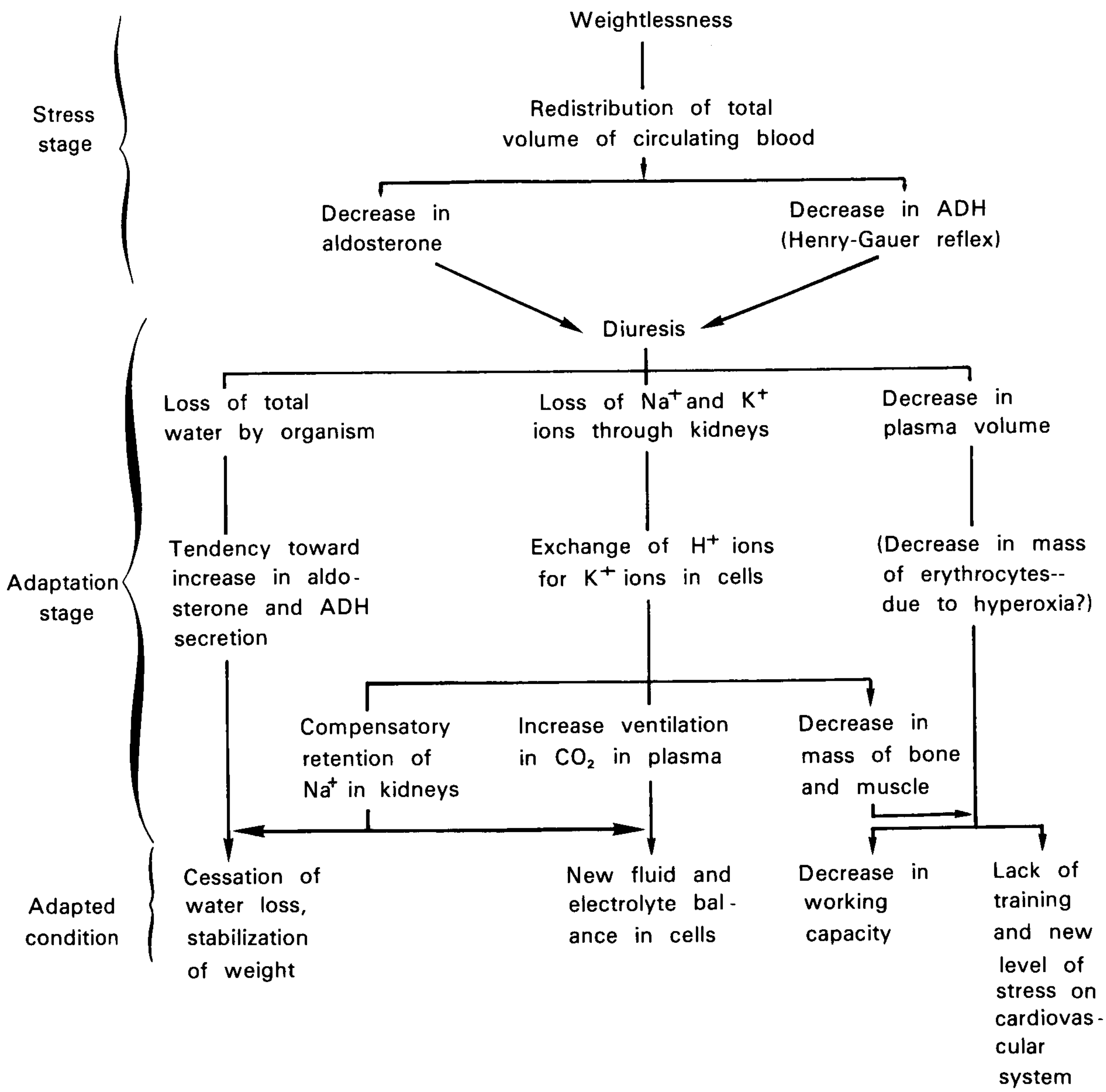

FIGURE 6.—Proposed process of adaptation to weightlessness [159a].

TABLE 6.—*Vestibular-Related Symptoms Experienced by Apollo Astronauts* [19]

Mission	Astronaut	Motion sickness history			Illusions/motion sickness symptoms in space flight			
		In land, air and sea vehicles	In zero-G parabola	In S/C egress or egress training	Tumbling illusions	Stomach awareness	Nausea	Vomiting
	A	×						
7	B	×	×	×				
	C	×		×	×			
	D	×				×	×	×
8	E	×	×	×		×	×	
	F	×	×			×		
	G							
9	H			×	×	×		
	I	×	×	×		×	×	×
	J	×						
10	K	×						
	L	×				×		
	M	×	×	×				
11	N	×	×	×				
	O	×	×					
	P	×						
12	Q							
	R			×				
	S(E)	×	×	×				
13	T					×	×	×
	U					×		
	V	×						
14	W	×						
	X							
	Y(H)			×				
15	Z		×		×	×		
	AA							
	BB(X)	×						
16	CC	×	×					
	DD	×	×					
	EE(L)	×	×			×		
17	FF	×	×			×		
	GG	×	×					

iness for carrying out compensatory reactions associated with action of the hydrostatic factor.

A constant stay in bed for a long period changes the magnitude and direction of hydrostatic forces, while immersion in water promotes their neutralization, since the immersion medium causes an equivalent counterpressure through the soft tissues on the vascular walls. In a state of weightlessness, action of the hydrostatic pressure is completely eliminated. The result of all these processes is a relative redistribution of blood from the lower half of the body to the upper half.

Hyperemia of man's cutaneous coverings, the development of edema in the nasopharynx and facial tissues under weightlessness conditions, may also be linked to the mechanism of blood redistribution [23, 184, 260]. Electroplethysmographic studies, conducted during brief weightlessness in aircraft, revealed an increase in filling the chest vessels and organs with blood [181, 244]. In an experiment with a monkey aboard US Biosatellite III [168], also during water immersion of humans, central venous pressure increased. During a prolonged stay in a horizontal position, stagnant dilation of the vessels of the eye fundus resulted [63].

Relative increase in the central blood volume accompanying decrease in hydrostatic pressure, according to Gauer et al, is approximately 400 cm^3 [73]. It is an instantaneous reflex mechanism that leads to plasma loss and decrease in the total volume of circulating blood to a level at which filling the central veins with blood corresponds to the homeostatic norm. The receptor zone of this reflex consists of volume receptors located primarily in the region of the left auricle [73, 75, 114]. Impulses from the volume receptors, resulting from distension of the left auricle, travel along the vagus to the medulla oblongata and the supraoptical region of the hypothalamus, and inhibit secretion of the antidiuretic hormone (ADH). ADH is stored in the neurohypophysis from which it is excreted into the blood. Decrease in ADH concentration in the blood leads to a drop in reabsorption of water and sodium in the kidneys, increased diuresis, and plasma loss. At the same time, thirst decreases and a negative water balance is established. Distention of the left auricle can also cause reflex spasm of the arterioles in the pulmonary circulation (Kitayev reflex) with subsequent pressure rise in the pulmonary artery system and an increased load on the right ventricle [139].

In experiments with laboratory simulation of weightlessness, the plasma loss was 300–800 ml [157, 177, 253]. During the postflight period, the astronauts in most cases also showed a drop in the volume of circulating plasma of 100–500 ml (up to 13%) [18, 20].

The processes of restructuring water-salt exchange when relative dehydration develops in the absence of hydrostatic pressure of blood take place quite rapidly, primarily during the first 48 h exposure, after which the water exchange settles at a new, lower balanced level [214, 253]. There are decreases in intensity of diuresis and the amount of water used [25].

Blood thickening caused by plasma loss is accompanied by increase in hematocrit [29, 102, 231, 259] and blood viscosity, although there may be a decrease later in the mass of erythrocytes [23, 177, 178]. As a result, the ratio between formed elements of the blood and plasma returns to normal [102]. In the late stages of experimental simulated weightlessness, the volume of circulating blood tends to increase [5, 198, 254]. Since no decrease in the volume of circulating plasma was observed following the 14-d flight of Gemini 7, it is necessary to assume the existence of mechanisms for compensation of plasma loss. One such compensation may be related to increased aldosterone concentration during flight [20, 23]. This hormone, produced in the adrenal cortex, promotes sodium and water retention in the organism as a rule. The production of, and causes of, increased aldosterone excretion in urine during space flight are matters requiring further research. The possibility cannot be excluded that restoration of circulating plasma volume against a background of prolonged absence of hydrostatic blood pressure can also depend upon change in sensitivity of the volume receptors in the left auricle.

Fluid loss serves as one of the reasons for decrease in body weight which is recorded frequently postflight, and after simulated weightlessness experiments [7, 34, 95, 214, 217, 218, 259, 260]. The magnitude of this decrease, averaging

2–5% of the original body weight, has little to do with duration of the action; it is compensated relatively rapidly by increased water consumption and reduced diuresis (Fig. 7). In a test with a waterload for the Soyuz-9 crew following their 18-d flight [260], there was slower restoration of weight and incomplete water retention. This may be explained either by considerable changes in sensitivity of volume receptors, or because weight losses were linked primarily not with dehydration, but with a decrease in muscle mass. Factors that form the basis of muscle atrophy will be discussed in the next subsection under **Reactions Caused Primarily by Lack of Weight on the Musculoskeletal System.**

Lack of hydrostatic pressure may also result in the development of changes in venous tone (especially vessels of the lower extremities), which are regulated under terrestrial conditions primarily by variations in hydrostatic pressure. Experiments with simulation of weightlessness led to change in the reflex stimulus. Rigidity sets in and distention and contractibility deteriorate [8, 171, 200]. The tendency toward decreased distensibility in leg vessels was observed in cosmonauts postflight, although it was previously reported that this parameter returned to normal [18, 20].

Orthostatic Stability

Prolonged deprivation or decrease of hydrostatic pressure of blood is followed, consistently, by deterioration of the postural reaction of the cardiovascular system. Decrease in orthostatic stability was also observed following the first manned space flights [161, 219]. This observation

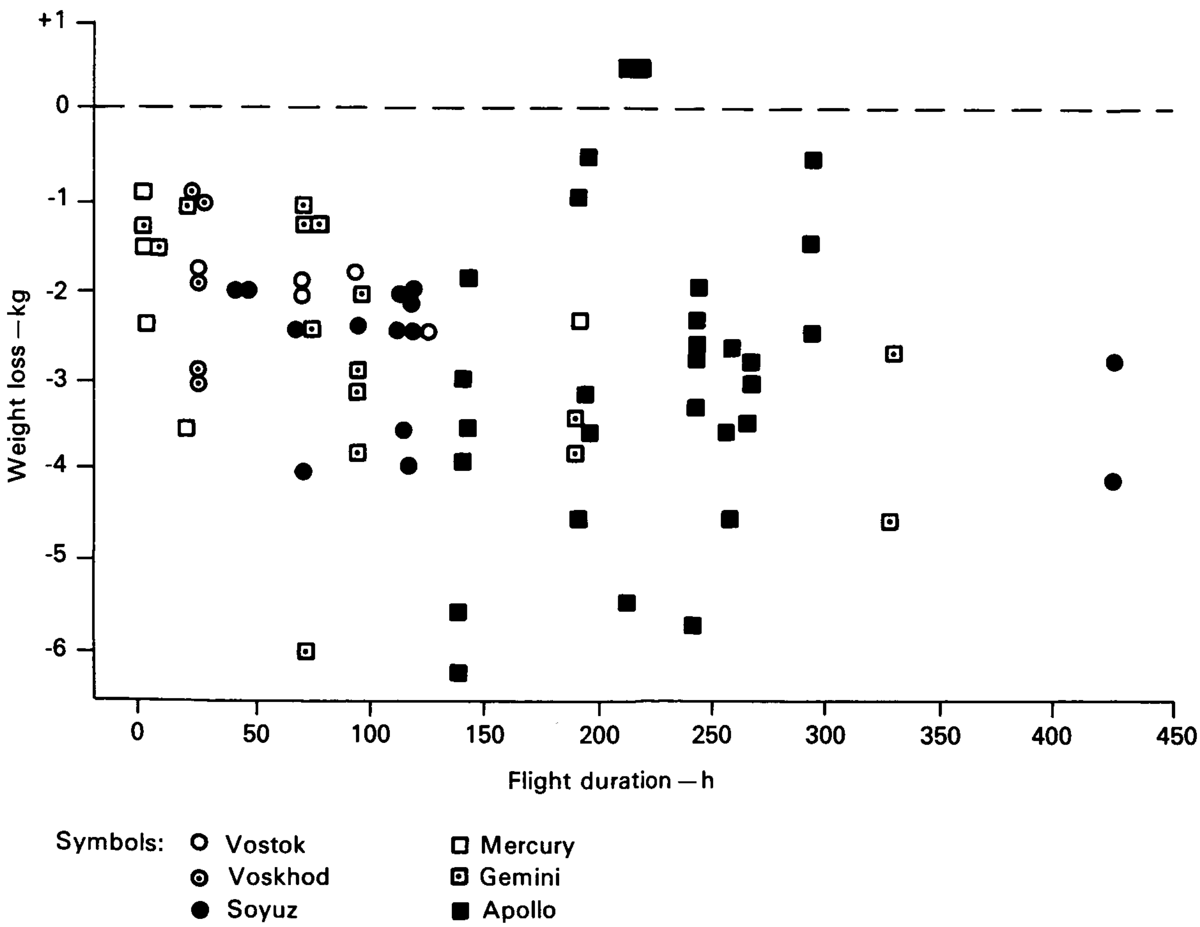

FIGURE 7.—Changes in body weight following space flights of varying duration.

was later confirmed repeatedly [23, 58, 77]. Orthostatic disturbances are also known to appear systematically after studies involving water immersion and bed rest.

The origin of the orthostatic deficit is linked essentially to dehydration phenomena and more precisely to decrease in total volume of circulating blood, inasmuch as it intensifies the decrease in returning venous blood to the heart with the body in a vertical position. Dehydration of any origin (blood loss, limited water use, thermal stress) has a negative influence on tolerance to influences associated with redistribution of blood to the lower extremities [95, 105, 182].

Not all authors have found clear correlation between the degree of dehydration or decrease in circulating blood volume on the one hand, and severity of orthostatic disturbances on the other, from which it can be concluded that this is not the only mechanism that takes part in formation of orthostatic instability [41, 200, 229, 253]. Other factors are also quite important in the origin of orthostatic problems following a stay in weightlessness or under simulated weightless conditions: decreased muscle tone, particularly in the lower extremities [56, 123, 157, 178]; capacity of the venous deposit in the lower half of the body [8, 171, 200]; permeability of vascular walls and loss of plasma into intercellular spaces [56, 251]; characteristics of neurohumoral regulation of functions in the vertical position; and fatigue [41, 96, 154, 169, 189, 200, 213].

The phenomena associated with orthostatic instability were very pronounced after the Soyuz-9 crew's 18-d flight [130]. This attaches considerable practical significance to timely diagnosis of potential orthostatic instability, which can be accomplished using functional tests associated with measured limitation of the return of venous blood to the heart. There is a high degree of correlation between reactions to the orthostatic test and the Valsalva test [53]. The test involving action of negative pressure on the lower half of the body is particularly informative [85, 182, 267, 268]; it may be performed during flight and is used actively in preflight and postflight testing of cosmonauts [17, 18, 81].

Dehydration caused by lack or reduction of hydrostatic blood pressure apparently is also one of the reasons for deterioration of tolerance to a number of other stressful influences, particularly accelerations and physical stresses. In any case, experimental dehydration exceeding 4% body weight (according to Greenleaf et al) led to disturbances involving isometric muscle contraction, physical working capacity, and tolerance to longitudinal accelerations ($+G_z$) [105].

These data confirm that the end effects resulting from the mechanism of blood redistribution in a state of weightlessness are very serious. Therefore, it is understandable that at the present time considerable emphasis is being placed on developing measures to prevent changes associated with lack of hydrostatic blood pressure in the weightless condition.

Reactions Caused Primarily by Lack of Weight on the Musculoskeletal System

Elimination of weight stress from the support-motor apparatus under conditions of weightlessness serves as the positive factor for a number of systemic changes, for which the pathophysiological basis is "disuse."

The lack of a need for active opposition to gravitational forces and maintenance of posture, decrease in muscle effort to move the body and its individual parts in space, on the basis of theoretical consideration alone, necessarily leads to decreases in energy exchange and oxygen transport requirements in the system. Insufficient loading of the muscle system and supporting structures, significant restructuring of motor coordination in the unsupported state also create preconditions for changes in metabolism, neurohumoral mechanisms for regulation of somatic and vegetative functions, and development of the so-called hypodynamia syndrome.

Prolonged experiments on the ground with controlled limitation of motor activity, especially its motion (hypokinesia) and force (hypodynamia) components, indicated a systematic decrease in basal metabolism ranging from 3–7% to 20–22% [56, 138, 159, 173]. Indirect determination of the gas exchange level under spaceflight conditions, carried out by Soviet and US investigators on the basis of results of chemical analysis of regeneration material, showed a slight decrease in energy consumption to 83.5–97.2 kcal/h [23, 261]. Individual direct measurements of the gas exchange level during space flights do not permit final conclusions, since both increases and decreases in oxygen consumption have been found [133, 135].

The decrease in energy metabolism is one of the reasons for decrease in food consumption; such observations were made in studies involving water immersion and hypodynamia [101, 214]. Energy expenditure from food by US astronauts in Gemini flights varied widely from 1000 to 2500 kcal/d while in the Apollo program there was a decrease to an average 1680 kcal/d [18, 23].

Demineralization of bone tissue, frequently recorded in terrestrial experiments involving hypodynamia and following termination of actual space flights, is evidently the consequence of a decreased weightload on the skeleton, since simulation of this load decreases demineralization [17, 20, 26, 112, 151, 163].

Decrease in optical density of the calcaneus (heel bone) postflight reached 15–20% in some cases, exceeding somewhat the values recorded for comparable periods of bed rest. The method of photon absorption for the Apollo 14 crew failed to reveal any symptoms of bone demineralization [21].

Reports indicate that urinary calcium losses in 2 weeks of simulated weightlessness amounted to 2 g and hence as much as 6–12 months in a state of weightlessness would be completely harmless to man [57]. In contrast, other theories hold that calcium losses caused by high physiological activity can lead to a number of functional disturbances, particularly involving the specific nature of the cardiac muscle, conduction of nerve impulses, and blood coagulation [127]. Possible changes in the mechanical strength of the skeleton due to its decalcification must also be taken into account [98]. On the basis of comparative physiological studies, it has been concluded that decrease in weightload on the bone-support apparatus decreases the erythropoietic function of the bone marrow [147].

Muscular Effects

Insufficient loading of the muscle system. which develops even in brief weightlessness, in the form of decreased bioelectrical activity of neck, back, and pelvis muscles [280], results in a number of specific problems. In experiments with hypodynamia, following terminated space flights, there is a decrease in the volume of muscles, particularly those of the lower extremities [45, 180, 189]. Analytical studies with animals permit qualifying this phenomenon as muscular atrophy [106, 196, 207]. At the same time, a change in protein metabolism and negative nitrogen balance develops [69, 214, 238]. Resynthesis of protein and its rate of amino acids inclusion likewise decrease [68, 234]. Postflight, cosmonauts have shown increased urea content in blood, increased creatinine excretion in urine [7, 77, 258], and decrease in total potassium content in the organism [14, 15, 21], which also indicates a breakdown of muscle proteins.

The possibility cannot be excluded that development of destructive processes causes increased sedimentation rate, neutrophilic leucocytosis in the lymphopenia and eosinopenia, which are recorded frequently in cosmonauts following return to Earth. These changes may, however, be due to postflight stress reactions. In support of this hypothesis, there have been increases in urinary corticosteroids and in their concentration in the blood serum following flight, also hyperglycemia [18, 20, 21, 69, 180, 217, 218]. On the other hand, during weightlessness and during laboratory experiments, a decrease in activity of the corticoadrenal system has been observed [96, 167, 213, 214, 263].

The nature of the motor activity and nutrition under weightless conditions also affects the condition of lipid metabolism, evidenced by increased content of cholesterol, lecithin, and nonesterified fatty acids in the blood [77, 88, 196, 218, 219, 258]. The decrease in the levels of cholesterol of United States astronauts probably was related to the type of diet and to the relatively low food consumption [18].

Weightlessness, as well as experimental hypodynamia, lead to decreases in muscle tone, muscular strength, tolerance, and physical work capacity [45, 65, 137, 152, 157, 159]. During the first few days of recovery, there is usually evidence of serious motor coordination disturbances regarding both statics and dynamics [108, 204, 221].

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These changes in the support-motor apparatus cause deterioration of tolerance to all those stressful stimuli which impose increased requirements on the muscle system in particular.

Cardiac Effects

During hypodynamia, the decrease in muscle tone, physical stress, and energy exchange decrease the requirements imposed on the system for oxygen transport and gradually lead to lack of resistance in the cardiovascular system in regard to various stresses. In hypodynamia lasting more than 10 d, an increase in pulse rate at rest has been observed which is characteristic of deconditioning [122, 188, 216, 235, 254]. The systolic blood volume decreases under these conditions according to a majority of researchers, although the opposite view is sometimes held [39, 87, 183, 188, 198, 216, 235]. The arterial pressure, during the initial period of hypodynamia, shows the hypotensive type of reaction predominantly, while later the hypertensive variety is more prominent [123, 188, 223]. Such changes in pulse frequency and arterial pressure are considered by many a predominance of sympathetic effects in regulating cardiac activity due to functional insufficiency of the vagus [179, 202, 216].

During the 18-d Soyuz-9 flight, following initial decrease and subsequent stabilization of the crewmembers' pulse rates, which was usually observed on shorter flights, there was a tendency toward increase in this parameter during the last week of the stay in weightlessness [129, 260]. Reactions of the arterial pressure showed an initial hypotensive phase followed by the pressure returning to the original level and stabilizing [7, 23, 58, 136, 260]. There was also a tendency toward increased variability of the arterial pressure parameters and a slight drop in the pulse pressure [17, 258].

When a horizontal position is prolonged, the electrocardiogram shows position changes, relative slowing of the intraauricular, atriventricular, and intraventricular conductivity as well as the $T_{v1} > T_{v6}$ syndrome [122, 123, 262]. Changes in phase structure of the cardiac cycle during laboratory simulated weightlessness usually combine in the sympton complex called the *phase syndrome of cardiac hypodynamia* [123, 131, 188]. The symptom complex includes: lengthening of isometric contraction phase, shortening of expulsion period, decrease in rate of intraventricular pressure rise, intrasystolic index, and increase in myocardial stress index. In pathology, this syndrome is encountered in various forms of myocardial ischemia and reflects a disturbance of its contractility. Although several weeks are required for development of these symptoms with deconditioning hypodynamia effect on the cardiovascular system, some have already become evident in varying degrees during periods spent in weightlessness.

Electrocardiographic studies performed under spaceflight conditions showed no significant changes in ECG peaks and intervals. The majority of indices changed, as a rule, in accordance with pulse rate changes or reflected the position changes. It was frequently noted that there was some lengthening of the time for auriculoventricular conductivity and a tendency toward decrease in amplitude of the T-spike, indicating deviation in the conductivity function, and in intensity of the cardiac muscle metabolic processes during weightlessness [191, 194, 217]. Individual phasal changes have also been observed during space flight which could be considered decreased cardiac muscle mechanical activity [9, 191], which include: decrease in amplitude and duration of seismocardiographic oscillatory cycles, increase in electromechanical delay, mechanoelectrical coefficient, and mechanosystolic index. Increase in the electromechanical delay, caused in one Gemini 5 astronaut, was linked with vagotonic reaction [60, 240]. Symptoms of deterioration in the myocardium contractile function were recorded in cosmonauts soon after landing [217, 258].

Hence, elimination of weightload on bone and muscle apparatus is a distinctive and important causative mechanism in the development of various disturbances attributed to weightlessness. It is sometimes given primary responsibility, although this leads to insufficient evaluation of other pathogenetic mechanisms [126, 157]. Hypodynamia is widespread in clinical practice and there is an analogy to this mechanism in daily life. Therefore, problems in investigating the influence of hypodynamia on the organism and combating its consequences are not limited to space medicine, but have general clinical significance.

Exposure Limits Derived from the Effect of Prolonged Weightlessness on the Human Organism

Reactions produced by the influence of weightlessness on the function of afferent systems, distribution of blood and load on the bone and muscle system, essentially reflect accommodation of the organism to new environmental conditions which proceeds along paths that could be disuse atrophy. Prolonged weightlessness can lead to destructive processes, a drop in the organism's functional capacities and its resistance to various stress effects. In this connection, it is advantageous to consider certain final reactions that can limit or reduce man's effective role in further conquest of space.

Deconditioning is one of the most general symptoms of an unfavorable weightlessness influence on the organism. Its individual symptoms (deterioration of working capacity, rapid fatigability) are obvious in the course of flight [217, 258]. However, the phenomena of deconditioning are manifested more clearly upon return to Earth. Decreases in body weight, muscle mass, mineral content of bones, and in strength, tolerance, and physical working capacity limit tolerance of stressful influences characteristic of this period: G-forces and the Earth's gravitational effect [217]. In particular, following the 18-d flight, the sensation of weight was felt by crewmembers as a force of 2–2.5 G; general weakness, dizziness, and increased fatigue developed [260]. US astronauts noted that after the flight their clothing seemed much heavier [17].

Studies involving laboratory simulation of weightlessness that produce symptoms of general physical deconditioning demonstrate the possibility of psychic function asthenization. During 3 weeks or more of hypodynamia, there were frequent developments of restlessness, irritability, fixed ideas, conflict, and in some cases, psychic disturbances [30, 212]. These general deconditioning phenomena, therefore, may be factors to limit safety and effectiveness in long space flights.

Disturbances of motor functions under spaceflight conditions apparently are not critical, since motor coordination habits in weightlessness develop quite easily. The problems involving coordination of motion that can develop during readaptation are more unfavorable. These problems developed in a mild form in studies involving prolonged bed rest and in serious form following the 18-d space flight [108, 204, 221, 260].

Considerable changes in physical working capacity and tolerance can also seriously limit cosmonauts' ability to move around after flight. Since the magnitude of coordination problems is a function of exposure duration to hypodynamia and weightlessness, this situation must be taken into account as presenting important limitations in flights of increased duration.

Orthostatic instability takes the form of pronounced increase in the physiological state of changes, development of dizziness, weakness, nausea, and particularly a syncopal condition in the vertical position. It constitutes a serious post-flight problem. While orthostatic instability symptoms following brief flights were short and easily overcome, after the 18-d flight they were manifest in a sitting position and were of considerable duration [23, 130].

A comparison of results from the 14-d Gemini 7 flight with shorter flights does not support any relationship between severity of orthostatic disturbances and duration of exposure to weightlessness [20]. Preliminary data from medical examination of the Skylab crew following their 28-d flight also indicates that orthostatic problems were very moderate in two of the three astronauts. Hence, disrupted stability in the vertical position is a function not only of duration of weightlessness, but also of such factors as living conditions and the use of protective measures in flight.

Changes in immunological reactions and resistance to infection were noted in simulated weightlessness experiments and after an 18-d space flight [49, 175, 260]. These alterations, linked to general deconditioning and metabolic changes, were accompanied by increased sensitivity to disease, which could be critical during flight [84]. Illness can also be transmitted from one crewmember to another through pathogenic microbes and fungi [18]. Therapy under these conditions may be limited by change in the organism's reactivity in regard to pharmacologic preparations resulting from the action of weightlessness [243, 246]. On short flights, no significant changes involving immunological reactivity were observed [2].

Neurologic problems have been recorded during prolonged (more than 30 d) hypodynamia [189]. Symptoms of interhemispheric asymmetry and dextrolateral pyramidal insufficiency developed which were linked to problems involving the brain hemocirculation and changes in level of afferent stimulation [174]. Similar problems could arise on long flights [181], particularly deterioration of motor function and working capacity.

Changes in coagulability involving the development of hemophilic reaction were noted in prolonged studies in simulated weightlessness [42, 61]. Some cosmonauts developed a condition postflight of a decreased number of blood thrombocytes [180, 218, 219], which also indicated hemophilic change. Blood coagulability is a function of more complicated relationships between the coagulatory and anticoagulatory systems. The possibility of unidirectional changes in both components must also be considered, which took place in experiments aboard the Cosmos-110 biosatellite [4]. Blood coagulability problems in weightlessness deserve further research.

Other changes in the organism's functional condition may limit the length of a safe stay in prolonged weightlessness. Some changes are determined by restructuring processes of nervous and hormonal mechanisms which regulate vegetative and motor functions in this state. Others depend upon the degree of structural changes (for example, muscle and bone tissue), deconditioning of the cardiovascular system, and metabolic changes.

However, during all the periods of weightlessness so far, the most critical form of these changes is the problems manifest in the readaptational period. The most important are decreased tolerance to G-forces, vertical posture, deterioration of physical working capacity, and coordination of basic motor activities. Therefore, it is highly important for medical safety on long space flights to develop and introduce measures for preventing these problems.

PROTECTION OF THE HUMAN ORGANISM AGAINST ADVERSE EFFECTS OF WEIGHTLESSNESS

Preventive and Therapeutic Measures

An evaluation of phenomena associated with adverse effects of the influence of weightlessness on the human organism necessitated creating conditions for the astronaut to alleviate the effects of physiologic and psychobiologic adaptation to weightlessness. Two general concepts for such prevention (pointed out previously) are currently being developed [37, 211]. One concept would prevent adaptation of the organism to weightlessness; the other would protect the astronaut against undesirable consequences or partial adaptation. It has not been determined at present which approach is more effective.

Adaptation to weightlessness can be prevented only by developing a constant and sufficiently complete equivalent of terrestrial gravitation aboard spacecraft. The introduction of artificial gravity appears to be the most extreme method of prevention, but at present there is no justification for this complicated and costly solution. The rotational mode involves a number of technical problems that arise as the radius of the rotating platform increases. A major problem is weight limitations, added to which are complexity of the orbital design, gravitational gradient of rotation, retention of a stable orbit, fuel problems, as well as control and supply requirements which remain nearly insoluble. Possible side effects of prolonged stays in a constantly rotating system have not yet been estimated. In the final analysis, it may be necessary to resort to this method for theoretical and experimental studies [24, 79, 279], although both engineers and biomedical specialists are trying to get around it [165].

The second concept is more realistic for current needs of astronautics, since it allows partial adaptation of the organism to weightlessness, but also provides for measures that can be taken to prevent or reduce the principal unfavorable consequences of adaptation. Solution of the problem will be satisfactory if the preventive measures by the crew during the flight and directly after landing preserve their health and working capacities. The effectiveness of the protective measures will, therefore, be based primarily on maintenance of a sufficient level of physical working capacity, motor coordination, and orthostatic stability, since changes in these functions postflight appear to be the most critical. Such measures may be comparable with flight conditions in terms of technical and operational characteristics and medically, will not produce discomfort or harmful side effects.

The most promising trends in preventive measures are governed by those concepts regarding mechanisms of functional changes in weightlessness. In a simplified system of pathogenesis for disturbances caused by weightlessness effects, some of their possible trends and methods of prevention are charted in Figure 8 [81].

The most natural and feasible technique, evidently, is to prevent loss of hydrostatic blood pressure and weightload on the musculoskeletal system. If it is possible to block these primary effects, the long chain of secondarily produced modifications could be prevented, including those causing most of the readaptation difficulties. Selecting a method for offsetting changes in activity of the afferent systems during weightlessness is more complicated. Preventive measures (e.g., negative pressure on the lower half of the body), promoting blood flow to the legs, theoretically can create sensations characteristic of a vertical posture [81]. However, it is not possible to provide gravitational stimuli for specific gravity receptors without resorting to artificial gravity.

Preventive and therapeutic measures can be directed not only at the primary or causative effects of weightlessness, but also at the lower levels of the pathogenetic chain (represented accordingly in Fig. 8).

A more detailed list of preventive measures that have been used in ground experiments involving simulated weightlessness and which are partially suitable for actual space flight may be found in Table 7. Classification of preventive measures based on their physical nature was used in the listing.

In the prevention of adverse effects of prolonged weightlessness, significance is placed on preflight selection and training of astronauts, and postflight restorative therapy. These subjects have been discussed in detail in other chapters of this text; only those means and methods meant for use in space flight and immediately thereafter will be considered in subsequent sections of this chapter. To achieve systematic arrangement of experimental data obtained in testing individual preventive measures, their pathogenetic effects are used as a basis.

Preventing Primary Effects of Lack of Hydrostatic Blood Pressure in Weightlessness

The logical prevention of consequences from unusual blood distribution associated with a lack of hydrostatic pressure is in artificially creating the effects of hydrostatic pressure. Water immersion and prolonged bed rest have been used to test various methods and devices.

Inflated cuffs, which enclose the extremities, are intended primarily to reduce return of venous blood to the heart and simulate conditions of the human in a vertical position on Earth. Narrow cuffs are usually applied to the upper part of the thigh [81, 100, 178, 229, 250, 255]. Pressure levels produced usually do not exceed 70–75 mm Hg and the ratio between the length of compression periods and the intervals between them vary broadly in different experiments—from 1:1 to 5:10 min. Numerous laboratory tests do not indicate a reliable and clearly reproducible protective effect, although in some instances this effect was observed. The inflated cuffs used during space flights also failed to yield conclusive results [58].

Thigh cuffs used to impede venous-flow in an experiment involving 70 d hypodynamia increased vessel tensility in the legs in comparison with observations from tests under analogous situations without use of the cuffs [200, 255]. Reserve capacity of the venous deposit increased, and with the body in a vertical position, a relatively large amount of blood accumulated in the legs. As a result, orthostatic problems were not eliminated. Hence, physiologically unpleasant

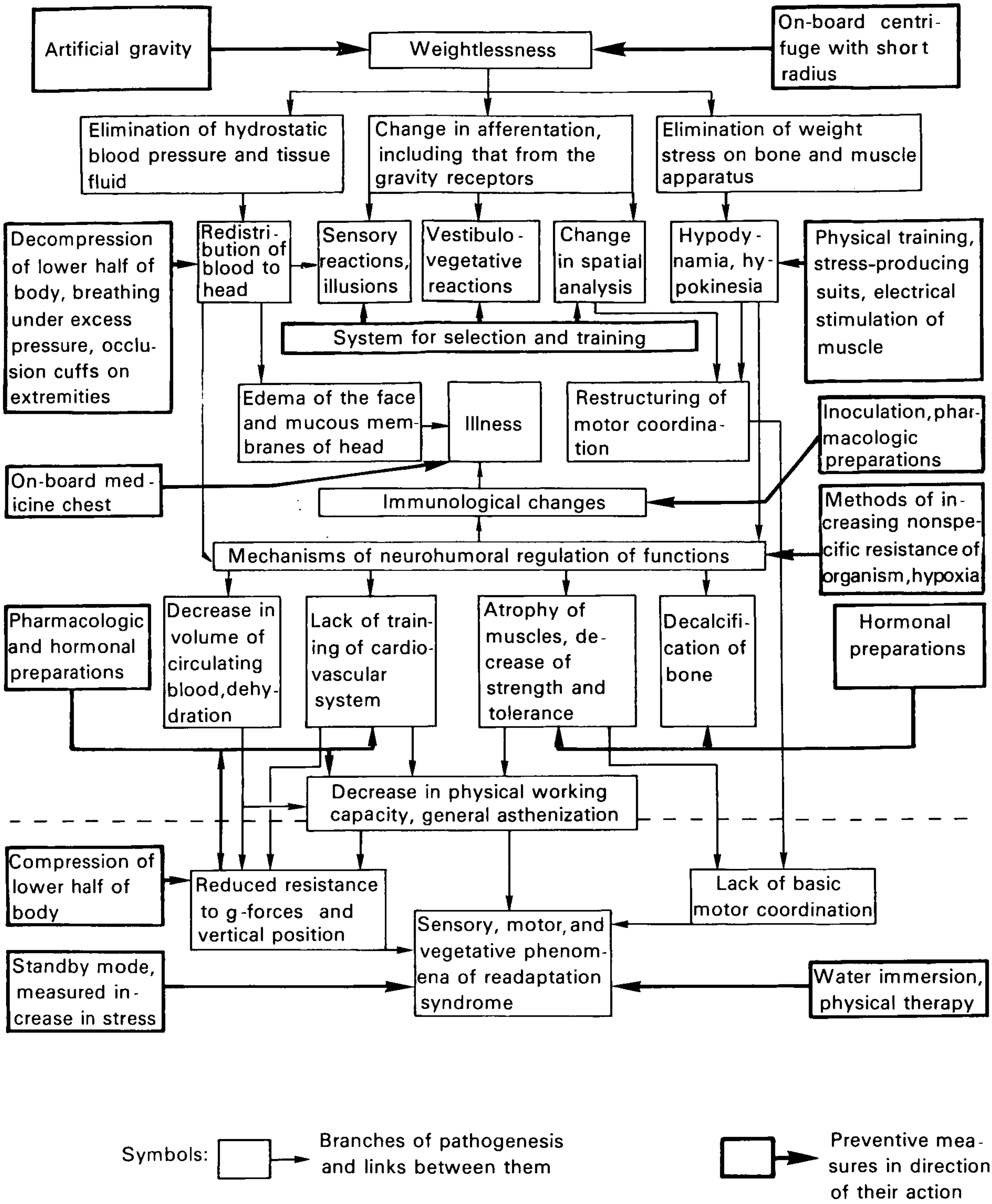

FIGURE 8.—Pathogenesis of problems caused by influence of weightlessness and directions of preventive actions. (Modified version of the system in [81])

TABLE 7.—*Means of Preventing Adverse Effects of Long-Term Weightlessness*

Partial adaptation to weightless state	
Physical exercise	**Acceleration**
Calisthenics All kinds of sports Tumbling, diving, zero-G training Isometric & isotonic contractions Bicycle and hand ergometers Head movements during zero-G	On-board centrifuge Trampoline Oscillating support Vibrating bed Space station rotation
Controlled environment	**Drugs and medication**
Hypoxia Low temperature Diets	Aldosterone Antidiuretic hormone Plasma expanders 9α-fluorohydrocortisone
Pressure	**Counteractives**
Pressure breathing Positive pressure cuffs Elastic garments Lower body negative pressure Anti-G suit	Glucose Pitressin Anabolic hormones Electrostimulation
Complete adaptation	
Preconditioning of organism to subgravity level or zero-G state; reconditioning organism to force of normal terrestrial gravitation	

side effects from the occlusion method predominated over those effects for which it was intended.

Pressure breathing (on the order of 200–300 mm water column) promotes expulsion of blood from the lesser circulation into the greater, restricts return of venous blood to the heart, and prevents atelectases caused by stagnation phenomena in the vessels of the lesser circulation [81, 120, 148]. When respiration under excess pressure was combined with compensatory counterpressure on the head and upper part of the body, blood was redistributed to the lower part of the body. This adequately simulates the presence of hydrostatic pressure with resulting consequences. In particular, the use of a G-suit while pressure breathing produces a gradient involving an increase in hydrostatic blood pressure in the lower half of the body, so that the level of compensation in such a suit gradually decreases toward the legs [27].

Excess pressure in the lungs during 6-h water immersion inhibited diuresis, salt excretion, and prevented orthostatic difficulties [120]. Another important parameter in characteristics of the method described is the level of variations in intrapleural pressure during respiration. Ventilation of the lungs under oscillating pressure increases diuresis [75]; similar data were obtained in 18-h immersion in water to the level of the neck [81]. For 2.5 h, subjects inhaled from the atmosphere and exhaled into water (resistance to expiration was 200 mm water column). The amount of urine excreted and negative water balance increased, while the orthostatic problems were not prevented. In total water immersion tests, respiration under pressure equivalent to external pressure on the chest reduced severity of changes in the water/salt balance and promoted orthostatic stability [117]. It can be concluded from these results that the principle of breathing under excess pressure is well-founded pathogenetically, and is promising. With appropriate structural designs, it could be used more widely in experiments and possibly during space flights.

Lower Body Negative Pressure (LBNP)

The method of producing lower body negative pressure (LBNP) is similar to that described above, differing from it primarily in the nature of the apparatus used [81, 156, 167, 201, 228, 231]. A device that produces slight negative air pressure around the lower half of the body makes it possible to redistribute blood as if there was excess pressure on the upper half of the body and lungs, and the lower half at normal pressure. However, both these methods fall short of completely simulating characteristics of blood redistribution when in the vertical position, where filling various parts of the body with blood is a function of smooth increase in hydrostatic pressure. When there is pressure change on only one level (e.g., around the waist), blood is gradually redistributed. Experimental studies have shown that even this incomplete simulation of the hydrostatic factor causes fluid stagnation in the organism, normalization of circulating plasma volume, and orthostatic stability under conditions of simulated weightlessness.

The hypobaric levels acting on the lower half of the body usually amount to 25–50 mm Hg in various experiments (below atmospheric pressure), while duration of action is from 1–2 to 10–12 h/d. Both constant and varying pressure values are employed, as well as daily practice sessions or training cycles during the last days of the experiment. In other words, the search for optimization of the technique is still ongoing. In particular, an increase in ADH secretion and stimulation of the sympathetic nervous system are due solely to an underpressure of 40 mm Hg or more [210]. A 15-min daily exposure to LBNP at a level of 70 mm Hg not only prevents a drop in orthostability of subjects deconditioned by 5-d water immersion and bed rest, but also significantly increases the level of this resistance in regard to the original level [54]. However, lower values of negative pressure obviously can have a positive physiologic effect. Thus, the influence of LBNP at the 30 mm Hg level produced the same changes in activity of the venous blood renin as did the orthostatic test performed at a 70° angle [67].

In water immersion experiments, when compensatory counterpressure of water on the lower half of the body was decreased by a total of 24–25 mm Hg, there was effective retention of body fluid, increase in body weight, and orthostatic stability in seven of eight subjects to degrees higher than those prior to the study [201]. During the LBNP sessions, there was increase in functional residual capacity, as well as in vital and total capacities of lungs [62]. By simulating natural orthostatic mechanisms, periodic LBNP sessions can prevent orthostatic instability in space flight without having to resort to more complicated devices.

Simulated Weightlessness Experiments

Promising results for prevention of unfavorable reactions were obtained by exposing subjects to accelerations on centrifuges with a short (about 2m) arm, where G-forces at the head level were close to zero and at leg level reached 2–3 G-units. The effect of longitudinal forces ($+G_z$), developed on such centrifuges, simulate hydrostatic pressure and thus affect the musculoskeletal system and gravity reception [183, 187, 205, 209]. These simulated weightlessness experiments produced increase in ADH, renin, and catecholamine secretion, decrease in diuresis and mineral excretion and restoration of circulating blood volume to normal [187, 205, 209]. Changes in ECG under the influence of longitudinal G-forces are linked to an increase in sympathetic tone [50].

Test subjects' work capacity and tolerance to acceleration on short-radius centrifuges are less than on centrifuges with relatively long arms [172, 185], which is related to the considerable gradient magnitude of G-forces acting on the body. After such rotations, certain problems affecting motor coordination developed. A total of only four rotations at $+4\ G_z$ force (level of the legs) of 7.5 min each noticeably prevented orthostatic instability, if orthostatic instability can be judged on the basis of collapse [37, 211]. However, pulse and blood pressure reactions to the orthostatic test were not improved. The centrifuge provided little protection against decrease in plasma volume during prolonged bed rest. Hence, a comprehensive evaluation of advantages and limitations of this preventive action remains to be carried out. If the need for such devices and their effectiveness is sufficiently well-established, the weight, power, volume, and control penalties, as well as side effects imposed by a short-arm centrifuge could be made acceptable to future spacecraft [33]. Shock stresses, which act in the direction of the longitudinal axis of the body and cause blood redistribution along the major vessels, can be included to a certain extent, among the group of methods discussed here [41, 265, 274].

Pharmaceuticals

Preventive action aimed at certain intermediate links of the pathogenetic chain can be effected with pharmacologic and hormonal preparations [73, 167, 197, 200, 229, 243, 245, 246]. Such substances proved effective in laboratory experiments and prevented phenomena of deconditioning and orthostatic instability following a certain period in a horizontal position [32, 118].

Restoration of a low volume of circulating blood due to retention of fluids and minerals may be achieved with hormonal preparations: vasopressin, pitressin, and 9 α-fluorohydrocortisone [32, 57, 119, 268]. Healthy subjects who received 9 α-fluorohydrocortisone for two 10-d periods of bed rest and two 10-d periods of normal (ambulatory) activity had larger volumes of plasma, more favorable pulse rate reaction in the orthostatic test and physical exercises, and their pulse rate restoration was the same as before the experiment [32]. Not all the preparations were equally effective. During bed rest and water immersion, pitressin suppressed diuresis and stabilized plasma volume, but did not prevent orthostatic stability [119]. A relative increase in tolerance of gravitational effects following tests with water immersion and prolonged hypodynamia was obtained with preparations (phenamine, caffeine, securinine) that stimulate the CNS, heart, and transversely striated muscles [200, 243]. Evidently, using such preparations during the most important portions of the flight, particularly before landing, is justified, regardless of their varying effects under these conditions [216].

G-Suits

In conjunction with postflight conditions, for preventing orthostatic disturbances, G-suits are recommended [81, 177, 178]. This prevention method promotes significant decrease (and in some cases, normalization) of the orthostatic reactions following simulated weightlessness experiments; the protective effect is reduction of blood volume in the lower extremities in the vertical position. The effect is particularly pronounced when prevention of orthostatic instability is accomplished on a complex basis and includes, with other influences, negative pressure on the lower half of the body during simulated weightlessness [81]. Satisfactory results were obtained with pressures on the order of 35–50 mm Hg produced in G-suit compartments. Prolonged (to 10–11 h) continuous wearing of G-suits with inflated compartments was tolerated with full satisfaction and did not lead to local or general unfavorable reactions. An elastic undergarment (fashioned on the pattern of a leotard) that exerted pressure on the lower half of the body also had favorable influence on resistance in the vertical position in both healthy individuals and those deconditioned following prolonged bed rest [252].

Establishing a backup system with gradual, measured increase in time in the vertical position is another theoretically possible way of relieving orthostatic stress postflight. Positive effects were obtained with orthostatic training by alternating 30-s passive changes in body position from 45° head down to 90° head up [176].

Prevention of principal consequences of lack of hydrostatic pressure under conditions of weightlessness, particularly orthostatic instability, is quite possible according to laboratory studies. Feasible methods are using negative pressure action on the lower half of the body at the end of the flight, pharmacologic stimulants 1 h prior to descent from orbit, a G-suit immediately after landing, and recommended procedures during readaptation.

Preventing Adverse Effects of Hypodynamia

Compensation for weight stress deficit on the musculoskeletal system under conditions of weightlessness by means of other stress-producing methods is a significant trend in preventive measures [271]. Such procedures require additional oxygen, food, and electrical energy aboard the spacecraft, which are not optimal technologically [233], but medically are considered advantageous. Vast experience in the physiology of sports, sports medicine, physical exercise for improved condition and therapeutic purposes supports the favorable effects of physical exercise, particularly on a methodological basis and as a planned regimen.

When insufficiency of muscle stress is caused by unfavorable changes in the condition of the organism, physical training is not only justified, but also necessary. Physical exercise studies with controlled limitation of motor activity, its spatial and force components, has promoted normalization of phenomena associated with the hypodynamic syndrome. Changes involving gas exchange [138, 173], nitrogen metabolism [234], the cardiovascular system [150, 198, 216], neuropsychic functions [30, 163, 189, 212] and immunobiologic reactivity [49] have been less prominent. The positive action of physical training has also been observed in states of the musculoskeletal system, physical working capacity, motor coordination [44, 100, 126, 137], and stress tolerance [44, 148].

Physical Exercise

Relatively few effects have been noted from physical training for preventing changes in mineral and fluid balance and orthostatic problems [41, 100, 126, 178, 242, 253], although certain positive results have been obtained [44, 202]. With physical exercise during strict bed rest for 5 weeks, subjects retained working capacity and showed no decrease in renin content of plasma as a response to venous blood stagnation in the lower extremities, although fainting states during orthostatic tests were frequent [158]. When physical exercise is performed during bed rest, there are decreases in the excretion of urine, sodium chlorine, and creatinine [71]. It may be assumed that retention of fluids and minerals may decrease as a result of sweating.

Evaluation of the results of physical training must take into account the degree of stresses, training programs, nature and structure of exercise, and training methods. There are advantages associated with training that include inertial shock effects along the longitudinal axis of the body (simulation of jumps in the horizontal position with use of shock absorbers and a solid support for legs for a reciprocating movement of the bed between two trampolines) [41, 265, 274]. Stimulation of the vessels in performing these exercises, as well as effects of vibration during bed rest can satisfactorily maintain the ability of blood vessels to compensate for decreased hydrostatic forces under reduced gravitation. Exercises for the lower extremities are important, which can decrease the tendency toward venous blood stagnation in the vertical position due to maintenance of tone, strength and mass of muscles, and possibly ability of vasoconstrictive mechansims to react to intravascular hydrostatic forces caused by gravity. In studies with 2 months' bed rest and various exercises, investigators gave preference to isotonic rather than isometric weight lifting [34]. Nevertheless, isometric exercises were also capable of reducing muscular atrophy [212], and made possible reduction of CNS sensory and musculomotor stimulation and normalized psychologic functions.

The necessary amount of physical stress varied widely, to values of 1000–1300 kcal/d, yet significantly smaller stresses produced satisfactory results [44, 274]. Springs of rubber expanders, bicycle ergometers, treadmill-type devices, and stress suits that create an axial static stress on the body by elastic cords are most frequently used for studying physical training [10, 81, 275]. Better results can be achieved by using methods and means of physical exercise to ensure primarily loading the antigravitational muscles, but which can also simultaneously affect other muscle groups.

It is desirable to maintain important motor actions such as walking and running in weightlessness or its simulation. An exercise device used in ground tests, which had a vertically mounted treadmill to which the subject (in a horizontal position) was attached by means of rubber straps, was found satisfactory. Constant static stress is imposed in the direction of the body's longitudinal axis making it possible to walk, run, jump, do situps, and lift weights under simulated weightlessness. This type of simulator promoted significant normalization of motor and vegetative functions and facilitated recovery following 70 d bed rest [81, 84, 274]. Total normalization of the hypodynamic symptoms could not be achieved in this study, which are observed with other methods of physical training [39, 100, 126, 152, 175]. No positive effects were found with physical training involving simulated weightlessness [41, 178, 188, 214, 242, 253], which is probably an extreme point of view. It can be explained by the kind of training method used or study of parameters linked pathogenetically only slightly with the nature of the motor activity. It can be concluded that all symptoms of unfavorable effects of weightlessness cannot be prevented by singular methods, but must be approached on a complex basis.

Although experience with physical exercise under spaceflight conditions is still limited [23, 59, 80, 180, 260], there is no doubt about the desirability of its further use in weightlessness. The Gemini 7 crew performed exercises with isometric contractions, and showed fewer bone tissue changes in terms of quantitative parameters determined by radiodensitometry than did astronauts without exercise [20]. Cosmonauts aboard the Salyut orbiting station had a positive opinion of physical training in flight [81]. Preliminary reports indicate successful and effective use of physical training aboard the Skylab orbiting station.

The question of nature, intensity, and even need for increased physical training of astronauts preflight is less clear. Opinions are partially contradictory. Theoretically, it might be assumed that a less physically trained organism, with all other conditions equal (sex, age, and so forth) would adapt better to lack of muscular activity than one highly trained. Abrupt cessation of training of qualified athletes will lead to disturbances of metabolism and functions of the nervous, cardiovascular, and other systems. Similar dangers in space flights are considered nonexistent [144, 145]. Planned physical preparation for weightless conditions is considered necessary, with emphasis on general tolerance that increases the organism's resistance to prolonged hypodynamia. It is reported that athletes withstand hypodynamia better than untrained persons and their recovery of the original condition is relatively more rapid [123].

In studies with water immersion, inhibition of the diuretic reaction and higher resistance to stress effects were found in athletes, compared with untrained persons [28]; however, changes involving blood proteins and electrolytes were the same for both groups [29]. It has been suggested that reflexes regulating their fluid volume have adapted to blood volume changes in athletes, since physical exercise is frequently accompanied by such changes.

Dissenting views on the role of the original condition for hypodynamic stress tolerance state that physical training does not constitute any advantages regarding tolerance to gravitational stresses (accelerations and orthostatic tests), although according to other data, athletes endure these effects better than untrained persons [52, 142, 227, 250]. In the deconditioned state and particularly after prolonged bed rest, changes in orthostatic resistance and physical working capacity in athletes were similar in trends and intensity to those in untrained persons [250], although physical training had a definite effect on tolerance to hypodynamia [122]. The combination of physical exercise with orthostatic training is not sufficient to prepare the organism for hypodynamia conditions [176]. Previously trained rats showed higher resistance to hypodynamia only during the initial phase of the experiment; at subsequent stages, changes in their muscular and motor nerve fibers became more pronounced than in untrained animals [106].

The problem of determining the optimum level and duration of physical exercise preflight evidently has not been solved. Nor is it clear whether it will be necessary to modify physical exercise systems in flight since the crew's physical condition will be deteriorating as compared to preflight levels. In prolonged ground tests, the amount of stress, which was satisfactory in the initial stage of hypodynamia, became excessive at later stages and led to overtraining symptoms. This question needs special study.

Other Methods

In preventive changes, due more or less to lack of weight stress on the musculoskeletal system, other methods of affecting various links of this pathogenetic chain may be used. Electrical stimulation of muscles, use of hormonal preparations that normalize protein and calcium metabolism, and methods of increasing the organism's resistance to infections appear promising [116, 197, 214]. Thus, in the prevention of the hypodynamic syndrome, a realistic concept is to apply constant variable stress on the musculoskeletal system, and use pharmacologic preparations.

The action of most of the preventive measures mentioned is not strictly selective, but frequently extends to combined branches of pathogenesis and thereby goes beyond the limits of the proposed classification, which emphasizes only primary effects for which a specific measure was designed. For example, the effect of LBNP, in addition to blood redistribution, is likewise accompanied by an axial load on the organism, the magnitude and point of application of which are determined by design of the vacuum device or garment. LBNP can also create sensations that are characteristic of the force of gravity action. A vacuum device used during bed rest creates, in particular, the feeling of being in a vertical position. A broad spectrum of action, which affects all triggering mechanisms associated with weightlessness, is obtained by the use of on-board centrifuges. Desirable preventive effects may be achieved only with a combination of preventive measures aimed at various links of the pathogenetic chain.

Methods of Nonspecific Prevention

Within the total system of prevention measures, it is necessary to take into account the possibility of an increase in the organism's nonspecific resistance. An obvious trend in this direction is a decrease of harmful effects of stress in space flight. For example, severity of the vestibulo-vegetative symptoms may cause additional dehydration and deconditioning of the organism in flight. In this connection, the system for preflight selection, vestibular training, and measures to stabilize the spacecraft constitute conditions that indirectly ensure better tolerance of weightlessness. Decreased noise level, temperature optimization, and appropriate hygienic and living conveniences also promote weightlessness tolerance. Light clothing during flight instead of constantly wearing space suits would decrease adverse effects of weightlessness in a 14-d flight compared with one of 8 d [23].

In the prevention of deconditioning, sufficient fluid intake and a balanced diet are also important. When increased excretion of vitamins was observed during prolonged hypodynamia, vitamin saturation of the diet had to be increased [214]. Additional calcium and potassium were added to the diet because of their increased losses during weightlessness [21, 23]. The addition of phosphates to food decreases both urine excretion and calcium losses in the blood, according to ground studies. The taste of food and beverages aboard spacecraft must ensure stimulation of appetite that has diminished from weightlessness.

The astronauts are occupied during flight with demanding operational and scientific activities, and their general state depends largely on the severity of fatigue. Thus it is necessary to provide appropriate conditions for rest, especially sleep, which, during flight, amounts to no more than 5–6 h/d [17, 23]. To prevent general deconditioning and undesirable mood changes in members of Antarctic expeditions, Soviet scientists recently tested so-called recovery preparations, which included ascorbic acid, glucose, phytin, lipocerebrin, calcium pangamate, thiamine bromide, methionine, calcium pantothenate, nicotinic acid, riboflavin, glutaminic acid, and elenium [121]. An EEG established that these preparations reduce severity of unfavorable changes in brain activity and individual behavior under prolonged exposure to sensory deprivation and stress. Although these results were obtained under terrestrial conditions at low altitudes, associated with moderate hypoxia, use of the preparations in space flight must be considered.

Additional factors that intensify the organism's reaction to weightlessness can also be evaluated from studies aboard biosatellites [1, 170, 196]. Serious problems in animals during these experiments evidently were caused not only by weightlessness, but also by rigid immobilization, loss of appetite, and isolation. Elimination of harmful effects associated with space flight may also decrease the unfavorable effects of weightlessness.

Another approach to increasing the organism's nonspecific resistance to counteract weightlessness may be the use of conditioning measures used widely under terrestrial conditions—ultraviolet irradiation and acclimatization to high altitude [149, 155, 247, 248]. In simulated weightlessness experiments, hypoxia prevented a decrease in erythrocyte mass but did not prevent plasma loss [231]; there were also decreases in electrolyte excretion, total urinary nitrogen, and bone substance demineralization [163]. Physiologic reactions to hypoxia are considered counter-reactions in the hypodynamic syndrome, similar to reactions to physical training [155, 237]. Within the total of preventive measures, periodic changes in spacecraft gas composition and other environmental parameters may find justifiable usage in time [82].

These nonspecific prevention methods are being partially used in modern space exploration programs. An increase in spacecraft internal volume and improved living conditions on-board is contributing markedly to reducing unfavorable reactions to weightlessness. The potential for increasing tolerance to this spaceflight factor is far from being exhausted; the search for effective methods of nonspecific prevention must continue.

A combination of preventive measures tested during Salyut orbiting station flight indicates adequate selective approaches and preventive measures [81]. The crew willingly used a physical exercise trainer, vacuum device for the lower half of the body, and G-suits. While the effectiveness of these measures has not yet been evaluated, a first step toward progress in this field of space medicine has been taken. The approach to devising a system of preventive measures was successfully demonstrated on the 28-d, 59-d, and 84-d flights of Skylab.

SUMMARY OF SKYLAB MISSIONS

The Skylab flights confirmed man's tolerance and ability to function properly in today's spacecraft. There were no major changes in cardiac functions; standardized exercise loads were incorporated into the on-board protocol to increase sensitivity of the vectorcardiograms for deconditioning effects. Significant in-flight changes included decreased resting heart rate, increased QRS magnitude and duration, anterior shift of QRS and T vectors, and increased T vector magnitude. There was a slight impediment of ventricular return or stroke volume. LBNP, also used to assess cardiovascular responses during weightlessness, usually exceeded those typical on Earth. These changes appeared early in-flight and continued, with periodic fluctuations, throughout the shorter missions.

In body biochemistry, fluids, electrolytes, and urinary calcium excretion increased, and total calcium balance shifted from slightly positive to equilibrium. The urinary creatinine level was unaffected. There were no changes in potassium balance, but phosphorus, nitrogen, magnesium, and sodium were excreted at a higher rate in-flight. Thus, a continuous mineral deficit may be associated with muscle and tissue loss. The actual body mass loss and muscle atrophy in Skylab 2 and 3 missions apparently was corrected in Skylab 4, probably through physical exercise, LBNP, and improved diet. The volume loss was unproportionally high for the lower extremitites of the body, but the fluid and tissue shifts from the legs upward, which had caused an increase of the astronauts's body size in space, were temporary and reversed after return to normal gravity.

Red cell mass decreased in the shorter Skylab mission, but this trend was transient and no destruction of red cells was found in the 84-d flight. In Skylab and Apollo, plasma volume decreases continued to be smaller than those reported after comparable periods of bed rest. Changes in cortisol and aldosterone metabolism, known to accompany weightlessness (but not bed rest), and red cell mass decreases probably explain the plasma volume findings.

Only minor changes were observed in the functional capacity of erythrocytes, determined by measuring concentrations of selected intracellular enzymes and metabolites. Tests of red cell osmotic regulation indicated some elevation in activity of the metabolic-dependent Na-K pump, with no significant alterations in the cellular Na and K concentrations or osmotic fragility. A transient shift in red cell specific gravity profile was observed on recovery, possibly related to changes in cellular water content.

Measurements of hemoconcentration (hematocrit, hemoglobin concentration, red cell count) indicated significant fluctuations postflight reflecting observed changes in red cell mass and plasma volume. There was no apparent reticulocytosis during the 18 days following the first Skylab mission, in spite of significant loss in red cell mass. However, the reticulocyte count and index increased significantly 5–7 d after completion of the second, longer duration flight.

There were no significant changes in either white blood cell count for differential. However, capacity of lymphocytes to respond to an in vitro mitogenic challenge was repressed postflight, and appeared related to mission duration. Only minor differences were observed in plasma protein patterns. In the second mission, changes in proteins involved in the coagulation process suggested a hypercoagulative condition. Interindividual variability was demonstrated in most experimental indices measured; however, constant patterns have emerged which include body weight change; increases in plasma renin activity; and elevations in urinary catecholamines, ADH, aldosterone, and cortisol concentrations. Plasma cortisol decreased in immediate postflight samples with subsequent increase in 24-h urines. Measurements of Skylab-2 and Skylab-3 crews after 28 and 59 d weightlessness, respectively, revealed significant losses only in the os calcis of the Skylab-3 scientist pilot. The Skylab 4 results lay within predicted limits.

Physiological measurements taken in-flight showed reduced diastolic blood pressure during exercise tests on the bicycle ergometer. There was also an increase in heart rate response during exercise after the Skylab 3 (59-d) mission. Performance loss during the first 4 d in weightlessness ranged about 25–40%.

Time-motion studies indicate that the initial changeover from preflight to in-flight (or, from 1-G to zero-G) was accompanied by substantial increase in performance time for most work and task activities. Equally important was that crewmen adjusted rapidly to the weightless environment and became proficient in developing techniques to optimize task performance.

In the first two Skylab missions, motion sickness posed an operational problem, some of the astronauts manifesting symptoms after entering the workshop and after splashdown. In the workshop, symptoms persisted as long as 3–5 d, although the drug combination I-scopolamine + *d*-amphetamine proved an effective countermeasure. In one of the Skylab experiments, susceptibility to motion sickness in the workshop (on and after mission day 8) was compared with susceptibility preflight and postflight.

There were motion sickness attacks in the Skylab 4 crews, the etiology of which is still unclear. It is hypothesized that the vestibular system in conjunction with the fluid shift phenomenon may produce the motion sickness syndrome in the early phase of weightlessness, depending upon such factors as duration of transition time, type and speed of head movements, motion of the spacecraft, and other pertinent environmental factors.

The astronauts experienced various types of stress during Skylab 2, 3, and 4 missions. However, physical exercises were efficient morale boosters, and overall, housekeeping, operational, and scientific tasks were never compromised. The men generally slept well, displaying slightly modified (less REM) sleep patterns. In summary, they adapted surprisingly well to longer periods of weightlessness and readapted quickly to the terrestrial gravity.

The results obtained during space flights and from completed laboratory studies show that man is capable of withstanding the effects of reduced weight or weightlessness for almost 3 mo. During the first decade, since the beginning of the conquest of space by man, more than 50 astronauts and cosmonauts have participated in flights that total more than a year. Weightlessness, then, has ceased to be a mysterious and hidden factor. Scientific facts have made it possible to discard a number of false threats and discover real ones resulting from the influence of weightlessness on the human organism, replacing a variety of hypotheses. However, most important in scientific research related to weightlessness has been not only analysis of results of previous flights, but also determination of possible further increase in flight duration.

A retrospective analysis of the state of the art indicates that the level of scientific theoretical thought at all stages in the development of astronautics has been sufficient to satisfy practical requirements in a timely fashion. Long before the practical need for eliminating unfavorable effects of prolonged weightlessness on the human organism, US and USSR laboratories had begun testing effective preventive measures. It was precisely the development of these measures that made it possible to plan space flights of increasing duration. However, as the length of the flights increase, new problems may arise, making even more important further studies linked to the effects of weightlessness on the human organism [266].

Four major areas of biomedical concern have been defined. The first consists of factors which bring about deconditioning of the cardiovascular system, changes in bone density and muscle mass, alterations in body fluid volume, orthostatic intolerance, loss of exercise and work capacity, and general systemic asthenia. Time course and end point of this process have not yet been established.

Researchers must pay serious, ongoing attention to blood circulation during weightlessness. Increased filling of vessels in the lesser circulation with blood in the absence of hydrostatic pressure can theoretically lead to arteriole spasms, increased pulmonary artery pressure (Ketayev reflex), and increased load on the right ventricle. Since this theory is in agreement with experimental data concerning increased central venous pressure in monkeys during weightlessness, and with the electrocardiographic recordings indicating increased load on the right ventricle during bed rest, the possible consequences of these circulatory changes must be evaluated clinicophysiologically.

The second area of concern encompasses neurosensory changes associated with the weightless state or transition into it. Specifically, attention is focused on motion sickness, presumably caused by alterations in vestibular response to zero-G. Although several astronauts experienced disturbances of well-being, they all recovered during weightless exposure. The relationship between individual history of motion sickness and weightlessness is still not clear. The combined effects of zero-G with other environmental conditions, such as sensory impoverishment, restriction of movements, hypokinesis, and emotional factors are still unknown. Various concepts and models of synergism must be tested and verified.

The third problem area, adaptation to weightlessness, concerns the process as well as its desirability. Various body systems and functions which have been defined, based on experimental and theoretical evidence, are involved in the adaptation process.

Evidence accumulated in exposures to actual and simulated weightlessness shows that, in the course of 1–2 mo, the functional state of the organism becomes relatively stable. However, there is certain danger that other factors may limit the flight duration, including increased susceptibility to illness, especially those connected with lowered resistance to infection, and neuroemotional changes. Changes during the adaptation and readaptation period will probably not differ significantly from those already known. However, the acuteness of a number of changes may increase (e.g., bone demineralization and muscular atrophy) if prophylactic measures are not taken. In short, prediction based on results of laboratory experiments will doubtlessly require further refinement and correction on the basis of data from longer actual flights.

In present schematic models of the adaptation process, much of the current data can be arranged in logical relationship. As new information is gained, these models will make it possible to determine more precisely the roles of the mechanisms responsible for the adaptation process, thereby supplying information necessary for effective prevention and therapy. Data obtained under laboratory conditions and during flights correlate, which resolves the question of adequacy and value of simulated weightlessness experiments performed on Earth.

The fourth area of concern is the development, testing, and perfecting of prophylaxis to prevent unfavorable effects of prolonged weightlessness on the human organism. This will serve to increase flight safety, fitness of the crew, and effectiveness of space missions. Evidence indicates that the extent of astronauts' adaptation to weightlessness, and to other force fields, can be manipulated by various means. A preventive medicine program for long-duration space missions, using combinations of effective countermeasures, may eliminate the need for artificial gravity in space vehicles. Investigations should be undertaken to provide optimum biomedical control techniques for future manned space missions.

An appropriate research program, conducted in-flight and on the ground, must be developed to obtain the information lacking. More precise measurement techniques, adequate equipment and instrumentation for in-flight experiments are needed, and new tests must be added. The biological factors that determine the organism's deconditioning process as well as its reconditioning during weightlessness must be fully determined. Reliability of the *human factor* in space is of importance for extended space flight equal to that of reliability of the space vehicle system. Hence, scientifically well-founded methods to prevent adverse effects of prolonged weightlessness on the human organism must be designed and utilized.

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