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Volume II, Book Two

ECOLOGICAL AND PHYSIOLOGICAL FOUNDATIONS OF SPACE BIOLOGY AND MEDICINE

CONTENTS

VOLUME II, BOOK TWO

(Chapters 1 through 9 of Volume II may be found in Volume II, Book One.)

INTRODUCTION

Space flight inevitably exposes the human to a number of unusual environmental stresses, both physical and mental, which can be divided into three broad basic groups: (1) elements resulting from flight dynamics which include acceleration, vibration, noise, and weightlessness; (2) elements characteristic of outer space as an inhabitable environment including the various radiations—ultraviolet, infrared, radio, microwave, and ionizing, and lack of a gaseous atmosphere supportive of life; and (3) elements intimately related to man living confined for a time in spacecraft cabins that involve problems connected with isolation as a member of a very small community, artificial atmosphere requirements, and altered biologic rhythms. The monumental personal and coordinated group responsibilities required for success of the flight mission, extraordinary working conditions in confinement, novelty of the situation and, indeed, the possible boredom attendant upon a long flight, are fraught with potential dangers that can significantly increase neuroemotional and psychologic stresses.

The material in world scientific literature in the field of aviation and space medicine and biology and related topics since the year 1920 is voluminous; it would be futile to attempt to review and reference all of it in one volume. Consequently, the authors of each chapter prepared a *critical* presentation of the present state of knowledge on the chapter topic. Information in each chapter emphasizes fundamental principles involved and summarizes laboratory experiments and spaceflight data. Wherever possible, the authors reference major publications with extensive bibliographies such as review papers, monographs, and other studies. The reader is referred to these publications for more complete bibliographic citations.

Although each chapter is relatively brief and concise, it became necessary to divide Volume II into two parts. In Book One of Volume II, the topics concern influence on the organism of artificial gaseous atmospheres, thermal properties, and altered atmospheric and dynamic flight factors. Book Two is an examination of influence on the organism of radiant energy, psychophysiologic problems of space flight, methods of physiologic investigations in flight, and transmission of information.

The extraordinary advances documented here have directly influenced methodology in related scientific fields; advancements in aerospace medicine have been applied to the practice of clinical medicine. Examples include progress in knowledge of pulmonary function and respiration tests, biomedical monitoring of the critically ill, materials for artificial heart valves and prosthetic devices, electronic pacemakers, development of fiber-optic lighting for endoscopic procedures, use of high-energy particles and heavy nuclei in radiobiology and therapy, and more efficient collection, storage, and retrieval of medical information.

In a rapidly advancing field of study and development, the solution of one problem frequently introduces new and even more challenging problems to be explored. Space biology and medicine is no exception. The authors of each chapter have identified those areas in their specialties where further investigations are needed to solve problems and answer questions which at present are unresolved.

In the field of space physiology, the problem of man's adaptation to weightlessness and subsequent readaptation to the gravitational force of Earth demands further intensive investigation. The mechanisms of adaptation and levels in the organism at which these occur, as well as the time sequence for retention of acquired adaptation, are phenomena that demand more comprehensive and in-depth study. The Skylab program has provided a tool whereby these problems and many others discussed in this volume can be intensively studied in the future.

The preparation of any book would not be possible without the direct support and assistance of numerous persons. Our sincere gratitude is extended to all those who actively participated in the preparation of this volume. This includes the authors, and a great number of specialists who compiled preliminary surveys of the literature and thereby significantly lightened the burdens of the authors. We wish to express our deep thanks to the translators whose tasks were complex and to the reviewers whose constructive comments and criticisms increased the quality of the chapters.

In conclusion, we consider it vital to note the significant contributions to the general ideas, policies, and structure of the volume made by Professor L. D. Carlson and the late Academician V. V. Parin.

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Part 3

EFFECT OF RADIANT ENERGY FROM SPACE ON THE ORGANISM

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Chapter 10

RADIO-FREQUENCY AND MICROWAVE ENERGIES, MAGNETIC AND ELECTRIC FIELDS

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Ordinarily, man exists in equilibrium within very narrow ranges of physical influences of the Earth, such as temperature, pressure, electromagnetic radiant energies, and geomagnetic fields. The advent of space travel has imposed the problem on man of taking him out of his normal sphere of environment.

In this chapter, the biologic effects of radiofrequency and microwave energies as well as electric and magnetic fields will be considered in relation to their influences on man's functional capabilities. It is most unlikely that these energies constitute a hazard to space flight under ordinary circumstances. Nevertheless, it is not only of academic interest but also of practical importance to review what we know about the influence of these energies on the physiology and behavior of organisms, to provide a basis for assessment and prediction of how man will fare in space.[1]

PHYSICAL CHARACTERISTICS

A common characteristic of electromagnetic fields (EMF) in all ranges—from geomagnetic and geoelectric fields of the Earth to solar radio emission—is the periodicity of their intensity changes: daily, monthly, and seasonal. A second common characteristic of the Earth's electrical field and of the atmospheric and radio-emission fields is their approximately identical minimum average intensity in the environments, on the order of 10^{-5} V/m (for radio emission in the atmosphere, for atmospherics, and for the electric field in a water medium). Along with periodic changes around this average value, spontaneous changes also occur (increase in intensity) in the EMF of the biosphere which vary from doubling their average level to exceeding it hundreds of times (radio emission) [211].

In future space operations, in addition to electromagnetic radiation, individuals may be exposed to a wide range of magnetic field intensities and gradients. Regular and irregular variations, thought to be caused by electric currents in the upper atmosphere, are superimposed on the steady geomagnetic field. Although electric currents are of a magnitude of several million amperes, the current density is very low. Also, the electric field which is intrinsically

[1] The material in this chapter constitutes review and evaluation of the pertinent literature by the author, in collaboration with Yu. I. Novitskiy, Z. V. Gordon, A. S. Presman, and Yu. A. Kholodov, whose contributions are gratefully acknowledged.

Additional support for this chapter was provided by Mrs. Margaret Anderson Bush, who not only typed several drafts of this manuscript with exemplary patience and competence, but also assisted in organizing and checking the bibliography. The author wishes to acknowledge her assistance with extreme gratitude.

linked with the current system is of an order of magnitude (10^{-4} V/cm), which apparently is completely harmless [64]. The physical characteristics of electromagnetic, magnetic, and electric fields in space are detailed in Volume I, Part 1, Chapter 2, providing further information.

To provide a basis for understanding the biologic effects of radio-frequency and microwave energies, review of some fundamental aspects of electromagnetic radiation is indicated. The nonionizing electromagnetic (EM) spectrum encompasses wavelengths from 3×10^8 meters to 3×10^{-2} nm, the energies of which can be propagated in a vacuum or through a number of media (air, water, tissue). Electromagnetic energy is generated through the change in the state of motion of an electron, this change being accompanied by the emission or absorption of EM energy. The EM waves vary in space and time, and the wavelength is inversely proportional to the magnitude of energy change. The physically varying qualities are actually a set of quantities: electric (E) and magnetic (H) field vectors. These vector quantities are related to each other perpendicularly and sinusoidally, and a resultant of the two vectors is the propagated EM wave. Measurable quantities which characterize the waves are: frequency of the sinusoidal activity, peak-to-peak length between the sine wave components (wavelength), and energy content.

The magnetic field is a geophysical phenomenon of unknown origin. The Earth is in a geomagnetic field imposed from the North and South Poles of the planet. Other properties of the magnetic field are its direction, homogeneity, and strength.

The energies of the electromagnetic spectrum (Fig. 1) [156] are propagated in the form of waves that act as small bundles of energy with many of the properties ordinarily ascribed to particles, which are called photons or quanta. The energies residing in photons (E) are directly proportional to the frequency of oscillation of the specific electromagnetic radiation associated with them by the formula $E = hv$, where h is Planck's constant. The photon energy measured in electron volts (eV) and the frequency of an electromagnetic wave are inversely proportional to the wavelength.

The radio-frequency (RF) portion of the electromagnetic spectrum is considered to extend from 0.03 MHz (very low frequency–VLF) to 300 000 MHz (extremely high frequency–EHF). On a functional or operational basis, frequencies in the region from 100 MHz to 300 000 MHz (300 GHz) are designated microwaves. The various RF bands are shown in Table 1. Radio-frequency energy, when propagated, is categorized into two discrete modes known as continuous wave (CW) and pulsed.

TABLE 1.—*Radio-Frequency Bands*

Frequency (MHz)	Designation	Definition
0.03	VLF	Very low frequency
0.03–0.3	LF	Low frequency
0.3–3	MF	Medium frequency
3–30	HF	High frequency
30–300	VHF	Very high frequency
300–3000	UHF	Ultrahigh frequency
3000–30 000	SHF	Super high frequency
30 000–300 000	EHF	Extremely high frequency

Biophysics

As the frequency decreases, the EM energy of the emitted photons is insufficient, under normal circumstances, to dislodge orbital electrons and produce ion pairs. The minimum photon energy capable of producing ionization in water, and atomic oxygen, hydrogen, nitrogen, and carbon, is between 12 and 15 eV. Inasmuch as these atoms constitute the basic elements of living tissue, 12 eV may be considered the lower limit for ionization in biologic systems. Since the energy value of 1 quantum RF is $0.024\text{–}4.0 \times 10^{-6}$ eV, the type of electronic excitation necessary for ionization is not possible, no matter how many quanta are absorbed.

The nonionizing radiant energies absorbed into the molecule either affect the electronic energy levels of its atoms, or change the rotational, vibrational, and transitional energies of the molecules. In biologic systems, absorbed RF energy is transformed into increased kinetic energy of the absorbing molecules, thereby producing a general heating of the tissue. Such heating results from both ionic conduction and vibration of the dipole molecules of water and proteins [125].

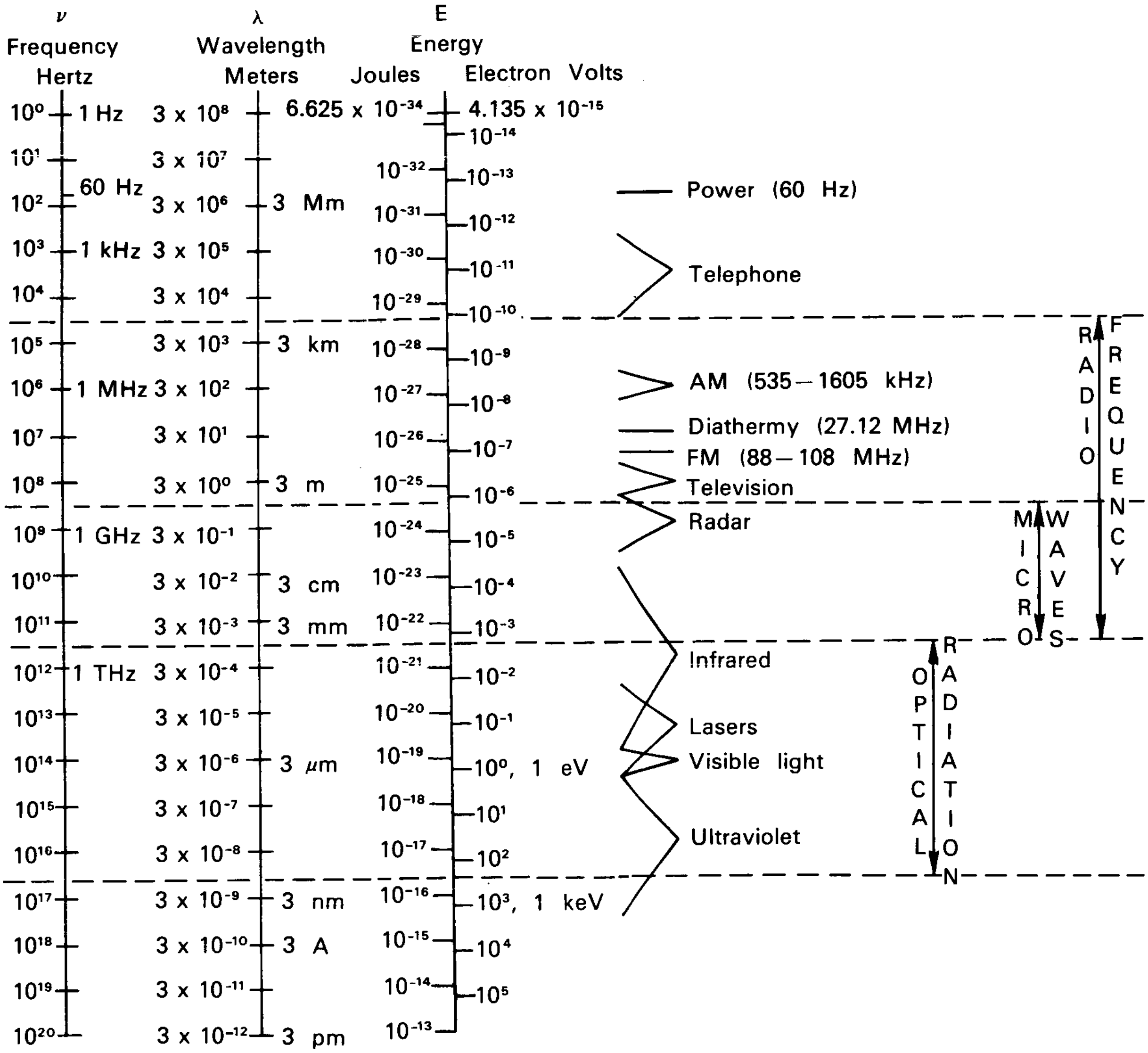

FIGURE 1. Nonionizing electromagnetic radiation (adapted from Ref. [156]).

The absorption of RF energy is dependent upon the electrical properties of the absorbing medium, specifically, its dielectric constant and electrical conductivity. These properties change as the frequency of the applied electrical field changes. Values of dielectric constant and electrical conductivity and depth of penetration have been determined for many tissues [260]. The absorption of RF energy is high and the depth of penetration low in tissues of high water content such as muscle, brain tissue, internal organs, and skin, while the absorption is lower in tissues of low water content such as fat and bone. Reflections between interfaces separating tissues of high and low water content can produce standing waves accompanied by *hot spots* that can be maximum in either tissue, regardless of dielectric constant or conductivity [125].

In considering the biologic effects of RF energy, the wavelength or frequency of the energy and its relationship to the physical dimensions of objects exposed to radiation become important factors. Absorption of energy radiating from a source into space also depends upon the relative absorption cross section of the irradiated objects. Thus, the size of the object with relation to the wavelength of the incident field plays a role [1].

A complete description of RF or microwave energy-tissue interactions is not possible in this chapter. Several excellent reviews, however, are available [1, 106, 125, 157, 185, 221, 245, 253–256, 260–263, 306].

PATHOPHYSIOLOGIC ASPECTS OF RADIO-FREQUENCY RADIATION

Systematic research on the biologic effects of RF radiation was begun immediately after World War II [282]. The results of these investigations are available in reports of the "Tri-Service Program" [189], reviews [50, 128, 187, 199, 245], books [98, 185, 211, 221, 293], and symposia proceedings [49, 73]. Glaser [86] has recently prepared a comprehensive bibliography of the literature on RF and microwave bioeffects.

Extensive investigations into microwave bioeffects during the last quarter century show conclusively that, for frequencies between 1200 and 24 500 MHz, exposure to power density of 100 mW/cm^2 for 1 h or more could have pathophysiologic manifestations of a thermal nature. Such manifestations would be characterized by temperature rise, which is a function of the thermal regulatory processes, and active adaptation of the animal. The end result is either reversible or irreversible change, depending on the conditions of the irradiation and the physiologic state of the animal. At power densities below 100 mW/cm^2, however, evidence of pathologic changes is nonexistent or equivocal. A great deal of discussion, nevertheless, has been engendered concerning the relative importance of thermal or nonthermal effects of RF and microwave radiation.

The results of some in vitro studies have been considered as evidence of nonthermal effects of RF radiation. Although some investigators still question the interpretation of these so-called nonthermal effects [187, 188, 199, 245, 251, 269, 270], several support *nonthermal* interactions between tissues and electric and magnetic fields [141, 185, 211, 221, 232].

The phenomenon of pearl-chain formation is suggested as evidence of *nonthermal* effects of RF. This phenomenon can be seen when suspended particles of charcoal, starch, milk, erythrocytes, or leukocytes are placed in a CW or pulsed RF field in the range 1–100 MHz. The particles become oriented into a chainlike form parallel to the electric lines of force. For each particle type there is a frequency range where the effect occurs at minimum field strength [125]. Apparently some pearl-chain formation is due to the attraction between particles in which dipole charges are induced by the RF fields [251]. It is also of interest that bacteria, planaria, and snails react to relatively weak electric and magnetic fields [37].

It is unlikely that any histologic structure exists in the body that is superficial, sufficiently large and free to be oriented [269]. The effect occurs in biologic tissue at field levels where there will be damaging thermal effects; therefore, pearl-chain formation has no biologic significance as far as the human body is concerned [251, 270].

The literature on the biologic effects of radio- and low-frequency (≤ 30 MHz) electromagnetic radiation has been reviewed by several authors [21, 141, 185, 190, 211, 232]. Bollinger [35] has reported on an extensive biomedical study of low-frequency RF radiation. Short-term (1 h) exposures of monkeys to 10.5, 19.3, and 26.6 MHz, under the experimental conditions which employed 100 to 200 mW/cm^2, did not produce discernible biologic effects.

An acoustic response corresponding to the frequency of modulation has been reported in individuals exposed to radars of relatively low average power [79]. This phenomenon apparently is not due to direct stimulation of neural fibers or cortical neural tissue, but rather to stimulation of the cochlea through electromechanical field forces by air or bone conduction [108, 276].

Thermal Effects

Body temperature increase during exposure to microwaves depends on: (a) the specific area of the body exposed and the efficiency of heat elimination; (b) intensity of field strength; (c) duration of exposure; (d) specific frequency or wavelength; and (e) thickness of skin and subcutaneous tissue. These variables determine the percentage of radiant energy absorbed by various tissues of the body [262, 263].

In partial body exposure under normal conditions, the body acts as a cooling reservoir, which stabilizes the temperature of the exposed part. The stabilization is due to an equilibrium established between the energy absorbed by the exposed part of the body and the amount of heat carried away from it. This heat transport is due to increased blood flow to cooler parts of the body, which are maintained at normal temperature by heat-regulating mechanisms of the body such as heat loss due to sweating evaporation, radiation, and convection. If the amount of absorbed energy exceeds the optimal amount of heat energy which can be handled by the mechanisms of temperature regulation, the excess energy will cause continuous temperature rise with time. Fever, and under some circumstances, local tissue destruction can result [262, 263].

Threshold for Perception

Awareness of microwave exposure is developed by several mechanisms including cutaneous thermal sensation or pain. The physiology of thermal sensation and pain in relation to microwave perception has been reviewed by Michaelson [190]. The subjective awareness of warmth could be an indicator of microwave exposure, and several investigators have established the thresholds for microwave-induced thermal sensation and pain in man [54, 55, 115, 259, 304]. The results of these studies are shown in Table 2; the data suggest that cutaneous perception could constitute a warning mechanism to prevent exposure to microwaves at possibly injurious levels.

Cataracts

Microwaves have been shown to produce cataracts in some experimental animals, and there are reports of microwave-induced cataracts in man. The techniques used and interpretation of results and conclusions, however, are quite often equivocal. Careful review of these reports indicates insufficient quantitation and correlation of pathophysiology with the level of microwave radiation. The literature on this subject is discussed by several reviewers [39, 128, 178, 187, 188, 190, 195, 199, 200, 245, 272].

Carpenter and associates [45] reported that single or repeated exposure of rabbits' eyes to 2450 MHz pulsed or CW can cause clouding when the lens temperature increases 4°C. The greater the power density the higher the temperature, and the time required to produce lenticular clouding was decreased. Latency time observed for lens changes averaged 3.5 days. Baillie [3] determined that lens opacification is a temperature-dependent phenomenon. Carpenter [45] also suggested a cumulative effect on the lens from repeated *subthreshold* exposures of rabbits' eyes to microwaves. The reported cumulative effect, for all practical purposes, is accumulation of damage resulting from repeated exposures, each individually capable of producing some degree of damage; no cumulative rise in temperature occurs if the interval between exposures exceeds the time required for the

TABLE 2.—*Stimulus Intensity to Produce a Threshold Sensation* [1]

Exposure time (s)	3000 MHz	10 000 MHz		Far infrared	
	Power density (mW/cm^2)	Power density (mW/cm^2)	Increase in skin temp. (°C)	Power density (mW/cm^2)	Increase in skin temp. (°C)
1	58.6	21.0	0.025	4.2–8.4	0.035
2	46.0	16.7	0.040	4.2	0.025
4	33.5	12.6	0.060	4.2	
20	3100.0 [2]				
60	1800.0 [2]				
120	1000.0 [2]				

[1] Data from Cook [54] and Hendler [115].
[2] Threshold for pain sensation.

tissue to return to normal temperature. The concept of cumulative effect in relation to microwave-induced cataractogenesis is discussed by Michaelson [187].

Zaret and associates [313] performed ophthalmologic studies among selected microwave workers and reported no late lens defects peculiar to microwave exposure. They did note a small, statistically significant increase in posterior polar defects but no decrement in visual acuity. In other studies, it has been shown that lenticular markings of a possible congenital nature may reach a certain magnitude and progress no further, even when there is no change in the occupational setting [272]. It should be noted that the reports by Zaret and associates [313] are not accepted by the community of ophthalmologists. The reports, in general, do not indicate any relationship between the actual power level and pathology. Analysis of the reports of microwave-induced cataracts [117, 155, 201, 273] permits the conclusion that, as a rule, the development or detection of cataract coincide only accidentally in time with the exposure to microwaves and, it was actually due to other causes such as uveitis, congenital clouding, or the like [272]. It should also be recognized that individuals studied in such surveys could have been exposed to ionizing radiation as well as to microwaves.

In actual radar or microwave-communication operation, it is important to note that a technician is rarely exposed to high-intensity microwaves for a potentially harmful time, since he would probably feel the heat due to energy absorption which would serve as a warning. Apparently, damage to the lens from exposure to microwaves may seldom occur (if at all), and only under unusual circumstances. Under normal working conditions, personnel are exposed at levels representing several orders of magnitude below the level with which various changes in the lens are produced experimentally. Exposure to a rotating radar antenna is no practical threat to the lens, even at high power densities [272]. There are no experimental data demonstrating cataract formation associated with whole-animal exposure [187, 195, 272]. On the basis of present knowledge of conditions under which experimental *microwave cataract* arises and its diagnosis and treatment, it must be acknowledged that none of the cases of microwave-induced cataracts in man described in the literature is fully verified. Well-controlled prospective epidemiologic studies associated with accurate records of microwave exposure will be required to determine if occupational exposure to power densities in the range of 10–100 mW/cm^2 can result in cataract formation [272].

Effects on Reproduction

The testes. The effect of microwaves on the testes has been studied [74, 95, 123, 266]. Exposure of the scrotal area at high-power densities ($>$ 250 mW/cm^2) results in varying degrees of testicular damage such as edema, enlargement of the testis, atrophy, fibrosis, and coagulation necrosis of seminiferous tubules in rats, rabbits, or dogs exposed to 2450, 3000, 10 000, or 24 000 MHz.

Ely et al [74], using 2880 MHz, tried to determine the lowest power density which would produce minimal changes in the most sensitive animal of a group of dogs. They found 5 mW/cm^2 to be the *threshold* for testicular damage, for an indefinite exposure. The field intensity required to maintain a threshold temperature was chosen from the most sensitive of the 35 dogs exposed. The threshold temperature of 37°C was the lowest damaging temperature found in this study. It should be noted that this was based on a single animal which may be spurious; sufficient controls were not used, and, there may have been a normal incidence of histologic damage in unexposed animals. The authors point out that the damage observed at such low-power levels is slight, almost certainly fully recoverable, and the response of the testes to heating from a radar source is similar to that from other sources of heat. The same effect, which is reversible, can also be caused by a hot bath or constrictive clothing and should therefore not be considered hazardous. It is questionable, therefore, whether such effects should be legitimately considered as a basis for appraisal of hazard from microwave exposure [128].

Whole-body exposure of dogs to 24 000 MHz [61] or guinea pigs to 3000 MHz [77] did not affect reproduction. Exposure to 3000 MHz, 8 mW/cm^2 did not affect mating of mice or rats [204].

Reports of human sterility from exposure to microwaves are questionable. Barron and associates [17, 18] found no evidence of fertility changes in their surveys of humans. There is one case report of altered fertility in a man from unusually high exposures to microwaves [244]; without preexposure examination of this individual, any causal relationship is tenuous. The patient, a repairman at a weather radar installation, frequently performed maintenance on the radar antenna while the equipment was in operation; he did not wear protective clothing. On occasion, while working near the microwave beam, the patient noted a sensation of warmth. He was exposed repeatedly to microwave power densities more than 3000 times the currently accepted safe level established by the US Air Force.

The testes are sensitive to temperature elevation because of their physical location relative to the body surface and poor ability to dissipate heat by means of the vascular system. Any clothing that prevents maintenance of an intrascrotal temperature that is at least 1 °C below body temperature will significantly lower sperm output. Testicular reaction to heat injury resulting from RF radiation appears to be the same as the reaction to high fever associated with many illnesses.

The ovaries. Gorodetskaya [96] has reported that exposure of 2- to 3-month-old mice to 10 000 MHz, 400 mW/cm^2 for 5 min caused a decrease in the number of estral cycles with increase in duration of individual cycle stages. One month after exposure, the estral pattern was reestablished.

The mating of normal females and microwave-irradiated males resulted in a decrease in number of progeny, lower average weight of offspring, and increase in number of stillborn. When mated with normals, microwave-treated females produced weaker offspring than did similarly treated males.

Deformed offspring were observed exclusively from microwave-exposed females. Histologic studies revealed degenerative changes in the germinal epithelium. In the ovaries, follicular epithelial cells were degenerated with pyknotic nuclei. Comparison of changes in testis and ovary indicate the female gonads to be more sensitive. Similar but less pronounced changes result from convectional heating.

In other reports, reproductive studies on guinea pigs exposed to 3 GHz microwaves [77] and dogs exposed to 24 GHz indicated no adverse effects from exposure [61]. Exposure of rats and mice to 3 GHz (ca. 10 mW/cm^2) had no detectable effect on mating behavior [204].

Timeskova [289] studied the influence of microwaves on testicular function, impregnation, the course of pregnancy, and the offspring of sexually mature rabbits subjected to whole-body irradiation with centimeter microwaves at 100 mW/cm^2 with an exposure time of 15 min. Their rectal temperatures rose by 3°—4°C. In these experiments it was found that the granulosa cells in the mature and maturing follicles of the rabbits degenerated and decomposed. The irradiated females were difficult to mate and were impregnated only after 6 or even 10 days with the male. It should be pointed out that 100 mW/cm^2 is an unrealistically high power density and will no doubt cause such effects by the extreme thermalization.

Two female beagle dogs were exposed to microwave radiation of 24 000 MHz at a power density of 20 mW/cm^2. During a period of 20 months, one dog was exposed for a total of 2631 h (6.7 h/d, 5 d/wk). Another dog was exposed for a total of 3670 h (16.5 h/d, 4 d/wk). Both dogs reproduced normally. One animal had a litter of five (one stillborn) after 1500 h exposure; the other dog had two litters—five puppies (two stillborn) after 200 h exposure, and four puppies (one stillborn) after 1850 h exposure [61].

Although some experimental data indicate that high power densities can affect the testes and ovary, it is apparent that these responses are a result of the heat which develops in the animal. The experimental evidence tends to support the conclusion that the effects of microwave radiation on the gonads are primarily of thermal origin.

There is little information on the response of the human female. Rubin and Erdman [246] observed that neither conception nor pregnancy in humans was disturbed by therapeutic microwave diathermy application. Disturbance in menstruation is mentioned by Osipov [217] as one of the effects of an electromagnetic field on the individual, although results of other studies of women working 3 to 11 years in microwave fields do not support this report [218].

Effects reported by Marha and associates [184, 185] include: decreased spermatogenesis, altered sex ratio of births, changes in menstrual patterns, retarded fetal development, congenital defects in newborn babies, and decreased lactation in nursing mothers. They also report an increased incidence of miscarriages in women working with microwaves. Because of these reports, adolescents and gravid females are not permitted to work with HF, VHF, or UHF equipment as a preventive measure [185]. According to these authors, such effects occur at thermal microwave exposure intensities (greater than 10 mW/cm^2). It must be noted that in some countries a far greater number of women are employed in the industrial work force than in others; many of these women work swing shifts after taking care of their families during the day. The influence of such interacting variables may have been overlooked in these surveys. More details are needed relating work cycle/work shift information of the affected women, how it affects the menstrual patterns, and lactation of nursing mothers who are part of an occupationally equivalent control population, especially with respect to work shift. These reports raise the question: What effects do working a regular job, or irregular shifts, have on lactation and menstruation in general? Also: What is the incidence and prevalence of miscarriages in the general working population that is equivalent to the microwave-exposed group in every way except exposure?

Visceral Pathophysiology

In rats exposed whole-body to 2450 MHz, 100±15% mW/cm^2, from 8–15 min for 1–28 exposures, histopathologic examination of the organs (testis, eye lens, liver, spleen, lung, kidney, heart, thyroid, and brain) was made. The only significant observation in the microwave-exposed group was atrophy of the tubules of the testis. No other significant histopathologic changes were observed in the microwave-irradiated rats [129]. It should be noted that the power density was extremely high, especially for rats.

In a study by McLees et al [179] in which partially hepatectomized rats were exposed to 13.12 MHz ca 1 mW/g, examination of liver sections obtained immediately after 28 to 44 h exposure failed to reveal any definite pathologic changes. There was no evidence of hepatocyte swelling or erythrocyte accumulation.

Delay in gastric emptying time has been described in dogs exposed to 300–3000 MHz 1 mW/cm^2 for 30 min [99, 281]. Repeated exposures resulted in diminution of the effect. Increased gastric evacuation was noted after partial denervation of the stomach. Similar results were obtained in guinea pigs exposed to 3000 MHz, 0.5–1 mW/cm^2 [281]. In a study of stomach secretory function, when dogs were irradiated with 300–3000 MHz, 1 mW/cm^2, secretion of gastric juices in response to meat was suppressed significantly, especially during the first (nervous reflex) phase, and its acidity was lowered [281].

According to Subbota [281], under exposure to microwaves of low, "nonthermal" intensity, the dominant picture is suppression of the evacuatory motor function of the gastrointestinal tract. Since the opposite appears on partial denervation of the stomach, it must be assumed that microwaves at "nonthermal" levels have a dual effect on this gastrointestinal tract function: mediated action (through changes in function of the CNS) and a direct effect on the organ or its local innervation. Possible humoral-chemical changes capable of producing the same shifts should not be excluded.

Pitenin and Subbota [226] have reported that local irradiation of the anterior celiac region in rabbits (which corresponds to the epigastric region in man) causes selective injury to the stomach mucosa. After 10 min exposure to 2450 MHz, 110–120 mW/cm^2, half the animals developed gastric ulcers on the anterior wall of the stomach, i.e., on the wall nearest the source of radiation. All other tissues through which the microwave energy had penetrated before reaching the mucosa remained practically undamaged. The temperature of the stomach contents did not rise above 40°–42°C. At still higher radiation intensities (150 mW/cm² and more), ulcers were found in practically all the animals.

It appears that the amount of temperature developed in the visceral organs during 2450 MHz microwave irradiation may be a function of animal size as well as duration and intensity of radiation. Imig and Searle [122], and Searle et al [264] showed that the amount of temperature developed in visceral tissues during exposure was inversely related to animal size, being greatest in rabbits, next in small dogs, and lowest in large dogs.

Effect on Hematopoietic Tissue and Blood

Analysis of blood changes has been carried out by numerous investigators because of its easy accessibility and availability of quantitative techniques, to study the biologic effects of microwaves and RF. Most of the data are based on studies with rodents, rabbits, and dogs under controlled exposure conditions, or in man where field intensities and duration of exposure are not easily measured.

A number of authors state that the blood picture is not affected noticeably by RF or microwaves [17, 57, 169, 233], however, leukocytosis, lymphocytopenia, eosinopenia, alteration in red blood cell lifespan and bone marrow function, as well as a drop in hemoglobin have been reported [87, 118, 119, 120, 198, 247, 249]. The effect of microwave radiation on hematopoietic organs has also been studied. Some investigators have been unable to detect any shifts [300]. Kitsovskaya [145] observed only a slight decrease in the number of polymorphonuclear neutrophils. The time of onset and degree of hematopoietic change may be dependent upon the wavelength, field intensity, and duration of exposure [145, 194, 198]. It is suggested that leukocyte response is related to hypothalamic-hypophysial-adrenal stimulation due to thermal stress [193].

A significant decrease in leukocytes and erythrocytes was noted in rats after 7 h of continuous exposure to 24 000 MHz, 20 mW/cm² with recovery in 1 week; 10 min of continuous exposure to 20 mW/cm²; and 3 h of continuous exposure to 10 mW/cm² with recovery in 2 days [62].

In mice irradiated with 10 000 MHz at 450 mW/cm² for 5 min, decreases in erythrocyte, leukocyte, and hemoglobin values were noted immediately, and at 1 and 5 days. Hematologic recovery was evident 10 days after exposure. Convectional heat produced less distinct changes, with more rapid recovery than when exposed to microwaves [97]. Leukocytosis was reported in mice enclosed in a slowly rotating polystyrene cabin, irradiated daily for 16–19 months at 10 000 MHz, 100 mW/cm², 4.5 min/d. The rectal temperature rose an average of 3.3°C after each radiation treatment [228].

Hyde and Friedman [121] studied the effects from exposure of mice to 3000 MHz, 20 mW/cm² and 10 000 MHz, 17, 40, or 60 mW/cm² up to 15 min. No significant effect on total or differential leukocyte count or hemoglobin concentration was noted immediately or 3, 7, or 20 days after exposure. There were no changes in femoral bone marrow other than inconstant, slight increase in the eosinophil series of the exposed animals which was not reflected in peripheral blood counts.

Kitsovskaya [145] subjected rats to 3000 MHz according to the following schedule: 10 mW/cm², 60 min, 216 days; 40 mW/cm², 15 min, 20 days; 100 mW/cm², 5 min, 6 days. At 40 mW/cm² and 100 mW/cm², total red blood cell count (RBC), white blood cell count (WBC), and absolute lymphocytes were decreased; granulocytes and reticulocytes were elevated. At 10 mW/cm², total WBC, and absolute lymphocytes decreased, and granulocytes increased. Bone marrow examination revealed erythroid hyperplasia at the higher power levels. The blood did not return to normal state months after the series of irradiations was discontinued.

Baranski [5] exposed guinea pigs and rabbits to 3000 MHz pulsed or CW 3.5 mW/cm² power density for 3 months, 3 h daily. Peripheral blood, bone marrow, lymph nodes, and spleen were examined. Increases in absolute lymphocyte counts in peripheral blood, abnormalities in nuclear structure, mitosis in the erythroblastic cell series in the bone marrow and in lymphoid cells in lymph nodes and spleen were observed. Baranski suggests that extrathermal complex interactions seem to be the underlying mechanism for the changes.

Budd et al [40] investigated the sensitivity of the fetal rat hematologic system following in utero microwave irradiation. Pregnant Sprague-Dawley rats were exposed one at a time to whole-body 2450 MHz 100 mW/cm^2 CW microwaves at 15 days gestation. Under these conditions, the rectal temperature of the pregnant rats increased 4.2°C above that of the controls. Hematologic changes were measured in the pregnant rats at 4 h, 24 h, and 5 d postirradiation (shortly before the fetuses were removed). Body and spleen weights, and hematologic changes were measured in the fetal rats at 20 days gestation. No significant differences were found between control and microwave-exposed pregnant rats in body weight, total leukocyte count, erythrocyte count, hematocrit, or hemoglobin value. Microwave-irradiated fetuses had significantly lower spleen weights ($P < 0.05$), total leukocyte counts ($P < 0.01$), and somewhat lower hemoglobin values ($P < 0.10$) than controls. No appreciable differences were observed between microwave-irradiated fetuses and their controls in body weight, ^{59}Fe uptake in blood, or fetal resorption. The lack of any effect in the pregnant rat exposed to 100 mW/cm^2 or any greater effect in the fetus than that evidenced is worthy of note.

Spalding [278] exposed mice to 800 MHz 2 h daily for 120 days in a closed system (wave guide) at an incidence level of 43 mW/cm^2. Body weight, red and white blood cell count, hematocrit, hemoglobin, growth, voluntary activity and life span remained normal. Ivanov [124] reported distinct changes in the proportions of white and red bone marrow stem cells in rabbits chronically exposed to meter waves at 1 mW/cm^2.

In dogs exposed whole-body to microwaves there was a marked decrease in lymphocytes and eosinophils after 6 h, 2800 MHz 100 mW/cm^2 [195]. The neutrophils remained slightly increased at 24 h, while eosinophil and lymphocyte values returned to normal levels. Following 2 h exposure at 165 mW/cm^2, there was slight leukopenia and decrease in neutrophils. When the exposure was 3 h, leukocytosis was evident immediately, and was more marked at 24 h, reflecting the neutrophil response. There was a moderate decline in lymphocytes immediately following 2 to 3 h exposure, with recovery to the preexposure level at 24 h. Following 2 h exposure, there was slight decrease in eosinophils which was unchanged at 24 h. Eosinophil change was negligible at the termination of 3 h exposure and moderately decreased at 24 h.

After exposure to 1285 MHz, 100 mW/cm^2, for 6 h, there was an increase in leukocytes and neutrophils. At 24 h, the neutrophil level was still noticeably increased from the preexposure level. Lymphocyte and eosinophil values were moderately depressed and at 24 h, slightly exceeded their initial values.

Six hours of exposure to 200 MHz, 165 mW/cm^2 resulted in a marked increase in neutrophils and a mild decrease in lymphocytes. The leukocyte count was further increased, and the lymphocytes markedly increased the following day. Eosinophils were moderately decreased [195].

Comparison of leukocyte changes over a 60-day period after a 6-h exposure at 100 mW/cm^2, 2800 MHz or 1285 MHz, revealed that 1285 MHz had a slightly greater and more prolonged effect on leukocyte response. Recovery of leukocytes and neutrophils to the preexposure level occurred 1 to 2 weeks after 1285 MHz and within 1 week after 2800 MHz exposure. A 25 to 40% lymphocyte increase from the preexposure level was noted from 1 day to 2 years after 1285 MHz exposure. The reticulocyte count was moderately diminished during this period. Lymphocytopenia from 2800 MHz was followed by recovery to 95% of initial value in 24 h and a gradual decrease to 54% of initial value by 60 days.

Early and sustained leukocytosis in dogs exposed to thermogenic levels of microwaves may be related to stimulation of the hematopoietic system, leukocytic mobilization, or recirculation of sequestered cells. Eosinopenia and transient lymphocytopenia with rebound or overcompensation when accompanied by neutrophilia may indicate increased adrenal function.

Rhesus monkeys were exposed to 10.5 MHz, 200 mW/cm² for 1 h; 19.27 MHz, 170 mW/cm² for 4 h, and for 13 consecutive days 4 h each day at a power density of 115 mW/cm²; and 26.6 MHz, 100 mW/cm² for 1 h. Hematologic examinations which included hematocrit, total white cell count, differential count, and morphologic evaluations, indicated no obvious effect of RF exposure on the formed elements of the blood. Hematocrit, total white cells, and differential cell estimations fell within the range of normal. Platelet level remained normal, and there were no changes in the clotting mechanism. Histologic examination of bone marrow and spleen revealed no evident pathology [205]. The authors concluded that RF exposure had no effect on the hematopoietic system.

There are few reports of RF—or microwave-induced hematologic changes in man. In surveys of military and industrial radar personnel, variable hematologic changes have been reported [17, 18, 57, 110, 160, 170, 203, 275]. Reticulocytosis has been noted in some studies [160, 275].

Barron et al [18] reported an apparent decrease in polymorphonuclear cells and increase in eosinophils and monocytes in a group of occupationally exposed workers. In a later report, however, these authors [17] found the decreases incorrect, due to variation in a laboratory technician's interpretation.

Baranski and Czerski [7] reported on the hematologic examination of a large group of people occupationally exposed to microwaves. They concluded that a small drop in the number of erythrocytes takes place in all individuals exposed to microwaves; incidence is related to length of employment and degree of exposure. Various leukocyte shifts occur in the first year of employment, with normalization later, a symptom which does not appear in groups having worked for 1 to 5 years. A tendency toward lymphocytosis with accompanying eosinophilia is apparent in persons having worked more than 5 years under conditions of low and medium microwave exposure. Three groups of leukocyte changes occur in persons exposed to substantial irradiation for more than 5 years: most frequent are absolute and relative lymphocytosis accompanied by eosinophilia and monocytosis, or relative lymphocytosis; next is absolute lymphocytosis with monocytosis; and neutrophilic leukocytosis is last. About 50% of persons exposed to microwaves show a moderate drop in platelet number. This poses the question if exposure to x-rays or other environmental factors may not be the entity, or at least a contributor, in such findings [221].

Cardiovascular Effects

Several investigators report that exposure of animals or man to electromagnetic radiation may result in direct or indirect effects on the cardiovascular system [68, 89, 151, 159, 209, 212, 215, 216, 230, 233, 279, 301]. Some authors suggest that exposure to microwaves at intensities that do not produce appreciable thermal effects may lead to functional changes, which are observed in connection with acute as well as chronic exposures [89, 233].

Disturbances of the blood circulation that have been described [101] are evidenced by change in blood flow [241], usually an increase in flow which is proportional to both the intensity and duration of exposure [242]; a decrease is observed only in denervated extremities. These phenomena are related to vasodilation. Negative results, however, have also been reported in studies of persons working with radar [247]. Aberrations in vascular reactions, such as oscillation of vascular tonus [75], have also been reported.

Increased heart rate has been observed after exposure to power densities of 50–130 mW/cm² for variable periods ranging 10–140 min [56, 186, 279]. Slowing of heart rate is reported by some investigators with low (or which they consider nonthermal) levels of microwaves [137, 249, 300, 301]; others have reported increased heart rate with low-level microwave exposure over the dorsal aspect of rabbits [235, 236].

Decrease in blood pressure from microwave exposure has been reported by some investigators [89, 92, 137, 214, 249] while by others, an increase in blood pressure [56, 176, 224]. Also, blood pressure rises slightly at first and then begins to fall [2, 16, 247], an effect which can be pronounced and last for several weeks following exposure. To confuse the picture still more, a decrease in blood pressure in man and an increase in blood pressure in the rabbit under comparable irradiation has also been reported [15, 16]. These somewhat contradictory reports indicate that the relationship is quite complex and these discrepancies reveal several defects in some experiments which should be recognized, such as frequency, power density of microwaves, duration of exposure, animal restraint, and inadequacy of statistical analysis [286].

Subbota [281] has noted that when rabbits were chronically exposed to 2450 MHz, 10 mW/cm^2, little change in arterial pressure was evident. However, hemodynamic shifts were quite clearly in evidence even at 1 mW/cm^2. No hemodynamic shifts were observed beginning with the fourth or fifth treatment. When the rabbits were exposed to 50 mW/cm^2, the arterial pressure dropped, then recovered its initial level after 1–2 h. Characteristically, these effects were registered only after the first few microwave treatments, and later, as the treatments were repeated (once every 1–3 days), the arterial pressure change became smaller in degree until disappearance at the ninth or tenth treatment. The rectal temperature rise was 1°–1.7°C after the first exposure, but 0.7°–0.9°C after nine to ten treatments.

Presman and Levitina [235, 236] reported a differential effect on the heart rate of rabbits; the animals were exposed to 2450 MHz (CW), 7–12 mW/cm^2, for 20 min. Ventral exposure resulted in bradycardia (slowing of heart beat). Irradiation of the dorsal portions of the head produced an acceleration. In a later study the same investigators used pulsed 3000 MHz at a power density of 3–5 mW/cm^2. Under these conditions, irradiation of the ventral aspect of the animal caused a shift of rhythm in the direction of acceleration. This effect was far more pronounced with the pulse-modulated radiation than with CW. The investigators suggest that the possible cause lies in the deeper penetration into the tissue of the modulated waves. Presman also interprets these data as indicating an effect on the parasympathetic nervous system (vagus nerve) during ventral irradiation and on the sympathetic nervous system during dorsal exposure.

Levitina [159] has suggested that the peripheral nervous system is the mediator between microwave radiation and its possible effects on heart rate. Irradiation of ventral body areas of rabbits with high power density-pulsed microwaves resulted in a lower pulse. If the skin was anesthetized, cardiac rate did not change. The author concluded that the reduced cardiac rhythm, as the result of ventral exposure, was due to microwaves acting on the skin receptors.

McAfee [175] points out how data can be misinterpreted to be the result of some unknown effect of microwave radiation, when hyperthermal effects are not involved. In cats, when peripheral nerves are stimulated by 45°C temperature, adrenal medullary secretion occurs and a rise in blood pressure is developed as a result of adrenaline secretion [173]. The halogenated hydrocarbon anesthetics in combination with injected adrenalin frequently produce ventricular arrhythmias [132]. If an animal is irradiated with microwaves and the analeptic effect is elicited deliberately or accidentally, a sequence of events will be observed identical to that obtained by simply injecting adrenalin. With some anesthetic agents the heart rate increases in dogs, and in unanesthetized animals heart rate is modified by an analeptic response if such response is accidentally produced [173]. McAfee [175] questions whether experiments on the effect of microwave radiation on heart rate are carefully controlled for this possibility. If so, it is not mentioned in the literature.

In rabbits and dogs, whole-body irradiation (100–200 mW/cm^2) causes brief constriction and subsequent dilation, especially in the veins of the pia mater [279]. Dogs exhibit slowing of heart rate with alteration in the electrocardiogram during 3000 MHz, 5 mW/cm^2 exposure. Bradycardia, sinus arrhythmia, retardation of auricular and ventricular conduction, changes (usually a decrease) in the P- and T-deflections, and a broadening of the QRS complex are observed [301]. More marked and persistent electrocardiogram (ECG) changes are noted in dogs with experimentally induced myocardial infarction than in normal dogs when exposed to microwaves [301]. Changes in the heart rate, coagulation time, and a fall in blood pressure have been reported in dogs exposed for 30 min at 5 mW/cm² 3000 MHz microwaves [233].

Hemodilution is an early manifestation of any heat stress in the mammal, and it occurs during the first 30 min exposure prior to temperature increase. As the exposure is prolonged, hemodilution is reversed as a result of dehydration, and hemoconcentration follows. The early hemodilution possibly reflects an influx of extravascular fluid as a result of the extensive peripheral vasodilation. This permits dissipation of absorbed heat.

Hemodynamic response of the dog exposed to 2800 MHz pulsed resembles that of acute heat stress as manifested by early hemodilution followed by hemoconcentration. As the exposure is prolonged, hemoconcentration becomes more evident. Dogs exposed at 165 mW/cm^2 show a body weight loss of 2.0%/h. At 100 mW/cm^2, there is weight loss of 1.25%/h, and hemodilution occurs, contrasted with hemoconcentration evident at 165 mW/cm^2 [195].

Functional damage to the cardiovascular system indicated by hypotonus, bradycardia, delayed auricular and ventricular conductivity, and decreased height of ECG waves in workers in RF fields is reported [67, 212, 215, 216].

Drogichina and associates [68] have reported the clinical observation of persons chronically exposed to intense radiation, indicating that in individual cases, the "angiodystonic" manifestations caused by chronic exposure to super high frequency radiation may develop further into more serious autonomic and cardiovascular pathologies. These are characterized by a tendency to angiospastic reactions and cerebral autonomic vascular attacks accompanied by pronounced arterial pressure lability and coronary spasms with corresponding changes in ECG. Osipov [217], however, points out that these changes do not diminish work capacity, and are reversible. Although temperature rise cannot be measured in these individuals, Osipov feels that this is a reflection of the lack of precise instrumentation, and prefers to consider these changes due to microthermal rather than nonthermal effects.

According to a group of authors, the symptoms of chronic exposure to cm waves (the level of vasomotor disturbances) are divided into three stages [185] of: (a) initial, compensated; (b) gradual changes; (c) where changes proceed rapidly. The degree of change depends on intensity and duration of exposure.

It would appear that functional cardiac changes can result from microwave exposure which, doubtless, are due to autonomic nervous system response to thermal effects. It has been noted that McAfee [173] indicates that thermal stimulation of the peripheral nerves produces the neurophysiologic and behavioral changes observed. Interaction between the peripheral nervous system and the central nervous system would account for the reported effects on heart rhythm, blood chemistry, and ECG. On the other hand, Tolgskaya and Gordon [291] observed morphologic modification of receptors after one exposure to microwaves, changes which decreased with repeated exposures. They suggest that receptors of the reflexogenic zone of the curve of the aorta, the carotid sinus, and all layers of the auricular wall are highly sensitive to microwaves.

Central Nervous System (CNS)

The suggestion that microwaves may interact with the central nervous system by a mechanism other than heating has been made by various investigators [89, 90, 141, 162, 185, 201, 211, 221, 231, 232, 236, 249, 291, 300], who stress that the CNS must be considered as moderately or highly sensitive to radiation injuries. Their conceptual basis for this is centered largely about Pavlovian conditional response studies.[2]

These reports, chiefly from Soviet and other East European investigators, are based on a definition of thermal as those effects associated with measurable local or whole-organism temperature rise from an equilibrated baseline. Most

[2] It should be pointed out that although the nervism principle of I. M. Semenov and I. P. Pavlov constitutes one of the most important theoretical bases for Soviet medicine in general, specific studies are based on the theoretical foundation of the special scientific discipline within the framework of which a given effect is being studied, i.e., encephalography, biochemistry, cardiovascular pathophysiology, and so forth. (Personal communication from Professor S. V. Gordon)

other investigators use the term thermal in a somewhat different sense, taking into account that an organism can be affected thermally without demonstrable temperature rise. In fact, a rise in temperature means that the functional reserves of the organism for maintaining homeostasis have been exceeded.

In one of the earliest studies on neurologic effects of microwaves by Oldendorf [213], evidence was found of focal coagulation necrosis in rabbit brains exposed to 2450 MHz. The first report on the effect of microwave energy (in the cm range) on the conditional response activity of experimental animals was made by Gordon et al [93]. In subsequent years, the study of the nonthermal effects of microwaves gradually occupied the central role in electrophysiologic studies in the Soviet Union [211].

Baldwin, Bach and Lewis [4] found that exposure of monkeys to 225–400 MHz was followed by neurologic signs of agitation, drowsiness, akinesia, and eye signs, as well as autonomic, sensory, and motor abnormalities. There were signs of diencephalic and mesencephalic disturbances; alternation of arousal and drowsiness, together with confirming electroencephalogram (EEG) signs. The response depended on orientation of the head in the field and reflections from the surrounding enclosure. Rabbits whose heads were exposed for 30 min to 3–300 MHz showed increased excitation of cortical and other visual analyzers [291].

Chickens, pigeons, and sea gulls exposed to 9300 and 16 000 MHz (pulsed) 10 mW/cm^2 showed sustained extensor activity of wings and legs commencing within a few seconds. These birds showed distress and unsteady gait [283]. Whole-body exposure of chicks to 24 000 MHz produced staggering gait and muscular weakness [63]. Rats given head irradiation at 24 500 MHz tried to avoid the microwave field, suggesting awareness of a stimulus [136]. The most conspicuous effects were muscle spasms, tremors, and clonic convulsions. This stimulation was capable of arousing a rat from deep surgical anesthesia. In a study with audiogenic seizure-susceptible mice and rats sensitive to sound stimulation, Kitsovskaya [144, 146] found that the seizure response to noise was suppressed after exposure to 3000 MHz pulsed microwaves at an average power density of 10 mW/cm^2.

Tolgskaya [294] studied the effects of pulsed and CW 3000 and 10 000 MHz microwaves on rats at various intensities. Emphasis was placed on morphologic changes. The more pronounced morphologic changes in the nervous system following 3000 MHz than 10 000 MHz at 1-10 mW/cm^2 was interpreted as evidence of a nonthermal effect. Pulsed waves were more effective than CW. The greater effectiveness of pulsed microwaves was also noted by Marha [183].

Conditional responses (CR). Troyanskiy and Kruglikov [296, 297] exposed rats to SHF fields. Radiation at thermal (50 mW/cm^2) and nonthermal (10 mW/cm^2) intensities affected intrauterine development and led to changes in function of higher centers of the central nervous system in prenatally irradiated animals. Exposure of pregnant rats at an intensity of 10 mW/cm^2 accelerated postnatal development, and made conditional response indices worse in their offspring. Animals prenatally irradiated at an intensity of 50 mW/cm^2 and those derived from crossing exposed males with nonexposed females exhibited similar changes such as anomalies, deformities, peculiarities of higher nervous activity [296]. In the offspring of exposed animals, besides abnormalities and developmental anomalies, disturbances in the functions of higher sections of the CNS were also observed in the form of delayed development and alteration of electrodefensive and motor-food conditioned reflexes [297].

Yakovleva and associates [309, 310] reported that single and repeated exposures of rats to microwaves, 5–15 mW/cm^2, weakened the excitation process and decreased the functional mobility of cells in the cerebral cortex. Edematous changes throughout the entire cross section of the cortex were most often noted. The greatest number of altered cells was with repeated exposures at 15 mW/cm^2 [310]. In another study with cats, the background bioelectric activity recorded in efferent fibers of renal, splenic, and lower mesenteric nerves under single exposure to 30 mW/cm^2 increased in 50% of the cases [309].

Lobanova [165] summarized her findings at

3000 MHz suggesting two phases are determined in changes in CR during exposure: an increase in excitability of the central nervous system, i.e. a weakening of active inhibition; and a second phase of weakened excitation, with the development of external inhibition. In a later study, however, Lobanova and Goncharova [166] reported that chronic exposure of animals to RF in the 155–191 MHz range for 4.5 months at "low intensity" does not have a marked effect on their CR.

In conditional response studies in dogs irradiated with 50 MHz to specific zones of the cerebral cortex, exposure at 7–14 W output power elicited no response; 20–25 W caused defensive reactions and deterioration of discrimination [162]. Subbota [280] found alteration of conditional response in dogs exposed to SHF (3000–30 000 MHz). The exposure time was 1–2 h. The direction of changes in intense radiation, in the majority of cases, was opposite that observed after weak radiation. At 5 mW/cm^2, increased salivation was observed as a positive CR with relative stability of differentiation. The latent period of CR in the majority of cases was shortened with 100 mW/cm^2. A positive CR was almost always depressed, and differentiations were delayed. Tests with repeated radiation indicated possible adaptation of the cortex to the EMF. On the other hand, no disorders of behavior were noted in two female dogs irradiated whole-body several hours a day for more than a year with 24 500 MHz microwaves at 20 mW/cm^2; their behavior was normal during the whole experiment [61]. In rabbits, brief exposure to 10 mW/cm^2 VHF (30–300 MHz) intensified conditional responses to different stimuli, whereas prolonged exposure produced an inhibitory effect. Selective sensitivity of the brain to this frequency was demonstrated by reversible structural changes in the cerebral cortex and diencephalon [138].

Promtova [237] pointed out in CR studies the importance of the initial functional state of the animals. In healthy dogs, an increase was first noted in food-conditioned reflexes with differentiation maintained, followed by a phase of sharp decrease in CR and retardation of differentiations. In dogs with disturbed higher nervous activity, the action of UHF (300–3000 MHz) worsened the pathologic state of brain cortex in the first phase, and normalized higher nervous activity in the second phase. According to Subbota [280] under the effect of weak and intensive SHF fields (300 MHz–300 GHz), changes in higher nervous activity can occur in three ways:

(a) because of direct penetration of electromagnetic waves into brain;
(b) reflexively, because of stimulation of the receptor apparatus; and
(c) by a humoral-chemical route.

Activity. Lobanova [164] exposed rats to 3000 MHz pulsed microwaves, after which the animals were tested for swimming time. A decrease in endurance was noted among rats exposed to power-time combinations ranging from 100 mW/cm^2 for 5 min to 10 mW/cm^2 for 90 min.

Cortical effects. Several investigators have reported that RF or microwave exposure produces alterations in the electroencephalogram (EEG) [4, 109, 139, 140, 141, 143, 161, 274, 311]. Stimulation is often followed by increased amplitude and decreased frequency of EEG components, or by decreased amplitude and increased frequency. The general character of the observed EEG alterations is constant throughout a wide range of intensities (0.02 mW/cm^2 to ~ 100 mW/cm^2). In general, the percentage of cases evidencing alterations increases with increasing intensity. However, one investigator revealed a greater percent of responses at 0.02 mW/cm^2 than at intermediate intensities [161]. The EEG responses show a substantial delay which decreases with radiation intensity from about 100 s at 0.02 mW/cm^2 to about 20 s at 10 mW/cm^2. Apparently, the observed responses are unaltered when visual, auditory, and olfactory channels are blocked [141, 161]. Comparable neuroelectric changes have been observed in a strip of cortex isolated by cutting from surrounding tissue [141].

EEG tracings in rabbits exposed to 3000 MHz (pulsed) 5 mW/cm^2 showed slight desynchronization from the motor region; at 20 mW/cm^2, variations in the amplitude were observed. Rabbits irradiated with 300 to 3000 MHz showed changes in the EEG; 300 MHz had the greatest biologic effect while 3000 MHz had proportionately less pronounced effects. Pulsed microwaves produced a greater effect than CW microwaves. Rabbits exposed to 40 MHz, 0.1 mW/cm^2, show EEG changes in the cortical and subcortical brain structures produced by a 3-min exposure [47]. An SHF field (3000 MHz–300 GHz), 40 mW/cm^2, 1 min, on the head of a rabbit caused changes in the background activity of neurons in the optical cortex of the brain [48]. The SHF field facilitated responses of the neurons to a flash of light. According to the author, judging from morphologic data, glial elements could be more sensitive than the neurons. Exposure of rabbits to 300, 577, or 2400 MHz (CW) for 5 min at power levels as low as 0.02 mW/cm^2 resulted in EEG changes in more than 50% of the animals studied [109, 141, 314]. Other investigators [8], however, reported that rabbits exposed to 3000 MHz (CW) or 10 000 MHz (pulsed) at 5 mW/cm^2 showed no changes in EEG tracings. These reports suggest that microwave radiation may affect hypothalamic and midbrain functioning, and strong inferential evidence exists for an effect on cerebral, cortical, and reticular system function [286, 311]. According to Gvozdikova and associates [109], the greatest cortical sensitivity occurs in the meter range, less in the decimeter, and least in the centimeter band.

Reviewing the literature on EEG effects requires awareness of certain deficiencies in this methodology. There is not always a one-to-one correspondence between functional state and character of EEG recording—which may lead to mistaken interpretation of the functional consequences of changes in the character of spontaneous activity as the result of exposure to microwaves. Spontaneous activity is easy to measure, but extremely difficult to interpret [113].

Frey [81] has elicited evoked potentials in the brain stem of cats by exposure to pulse-modulated UHF energy. The threshold power density necessary to evoke the potentials was approximately 30 μW/cm^2 average and 60 mW/cm^2 peak. Frey suggests that the potentials were neural rather than an artifact. Within the carrier-frequency range used (1.2–1.525 GHz), there appeared to be a reduction of effect at the highest frequency. Variation in power density had a distinct effect on the evoked potential.

Behavioral effects. Justesen and King [126] studied the behavioral effects in rats exposed in a closed-space situation to 2450 MHz. Average power densities approximated 2.5, 5.0, 10, or 15 mW/cm^2. A major finding was—rate of recurrence of an iterative (phasic) tongue-licking reflex increased and then fell off as dose increased to 14 mW/cm^2. At the high level of 14 mW/cm^2, invariably there was a behavioral state suggesting flaccid paralysis. The animal recovered within 5–10 min after removal from the experimental chamber and thereafter exhibited no behavioral signs of stress.

Readings from rectal thermometers were taken immediately before and after 0, ~ 4.5, 9.6, and 14 mW/cm^2 exposures. The 0 and ~ 4.5 mW/cm^2 levels were associated with small but statistically unreliable rises in average temperature after 60 min intermittently presented irradiation. The ~ 14 mW/cm^2 exposure reliably increased temperatures after 19 min intermittent irradiation—and after 60 min two of the animals exhibited temperatures greater than 44°C. The temperature data confirmed an impression growing from earlier behavioral observations that the rat is highly variable in individual thermoregulatory capability. Rats were presented 2450 MHz energy as a cue for obtaining sugar water, but none discriminated the cue. In essence, Justesen and King [126] found no chronic ill effects behaviorally or neurohistologically from fairly long-term intermittent exposures approximating 2.5 to 15 mW/cm^2; although some acute effects were observed, none was (or is) incompatible with the supposition that thermalization was the only consequence of irradiation.

Nealeigh et al [207] found that exposure of Sprague-Dawley rats to 2450 MHz, 50 mW/cm^2, immediately prior to running in a Y-maze, significantly improved performance. It is suggested that microwave exposure may produce effects similar to a variety of CNS stimulants which act by facilitating consolidation of the memory trace. In another study by the same investigators, 10-week-old beagle pups were tested in an approach runway after whole-body exposure to 2450 MHz microwaves, and showed no appreciable changes in performance and/or motivation.

In the context of behavioral effects, it should be noted that behavior is not a simple process and that behavioral effects represent the algebraic sum of different effects in different systems. Such effects could be a response to subtle temperature input signals which may arise in many body structures.

Effect on learning ability. Conditional response studies have indicated alteration in learning as a consequence of RF or microwave exposure [16, 89, 168, 280]. Retrograde amnesia and depressed learning have been described in rats exposed to microwaves [38, 127]. The field intensity in these studies evidently was quite high. Behavioral effects, nevertheless, have also been demonstrated with apparently low-intensity fields according to the authors [149, 150, 284]. It should be noted that more precise power density measurements [107] revealed thermally significant levels in some studies [149, 150].

Subbota [280] noted alternating arousal and drowsiness effects in dogs subjected to pulsed UHF fields. Turner [299] has suggested that the phenomenon of pulsed-energy sleep may be related to the effects described above. In this technique, a low-intensity current (0.2 mA) is applied to the brain between occipital and orbital electrodes; the current is pulsed at a rate between 1 and 100 pps, with a pulse duration of 0.3 ms. Under these conditions a sleeplike state (apparently quite similar to normal physiologic sleep) is observed. In the USSR, pulsed-energy sleep has been used as therapy for psychopathologic conditions [286].

Histopathology. According to some authors, morphological and histochemical studies of the nervous system show cellular changes following 3000–30 000 MHz exposures at 10 mW/cm^2 [290, 292, 293]. Degeneration of neurons in the cerebral cortex and retrograde changes in the kidney and myocardium of rabbits have been produced by exposure to 200 MHz. Exposure of rabbit heads to 2450 MHz resulted in focal lesions in the cerebral cortex. Whole-body exposures of rats to 1430 MHz produced lesions of the brain [213, 266, 291].

Rabbits exposed to 3000 MHz (pulsed or CW), 5 to 20 mW/cm^2, showed evidence of brain injury. Cells of cortex, cerebellum, and subcortical structures had deficient tigroid content, vacuolization in some cells, proliferation of glial cells, congestion of the meninges, and superficial cerebral cortex vessels were frequently observed at 30 mW/cm^2. Some red cell effusion and enlarged perivascular spaces were noted. There were more pronounced morphologic changes in the nervous system of rats following 3000 MHz than after 10 000 MHz at 1 to 10 mW/cm^2; pulsed waves were more effective than CW [291]. Exposure of cats for 1 h to 10 000 MHz 400 mW/cm^2 resulted in injury to cerebral and spinal cord nerve cells; changes occurred in tigroid substance and other components of nerve cells [33]. Rabbits exposed to 10 000 MHz (pulsed) 5 mW/cm^2 showed no evidence of morphologic damage to the brain [8]. Exposure of dog head to 2450 MHz (CW) produced no effect on brain or cerebrospinal fluid [265].

Gordon et al [92] found that "low-intensity" microwaves produced only slight morphologic changes in the axon-soma and axon-dendrite interneuron connections of the cerebral cortex and in the receptor and interoceptor apparatuses in various receptor zones (skin, intestinal wall, wall of urinary bladder, myocardium, and aorta). In addition to these changes, low-intensity irradiation led to histochemical shifts in the form of reduction in the nucleoprotein content of various cells and tissues. These changes were reversible and disappeared within 3–4 weeks. Further evidence for morphologic change in the CNS under low-power densities was found by other investigators [168, 220, 294]. In all these studies, the morphologic changes noted centered around rearrangement and atypical appearance of the synaptic area. Kevork'yan [137] points out that a "gelatinization" of the synapse takes place during short exposures to UHF radiation, this effect being reversible.

Tolgskaya and associates [168, 290, 291, 294, 295] have investigated the influence of pulsed and CW 3000 and 10 000 MHz on the morphology of nervous tissue in rats and rabbits. In brief, with exposure to 3000 MHz (110 and 40 mW/cm^2), severe clinical symptoms of overheating were observed, often leading to death. Severe vascular disorders such as edema and numerous hemorrhages of the brain and internal organs were morphologically predominant.

In repeated, but less prolonged, exposure to high and medium levels, vascular disorders and degenerative changes in internal organs and the nervous system were less severe. With repeated exposures, the animals better withstood successive exposures. They continued to gain weight, body temperature recovered quickly after irradiation, and overheating disappeared [294].

Similar effects in afferent nerve cells of cats were reported by Pervushin [220]. He used UHF at intensity levels of 0.5 to 10 mW/cm^2, and 30 mW/cm^2, for 2 h/d, 1–5 d, and reported particular sensitivity in preterminal sections of the afferent cells and in myelinated fibers; the non-myelinated fibers appeared to be unaffected.

At high field intensities, when death results from overheating (hyperthermia), the vascular changes are hyperemia, hemorrhage, and acute dystrophic manifestations [6, 66, 202, 208]. The changes described are greatest when in the site of direct irradiation. At lower field intensities, the changes are of a more general dystrophic character, and proliferation of the glia and vascular changes are not as prominent [66]. When the animal is sacrificed within 1 to 3 weeks after exposure, dystrophic changes are only isolated and there is no hyperemia [66]. It should be noted, however, after total-body irradiation, the histopathologic changes are present not only in the CNS, but also in other organs: myocardium, intestine, liver, gallbladder, and urinary bladder [36, 66, 116, 202, 208]. This was shown by Dolina [66] when rabbits were exposed daily to 3000 MHz CW 40–100 mW/cm^2 or 220–270 mW/cm^2 for 5–15 minutes. He found diffuse nervous system and circulatory system damage.

Some reviewers [188, 192, 195, 199] have suggested that investigations purported to show neurologic effects at nonthermal microwave intensities do not clearly indicate whether the changes produced by microwaves are due to generalized thermal effects or to more specific influences on particularly vulnerable tissues. There is no complete unanimity among the authors that have investigated conditional responses in different animals, in the evaluation of observed phenomena and understanding of their mechanisms. These studies are complex and require a special investigative approach [163].

In regard to the relationship of body temperature and physiologic functions, it is important to realize that temperature input signals arise in many body structures. The following have been identified experimentally: (a) preoptic anterior hypothalamus, (b) posterior hypothalamus, (c) midbrain, medulla, motor cortex, and thalamus, (d) spinal cord, (e) skin, (f) respiratory tract, and (g) viscera. All these, except the motor cortex and thalamus, have been shown to evoke behavioral and/or physiologic responses to changes in local temperature [112].

In regard to the sensitivity of neural tissue to microwaves, it should be understood that the intensity of electrical membrane potential of nervous tissue is generally measured in mV. The membrane potential of animal muscle and nerve cells is generally in the range of -70 to -110 mV; animal cells cultured in vitro may show values as low as -10 to -30 mV; and protozoan cells have been shown to display potentials in the range of -30 to -100 mV [177]. Because of their selective permeability, electrical double layers are formed at biologic membranes which cause differences of potential between both sides of the membrane. Therefore, the membranes are placed within electrical fields which are conditioned by electrical double layers. The power of these fields is considerable, which amounts to 10^5 V/cm with a potential difference of 100 mV and a membrane thickness of 100 Å. For microwave energy to be effective, therefore, tremendous fields must be exerted to cause any effects [32]. Microwave fields are only capable of applying a potential to a biologic membrane which is many orders of magnitude smaller than the resting potential and, for this reason, should be unable to excite or change normal patterns [254, 255, 256]. A great deal is known about the excitation of membranes by low-frequency and DC currents. In these cases, excitation is possible with current densities of the order of 1 mA/cm^2 in tissue. At higher frequencies, and particularly at microwave frequencies, higher current densities are required to cause excitation if it is at all possible. It is difficult to perceive, therefore, how microwave fields can affect excitable biologic membranes at power densities less than those which would cause thermal effects [256].

Observations in man. A number of effects in man referrable to CNS sensitivity has been described [89, 137, 185, 201, 211, 217, 221, 232, 249, 291], most of which are subjective—fatigability, headache, sleepiness, irritability, loss of appetite, and memory difficulties. Psychic changes have been observed that include unstable mood, hypochondriasis, and anxiety. Most of the subjective symptoms are reversible, and pathological damage to neural structures is insignificant. Microwaves rarely, if at all, cause hallucinations, syncope, adynamia, and other manifestations of the so-called diencephalic syndrome. It has been pointed out that much of the work is based on subjective rather than objective findings [219]. It should be noted that individuals suffering from a variety of chronic diseases may exhibit the same dysfunctions of the central nervous and cardiovascular systems as those reported as a result of exposure to microwaves.

Soviet and other East European investigators have contributed most of the reports on human effects of RF and microwave energies; the greatest emphasis is on effects produced at less than thermogenic power flux densities (< 10 mW/cm²). According to these authors, the responses of an organism to microwaves are directly or indirectly referrable to the central nervous system [91, 187, 192, 221, 232].

Neurasthenia syndromes. The observed neurasthenic effects from electromagnetic radiation have been organized into categories by wavelength, organ system, or clinical syndrome. Many of the reports in man can be classified as: (a) neurasthenic syndrome, (b) autonomic vagotonic dystonia, and (c) diencephalic syndrome [65]. Drogichina et al [68] report all three classes of symptoms in personnel subjected to microwave fields of a few mW/cm². The basic symptomatology and neuropathology underlying all these syndromes is reportedly due to the functional disturbance created in the central nervous system caused by reported nonthermal mechanisms. These effects do not result from an observable rise in body temperature, and are reported to occur at levels far below those required to produce a temperature rise. The symptoms are manifested by weakness, fatigue, vague feelings of discomfort, headache, drowsiness, palpitations, faintness, memory loss, and confusion. Such syndromes are completely reversible in most cases, with little or no time lost from work [217]. In contrast, other authors emphasize the resultant time lost from work, and necessary hospitalizations [90, 91, 158]. One author reported that physical activity in both organized and unorganized forms modifies the incidence of functional cardiovascular disorders in radar operators, but he stresses environmental factors and job immobility as contributing to the incidence [71].

Clinical observations of humans exposed to microwave fields have suggested that motor effects may be accompanied by sleep disturbances, lower resistance to fatigue, increased irritability, and memory concentration deficits [72, 137, 248, 249, 267]. Kevork'yan [137] reported that workers exposed to moderate intensity microwave fields are prone to a syndrome that includes sleep disturbances, memory changes, and fatiguing rapidly under work requiring mental concentration. Sadchikova and Orlova [249] also found general debility, listlessness, and increased irritability in individuals chronically exposed to low-to-moderate intensity microwave fields in an industrial environment. They classified the people according to exposure: (1) periodic to 3–4 mW/cm², (2) periodic to less than 1 mW/cm², and (3) constant to less than 0.1 mW/cm². In group (1), a vagotonic reaction was observed with symptoms of bradycardia, and prolongation of intra-auricular and intraventricular conduction. In those exposed continuously, group (3), the result reported was an asthenic syndrome with irritability. The control group, apparently, was not composed of matched workers, but of a group of college students between the ages of 25 and 40.

In regard to the question of neurasthenic responses, Cohen and White [52] have presented an extensive review of neurocirculatory asthenia (NCA) as a clinical syndrome that has implications in assessing the reported effects of low-level microwaves. Neurocirculatory asthenia presents as a familial disorder with a mean age of onset of 26 years (range 25–35 years). Twice as many cases are presented in females compared with males. The authors relate that onset of the syndrome in predisposed individuals is usually precipitated or made worse by emotion-provoking circumstances, medical illness, unaccustomed or hard muscular labor (particularly if involuntary), pregnancy, and in various situations in military service. Exact etiological relationships are unknown, but point toward environmental influences and familial predisposition.

It is relevant to point out that the effects reported by East European investigators have not been observed in the West, even at higher exposure levels. It is important, therefore, that thorough, well-controlled experimental and clinical investigations be undertaken to determine the presence of these reported effects, the levels of exposure at which they occur, and the extent to which they represent a hazard to the individual.

Olfactory-optical apparatus. Alteration of olfactory thresholds was found in occupationally exposed individuals in fields between 30 MHz and 300 GHz, which suggests sympathetic and parasympathetic inhibition [82, 87, 88, 130, 167]. Some reduction in the excitability of the olfactory and optical analyzers has been reported in workers [88, 167]. Increase in olfactory threshold [82, 130] and curtailment of chronaxie [130] have also been reported. Lobanova and Gordon [167] found lower olfactory sensitivities among 358 workers exposed to microwaves than among members of a control group. Among experimental subjects exposed continuously to power densities up to 1 mW/cm^2, the lowest sensitivity was in those exposed less than a year, or more than 6 years; among subjects exposed periodically to power densities up to several mW/cm^2, the sensitivity decreased with increased exposure time.

Cortical activity. Electroencephalographic examination has revealed various cortical alterations. Under the influence of weak, chronic microwave action, excitability and reactivity of the cerebral cortex decreased [302]; slow activity during the alpha rhythm was maintained; length of the latent period of awakening increased; and listlessness, sometimes of a paradoxical character, occurred [298]. The most pronounced changes were observed in persons with severe symptoms from the action of centimeter waves. The character of the changes (generalized paroxysmal activity), according to the authors [85], indicates functional damage at the mesodiencephalic level. Kolesnik and Malyshev [148] reported that accidental exposure of a man's head and upper trunk to 10 000 MHz, 10 mW/cm^2 for 15 min resulted in asthenia and on the EEG he showed lowered voltage, a rapid beta rhythm, and a slow theta rhythm.

Sensory effects. Sensory effects have also been reported in humans exposed to RF. When Grinbarg [100] applied the electrical field of 50 MHz energy through electrodes, the threshold for pain was raised. Sheyvekhman [271], using electrodes to apply the electrical field of 50 MHz energy for 5 min to human heads, found auditory threshold changes in the exposed individuals.

Frey [78, 79] has reported that individuals can detect pulse-modulated electromagnetic energy at wavelengths of 10 to 70 cm and at average power densities of 0.4 to 2.1 mW/cm^2. The reported sensations were usually auditory in nature and described as hissing, buzzing, or clicking sounds. Frey [80] believes that modulation is necessary for perception of microwaves. There is no evidence that this auditory sensation constitutes a risk of injury. Considering that many sources of auditory sensation exist in the normal environment and are not considered hazards, more evidence of hazard is required. This phenomenon is apparently not due to direct stimulation of neural fibers or cortical neural tissue but rather to stimulation of the cochlea through electromechanical field forces by air or bone conduction [108, 276]. Vogelman [307] points out that significant though inefficient rectification of microwave energy may be possible in vivo.

Proposed mechanisms of neural effects. Presman [231, 232] suggests that resonant absorption at super-high frequencies (GHz range) could cause transitions of molecules, especially protein molecules, to excited states. He also discusses changes in the Na^+ to K^+ gradient across cell membranes, because of different effects of microwaves on degrees of hydration of these ions, as well as changes in cell permeability by the disruption of protein hydration in the cell membrane. It must be emphasized that all this is speculative, with no experimental data given in support [221]. Presman [231] has also stated that the changes in functions of the nervous system produced by microwaves are not specific. Such changes are produced by any means of stimulation or variation of the excitability of the peripheral and central parts of the nervous system. Hence, naturally it can be assumed that the action of microwaves under this system may be due to stimulation or variation of the excitability of the nervous tissues. The elucidation of the physical and chemical mechanisms of microwaves on excitable structures involves considerable difficulties, since the physical-chemical mechanisms of excitability of living tissue in general is still far from clear.

MacGregor [180], who reviewed briefly some of the literature on influence of microwaves on the nervous system, suggested possible mechanisms of low intensity microwave influence on neural function [180, 181]:

A. Direct effects (primary effect on apparatus for neuroelectric ionic fluxes).
   1. Direct influence on ionic currents leading in turn to influence on transmembrane potentials in nerve cells.
   2. Localized heating.
      a. change membrane properties, thereby disrupt transport processes;
      b. induce convection currents, thereby disrupt transport processes;
      c. affect processes of synaptic transmission;
      d. affect processes of excitable membrane.
   3. Chemical or structural change in components of membrane, or in apparatus of synaptic mechanisms or of excitable membrane.

B. Indirect effects.
   1. Primary effect on cell metabolism.
      a. alter by heating or by structural change, properties of membrane, thereby disrupting nutritional transfer;
      b. cause structural change in an enzyme or any critical molecule at any stage of metabolic cycle;
      c. alter by localized heating, processes of metabolism at any critical stage.
   2. Primary effect reflects stress.
      a. neural response to disruption of any neuroendocrine control system;
      b. neural response to disruption of any physiologic process;
      c. neural sensory response to field directly or to localized temperature disturbances.

C. Disruption by any physical mechanism of hypothetical glial or electromagnetic organic control systems.

MacGregor [181] suggests that intracranial electrical fields associated with low-intensity microwave irradiation may induce transmembrane potentials of tenths of millivolts (or more) and that, therefore, such externally applied fields may disturb normal nervous function through this mechanism. On the other hand (already been pointed out), an RF field can be reinforced in the region of peripheral nervous tissue causing a temperature rise, even while nearby muscle and skin show no measurable temperature effect. Peripheral nerves heated above a minimum level may trigger spontaneously [173].

Schwan [256] has noted that membranes are short-circuited by currents of frequency above 100 MHz. The electrical field strength which exists in a nerve membrane is about 500 kV/cm. The field strengths applied by a microwave field to the human body are infinitely smaller, and hence, cannot evoke stimulation.

Many investigators do not accept the possibility of nonthermal neural stimulation, and explain these effects entirely upon local heating. Pinneo et al [225] postulated that many so-called nonthermal effects may actually be specific thermal effects on certain neural structures. They examined the thermal stimulation of peripheral nerves exposed to 3000 MHz and 10 000 MHz microwave radiation and infrared energies.

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Their experiments showed that all three sources of energy produced the same effects on the central nervous system. They suggested that experiments purporting to show nonthermal effects should be examined with the possibility in mind that a thermally induced neurophysiologic response may have occurred.

McAfee [171] feels that the neural effects of microwave stimulation are due solely to the thermal effects of the radiation and that these effects arise from stimulation of afferent pathways of the peripheral nervous system structures. Studies by McAfee and associates [171, 172, 173, 174, 176] provide convincing evidence that the presumed nonthermal effects on CNS from microwaves are a result of thermal stimulation of peripheral nervous structures. Studies claiming CNS effects of microwaves should include controls for possible peripheral nervous system effects such as those described. These studies provide an explanation for behavioral effects in terms of responses evoked by microwave-induced heating of afferent nerve fibers, and further demonstrate errors that can be encountered when comparing responses obtained by irradiation of different regions of the animals. Such experiments and conclusions deserve careful consideration when physiologic changes in animals exposed to microwaves are attributed to specific or nonthermal effects of microwave exposure.

It is apparent that the reports which claim the existence of nonthermal effects are equivocal. Additional research is needed, especially from a more quantitative point of view, to clarify this point. Specific effects quoted in the literature are biologically interesting but have not been clearly shown to be related to symptoms in man [245].

Regardless of what the mechanisms are, the important point is whether or not the effects attributed to these mechanisms do indeed exist, and if they exist, to what extent they represent harm to the organism. The East European investigators obviously feel that the effects they report are due to nonthermal interactions and warrant consideration. This is reflected in the East European standards for personnel exposure.

Standards

To insure uniform and effective control of potential health hazards from RF and microwave exposure, it is necessary to establish standards or protection guides. Similar to most biologic processes, there is a certain range of levels between those that produce absolutely no effects and those that produce detectable effects. Ideally, effect or threshold values should be predicated on firm human data. If such data are not available, however, extrapolation from well-designed, adequately performed, and properly analyzed animal investigations is required. In establishing a standard, it is necessary to keep in mind the essential differences between a *personnel exposure* standard and a *performance* standard for a piece of equipment. A more detailed discussion of microwave exposure standards is presented by Michaelson [190, 191] and Schwan [257].

There is no evidence of hazard to man from RF and microwaves under normal conditions of operation and exposure. Nevertheless, concern has been aroused about the safety of personnel in intense RF fields close to transmitting antennas operating in the MF/HF bands. Such environments are, in general, of a near-field type which preclude the measurement of power flux. In the frequency bands below 30 MHz, the potentially hazardous environments are generally within this complex (near-field) region [243]. Since hazard evaluation in this frequency range is a function of measurement in the near-field, attention should be paid to the problems inherent in such measurement.

The first proposal for 10 mW/cm^2 as a protection guide for microwaves was made to the US Navy by Schwan in 1953; it was based on simple physiologic considerations. The amount of heat which the human body can transfer to the external environment is, under normal circumstances, about 0.01 W/cm^2 body surface which may be raised about tenfold under very favorable circumstances. This means that the human body's ability to absorb radiant energy without causing a continuous temperature rise is limited to a value somewhere between 100 and 1000 W [262, 263].

These considerations, and the extensive body of experimental data then available from the Tri-Service sponsored studies [189], were reviewed by a committee of the American National Standards Institute (ANSI) which, in 1966, recommended 10 mW/cm^2 as the standard [250]:

> For normal environmental conditions and for incident electromagnetic energy of frequencies from 10 to 100 000 MHz the radiation protection guide is 10 mW/cm^2 as averaged over any possible 0.1 hour period.

This standard permits a maximum power density of 10 mW/cm^2 for 0.1 h or more; and a maximum energy density of 1 mW h/cm^2 during any 0.1-h period. This guide applies whether the radiation is continuous or intermittent and is intended for the general public as well as workers.

Guides and exposure levels in force today appear to be entirely safe. So far, there is no documented evidence of injury to military or industrial personnel, or the general public, from the operation and maintenance of radars and other RF and microwave-emitting sources within the 10 mW/cm^2 limit of exposure. A compilation of various standards is presented in Table 3.

Rogers and King [243] suggest that under plane-wave (far-field) conditions the body could endure an RF radiation power density greater than

TABLE 3.—*Recommended Maximum Permissible Intensities for Radio-Frequency Radiation*

Maximum permissible intensity	Frequency (MHz)	Country or source	Specifications
10 mW/cm^2	10–100 000	ANSI 1966; Canada 1966	1 mWh/cm^2 for each 6 min
	30–30 000	Great Britain 1960	Daily exposure
	100–100 000	US Army and US Air Force 1965 France (military) 1969	10 mW/cm^2 cont. exposure 10–100 mW/cm^2 lim. occup. $\text{Min.} = \frac{6000}{(X\text{mW/cm}^2)^2}$
		Sweden 1961	occupational
		German Fed. Republic 1962	
1 mW/cm^2	all	Sweden 1961 France 1969	General public prolonged occupat. exp.
	> 300	USSR 1965; Poland 1961	15–20 min/d (protective goggles required)
0.1 mW/cm^2	> 300	USSR 1965; Poland 1961	2–3 h/d
0.025 mW/cm^2	> 300	Czechoslovakia 1968	(CW) 8 h/d (occup.)
0.01 mW/cm^2	> 300	USSR 1965 Poland 1961 Czechoslovakia 1968	workday workday (pulsed) 8 h/d (occup.)
20 V/m E field 5 A/m H field	0.06–30	USSR 1965	
10 V/m	30–300	Czechoslovakia 1968	(pulsed) 8 h/d (occup.)
5 V/m	30–300	USSR 1965	

10 mW/cm² ($E_i \approx 200$ V/m) for frequencies in the HF band and suggest that an electric field strength of 1000 V/m can be considered the safe limit for continuous daily exposure to RF radiation in the range below 30 MHz. Schwan [257] points out, in his review of microwave radiation and standards criteria, that there are circumstances where standards based on flux levels fail. This happens in the presence of complex field patterns, i.e., in the near-field of antennas or in the presence of several fields generated by different transmitters or by reflecting surfaces. He suggests that under these circumstances, a tolerance current density in tissue of 3 mA/cm² may well serve as a better guide for work-related exposure in complex fields. This current density for simple fields corresponds to a flux of 10 mW/cm² between 100 and 1000 MHz. Therefore, protection guide numbers may be:

(a) 3 mA/cm²	for frequencies above 10 MHz
(b) 1 mA/cm²	for frequencies from 10 KHz to 10 MHz
(c) 0.3 mA/cm²	for frequencies below 10 KHz

In the USSR, maximum permissible intensities or recommended protection standards, established in 1959 (Provisional Sanitary Rules for Work with Centimetric-Wave Generators, USSR Ministry of Health, 1959), are based on observations of reactions reported from low-level exposure to RF or microwaves. These levels are indicated in Table 3. An intermittency correction factor of 10 has been proposed for intermittent radiation when radiating devices are used in circular- and sector-scanning modes [221]. In addition, levels of exposure differing by one order of magnitude are permissible because of possible field gradients and limits of accuracy of the measuring apparatus [90].[3]

The divergences between US and East European standards are, to a great degree, due to differences in basic philosophy—differences which appear in industrial hygiene and basic scientific research. The standard used in the US and most other countries is, as already noted, based on the amount of exogenous heatload which the body could tolerate and dissipate without any resulting rise in body temperature. This tolerance level was calculated to be 10 mW/cm² for continuous exposure. In contrast with US standards, the USSR maximum permissible exposures are based on *asthenia* syndromes reported by workers in the microwave field.

There is no evidence in Western world scientific literature that the present US standard of 10 mW/cm² represents a hazardous exposure level. If the general philosophy of industrial hygiene in the United States is considered, that for every *toxic substance* there exists a concentration or level below which no injurious effects will result and that not all effects represent hazards, this position becomes even more sound.

According to Magnuson et al [182], the industrial hygiene philosophy of the USSR basically consists of:

(1) The maximum exposure is defined as that level at which daily work in that environment will not result in any deviation in the normal state, as well as not result in disease.

(2) Standards are based entirely on presence or absence of biologic effects without regard to the feasibility of reaching such levels in practice.

(3) The values are maximum exposures rather than time-weighted averages.

(4) Regardless of the value set the optimum value and goal is zero.

Maximum permissible exposure (MPE) values are not rigid ceilings but, in fact, excursions above these values within reasonable limits are permitted and the maximum permissibles represent desirable values for which to strive rather than absolute values to be used in practice.

In view of the basic differences in industrial

[3] Although most East European countries follow the Soviet standard, Czechoslovakia, since 1968, permits a relaxation of 2.5 for CW emission, i.e. 0.025 mW/cm² in contrast to 0.01 mW/cm² for pulsed systems. In June 1973 Poland revised safety standards for radio-frequency radiation in the range of 0.3–300 GHz. The new standards enacted under Public Law No. 153 permit unlimited exposure of humans to field intensities of 0.01 mW/cm². Eight h/d exposure is permitted for intensities up to 0.2 mW/cm² for stationary fields and 1 mW/cm² for rotating fields. Exposures up to 10 mW/cm² are permitted for short periods (11.5 s in a stationary field; 4.8 min in a rotating field). Exposures greater than 10 mW/cm² are prohibited without approved safety equipment.

hygiene philosophy, it does not appear that the standards used in the US and USSR are as irreconcilable as would appear.

Protective Measures

Recommendations for protection against injurious levels of RF are described in various publications [94, 154, 221, 229, 239, 240, 268, 312]. These protective measures are for individuals and groups, by means of protective clothing, goggles, and shielding materials, and are based on technical and organizational principles.

EFFECTS OF ELECTRICAL FIELDS

The effects of static electric fields (SEF) and low-frequency (60 Hz) electric fields, discussed in this section, are of particular interest. Reports on biologic effects of SEF have been reviewed by Novitskiy et al [211], who note that in textile, woodworking, paper, and other industries, static electric charges are formed and accumulated from friction of materials with high dielectric properties. The number of people working in a static electric field increases as direct current, super high-frequency electrotransmission lines (400 to 750 kV) are put into production. Studies on animals [44, 46, 131, 227] indicate that SEF, if it does have a biologic effect, is quite weak and unimpressive. In discussing the biologic effects of electric fields, it is important to distinguish between where the body is in contact with two conductors at different potentials (two-contact case), and where the body is in an external electric field, insulated from conductors (no-contact case). The latter is of primary concern in this section. A brief discussion of the two-contact case may be helpful, however, in understanding the no-contact case.

When the body is in contact with two conductors at different potentials, current flows through the body. The biologic effects of "electric shock" have been discussed in a number of reviews [58, 59, 60, 133, 134, 135, 258]. Typical threshold values for 50–60 Hz currents lasting a few seconds are given in Table 4. The threshold for sensation is approximately 1 mA total body current. At approximately 10 mA the "let-go" threshold is reached, a level characterized by loss of ability to let go of a hand-held live conductor. A current of approximately 100 mA through the torso causes ventricular fibrillation in man which could result in death [258]. Keesey and Letcher [134, 135] recommend a safety threshold of 5 mA for the average person including children.

TABLE 4.—*Threshold Levels for Electric Currents*[1]

Human reaction	Total body current	Current density
Sensation	1 mA	0.1–1 mA/cm^2
Let-go	10 mA	0.1–1 mA/cm^2
Fibrillation	100 mA	about 1 mA/cm^2

[1] Adapted from Schwan [258].

Organs vary greatly in sensitivity and pathologic response to electric currents. Organic damage to the nervous system occurs in that portion of the brain or spinal cord where the current passes through. It is not specific and sometimes similar to that found in other types of cerebral injuries. Current effects on the skin are twofold: first, in passing through the skin, electric energy is transformed into heat which alters the structures along the path of the current; second, free discharge causes formation of electric sparks which leads to formation of third degree burns. Death from electrical injuries is usually due to cardiac or respiratory arrest. In most instances, cardiac arrest results from ventricular fibrillation. Respiratory arrest may be due to direct effects of the current on the respiratory center, or secondary to hypoxia of the cells of the center due to inadequate perfusion as a result of the ventricular fibrillation [76].

At the cellular level, biologic effect is a function of current density rather than total body current [84, 258]. A safety threshold of 5 mA would correspond to a current density somewhere between 0.1 and 1 mA/cm^2 [258].

In the no-contact case, an alternating field gives rise to a flow of current within the body. Schwan [258] has considered the possibility of low-frequency fields giving rise to dangerous current densities in the body. He showed that current density would be proportional to both field strength and frequency. His results, in Table 5, indicate that the field, to cause dangerous current densities, is two orders of magnitude

TABLE 5.—*External* 60 Hz *Fields Required to Produce Dangerous Current Densities in the Body*[1]

Current density	Field strength
0.1 mA/cm^2	1 MV/cm
1 mA/cm^2	10 MV/cm
Air breakdown	30 KV/cm

[1] Adapted from Schwan [258].

higher than the field strength at which air breaks down as an insulator, and sparking occurs.

A body of literature, nevertheless, indicates that there are biologic effects when animals are exposed to stationary and low-frequency electric fields. This literature has been reviewed by Novitskiy, Gordon, Presman, and Kholodov [211]. A wide range of physiologic effects has been reported, including changes in blood indices, heartbeat, and respiration, ranging in severity up to anaphylactic shock following repeated exposure, and to death. Widespread morphologic changes have also been reported. Field strengths at which effects were noted varied from approximately 50–5000 V/cm, with most reported field strengths between 200 and 2000 V/cm. For the most part, this work is difficult to interpret, since frequently, field strength and frequency are not specified, and in many cases the fields were pulsed rather than continuous wave.

In sharp contrast to the above-mentioned work, in a study by Knickerbocker, Kouwenhoven, and Barnes [147], 22 male mice were exposed to a 60-Hz field of 4 kV/in (1.9 kV/cm) for 1500 h during 10½ months. Careful observation failed to reveal any effect on the general health, behavior, or reproductive ability of these animals; necropsies performed after exposure failed to show any pathologic effects.

A number of studies carried out on persons occupationally exposed to high electric fields [211, 252] describe complaints such as listlessness, excitability, headache, drowsiness, and fatigue—attributed to exposure to high electric fields. The problem in interpreting such findings is that it is often difficult to determine which factors in the working environment are responsible for the observed symptoms, since all are noted in various occupational settings. Ulrich and Ferin [303] have suggested irregular shifts (i.e. night work) and dry air as possible factors in the initiation of the signs and symptoms cited.

Kouwenhoven et al [152, 153] have studied linemen, many of whom had spent several years working on high-voltage transmission lines. They found no physical, mental, or emotional effects which could be attributed to exposure to high electric fields.

In summary, neither animal experimentation nor clinical studies so far have provided clear evidence for harmful effect of human exposure to stationary or low-frequency electric fields. Until such evidence is found, the obvious dangers of electrical sparking should determine the limits of safe human exposure.

EFFECTS OF MAGNETIC FIELDS

A great amount of information has been accumulated during the last decade on the biologic effects of magnetic fields. Although all these works are not of equal value, the large number indicates the rapid development of this field [211]. In recent years, summary articles have appeared discussing questions on magnetobiology in detail [12, 13, 19, 20, 23, 24, 31, 41, 42, 43, 53, 83, 102, 111, 141, 210, 232].

In traveling to outer space, astronauts will leave not only the Earth's gravitational field, but also its familiar geomagnetic environment. Fortunately, unlike the zero-g environment, it is possible to create various magnetic environments in limited volumes on the Earth. With the aid of special coils or shielding materials, such systems can be used to study the possible effects of magnetic conditions along different paths of future spaceflight trajectories [83].

The existence of biologic effects of magnetic fields is now well-documented. Biomagnetic effects have been reported in a variety of systems [103, 211] that include bacteria [114], cell cultures [69, 206, 238], insects [51, 206, 285], plants [70], and other organisms, as well as mammals including man.

A few physical concepts may be helpful in understanding biomagnetic phenomena. Unlike external electrical fields (no-contact case), magnetic fields easily penetrate biologic materials so that the entire specimen experiences the field. In the case of a uniform field, the entire specimen experiences nearly the same field. In the case of a gradient field, the field becomes progressively stronger from one side of the specimen to the other.

Table 6 lists several possible interactions suggested as significant in causing biomagnetic effects. There is little direct evidence, however, to establish the significance of any of these mechanisms. In the case of gradient fields, paramagnetic substances may be attracted toward the stronger field and diamagnetic substances toward the weaker field; this phenomenon is not possible in uniform fields. In the case of alternating magnetic fields, indirect effects may be caused by magnetically induced electric currents.

TABLE 6.—*Possible Mechanisms for Biomagnetic Effects* [1]

Type of reaction	Reacting agent
Interaction	Transient free radicals
Diffusion	Membranes
Semiconductor effects	Neuronal function
Rate changes	Hormone secretion
Bond angles distortion	Enzyme–substrate
Rotational polarization change	Specific reactive sites molecules
Rate change	Quantum proton tunneling in DNA (genetic code effect)
Segregation	Paramagnetic and diamagnetic substances (gradient fields)
Induction	Electric currents (alternating fields)

[1] Adapted from Barnothy [13].

Relatively little is known about the specific effects on man of high- and low-intensity magnetic fields. Past studies in magnetobiology have been directed mainly toward determining the effects of magnetic fields that differ from those of the geomagnetic field in animals, plants, and simple chemical systems. Review of this material is available [42].

Since man has evolved in the Earth's geomagnetic environment, it is plausible to assume that removing him from this environment could have detrimental effects [83]. Very few human exposures to a magnetically quiet environment have been reported. A certain amount of experience, however, has accumulated during ordnance work inside degaussing coils. A health survey of personnel exposed to an almost magnetically quiet environment during most of their working days for several years revealed no ailment traceable to this unusual environmental exposure [22]. Effects are summarized in Table 7.

TABLE 7.—*Effects of Magnetic Fields on Man* [1]

Magnetic field	Time	Effect on man [2]
Alternating		Visual sensations—phosphenes
Nonchanging—up to 20 kG	15 min	No sensation in part or entire body exposure
5 kG	less than 3 d/yr man^{-1}	No aftereffects

[1] After Beischer [26].
[2] Taste and pain sensation caused by interaction with fillings of teeth sometimes described.

Animals have been experimentally exposed to very high fields. Beischer [25] exposed mice to uniform fields of up to 120 000 gauss [4] (G) and to a field of 45 000 G with a gradient of 7000 G/cm. Exposures were for 1 h. No changes were observed in either growth rate or hemogram for 8 months after exposure. More detailed experiments were carried out with squirrel monkeys in high fields. Changes were noted in the monkeys' electrocardiograms [27, 28] and electroencephalograms. Kholodov et al [142] have also reported changes in the EEG of rabbits exposed to fields of 800 oersteds (Oe). In terms of health hazards, the significance (if any) of these changes in ECG and EEG has not been established.

[4] Field strengths are commonly given as flux density (B) in gauss (G) or as field intensity (H) in oersteds (Oe). For purposes of this chapter the two measures may be considered numerically equivalent.

According to Beischer [26], in prolonged exposures (days to weeks), effects apparently are due to the gradual accumulation of physical and biochemical imbalances. Several effects reported in animals exposed to moderate fields (1000–10 000 G), for several days to several weeks, include growth retardation, hematologic changes [10], morphologic changes [14], and delayed wound healing [105]. It has been suggested [9] that these effects may be due to inhibition of mitosis, and that rapidly dividing tumors might be especially sensitive to the effects of magnetic fields. Experiments with tumor-bearing mice have given promising results [9, 11, 104], and the possibility of using magnetic fields in human cancer therapy should be given serious consideration.

The evidence of possible mutagenic effects of magnetic fields is mixed. Close and Beischer [51] found no genetic effects in *Drosophila* exposed to fields up to 120 000 G for as much as 1 h. Mulay and Mulay [206] also failed to observe genetic effects in *Drosophila* exposed to fields of 100 to 4000 Oe during one to three generations. On the other hand, Tegenkamp [285], also working with *Drosophila*, reported mutations and deviations in sex ratio in the offspring of flies exposed to fields up to 520 Oe for 24 h. Thus, the question of possible genetic effects remains unresolved.

Evidence that man can tolerate short exposures to high magnetic fields without apparent ill effects is indicated by workers in various physics laboratories in the US who were accidentally, or in the course of their work, exposed to up to 20 000 G for as long as 15 min. The only sensations noted to occur while in the field were taste sensations and mild tooth pain reported by some workers with metal fillings. No aftereffects were reported [22]. Individuals exposed to alternating fields have reported visual sensations, termed phosphenes [22, 211], which are considered an indirect effect due to induced electric currents.

A set of safety standards for human exposure to magnetic fields has been recommended by the directors of the Stanford Linear Accelerator Center (SLAC). The standards, shown in Table 8, reflect the results of animal experimentation and careful observation of personnel at the Center who were exposed to magnetic fields.

TABLE 8.—*Safety Standards for Magnetic Fields Recommended by SLAC*

Exposed part	Extended periods (h)	Short periods (min)
Whole body or head	200 G	2000 G
Arms and hands	2000 G	20 000 G

Novitskiy et al [211] have reported on a study by A. M. Vyalov of 1500 workers occupationally exposed to magnetic fields. They spent 20–60% of their workdays with their hands in fields of 350–3500 Oe, and their heads in fields of no more than 150–250 Oe. A number of general symptoms was reported, including headache, fatigue, low blood pressure, and decreased white blood cell count. A set of specific effects to the hands of a number of the workers, also reported, included sweating of palms, high skin temperature, subcutaneous edema, and shedding of skin from the palms. As a result of this study, Vyalov recommended the safety standards shown in Table 9,

TABLE 9.—*Safety Standards for Magnetic Fields Recommended by A. M. Vyalov* [1]

Exposed part	Field	Gradient
Whole body	300 Oe	5–20 Oe/cm
Hands	700 Oe	10–20 Oe/cm

[1] Adapted from Novitskiy et al [211].

which do not differ greatly from the SLAC standards for exposures of long duration. The lower value for maximum hand exposure in the Vyalov standard is probably a result of the aforementioned hand symptoms.

Very Weak Magnetic Fields

The normal geomagnetic field at the Earth's surface is approximately 0.5 G or 50 000 gammas (1 gamma $= 10^{-5}$ G), but varies somewhat both with geographic locale and with time. The physiologic significance, if any, of this weak magnetic field is poorly understood. It is possible to create an experimental area with almost no magnetic field either by shielding the area from, or compensating for, the geomagnetic field. Studies of the biologic effects of such magnetically quiet environments are of interest because of (a) the possibility of harmful effects when man travels in space, removed from the geomagnetic field, and (b) scientific interest in the possible physiologic role of the normal geomagnetic field.

In a number of studies on various organisms in magnetically quiet environments, various effects have been reported; this material has been reviewed by Conley [53]. Only studies on man will be considered here.

Numerous studies have suggested correlations between various health problems and either geographic variations in the geomagnetic field [211], or temporal fluctuations in the magnetic field in a given area [20, 211]. However, the significance of these relationships is indeed tenuous.

In two closely related experimental studies with volunteers in fields of approximately 50 gammas or less [29, 30], six men who spent 10 days in this low intensity magnetic field remained in good health and felt no ill effects. Various physiologic and psychologic tests were administered to detect any effects of the exposure; for the most part, the results were negative. There was, however, significant change in the critical flicker or fusion frequency threshold (CFF), or the frequency at which a flickering light cannot be distinguished visually from a constant one. These subtle changes in CFF cannot be considered harmful. They do indicate that removal of the geomagnetic field has a biologic effect, and suggest the possibility that longer exposures might cause more severe effects.

In conclusion, it has been shown that static magnetic fields have deleterious effects in laboratory animals, but there is little information relating potential human injury to field strength, field gradient, and duration of exposure. Given this lack of information, the recommended safety standards from SLAC (Table 8) and from S. M. Vyalov (Table 9) can be regarded only as tentative guidelines, subject to change on the basis of new information. Little is known about the biologic effects of human exposure to alternating magnetic fields, and meaningful recommendations for safety standards cannot be made at this time. Harmful effects have not been apparent when human volunteers were kept in a magnetically quiet environment for up to 10 days. There is evidence, however, suggesting that the normal geomagnetic field may have some physiologic role, the significance of which is not yet understood. Removal from the normal geomagnetic field should be considered as a possible hazard in future space voyages of long duration.

MECHANISM OF THE EFFECT OF EMW AND EMF

Since the quantum energy is too small in the RF and microwave bands to cause rupture of even the weakest chemical bonds in any biologic structures, several theories of a molecular mechanism of microwave action have been suggested:

- a specific thermal effect;
- nonthermal protein coagulation resulting from resonant vibrations of the side chains in the protein molecules;
- pearl-chain effect which involves orientation of suspended particles;
- disturbance of electromagnetic function regulation.

None of these hypotheses has yet been proved [222].

The mechanism whereby RF and microwave energy is absorbed is exceedingly complex, especially in the heterogeneous structures of a living organism. In accordance with the electrical properties of human tissues (dielectric constant, loss factor, conductivity), and varying with the particular frequency, RF energy can be absorbed by energy loss due to ion conductivity and dielectric loss due to relaxation of the dipole molecules of water. As electromagnetic oscillations increase, so does this latter phenomenon increase in importance. The result is that electromagnetic energy is turned into heat energy at the expense of the regulating oscillation of the water molecules and ions [91]. It is thought, too, that there may be a resonant absorption of radiation by protein molecules at super high and ultrahigh frequencies [305]. Damage to functioning of the cell's membrane apparatus may be the primary mechanism of action of electromagnetic energy absorption [211].

It may be assumed that the microwave field intensifies or suppresses metabolic processes (for example, tissue respiration) by influencing enzymatic activity. It has been demonstrated experimentally that metabolic changes are sensed by chemoreceptors. Consequently, information should then proceed to the CNS when there is surface microwave absorption (λ less than 10 cm) [222].

Presman [231, 232] has suggested that electromagnetic fields give rise to a regulatory process in the living organism (alongside the nervous reflex and humoral processes), i.e., that intracellular processes are controlled, along with interactions of organs and systems. Proceeding from these considerations, it is possible that this regulatory mechanism might be disturbed under microwave irradiation. Subbota and Kovach [282], however, do not concur, since there is no proof of the electromagnetic wave functional regulatory mechanism in the organism.

A specific (e.g. nonthermal) microwave effect has not been verified experimentally. Since biologic objects are electrically heterogeneous and since microwave-range electromagnetic fields have a known selective thermal effect on various tissues and organs, a difference between a microwave effect and a neutral heat effect is not necessarily due to an unknown extrathermal factor, but might well be a function of an uneven distribution of heat in the organism that could exert its own peculiar effect. The alleged nonthermal microwave effects may well be microthermal effects in the absence of conclusive experimental evidence to the contrary [217]. Investigations reported to show neurologic effects at nonthermal microwave intensities do not indicate clearly whether the changes produced by microwaves are due to generalized thermal effects, or to more specific influences on particularly vulnerable tissues. The lack of precise temperature-measuring or power-density measurement devices may play a part in the assumption of nonthermal or specific microwave effects.

An RF field can be reinforced in the region of peripheral nervous tissue causing a temperature rise, even while nearby muscle and skin show no measurable temperature effect. When peripheral nerves are heated above a minimum level, they may trigger spontaneously. Studies by McAfee [173] indicate that thermal stimulation of the peripheral nervous system may produce the neurophysiological and behavioral changes reported.

According to the best evidence available, the most important effect of microwave absorption is the conversion of the absorbed energy into heat, which, under proper physical and physiological conditions, may manifest itself by a temperature rise which is a function of the thermal regulatory processes and active adaptation of the animal. The end result is either reversible or irreversible change depending on the conditions of irradiation and physiologic state of the individual.

On the basis of published material on the biologic effect of low-frequency electric fields (EF), it is difficult to reach a conclusion about the biophysical mechanism of the effect of EF. There are contradictory data about the frequency-selective character of the biologic effect of EF, but there are still no data about the relation of the biologic effect to intensity and duration of EF action over a wide range of parameters [211].

Physiologic systems, from an electrical point of view, are assumed to be a combination of resistors and capacitors. When a steady direct current is passed through tissue, the tissue behaves like a simple electrolytic resistance path. In the presence of electrical currents, the body behaves like an electrochemical system. On the other hand, for anatomical reasons such as the presence of membranes, it generates potential differences between different parts of the body. Therefore, when considering the possibility of electric currents acting on the body, the end result will be integration of the intrinsic currents plus the externally applied currents [76].

When animals, isolated organs, neoplastic and non-neoplastic tissue cultures, and simple chemical systems have been exposed to high magnetic fields, a great variety of biologic effects has been produced [42]. So far, no definite magnetic dose-effect relationship has been established. Effects have been predicated on the basis of field strength alone, as well as on the inhomogeneity of the paramagnetic strength of the field.

The mechanisms proposed for the biologic action of magnetic fields, reviewed by Busby [42] and Grissett [102], include:

(a) generation of electromotive force in moving conductors;

(b) force exerted on moving charge carriers at critical sites;

(c) diamagnetic and paramagnetic effects—an impressed magnetic field alters the orbital character of electrons in a manner so that the magnetic field produced is in opposition to the externally applied field;

(d) rotational diffusion—an increase in magnetic field will reduce rotational diffusion and a decrease will enhance rotational diffusion leading to decrease in biochemical reaction rates;

(e) alteration of bond angles, which may influence chemical reaction rates;

(f) alteration of tunneling rate of protons in hydrogen bonds of macromolecular systems.

PROBLEMS REQUIRING FUTURE RESEARCH EFFORT

Since the intrusion of man into space involves drastic changes in his environment—changes which can range from reduced magnetic fields to very high fields created in the spacecraft (which may also include radio-frequency effects)—it is important to assess the need for research in these areas as related to space biology. Investigations in these areas are difficult. Definitive experiments that can be demonstrated readily and repeatedly and, hopefully, understood are lacking. It is a fact that any biologic consequence of a field, particularly if it is a weak field, is quite remarkable. Because of the challenging nature, it is most important that good, repeatable, readily demonstrable effects be sought and found; these effects need not be a great number, but must be unambiguous [277].

In general, the distinctive feature of the action of electric and electromagnetic fields is the dependence of the field effectiveness on the geometry of the object being affected. It is necessary, therefore, to know the physical properties of the object of study [211].

It is not always possible to use generally accepted electrophysiologic methods in studying the influence of microwave fields on the organism, since the sensors (electrodes, thermocouples) can act as receiving antennas so that substantial high-frequency voltages are induced during irradiation. These voltages may give rise to secondary but sometimes very strong stimuli ranging up to thermal coagulation of protein in tissues. Unfortunately, investigators have, at times, overlooked this [222].

In experimental studies on animals, it must be remembered that changes in the organism depend, to a major degree, on the geometric dimensions of the animals, due to the depth of penetration of microwave energy which varies with wavelength. It is known that at a given wavelength (for example, $\lambda = 10$ cm), vitally important organs in mice and rats may absorb the electromagnetic energy, while in dogs and especially in man, almost all of this energy is absorbed by the superficial tissues of the head, thorax, and abdominal wall. The brain, heart, and other vital organs may escape direct irradiation in these cases [222].

The features of the microwave effect on the organism are known at present only for certain discrete points in the electromagnetic spectrum. Information on the mechanism of action on various organs and organ systems is incomplete, and little study has been directed toward the peculiarities of the microwave effect on the permeability of cell membranes, tissue respiration, and other organic functions. Very little attention has been given to the combined influence of electromagnetic energy and various environmental factors (high temperature, oxygen deficiency); time-intensity relationships, the type of modulation, and other parameters should also be taken into account [222].

Since most reported low-level effects relate to behavioral and CNS changes, studies are needed to determine the nature and mechanism(s) of the nervous system's reactions, if any, to electromagnetic and magnetic fields and to investigate the degree to which the individual's performance capabilities may be affected. The neuroendocrine and central nervous systems, because of their important integratory and regulatory functions, should be given attention as possible sensitive areas. The question whether reported CNS changes in man, if they are validated, would be important enough to affect his performance at the low permissible doses, which do not endanger his health and comfort, should be resolved [83].

In any assessment of the hazards of exposure to nonionizing electromagnetic energy, it is extremely important to use a team approach of physical and biologic scientists working together. Physical scientists include individuals well-grounded in electromagnetic field theory and electronics. Biologic scientists include those with experience in genetics, behavioral sciences, physiology, biochemistry, and pathology, as well as individuals with broad or horizontal training in human or veterinary medicine. The physical scientists and biologic scientists should be complemented with biophysicists who provide a bridge between these two major orientations.

Specifically, the problem of dosimetry is overriding, for interpretation of biologic research is, without question, dependent on good dosimetric measurement. In addition to accurate measurement of the ambient electromagnetic fields, the amount of energy actually deposited in the tissue under investigation should be determined. Therefore, there is need for an accurate general purpose reader, the development of implantable probes should be encouraged, and an integrating dosimeter would be of considerable utility in hazards assessment. In this context, it should be remembered that, although good dosimetry and implantable probes are essential, they would be of no value without a precise definition of the biologic problem under consideration. Laboratories with proper EM sources, and exposure, dosimetry, and animal facilities are required.

It is important that research be conducted so that all aspects of the study are quantified, including the fields induced both inside and outside the tissues, type and degree of the effect, whether the effect is harmful, harmless, or merely an artifact, whether it is a thermal or nonthermal effect, and how it relates to the results obtained by other investigators. Body size of the experimental animal with appropriate scaling must be taken into account along with accurate in vivo dosimetry so that an investigator's results obtained with one animal species can be related to those of another investigator using other species. Since body absorption cross sections and internal heating patterns can differ widely, an investigator may think he is observing a low-level or a nonthermal effect in one animal because the incident power is low, while in actuality, the animal may be exposed to as much absorbed power in a specific region of the body as another larger animal with much higher incident powers. This points out the need for both physical and physiologic (comparative) scaling of animal species.

Particular attention should be paid to instrumentation problems—to the development of more adequate probes for making measurements in the presence of EMW or EMF. Field strength, electrophysiological, and thermal probes which will give artifact-free readings, will not distort the field in any way, and which will not give rise to inadvertent stimulation of the tissue due to induced currents, are essential before any degree of reliance can be placed on findings of altered physiology or behavior due to EMF or EMW.

More research is needed to determine the effects of physical characteristics of an exposed individual as well as the effects of external factors such as temperature, humidity, and air currents on his tolerance to EM fields. It is necessary to show the differences in effects and potential hazards in whole-body and partial-body irradiation under various EM exposure and heat stress conditions. Information is needed on the significance of maximum absorbed power density, average absorbed power density (per unit volume), and the average absorbed power density (per unit body surface area) to potential hazards for both continuous and intermittent exposures.

The greatest need today in the assessment of biologic effects of EMW, EMF, electric and magnetic fields is to maintain a realistic perspective on the nature of these radiations and the possible effects from exposure. The mechanisms which produce cell damage, the biological tolerance of the most susceptible tissues, and safe levels of intensity must be established in an organized fashion. Ultimately, clear differentiation must be made between hazard and biologic effect.

COMBINED STRESSES

During flight in space, man is subjected to an entire range of factors (electromagnetic radiation, accelerations, vibrations, weightlessness, changes in barometric pressure and gas composition, numerous emotional-psychic effects) which will act on him in a variety of combinations and sequences. Under occupational conditions, people working with microwave generators are subjected not only to the microwave, but also to other factors such as soft x-rays, noise, noxious gases (CO and others), and high and low temperatures in the environment. Their importance in pathogenesis of disease has not been adequately studied [221]. Interaction between stresses may manifest itself as addition of responses, the individual stress responses may be antagonistic and cause some canceling, or there may be simply no apparent interaction [308].

The subject of combined stresses which could have implications for space exploration has been reviewed or noted by several authors [34, 195, 232, 245, 308]. In recent years, information has become available on combined effects of RF and microwave energies and other factors on the organism. Synergism or other forms of interaction of microwaves and ionizing radiation have been noted by several investigators [196, 197, 233, 234, 287, 288]. Microwave modification of response to x-irradiation is related to duration and sequence of microwave exposures as well as the time between the exposure and the x-irradiation [195].

The effect of hypothalamic depressant drugs on the response to microwave exposure has been reported by Michaelson and associates [193, 195]. Studies have been reported on the influence of differences in ambient temperature on the response to microwave exposure [195]. Petrov and Yarokhno [223] noted inhibition of adaptation to hypoxia when rabbits were exposed to microwaves while inspiring air with a reduced O_2 content.

The potential of microwaves to increase or reduce the injurious effects of x-irradiation could have application in space operations and clinical radiation therapy. A possible mechanism may be that hypoxia reduces the formation and toxic effect of free radicals. Any molecular alteration may modify target molecules. Thermogenesis and stress may influence metabolism and endocrine response. The severe injury from x-irradiation at lethal dose levels may exceed or nullify any modifying capability of microwaves. The specific effects of frequency, power density, and x-ray doses and dose rates, and temporal separation of the two radiation modes have not yet been adequately determined, nor has the significance of this synergism been established for human exposure [245].

Adaptation to EF has resulted in increased resistance of mice to ionizing radiation exposure in the lethal range [131]. Interaction of magnetic fields with other factors has been reported as a reduction of ionizing radiation lethality by pretreatment with magnetic fields [3] and increase in lifespan in tumor-bearing mice [104]. On the other hand, in experiments on *Drosophila melanogaster*, synergistic effects of a magnetic field with x-irradiation, starvation, hyperoxia, or hypoxia were not observed [51].

These isolated reports of interactions of combined radiant energies as well as other factors suggest areas of investigation which could provide basic information on mechanisms of action as well as practical approaches to counteract undesirable effects of these radiant energies. Information should be obtained on the interaction of combinations of various radiant energies in addition to stresses on the body as a result of acceleration, gaseous atmospheres, toxic agents, hypoxia, exercise, heat, cold, vibration, weighlessness, and noise.

SUMMARY

The effort in this chapter has been to review, synthesize, and critically analyze the literature on human response (which, of necessity, requires concurrent consideration of other animal species) to RF and microwave energies, magnetic and electric fields. Although there is considerable agreement among scientists, there are lacunae of disagreement. It is especially recommended that apparent discrepancies be studied and analyzed in detail, taking into consideration all the biophysical factors inside and outside the body that might influence the individual's response, paying due regard to the regulatory systems that might be involved in regulation after exposure to these energies and fields.

The features of the microwave effect on the organism are known at present only for certain discrete points in the electromagnetic spectrum. Information on the mechanism of action on various organs and organ systems is incomplete. Very little attention has been given to the combined influence of electromagnetic energy and various environmental factors (high temperature, oxygen deficiency), time-intensity relationships, and the type of modulation.

Free international exchange of information and closer personal contact between scientists would help resolve the discrepancies and divergence of opinion in understanding biologic and clinical effects of exposure to RF and microwave energies, magnetic and electrical fields.

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Chapter 11

ULTRAVIOLET, VISIBLE, AND INFRARED RAYS [1]

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That portion of the electromagnetic spectral continuum which is bounded on the shortwave end by x-radiation and on the longwave end by the shortest microwaves is generally divided into three regions. Wavelengths between approximately 1.0×10^{-8} and 4.0×10^{-7} m (100 to 4000 Å) are described as ultraviolet rays since they lie in a spectral region beyond the shortwave limit of normal human vision. The wavelength band between about 7.5×10^{-7} and 1×10^{-3} m (0.75 to 1000 μm), waves too long to excite the visual process, is called the region of infrared rays. The narrow region which lies between the ultraviolet and the infrared, spanning less than one octave, contains those wavelengths (about 3.8×10^{-7} to 7.5×10^{-7}, or 380 to 750 nm) which are capable of stimulating the human sense of vision and which give the enormously important experiences of light and color.

Each of these three regions is characterized by certain biologic effects which its band of wavelengths produces, although there is some overlap at the arbitrary boundaries mentioned above, and some biologic processes (notably photosynthesis) require contributions from widely disparate spectral loci. Furthermore, many of the important actions of some wavelengths may involve the organism only secondarily, rather than by any direct absorption and utilization of the rays themselves. In order for electromagnetic energy to be detected, measured, or utilized, it must be made to impinge on an appropriate sensor or material. A ray of light is invisible and can be visually sensed only when it enters the eye either directly or by reflection from some substance. Ultraviolet radiation can be sensed through its effects on biologic systems, by causing it to excite a fluorescing material, or by other indirect means. Infrared rays are usually only sensed by reason of their heating ability, or by their action on one or another biological or chemical process.

The importance of ultraviolet, visible, and infrared rays to biological systems is immense; with very few exceptions, all life forms on Earth depend on the direct or indirect effects of these

[1] This chapter was prepared by combining separate material submitted by the two authors independently. The two manuscripts reviewed by the Joint Editorial Board were in good agreement in regard to content and emphasis, with one exception, that being the greater stress placed upon hygienic considerations by Professor Letavet. Space limitation in format required condensing the original material; however, the editors believe that all salient points have been included, and the references should be consulted for detailed information. Attention is called particularly to the material on safety and standards for radiation exposure developed by Soviet scientists.

wavelengths. At the same time, it is clear that exposure to excessive amounts of energy in these spectral regions can result in biologically harmful consequences which may range from minor impairment of function to death of the organism. A balance must therefore be maintained, so that optimal amounts of the radiations in question are provided. In the average terrestrial environment this balance has generally been achieved, partly through adaptive processes in evolution, and partly through purposeful modification of the environment, especially by man. In the hostile environment of space, which is characterized by extremes of radiative energy levels, it is necessary to modify the radiative environment to ensure that the needs of the organism are met but not grossly exceeded. In some cases, of course, it may be desirable to provide lethal levels of radiation for such specific operations as the control of microorganisms by ultraviolet irradiation. With this exception, however, the objective is to maintain levels of ultraviolet, visible, and infrared energies within biologically advantageous limits.

Although the visible part of the electromagnetic spectrum is very small in extent, this narrow range of wavelengths is of paramount importance to man because within it lies the adequate stimulus to human vision. Since vision is unarguably the most important of our senses, considerable emphasis must be given to problems associated with establishment and maintenance of the best possible conditions in the visual environment. While the visible spectrum is only a minute part of the electromagnetic domain, a tremendous amount of information about the world can be extracted, thanks to the exquisitely fine discriminations which the visual system is capable of performing. These discriminations, however, are best made under conditions where neither too little nor too much light energy is present, so that a prime objective in space operations is to provide light levels which lead to the highest possible discriminability of form, contrast, movement, color, and fine detail.

This chapter will discuss the radiation sources in the spectral regions under consideration, and describe the more important associated biological and psychophysiological effects. The problem of protection from excessively high or low levels of radiant energy in these spectral regions will be discussed, with suggestions for optimal levels.

SOURCES OF ULTRAVIOLET, VISIBLE, AND INFRARED ENERGY

The production of energy in the three spectral regions, ultraviolet, visible, and infrared, is associated in a general way with the different physical systems which are capable of emitting energy at the wavelengths involved. Visible light is produced, for example, from the change in energy level of the planetary electrons of atoms to a lower state, while infrared radiation is consequent upon vibrations and rotations at the molecular level. The Sun is the most important energy source in the spectral regions of interest here. It is the only significant natural source for most wavelengths, and only when solar energy is unavailable or insufficient must there be recourse to artificial energy sources. In each wavelength region, available manmade devices may be used to supplement or replace direct energy from the Sun.

Although the Sun radiates energy over a wide band of wavelengths (less than 1 Å to beyond 100 m), 99% of this energy is contained in the region from 0.275 to 4.67 μm, and about one-half lies within the visible spectrum. The solar irradiance spectrum has recently been redetermined by Thekaekara [15] for the range of wavelengths between 0.2 and 2.6 μm; he suggests adoption of the data in Figure 1 for practical purposes. Knowledge of the solar spectrum is important not only because of the direct biological and

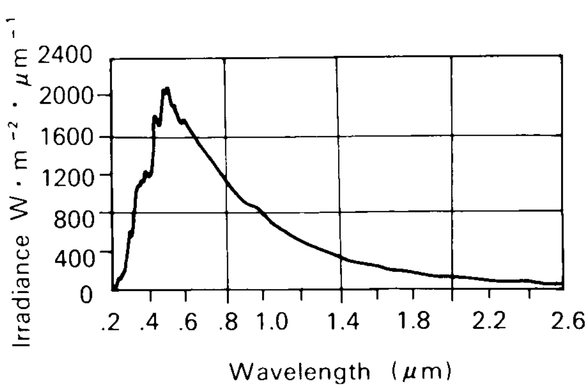

FIGURE 1.—The solar spectral irradiance curve outside the atmosphere. (From Thekaekara [15])

medical consequences, but also because of secondary effects arising from spacecraft heating by the near infrared, materials degradation in the ultraviolet, and influences on the radiation belts.

Ultraviolet Sources

Less than 5% of the Sun's energy is in the ultraviolet. Nevertheless, sufficient shortwave potency is present so that, even after attenuation due to the Earth's atmosphere, direct sunlight is active in a variety of biological processes. When solar energy in the ultraviolet region is lost, either through direct shadowing or transmission losses imposed by an intervening medium, it may be necessary to provide an artificial source to maintain a desired biotic effect. Such sources, long known, are available in a number of forms which are usually designed for maximum efficacy in one or another frequency band in the ultraviolet region, according to the intended use.

Since incandescent lamps are exceedingly inefficient sources of ultraviolet, radiating only a small fraction of their energy in the longer UV wavebands, an electrical arc is generally used instead. The most convenient types in space applications are the enclosed arcs of mercury, hydrogen, and xenon, with mercury most frequently chosen for reasons of cost, convenience, and reliability. (A discussion of ultraviolet sources of all types may be found in Koller [9]). Distribution of energy in the mercury arc depends heavily on the vapor pressure of the metal during lamp operation. At low pressures almost all of the emitted energy is at the mercury resonance line at 2537 Å; such lamps are widely used for germicidal effectiveness. When such a low pressure arc is contained in a quartz envelope, transparent to the 1849 Å line, part of the atmospheric oxygen in its vicinity is converted to ozone.

As the pressure is increased there is a broadening of the emission lines, a relative shift in spectral energy output toward the longer wavelengths, and an increase in the continuous background against which the bright lines appear. (See Ref. [9], p. 46.) Medium pressures, therefore, are used in lamps when the intention is to produce radiations in the medium and near-ultraviolet range. At very high pressures, mercury arcs radiate largely in the visible and near-infrared regions, and therefore are considered only secondarily as sources of ultraviolet.

Sources of Visible Light

Approximately one-half the Sun's energy is in the visible spectrum, which extends from about 380 to 750 nm. Because of this, and the intensity of solar radiation compared with relatively feeble artificial sources, the Sun is the single most important source of light. It is hardly surprising that many terrestrial biologic processes are either dependent upon, or influenced by, energy lying in this spectral region. The two peaks of the chlorophyll absorption spectrum lie near the ends of the light region, and the maximum sensitivity of most visual systems, including man's, is found quite close to the solar energy maximum. In Figure 1, the Sun's spectrum is essentially continuous throughout the visible light region, and aside from certain irregularities due to absorption by elements of the outer solar layers, is approximated by the energy distribution of an incandescent blackbody at 6000 °K for visible wavelengths. Artificial sources of visible light historically have been designed to approximate energy distribution, hence the color, of sunlight. In the long chronicle of manmade lights, from flames to incandescent filaments to fluorescent lamps to the most recent of electroluminescent devices, the first concern has been to supplement or replace solar energy with light that will permit normal visual function. Fairly recently, and only secondarily, has there been much effort to devise artificial lighting for other purposes, such as for growing plants.

The most common source of artificial light is the incandescent tungsten filament. In its simplest form, an incandescent lamp consists of a glass envelope filled with an inert gas or partially evacuated and a wire or ribbon of tungsten heated by passage of an electrical current. The distribution of energy from such a lamp in the visible spectrum depends upon the temperature to which the filament is heated, as shown in Figure 2. From the standpoint of visual

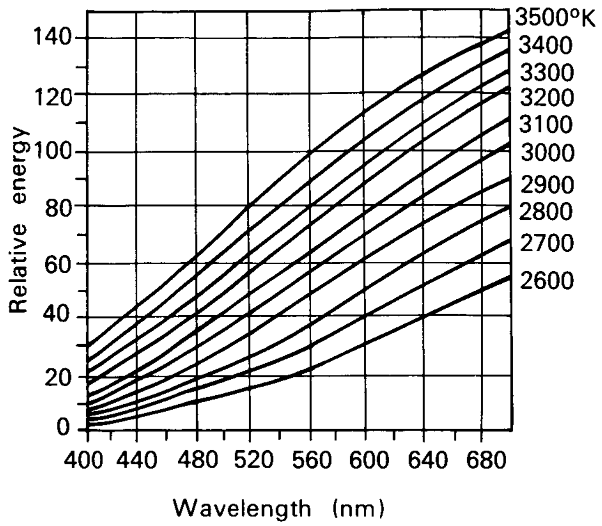

FIGURE 2.—Spectral energy distribution in the visible region from tungsten at different operating temperatures. (From Kaufman [8])

efficiency, higher operating temperatures are desirable, but this leads to short lamp life. The recent development of tungsten-halogen lamps represents a major step forward toward greater visual efficiency. In the tungsten-halogen lamp, the filament is operated at high temperature in an atmosphere of bromine or iodine vapor so that the evaporated tungsten redeposits on the filament instead of on the walls of the envelope. Any tungsten lamp, however, radiates a great deal of energy in the near-infrared, and many times this heat production may be intolerable. Moreover, when the purpose of the device is to generate light in the visible wavelengths, it is obvious that incandescent lamps are inherently inefficient. For these reasons, essentially, other means of converting electrical energy into light have been developed.

Fluorescent lamps ordinarily consist of a low-pressure mercury arc enclosed in a tube, the walls of which are coated with chemical phosphors which fluoresce when excited by the ultraviolet of the mercury spectrum. In comparison with tungsten lamps they are highly efficient and produce little infrared. As an example, a conventional 40-W tungsten lamp yields 465 lm,[2] while a 40-W fluorescent provides 2600 lm. Through the proper choice of phosphors, the energy distribution of fluorescent lamps may be adjusted over a wide gamut. Thus, lamps have been developed to show energy maxima in those spectral bands involved in photosynthesis, as well as to approximate daylight illumination. A great range of fluorescent lamps is presently available and their characteristics may be found in several lighting handbooks (see Ref. [8]). The life expectancy of fluorescent lamps is many times greater than the incandescents; about 7.5:1 for the two lamps mentioned above.

Other sources of visible light include open arcs, enclosed arcs, electroluminescent panels, photoemissive diodes, and a number of less important ones, such as luminescent phosphors and chemiluminescent fluid mixtures. The xenon arc, especially in its short-arc version, is a source with high efficiency and a spectral energy distribution close to daylight. Sodium vapor arcs achieve very high efficiencies, but radiate in the visible only at 5890 and 5896 Å. The concentrated arc lamp, which uses zirconium oxide as the negative electrode, is useful when only a small source is needed (0.127 to 2.79 mm). Open arcs, usually between carbon electrodes, are of little interest in space applications. Low energy sources, such as photodiodes and electroluminescent devices, find application mainly in visual displays and where high-intensity white light is not required, because of their tendency toward exotic emission spectra. Flashtubes, usually xenon-filled, are adaptable in visual signaling, for optical pumping of lasers, and wherever a short burst of high-intensity visible light is required.

Incandescent and fluorescent lamps will likely continue to be the most important practical sources of visible light, especially for general illumination, and photobiotic and psychophysiological activities. Lasers, although biologically and medically applicable in the clinic and in the laboratory, are only now being considered for operational biomedical uses in space flight. The special qualities of monochromaticity, tunability, coherency, and

[2] The lumen (lm) is the unit of luminous flux, that is, the radiant flux evaluated in terms of the response of the visual system. For a wavelength of 555 nm (the sensitivity peak of human photopic vision, v.i.), a lossless light source would produce 680 lm/W. Many factors in lamp design and operation act to lower the efficiency, especially the relatively high infrared emittance.

the high-power densities involved, make them exciting candidates for wider use in photobiological research.

Infrared Sources

All bodies not at absolute zero temperature radiate energy in the infrared region of the electromagnetic spectrum. The Sun, again, is the most important source of direct radiation; about 45% of its energy is emitted at wavelengths on the near-infrared (see Fig. 1). Cooler objects show energy maxima at longer wavelengths (suggested by Fig. 3) until, at terrestrial temperatures, a blackbody radiates with a peak intensity at about 10 μm. Much of the infrared radiation in the environment either comes directly from the Sun or indirectly by reradiation from matter so heated. By use of suitable materials of high thermal inertia, it is possible to store solar energy for use when the Sun's direct rays are absent or weakened. The many sources of infrared include fire and other exothermic chemical reactions as well as mechanical processes. Only those which use electrical input will be discussed here.

Any incandescent filament lamp is a rich source of infrared. Depending upon the operating temperature, from 75 to 80% of the energy lies in this spectral region, largely in the invisible range from 760 to 5000 nm. For this reason, the most common artificial source for obtaining infrared rays from electrical current is a tungsten lamp operated at a relatively low temperature so that the output maximum is shifted toward the longer wavelengths. In general, such lamps are used for the range from 760 to 4000 nm, while sheathed resistance radiant heaters are used for wavelengths from 1500 to 14 000 nm. The advantage of the latter is the capability to radiate the longer wavelengths that are absorbed by the glass or quartz envelope of an incandescent lamp, and they are extremely rugged and long-lasting. The important sources of energy in three regions of the electromagnetic spectrum (ultraviolet, visible, and infrared) have been indicated.

The list is by no means complete, but it should be evident that, in the absence of natural solar radiation, man has been able to devise artificial means for providing useful amounts of energy

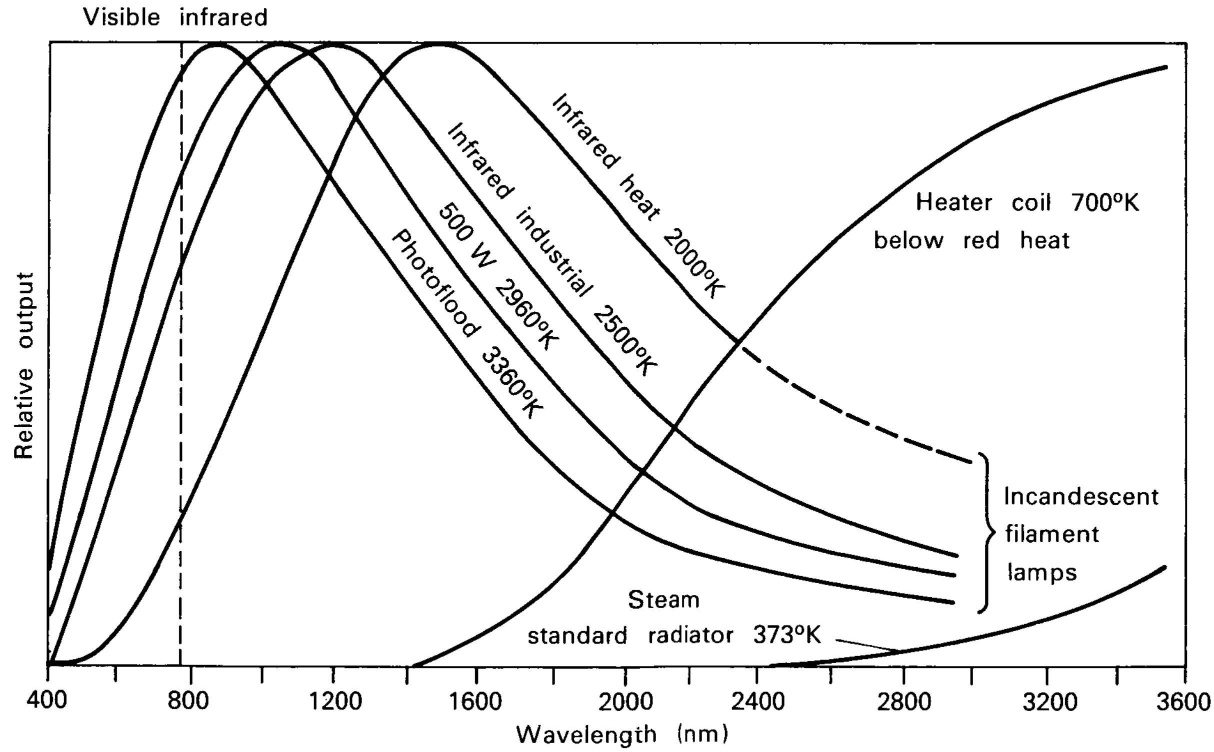

FIGURE 3.—Spectral energy distribution for some infrared sources. (From Kaufman [8])

in any desired spectral band. In the sections of this chapter that follow, the importance of these three spectral regions in space biology and medicine will be discussed.

THE VISIBLE SPECTRUM

The range of wavelengths between the approximate limits of 380 to 750 nm comprises the visible spectrum, since this band of energy is capable of stimulating the organs of sight and producing the sensation of light. Although this region of the spectrum exhibits other bioactive properties, including heating and activation of photosynthesis, its most important role in space operations is to act as the stimulus to vision. The human visual system, including the entire eye-to-brain complex, can perform a number of fine discriminations over a wide range of intensity levels. The literature on vision is vast; to summarize the accumulated knowledge would be beyond the scope of this chapter. Among compendia of the human visual response data, the works of Roth [14] and Davson [5] are highly recommended.

Visual sensitivity to the wavelengths of the light spectrum varies in two important ways. First, the eye shows a sensitivity curve which is roughly symmetrical about a maximum sensitivity peak. For vision in bright light this peak occurs at 555 nm; if this value is taken as unity, the sensitivity at 380 nm is 0.00004, while at 750 nm it is 0.00012. Second, at low light levels, the sensitivity maximum is shifted toward the blue end of the spectrum, occurring at about 505 nm when the eye is totally dark-adapted. The relationships are indicated in Figure 4. The implications are clear that wavelengths in the blue-green region are most efficient in stimulating vision, and that relatively large amounts of energy are needed at the violet and red extremes. When the eye is given adequate energy, it is possible to make very fine discriminations between wavelengths. Color discrimination is better in some spectral regions than in others (Fig. 5), and it is likely that this reflects the properties of the photosensitive pigments in the retinal cone cells, which are active in color vision. At low light levels, color discrimination is absent and only

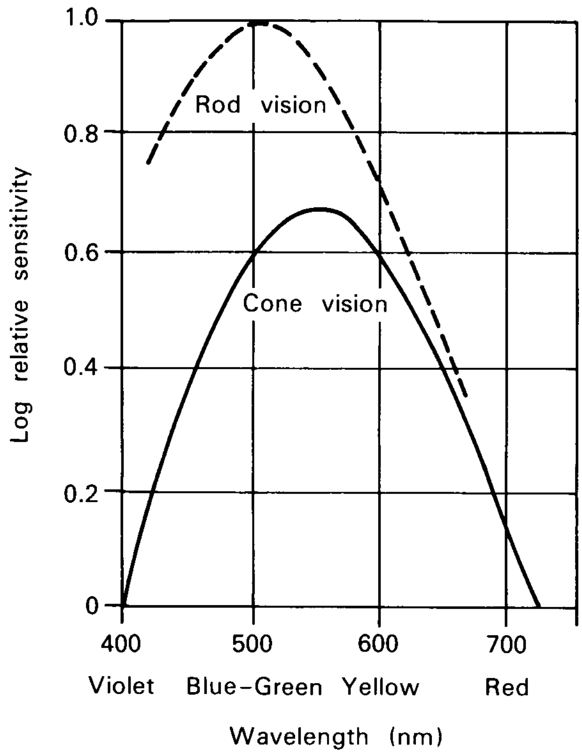

FIGURE 4.—Spectral sensitivity curves of human visual receptors. Cones are the retinal cells active in high-level, daylight seeing, and in color vision. Rods, which are more sensitive over much of the visible range, are responsible for night vision at levels too low for the cones to be stimulated, but color vision is not possible. (From Roth [14])

rhodopsin, the single photopigment of the retinal rod cells, is activated.

Useful vision is possible over a wide range of energy levels, although such visual functions as contrast discrimination, color vision, visual acuity, and the like are best performed in the upper part of this range.[3] The immense gamut of naturally occurring light levels on Earth and in space is shown in Figure 6. That the eye is able to perform successfully over so many orders of magnitude is due in part to the duplex nature of the retinal mosaic (rods and cones), partly to pho-

[3] Under fully dark-adapted conditions, the sensitivity of the eye is very great; for wavelength 507 nm the energy flux required for detection of light amounts to about 9×10^{-16} W. This amount of energy would require 150 million years to raise the temperature of 1 g of water 1° C. Put another way, the mechanical energy of a pea falling from a height of 1 in. would, if converted into luminous energy, be sufficient to give a faint impression of light to every man who ever lived.

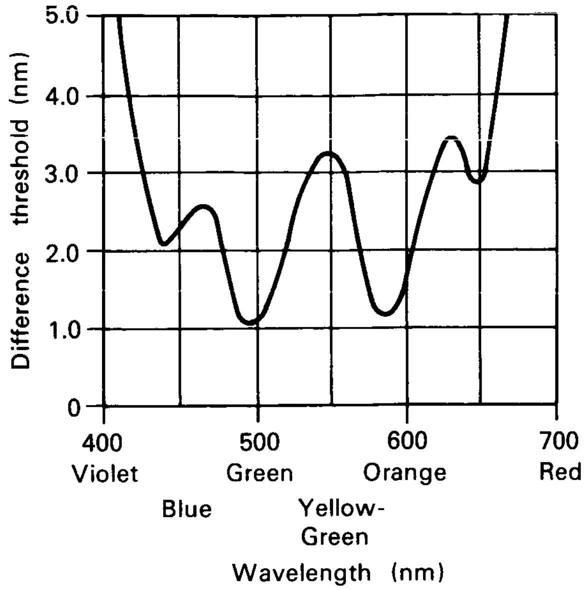

FIGURE 5. — Hue discrimination in the visible spectrum. Under optimal conditions wavelengths varying as little as 1 nm can be differentiated. (From Roth [14])

tochemical adaptation at the retinal level, partly to the adjustment of the iris, and partly to the fact that neural connections in the visual pathways and/or in the retina can change as a function of the light level. From the visual standpoint, sufficient light of the proper kind must always be available in space operations which depend upon human visual performance. This implies that the luminance of the critical visual tasks should be controlled to fall within the range roughly between 10 and 1000 millilamberts (mL) (30 and 3000 cd/m^2). The quality of illumination likewise is very important, for it is possible to make some of the necessary discriminations only when the energy of the illuminant is spread broadly throughout the visible spectrum. When light from the natural environment is too great, it must be reduced by filters, screens, visors, or occulting shields. When too little natural light is available, it must be supplemented by artificial sources, or, in some cases, redirected by means of reflectors.

In certain applications, notably when the spacecrew must maintain dark adaptation for observation of low-level phenomena, extravehicular activity in shadow, or any other activity in the relative dark, it is desirable to eliminate all light for up to about 30 min until the eye has reached its maximum sensitivity. If this is not practical, it is possible to maintain some useful vision during the adaptation process with deep red illumination (or wearing deep red goggles), which allows the rods to adapt differentially. Figure 4 indicates that wavelengths longer than 650 nm are suited to this purpose. During sleep or rest periods, it is also necessary to reduce or eliminate light from the eye, sometimes accomplished by complete shuttering of spacecraft windows and turning off all lights except those for emergency use.

Contrast Discrimination

Ordinary seeing depends upon differences in the luminances of objects or patterns in the visual environment. To detect an object against its background in the absence of a color difference between the two, a criterion amount of brightness contrast must be present. Luminance contrast is now universally defined by the ratio between the luminance difference between object and background and the luminance of the background itself, thus:

$$C = \Delta L / L_{bkg} \qquad (1)$$

Contrast, then, can vary between the limits of -1 (for objects of zero luminance against any background luminance) to plus infinity (for bright objects against a zero-luminance background). Many studies have been made of human contrast sensitivity as a function of such variables as size, shape, position in the field, presentation time, and the level of background luminance. These investigations have been well-summarized [5, 14]. The general form of the relationship for simple circular objects against uniform backgrounds is indicated by Figure 7. Luminance contrast seems to be much more important to the detection process than color contrast; color aids detection only when luminance contrast is insufficient or absent. Furthermore, to a first approximation, the detectability of objects of equivalent numerical contrast but opposite sign is the same.

Visual Acuity

The ability to discriminate fine detail is influenced by a number of factors, but the

Luminance				Object	Notes
cd/m²	mL		cd/m²		
3.2×10^9	1×10^9				
		7×10^8	2.2×10^9	Sun	Viewed from outside Earth's atmosphere
		4.4×10^8	1.4×10^9	Sun	Viewed from the Earth
3.2×10^8	1×10^8				
		8×10^7	2.5×10^8	A-Bomb	Fireball 4 miles from point of detonation of an 800 KT weapon
3.2×10^7	1×10^7				
3.2×10^6	1×10^6				
3.2×10^5	1×10^5				
		1.58×10^4	5.1×10^4	Venus	Assume albedo (r) of 0.59 viewed from outside atmosphere
		9.4×10^3	2.9×10^4	Earth	Viewed from space with cloud cover (r = 0.8)
3.2×10^4	1×10^4	6.4×10^3	2.0×10^4	Mercury	Viewed from outside atmosphere (r = 0.069)
		4.3×10^3	1.4×10^4	Earth	Viewed in January from outside atmosphere, no clouds (r = 0.39)
		2.9×10^3	9.2×10^3	Jupiter	Viewed from outside atmosphere (r = 0.56)
		2×10^3	6.4×10^3	Sky	Average sky on clear day
		1.2×10^3	3.8×10^3	Moon	Full Moon viewed from outside of atmosphere (r = 0.073)
3.2×10^3	1×10^3				
		9.6×10^2	3.1×10^3	Saturn	Viewed from outside atmosphere (r = 0.63)
		9×10^2	2.9×10^3	Mars	Viewed from outside atmosphere (r = 0.15)
		8×10^2	2.5×10^3	Moon	Full Moon viewed from Earth
		5×10^2	1.6×10^3	Sky	Average sky on cloudy day
		2.4×10^2	7.7×10^3	Uranus	Viewed from outside the Earth (r = 0.63)
		1.1×10^2	3.5×10^2	Neptune	Viewed from outside atmosphere (r = 0.73)
3.2×10^2	1×10^2				
		2×10^1	6.4×10^1	White paper in good reading light	

		1.6×10^{1}	5.1×10^{1}	Movie screen (indoors)	
3.2×10	1×10	1×10^{1}	3.2×10^{1}	TV screen	
		7×10^{0}	2.2×10^{0}	Pluto	Viewed from outside the atmosphere
3.2×10^{0}	1×10^{0}	8×10^{-1}	2.5×10^{0}	Snow in light of full Moon	
3.2×10^{-1}	1×10^{-1}				
		2×10^{-2}	6.4×10^{-2}	Lower limit for useful color vision	
3.2×10^{-2}	1×10^{-2}				
		7.5×10^{-3}	2.4×10^{-2}	Earth	Viewed from outside atmosphere with full Moon
		1×10^{-3}	3.2×10^{-3}	Upper limit for night vision	
3.2×10^{-3}	1×10^{-3}				
3.2×10^{-4}	1×10^{-4}				
		3×10^{-5}	9.5×10^{-5}	Earth	Viewed from outside atmosphere at night with airglow, starlight, and zodiacal light providing illumination
		1×10^{-5}	3.2×10^{-5}	Absolute threshold for dark adapted human eye, lower limit for night vision	
3.2×10^{-5}	1×10^{-5}				
1.6×10^{-5}	5×10^{-6}	1×10^{-5}	3.2×10^{-5}	Sky	Moonless night sky viewed from Earth
1.2×10^{-5}	4×10^{-6}				
9.5×10^{-6}	3×10^{-6}				
6.4×10^{-6}	2×10^{-6}				
3.2×10^{-6}	1×10^{-6}	1×10^{-6}	3.2×10^{-6}	Space background	Background luminance formed by starlight, zodiacal and galactic light

FIGURE 6.—The immense range of luminances in the terrestrial and space environments; albedo (r) is the ratio of reflected to incident visible light, with the reflected component collected over 4π sr. (From Roth [14])

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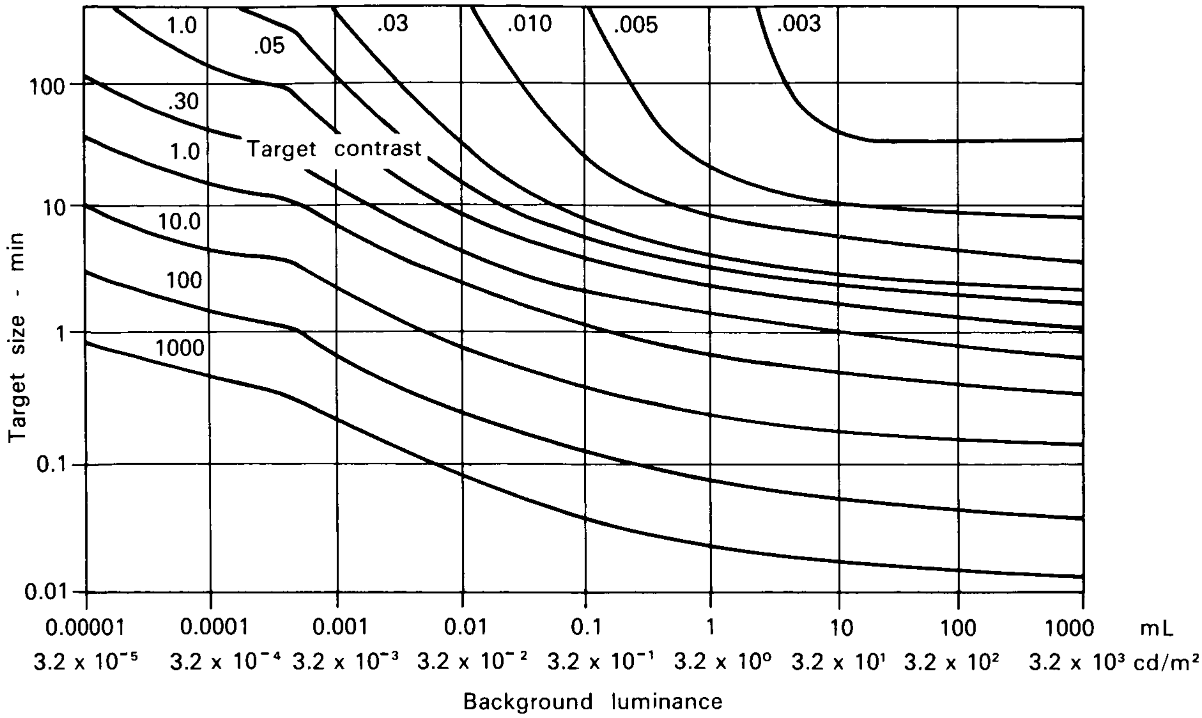

FIGURE 7.—Relationship between size of an object, background luminance, and object's contrast needed for visual detection. (From Roth [14])

underlying need is that the optical components of the eye be able to provide a well-focused image on the retina. Assuming that the refractive state of the individual is unimpaired, only those factors which tend to degrade normal visual acuity will be outlined. The luminance level of the task is of first importance. Either too little or too much light leads to poor performance, although for different reasons. At very low levels the relatively coarse mosaic of rods in the peripheral retina is stimulated, presumably with many receptors converging functionally upon very few fibers in the optical pathways. Also, at low levels, the pupil of the eye enlarges so that considerable spherical aberration comes into play. At very high energy levels visual acuity again deteriorates, which is thought due to excessive bleaching of the photopigments, glare effects (v.i.), and diffraction caused by a too-small pupil, although other factors may be present. Fortunately, the high-level effects on acuity are confined to a few limited situations, and can be controlled easily through use of attenuators.

The optimum luminance range for ordinary acuity is shown in Figure 8. Contrast likewise affects acuity, and more than a tenfold increase is needed in the size of the detail to be discriminated if the contrast drops from 0.50 to 0.02, according to Cobb and Moss [3]. Visual acuity is less also when the pattern is moving, or when the time allowed for observation is short. Loss in acuity is shown during high-altitude flight when no objects are in the visual field at optical infinity (Whiteside [18]). In this case, also at low adaptation levels, the eye tends to become myopic and distance acuity impaired. For the optimization, maintenance, and protection of visual acuity, the light environment should be controlled within those limits which enable best function, and, when possible, the objects of regard should be designed to have sufficient contrast for easy discrimination without error.

Other visual discriminations. While contrast discrimination and visual acuity are highly important components of visual performance, there are several other means by which information is extracted from the light patterns falling onto the retinas of the two eyes. Included are motion dis-

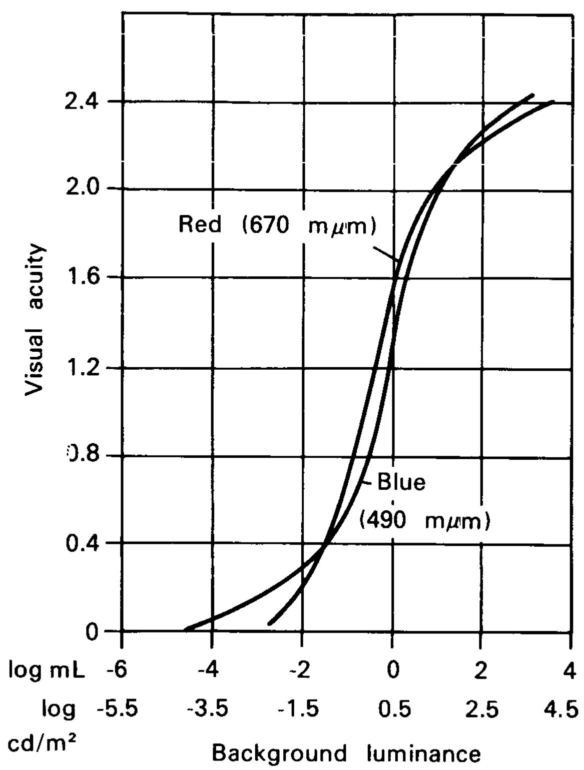

FIGURE 8.—Visual acuity as a function of background luminance for two different colors. (From Roth [14])

crimination, depth perception, the perception of intermittency (flicker), and others. References [3, 5, 11, 14] provide detailed discussion of these aspects of the seeing process.

Light as a Stressor

Occasionally light may act to degrade human performance. The most common and obvious instance is when too much light energy is present over the whole visual field, or the distribution of light is disadvantageous. In the former case, discomfort and disability result—discomfort from excessive pupillary contraction, squinting, and possibly, nystagmus; disability from the phenomenon of glare, which (in its precise definition) is a consequence of light scattering within the eye, leading to reduction in contrast of the retinal image. The problem of too much light over the whole field usually is easily controlled with visors, goggles, or an overall filter, which should be spectrally neutral. Glare, on the other hand, is frequently harder to control, requiring careful design of light sources, and special shielding from natural light such as direct sun rays or reflection of solar energy from highly reflecting surfaces. An additional strategy is to plan human activity so that the possibility of sudden confrontation by glare sources is eliminated.

The phenomenon of flash blindness is another visual stressor. This effect is consequent upon the eye being subjected to a sudden burst of high visible energy, usually unexpected. The results include startle, pain, and a more or less temporary loss of visual function—effects that are especially grave if the observer happens to be dark-adapted at the moment of exposure. Recovery time varies with the initial state of adaptation and with intensity and duration of the flash, its spatial and temporal distribution, and spectral energy content. Moderate exposures lead to momentary raising of the visual threshold, temporary loss of vision over the area affected (scotoma), and any performance decrement resulting from the startle pattern or other gross bodily response such as avoidance. Greater intensities and longer exposures may lead to more lasting disability and ocular pathology. (Consult Reference [4] for details.) Protection against flash blindness is easy only when the flash may be anticipated or when the onset is gradual enough for the natural blink response to be initiated. Research is in progress on the development of protective goggles and visors with rapid opacification times, but the ideal system has yet to be devised.

Either rhythmical or erratic changes in light level, especially if the energy extremes are great, can likewise be stressful. The amplitude and frequency of rhythmical variations, as well as the level of the prevailing average luminance influence the effects observed. In minor cases only mild annoyance or distraction may result, but in severe cases there may be serious interference with performance, not only through direct effects on the visual system but also through the development of somatic problems such as headache and fatigue. If the alterations in intensity are of the appropriate level and at frequencies at or near the alpha rhythm, there is a possibility of inducing seizures in certain individuals, especially those known to be epilepsy-prone. The prevention of all these untoward effects is through elimination of either aperiodic or periodic light fluctuations, or their attenuation to a level which is small relative to the steady ambient environmental luminance.

Standardization of the Light Environment in Space Operations

To ensure optimal performance and comfort for spacecrews much can be done by means of careful design of spacecraft and habitat lighting. Work sites should be arranged in accordance with established principles of illumination engineering; lighting recommendations for a great number of tasks have been developed. (For example, see Ref. [8].) Generally speaking, illumination levels for prolonged critical seeing should be in the range from 538–2152 lux (50–200 ft–ca) and the reflectance of surfaces should be such that the luminance ratios between a task and its surroundings are not excessive. Direct and reflected glare are to be avoided by proper placement of luminaires and attention to the optical properties of surfaces. In modern lighting practice in the USA, an effort is made to arrange the light environment in accordance with recommendations of the Illuminating Engineering Society [8]. exemplified in Figure 9. Special supplementary lighting, either fixed or portable, may be needed for tasks requiring best acuity and contrast discrimination. Polarizing materials can often be used to control reflected glare or, in crossed pairs, for the attenuation of sunlight.

Ratios	Type of seeing
1 to 1/3	Between task and adjacent surroundings
1 to 1/10	Between task and remoter darker surfaces
1 to 10	Between task and remoter lighter surfaces
20 to 1	Between luminaires (or windows) and surfaces adjacent to them
40 to 1	Anywhere within the normal field of view

FIGURE 9.—Recommended luminance ratios for prolonged critical seeing. These are maximum values; reductions are generally beneficial. (From Kaufman [8])

Soviet standards for minimum illumination of work surfaces are indicated in Table 1. Illumination standards in the USSR deal with precision of work in terms of the smallest object that can be distinguished (measured in millimeters); contrast between object and background; background characteristics; and lighting system. The illumination standards cover two types of lighting systems: general lighting systems, and combined lighting systems, in which local illumination concentrating light directly on work positions is added to general illumination.

Artificial Illumination Hygiene Standards

According to Soviet standards, the minimum illumination of work surfaces should correspond to the illumination levels, in lux units, in Table 1. The established illumination standards including those that specify two types of lighting systems were given in the previous subsection of this chapter.

General illumination is divided into: general uniform illumination (uniform distribution of light without consideration of arrangement of equipment); general local illumination (light is distributed with consideration of arrangement of work positions). The use of only local lighting in buildings is not permitted.

The standards specify that objects to be distinguished be located 0.5 m from the worker's eyes. These standards are increased by one order when the object is more than 0.5 m from the eye, and when stressed visual work is continuous for more than half the work day, also when objects on moving surfaces must be distinguished.

Soviet and US studies provide ample evidence that optimization of illumination levels leads to significant increases in productivity, accuracy, worker comfort, morale, and safety. (See Table 2.)

Since part of an astronaut's job involves extremely high precision and low and moderate contrast between the object to be distinguished and the surrounding background, an illumination

TABLE 1.—*Work Surface Illumination Standards*

Description of visual work	Smallest dimensions of workpiece	Subclass of visual work	Contrast	Illumination in lux	
				General lighting system	Combined lighting system
Highest precision	Less than 0.15 mm	a	Low	300	4 000
		b	Low		
			Moderate	300	3 000
			Low		
		c	Moderate	300	2 000
			High		
			Moderate		
		d	High	300	1 250
			High		
Very high precision	From 0.15 to 0.3 mm	a	Low	300	3 000
			Low		
		b	Moderate	300	25 000
			Low		
		c	Moderate	300	1 500
			High		
			Moderate		
		d	High	200	750
			High		
High precision	From 0.3 to 0.3 mm	a	Low	300	1 500
			Low		
		b	Moderate	200	750
			Low		
		c	Moderate	200	600
			High		
			Moderate		
		d	High	150	400
			High		
Moderate precision	From 0.5 to 1 mm	a	Low	200	600
			Low		
		b	Moderate	150	500
			Low		
		c	Moderate	100	400
			High		
			Moderate		
		d	High	100	300
			High		

level of 300 lux (lx) can be recommended as the level for general illumination of the working environment. It was necessary to resort to combined lighting for greater illumination of scales, instrument panels, and the like; the lighting level of these elements may be increased to 1500–2500 lx. Lower lighting levels, of the order of 50–100 lx, causing no irritation and creating the feeling of complete comfort and "home conditions," are recommended for astronaut rest areas.

The spectral energy content of artificial light should approximate that of sunlight, ideally. If this is not possible, the source should at least radiate at all wavelengths in the visible spectrum with neither large peaks nor significant voids; that is, the appearance of colors should be normal and neutral surfaces color-free.

Instruments, controls, and displays involving the visual system have been of cardinal interest to human engineers, so that extensive data are available to the designer. Handbooks of equip-

TABLE 2.—*Tolerable Weighted Mean Brightness of Work Surface*

Area of work surface in m²	Tolerable weighted mean luminance of work surface (units)
Less than 0.01	2500
From 0.01 to 0.02	1800
From 0.02 to 0.05	1300
From 0.05 to 0.15	1000
From 0.15 to 0.4	700
0.4 and larger	500

ment design (e.g. Morgan et al [11]) detail the visual considerations that lead to optimal performance.

Rest and sleep sites should be designed to have lower luminance, although complete darkness may never be desirable. Intermediate levels are recommended for periods of relaxation, and as low a level consistent with crew safety may be used during sleep.

In long-term space flight, such as manned interplanetary missions or in lunar or planetary habitats, it may be desirable to establish a program of lighting control designed to maintain the normal terrestrial circadian cycle. Although much of the existing data regarding circadian rhythmometry come from animal studies, it seems clear that the light regimen dominates such important biorhythms as susceptibility to radiation or to various noxious stimuli (see Ref. [1]). Finally, there are higher order psychologic effects from the use of light and color in the environment, including such relative intangibles as crew morale and interpersonal relationships.

THE ULTRAVIOLET SPECTRUM

Only a small part of the Sun's energy is in the ultraviolet region of the spectrum, which is shown in Figure 1. Nevertheless, sufficient radiation is present so that protection from prolonged exposure to direct solar rays must be arranged. Happily, this is quite easy, since ordinary materials (glass and various visor materials) that are transparent to visible wavelengths, afford excellent protection from the bioactive part of the ultraviolet spectrum. Moderate exposure of the human body to ultraviolet is, of course, salutary, and the shorter wavelengths have germicidal properties which are useful in spacecraft and habitat hygiene. Excessive exposures, depending upon the wavelengths involved, can result in damage to man's superficial skin tissues and ocular pathology. Although voluminous quantitative data exist regarding germicidal, antirachitic, and skin effects of ultraviolet [1, 8, 17], ocular damage in humans is only now being critically assessed, chiefly through excellent work by Pitts and colleagues [12]. It is possible here to give only a brief overview of the known effects of ultraviolet.

Germicidal Action

The bactericidal properties of ultraviolet radiation have been known for nearly a century, and abundant data relate lethal efficacy to both energy and wavelength. The germicidal action spectrum has been confirmed for numerous microorganisms, and the curve shown in Figure 10 is now well-established. In a general way, this curve follows the absorption spectrum of nucleic acid, and the ability of ultraviolet to inactivate cells depends upon their capacity for repair of DNA lesions, according to Todd and Tobias [16]. Since low-pressure mercury vapor lamps emit strongly in the 2537 Å line, very near the

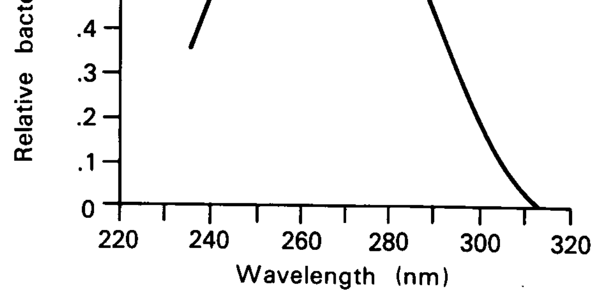

FIGURE 10.—Bactericidal efficiency of ultraviolet radiation. (Based on data of Kaufman [8])

action spectrum peak, these lamps are highly effectual germicidal devices, so that their application in general or local sterilization of living spaces and equipment is possible. Additional bactericidal and fungicidal action results from the generation of ozone by radiation of the 1849 Å line, if water vapor is present in the atmosphere. The deodorant property of ozone may be desirable in confined living spaces during long periods. The amount of ultraviolet energy required to inactivate a wide variety of bacilli, yeasts, molds, and viruses may be found in the literature [1, 8, 9, 17]. Temperature has little effect on the lethality of irradiation, but humidity is important; death rates are greatly reduced when the humidity is high. For this reason, germicidal lamps are often installed in ventilating and air-conditioning ducts where low humidities prevail

Action on the Skin

The two most obvious results of exposing human skin to either solar or artificial ultraviolet are erythema (sunburn) and pigmentation (tanning). Both effects have been studied quantitatively, and although there are wide individual differences in sensitivity, it is possible to describe the action spectra and time courses of each. In some individuals, there may be other consequences of exposure to ultraviolet, including polymorphic light eruption and skin cancer with wavelengths below about 3200 Å and urticaria solare both below 3200 Å and in the waveband from 4000 to 5000 Å (not a true ultraviolet effect). It may be assumed, however, that such idiosyncratic persons will not be selected for spacecrews. Both erythema and tanning depend upon the penetration and absorption of the cutaneous layers, and the observed differences in susceptibility between blond and dark skins must be due in large part to differences in the depth of penetration and the constituents of the various layers. (The *reflectivity* of both light and dark skins is essentially equal for ultraviolet wavelengths.) The transmission of human skin, layer by layer, is shown in Figure 11, which indicates that wavelengths below 4000 Å are totally absorbed before reaching the subcutaneous layer. Clearly, the biotic effects of ultraviolet on human skin are confined to approximately the upper 2 mm.

The action spectrum for erythema is shown in Figure 12. Reddening occurs after exposure

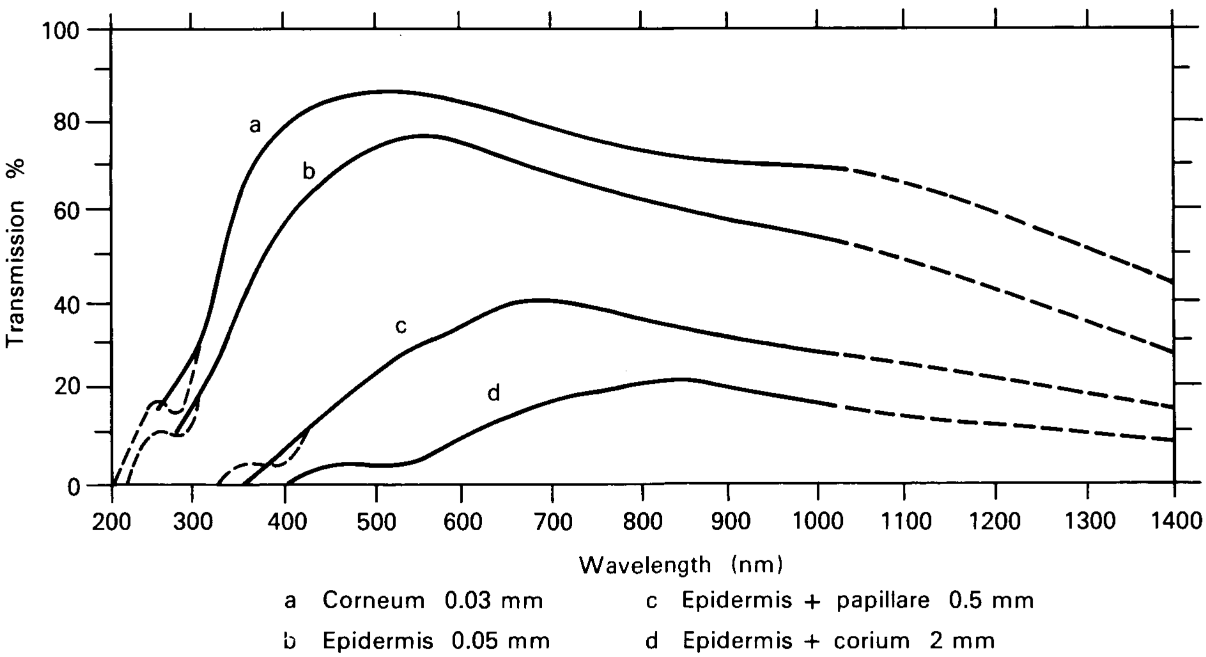

FIGURE 11.—Transmission of layers of human skin. (From Koller [9])

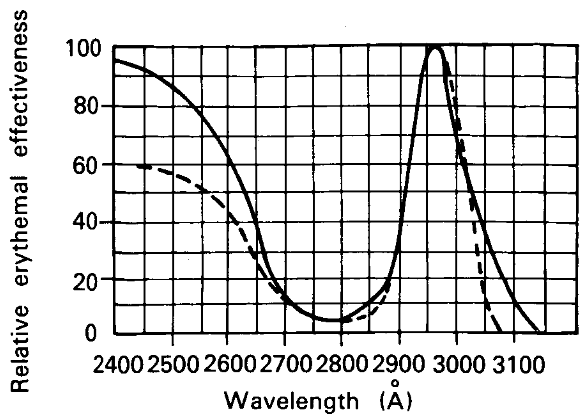

FIGURE 12.—Action spectrum for erythema. (Data from two sources as shown by Koller [9])

with a latency of 1–6 h and persists for 1 to 3 days. The degree of effect varies with exposure time and intensity, and the reference unit is called the minimum perceptible erythema (MPE). According to Koller [9], 2.5 × MPE results in vivid erythema, 5 × MPE in a painful sunburn, and 10 × MPE in blistering. Higher exposures can lead to necrosis. These values, however, are only approximate, based on noonday sunlight on the Earth's surface, which has a different energy spectrum from that of artificial sources or solar radiation outside the atmosphere. Also, the above factors are greater for longwave than for shortwave ultraviolet. The mechanism of ultraviolet erythema, which merely indicates dermal vasodilation, is probably through release of a histaminelike compound that reaches the lower vascular layers by diffusion.

Tanning of the skin is imperfectly understood, but two major phases have been described. The first phase has the same action spectrum as erythema, and follows it in time with a longer latency and much longer persistence. Presumably, tanning reflects the same photochemical changes that result in erythema, but the two effects may be only indirectly related. The second phase of tanning occurs in individuals previously exposed to ultraviolet. It differs from the first phase in that its action spectrum is broadened and displaced toward the longer wavelengths, with a peak at about 3460 Å, suggesting a different underlying photochemical mechanism [9]. Phase 2 tanning also shows essentially zero latency. The important point is that space crewmembers with a recent preflight history of tanning are likely to be more resistant to ultraviolet radiation of the skin.

Ultraviolet Photophthalmia

Exposure of the human eye to excessive levels of ultraviolet energy results in ocular pathology of various kinds and degrees of severity. It has been shown by Boettner and Wolter [2] that no radiation shorter than 3800 Å can penetrate to the retina of the adult eye, and that most of the energy below 3000 Å is completely absorbed in traversing the cornea and vitreous, i.e., before reaching the anterior surface of the lens. The effects of ultraviolet radiation on the eye are manifested only through its action on the superficial tissues. The symptoms of overexposure include changes in corneal epithelium, erythema of the lids, photophobia, and pain—effects that are usually transient, but may be dangerously incapacitating in certain space operations. Unlike the skin, the eye and its surrounding tissues do not develop a tolerance to ultraviolet exposure, therefore protection must be sustained despite repeated exposure. Pitts et al [12] describe the onset and course of ultraviolet photophthalmia thus:

> The ordinary clinical photokeratitis follows a characteristic course. After exposure, there is a period of latency varying somewhat inversely with the severity of the exposure. The latency may be as short as 30 minutes and as long as 24 hours but is typically 6 to 12 hours. Conjunctivitis sets in and is accompanied with an erythema of the skin surrounding the face and eyelids. There is a sensation of foreign body or 'sand' in the eyes, varying degrees of photophobia, lacrimation, and blepharospasm. These acute symptoms usually last from 6 to 24 hours, but almost all discomfort disappears within 48 hours. Very rarely does exposure result in permanent damage.

In a subsequent study, Pitts et al [13] present quantitative data regarding the human threshold for photokeratitis, which they found to be 0.05 ×

10^6 ergs/cm^2 at 280 nm. They also give the action spectrum for photokeratitis in primates (Fig. 13).

It is relatively easy to protect the eyes from abiotic ultraviolet radiation with suitable visor and goggle materials, but it must be emphasized that the photophthalmia consequent upon overexposure is very insidious, because of the long latency between exposure and development of symptoms. Accordingly, it is mandatory to exercise constant vigilance in the use of protective measures. Pitts et al [13] give formulas and calculations for protection against the ultraviolet levels encountered in the space environment, and show the protective characteristics of materials now used in the US.

THE INFRARED SPECTRUM

Radiation is one of four means of heat exchange between the organism and the environment. (The others—convection, conduction, and vaporization—will not be treated here.) Man and other organisms may either absorb heat from radiating bodies which are at higher temperatures than theirs, or lose heat by radiating energy to cooler bodies or to space. Man, as with other homoiothermic animals, requires that his environmental temperature exchange be within certain limits if he is to sustain comfort and unimpaired bodily function, both of which are essential to optimal performance. In the space environment the Sun is the most important source of infrared radiation, and the solar heating effect on both man and his spacecraft has been an important element in the design of vehicles and clothing. In much of the extensive literature about the pathologic effects of heat and cold, the response of the organism to alterations in body heat, due to all causes, is considered and the data referring to tolerance limits, effects of brief exposure, and acclimatization are almost never applicable to radiant heating or cooling alone. Nevertheless, radical alterations of either local or systemic temperatures due to radiant effects may have identical results, and some pathologies are uniquely produced by infrared radiation.

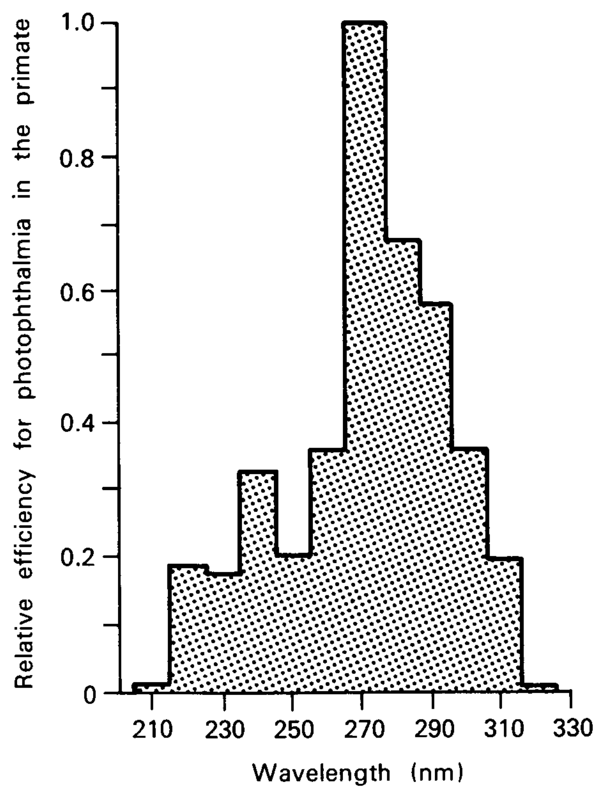

FIGURE 13.—Action spectrum for primate photophthalmia. (From Pitts et al [12])

Because infrared radiation can penetrate the skin more deeply than shorter wavelengths, the heating effect on subcutaneous vascular tissue is direct, and blood so heated circulates throughout the body to produce a systemic elevation in temperature. The transmission of human skin in the spectrum up to 1400 nm is shown in Figure 11. Radiative heat loss to the environment follows the same rules as absorption; clothing and spacecraft materials must be chosen so as to maintain thermal equilibrium within the somewhat narrow range required for optimum physiologic and psychologic states. The vast literature on heat tolerance, thermal balance, and protection has been summarized by Roth [14].

Pathologic Effects

Too much or too little heat is deleterious to the organism. Between the obvious extremes of freezing and burning of tissues, several pathologic conditions result from exposure to excess infrared radiation or from uncontrolled loss of body heat through the radiative mechanism. The former problem is remedied by removing heat, usually by conductive or evaporative means; the latter by providing supplementary heat from radiation, conduction, or convection. The three most debilitating systemic effects of excess heat are cramps, prostration, and pyrexia heat. The first is successfully treatable by increasing salt uptake. Heat prostration is a common syndrome caused by collapse of peripheral circulation, which is most frequently precipitated during strenuous physical activity. It is not associated with increase in internal body temperature, and may be prevented (and treated) by oral administration of water and salt. Heat pyrexia is graver, resulting from a breakdown of the body's heat regulatory mechanism. Rectal temperature is elevated and sweating diminishes or stops. Treatment is radical (usually immersion of the whole body in ice water), so that prevention is essential in space operations. Less severe pathologic effects of heat, such as discomfort, anorexia, mild dehydration, and excessive sweating, while relatively unimportant in the terrestrial context, may be critically important in space operations. Since the eyes are transparent to infrared energy in some wavebands (Fig. 14), the heating effect may lead to ocular

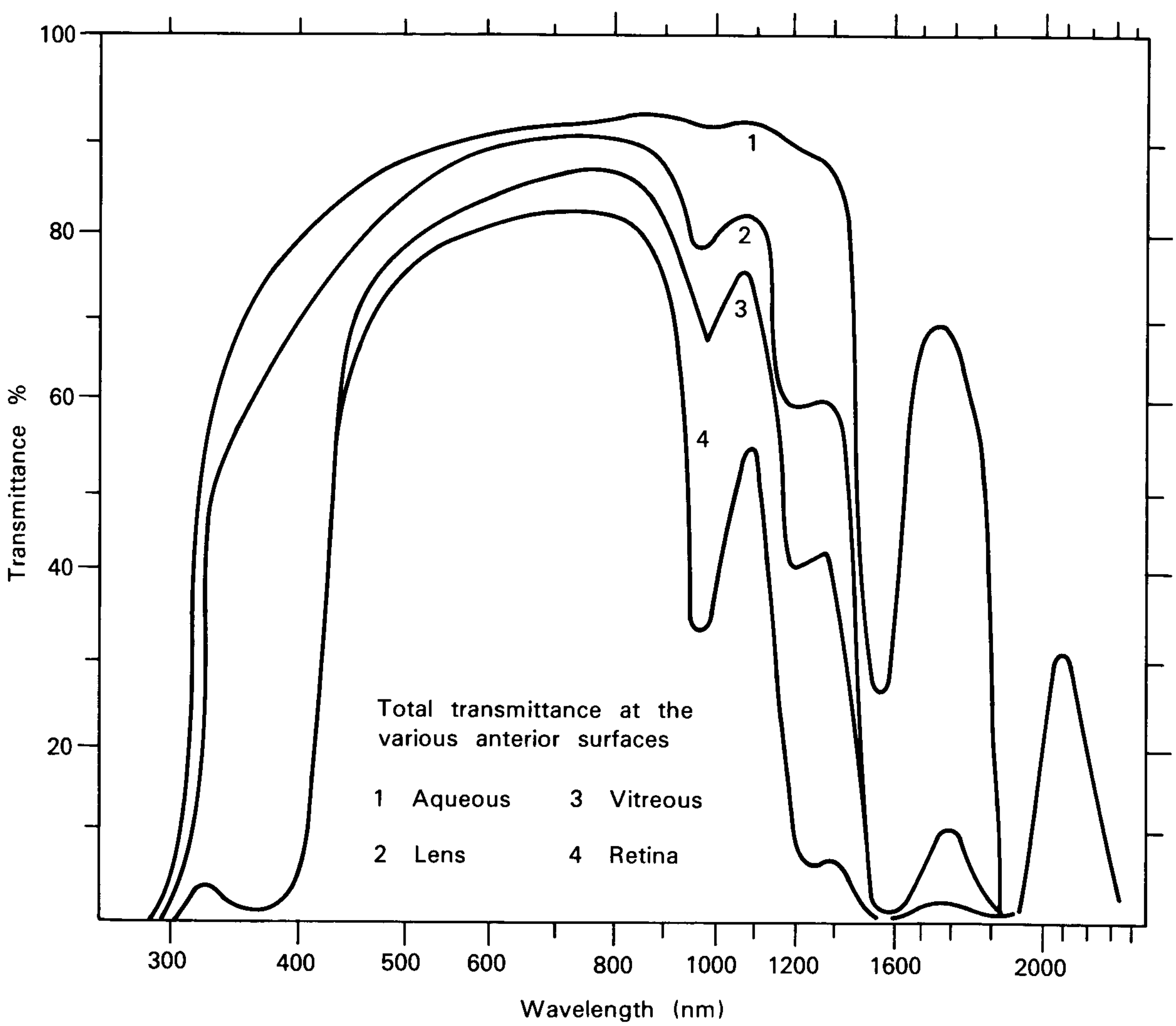

FIGURE 14.—Total transmittance of the whole human eye as a function of wavelength. Data for young adult eyes except for the region below 380 nm, which is for a child's eye; in adults, these wavelengths are completely absorbed by the lens. (From Boettner and Wolter [2])

pathology; the syndrome known as glassblowers' cataract is thought to be so caused, although the limited exposure times in space probably preclude its occurrence. Infrared radiation also has germicidal uses in the control of thermosensitive and hydrophilic microorganisms.

Standardization

To establish standards for infrared radiation in isolation is virtually impossible, for it is only one of several contributors to the thermal environment. Direct radiation works in concert with convection, conduction, evaporation, and reradiation in an exceedingly complex manner; the total thermal exchange pattern results from interplay of these factors. The radiant component in heat exchange is, of itself, complicated by crew motility, arrangement and surface temperature of different parts of the spacecraft or habitat interior, and local differences in wall temperature in the vicinity of feed-through equipment, windows, or any structural anomalies [14]. With the exception of studies on the threshold for pain caused by radiant heat, there are few quantitative data regarding the effects of infrared radiation (loss or gain) separated from the other elements in thermal exchange. In evaluating the many investigations of thermal stress, it must be remembered that infrared radiation may or may not be important, depending upon the structure of the total heat environment. Similarly, an attempt to establish radiant heat standards must account for both indirect and direct effects on the body.

Analysis of the integral heat exchange between man and environment establishes primarily the importance of individual means of heat transfer (radiation, convection, evaporation). It would not be reasonable to expect perfect agreement of data obtained by individual investigators. The figures of Hardy and DuBois [7] and Letavet and Malysheva [10] at room conditions of 20° C (presented in Table 3) are quite close.

Radiative heat transfer, according to Table 3, occupies the most important position. If the ratio of the radiative components is as large in heat exchange between man and his environment under usual comfortable conditions, when the

TABLE 3.—*Heat Losses of Man by Radiation, Convection, and Evaporation*

Forms of heat loss	Hardy and DuBois [7]		Letavet and Malysheva [10]	
	Heat losses			
	cal/h	%	cal/h	%
Radiation	45.7	59.1	41.7	55.6
Convection	11.0	14.2	11.5	15.3
Evaporation	20.6	26.7	21.8	29.1
	77.3	100	75	100

air temperature is equal to the room temperature, then a change of room temperature will naturally have a strong effect on body reactions and the heat sensations of man.

In tests with the temperature of all rooms at +40° C and at the same air temperature, disruption of the heat regulating functions naturally occurred for short periods, even in a state of rest, threatening overheating; moisture loss reached 300–400 ml/h. Reduction of the temperature of all rooms to +14° C eliminated almost entirely the overheating effect of air at a temperature of 40° C; moisture losses decreased from 300 ml/h to 75 ml/h; satisfactory feeling was restored and there were no complaints of discomfort, heat, or stuffiness.

By using cooled surfaces it is possible to completely eliminate or significantly alleviate the overheating effect of high air temperature. The use of cooled surfaces makes it possible to bring heat sensations very close to "comfort" at air temperatures that are uncomfortably close to overheating. For example, conditions very close to comfort were created at an air temperature of 25° C and raw chamber of 10° C, although in addition to comfort, cooling was evaluated sporadically. In the absence of cooling, an air temperature of 25° C is always assessed as uncomfortable. At low room air temperature, a comfort state can be achieved by infrared radiation. Industrial infrared heaters, usually called radiant heaters, may be various panel installations mounted on walls and ceiling, gas infrared radiators, and similar. The air temperature may be a few degrees lower when radiant heaters are used than with convective heating, since the direct effect of radiation on the body produces the required physiologic thermal equilibrium. When air heaters are used, the air temperature in the room is felt as pleasant at 20–22° C, but with radiant heating, the air temperature need only be 15–18° C.

Data collected on the dynamics of local radiative cooling suggest that the skin, to a certain extent, is transparent to the natural infrared radiation of body tissues. Thus, cooling of subcutaneous tissues and muscles can occur directly through the skin as a result of heat loss, also indirectly through infrared radiation.

In space travel, environmental conditions can be created under which the principles of infrared radiation action on the body, both radiative heating and radiative cooling, can be utilized for the purpose of providing favorable or "comfortable" conditions in the spacecraft environment (Table 4).

Protection against excessive heat gain or loss through radiation is accomplished in two major ways. The first is through the use of reflective materials in spacecraft, habitat, and space garment design. The second is by means of supplemental heating or cooling of either space suits or (in a shirt-sleeve environment) of the living areas. While a discussion of the many factors involved in materials and devices used in thermal control is beyond the purview of this chapter, it should be recognized that the bioengineering efforts of the past decade have successfully eliminated thermal stress in spacecraft, and during extravehicular activity, for prolonged periods.

TABLE 4.—*Time of Tolerance of Infrared Radiation at Various Intensities*

Radiation $cal/cm^2 \cdot min$	Source with $\lambda_{max(s)} = 3.6\ \mu m$	Source with $\lambda_{max(s)} = 1.07\ \mu m$
2	159	305
3	39.4	5.88
4	27.3	37.9
5	16.0	26.9
6	17.9	21.2
7	10.9	17.6
8	9.5	14.5

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Chapter 12

IONIZING RADIATION

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The first manned orbital space flight was accomplished by the Soviet cosmonaut, Yuri Gagarin, and many subsequent flights, including lunar landings by American astronauts, Neal Armstrong and others have proved the feasibility of exploring, with human participation, the properties of space nearest us and throughout the solar system. At the time of this writing, scientists of many nations are at work perfecting space stations—large manned orbital laboratories—where astronauts can remain for extended periods.

The success of manned exploration of the planetary system depends on many factors, including an understanding of the physical properties and biologic effects of ionizing space radiations which are being discovered and analyzed as part of the scientific exploration of space.

Man's safety in space depends not only on radiobiologic studies, but also, we are becoming increasingly aware, that our understanding of the origin of organic molecules in space and of evolution, maintenance, and transmigration of life on celestial objects also depends on these studies. Space-related radiobiologic studies have already yielded information that is useful not only to space science, but also to certain fields of biology and medicine on Earth.

Successful study of space has brought about the development of a new branch of science—*space radiobiology.*[2]

The Discovery of Cosmic Rays and Their Biologic Effects

The discovery of cosmic rays was connected with the question of how ionization changes with altitude.

In 1911, V. Hess completed several flights in a balloon, carrying with him a Wulf Electrometer [86, 87]. Greater ionization was revealed at a

[1] This author (C.A.T.) wishes to acknowledge assistance from Drs. Paul W. Todd, Pennsylvania State University, and Stanley B. Curtis, Donner Laboratory, University of California, Berkeley, who were consulted on various technical points. Gratitude is also expressed for the translating and editorial assistance of Della J. Mundy.

[2] In writing this chapter and attempting to translate material in different languages, the authors have agreed upon these abbreviations:

USA	*USSR*	*Definition*
GCR	GKI	Galactic Cosmic Radiation
LET	LPE	Linear Energy Transfer
rad	rad	Absorbed dose of ionizing radiation (1 rad = 100 erg/g)
rem	ber	Roentgen Equivalent Man (rad × RBE)
RBE	OBE	Relative Biological Effect
DNA	DNK	Deoxyribonucleic acid

height rather than at ground level. This led Hess, who received the Nobel prize for his discovery in 1936, to suspect the existence of a special radiation much harder than γ-irradiation and of extraterrestrial origin. At this time the radiation was called Höhenstrahlung, or "high altitude radiation." In 1923, Millikan and Otis, in measuring the absorption coefficient of cosmic rays in lead on the summit of Pike's Peak (4300 m), came to the conclusion that the absorption coefficient was of the same magnitude as that for γ-rays. In June 1925, the Soviet physicists, Myssowsky and Tuwim, at Lake Onega, were able to determine the coefficient of absorption for cosmic rays in water at a depth up to 10 m.[3] The results showed that the coefficient of absorption for the penetrating radiation was ten times less than that for γ-rays. In August 1925, Millikan and Cameron reached the same conclusion [120]. Since then, the existence of cosmic radiation has not been seriously questioned.

In 1927, Skobelzyn proved experimentally, by the use of Wilson cloud chambers, that cosmic radiation contains charged particles of extremely high energies [156]. In 1947, Freier and associates made the very important discovery, by flying photographic emulsions in high-altitude balloons, that nuclear particles with mass numbers up to 40 and with energies of several billion electron volts are continually entering the Earth's atmosphere [54]. These particles are now known as the heavy nuclei of galactic cosmic rays. In 1967, Fowler demonstrated the existence of *super* heavy particles, with an atomic number up to and perhaps beyond that of uranium ($Z = 92$), located within cosmic rays [53].

Radiation events in the solar system connected with solar flares were first discovered when a worldwide change in ground-level cosmic background radiation was observed in 1956. Since that time, numerous discoveries and measurements made in satellites by S. Vernov, J. Van Allen, and others have provided detailed information relating to the nature and composition of the Earth's radiation belt, solar wind and flares, solar and galactic heavy-ion radiation, and other related phenomena [177, 183].

By 1925, Nadson and Fillippov established that ionizing radiation can alter inheritable properties in yeast cells [125]. In 1926, Mueller succeeded in proving that some of the changes observed in postirradiation *Drosophila* were mutations which segregated according to the classical laws of genetics [123, 124]. Then the question arose of the possible role of cosmic rays in evolutionary processes. Rajewsky demonstrated that cosmic rays are mutagenic:

> The reports of H. Thomas, and of A. Delbrück and N. W. Timoféeff-Ressovsky published in Nature suggest the following considerations, and led us to give some provisional results from our own experiments.
>
> This question has often been discussed by various workers in genetics, and has usually been answered in the negative because of the known small intensity of cosmic radiation at sea level, and because of the amount of the mutation rate with x-rays and radium. The amount of air ionization was used as a means of comparison. As a matter of fact, on the basis of 2 ion pairs/cc^{S-1} for air ionization by cosmic radiation, the total dose is very small, even after prolonged exposure (e.g., about 2.5×10^{-3} R after 30 d). This dose is too small to cause mutation experimentally, compared with the dose of x-ray of 30 R which is necessary to produce an appreciable rise in mutation rate.
>
> An important fact, however, has been left out of consideration, which may be decisive: the showers and bursts which arise when cosmic rays penetrate matter and the resulting secondary effects. . . .
>
> In our tests we exposed a series of objects to the effects of cosmic radiation under suitable lead screening. The dimensions of the screens were calculated according to the Rossi Curve for showers, and the observations of Schwegler. Apart from the controls which were unscreened, we chose screens with an optimal wall thickness (maximum for showers) also screens least favorable to the production of showers.
>
> We give here just the results obtained with one fungus (*Bombardia lunata* Zickler).

[3] See Hess, V. F., and J. Eugster, op. cit., (1949) pp. 9–10.

In the case of this fungus we know, on the basis of former experiments, a few strains to be particularly stable as regards spontaneous mutation, but which display clearly recognizable mutation after exposure to x-rays. Cultures growing in Petri dishes were exposed in various series for periods of 4 to 6 weeks. At the end of exposure each culture was cut into squares of equal size and these were then further cultured separately in test tubes. Among these secondary cultures were a number which showed mutations, and these occurred more frequently under optimal screening than the control's unsuitably screened cultures.

The results are tabulated below:

Screening	Total number of secondary cultures	Number of cultures showing mutation	Percentage of cultures showing mutation
Controls and unsuitable screening	3095	22	0.71
Optimal screening	2721	85	3.1

It can be seen that the rate of mutated cultures is relatively large. Even granting that the actual number of mutations may be smaller than the number of mutated cultures, there nevertheless remains an excess of mutations under the optimally screened cultures compared with the rest.[4]

Koltsov wrote in the 1930s:

> We know nothing of the role of neutrons, protons and positrons as possible factors influencing mutation processes. But a practical problem—the provision of safety for our brave flyers in the stratosphere—urgently demands the quantitative and qualitative study of the biological effects of those radiations which are found in the stratospheres.

A. Piccard, who completed flights to the stratosphere in a balloon in 1931-1932, fully recognized the possibility of the existence of biologic effects due to cosmic rays.[5]

In 1931, Zirkle showed that α-particles with high linear energy transfer (LET) are biologically more effective than γ-rays; α-particles must directly strike the cell nuclei in order to have a lethal effect [196].

In 1934, academician L. Orbeli, promoting a plan of scientific investigation on the effects of atmospheric conditions on man and animals, remarked:

> We do not know what type of physiological effect these rays have, particularly those which are found in the upper layers of the atmosphere. A systematic study of this question by means of experimentation with humans and animals is needed.

The biologic experiments, carried out at first with balloons and later with rockets, could not provide convincing answers to the questions postulated because of the brevity and relatively low altitudes of these flights. The Swiss scientist, Eugster [49], described a variety of cosmic ray exposures. He compared effects on biologic objects stored in the Simplon Tunnel, located beneath a massive mountain and absorbing most of the cosmic radiation, with effects noted at the top of the Alps and in high-altitude balloons. Eugster developed the idea of investigating the effects of single cosmic ray particles on individual cells through the use of photographic emulsion to register the passage of particles.

Shortly after the discovery of heavy primaries in cosmic rays, Schaefer pointed out the possible hazard to humans of heavy-ion "thin downs" (or the events occurring at the end of a heavy-ion track as the particle comes to rest [148]) when flying at high altitudes. Krebs put forth the idea that multipronged nuclear stars can produce a biologic effect [96], and Tobias (1951, 1952) worked out methods for biologic research with cosmic ray particles [166].

Chase and associates in 1954 detected changes in hair color of black mice (C57bl) which were exposed to cosmic rays in high-altitude balloons [29]. A few gray streaks were also found, which

[4] From extract of Rajewsky's work in: Hess, V. F., and J. Eugster, *op. cit.* (1949) pp. 89–90.

[5] See Hess, V. F., and J. Eugster, *op. cit.* (1949) p. 11.

appeared to correspond to single-particle tracks. Experiments with mice on Mt. Elbrus and during flights on aerostats confirmed that hair graying occurred in separate areas.

Numerous biologic objects were then flown in balloons. For example, Slater and Tobias observed developmental malformations in maize exposed at 24 000–36 000 m (80 000–120 000 ft) in balloons for 48 h [157]. However, the practical difficulties of keeping biologic materials aloft for extended periods of time, such as necessary limitations in weight and size, have, in many cases, not allowed us to obtain statistically significant data on biologic effects of cosmic radiation. As a result, this has required simulating cosmic radiation at ground level.

Biologic studies with accelerated protons, deuterons, and helium ions were begun at the Berkeley cyclotron [168] in 1947, and later at Dubna [104].

Following the first manned orbital space flights, scientists from various countries (H. Strughold, N. Sisakian, V. Chernigovsky, R. Lovelace, V. Parin, O. Gazenko, and others) predicted that space biology and medicine were fast becoming new areas for scientific research.

Lebedinsky, Langham, Nefedov, Saksonov, and other scientists concluded that space radiation might present limitations for manned space flight. A committee of the US Academy of Sciences, headed by W. Langham, D. Grahn, and C. A. Tobias and other groups, such as Y. Grigor'yev and associates in the USSR, made detailed studies of the problem of space radiation hazards [63, 98].

Several fundamental theoretical and practical directions for research in space radiobiology resulted from such studies; these trends included:

- peculiarities of biologic effects due to various types of space radiation;
- combined effects of cosmic radiation and other extreme factors in space flight;
- radiation hazard on both short- and long-term flights and the establishment of permissible levels of radiation;
- methods of protecting astronauts and possible biologic links in the life-support system from cosmic radiation;
- system of dosimetric control;
- means of individual protection;
- pharmacologic means of protection from radiation injury.

The problem of evaluating radiation hazard for a given space flight is especially complex. The total dose, dose rate, and distribution of linear energy transfers (LET) must be determined. Shielding the spacecraft can modify the radiation spectrum. Evaluation of the significance of cosmic ray, heavy-ion radiation damage to structures essential for life in the human organism is an extremely important problem. Possible repair of radiation-induced injury should be considered, as well as direct influence on astronaut performance and long-term effects such as carcinogenesis. Synergism of all these factors under spaceflight conditions must also be considered in the evaluation of radiation hazard.

Results of the research conducted at the Dubna proton accelerator (50 to 730 MeV), at Serpukhov (70 GeV), and at several accelerators in the USA, as well as data obtained during space flights, made it apparent that the space radiation hazard on short flights (less than 1 month) is minimal. Orbits within the lower radiation belt, however, should be avoided, and certain regions of this belt must be crossed as rapidly as possible. Operational, dosimetric control should be provided and solar flares predicted. In the event of a very large, unexpected solar flare, it might be advisable to postpone or terminate a flight.

The problem of radiation hazard is more complex on long flights, at large orbital radii, and on lunar or planetary journeys (duration greater than 1 month). In order to evaluate the hazard on such flights, two types of research appear to be necessary.

First, it is necessary to know the hazard from continued exposure within the limits of the Earth's atmosphere (the level of background radiation on Earth) compared with the level found in space. Second, the nature and severity of hazardous effects from heavy particles in galactic radiation must be understood.

An experiment designed to continue for several years was initiated in the USSR in 1966

[72], in an effort to answer the first question. The experiment, which became known as the "Chronic Irradiation Experiment," was conducted with 246 dogs under simulated long-term spaceflight conditions. The data obtained from this experiment permit evaluation of the effects of 3- to 6-yr continuous irradiation at different annual doses (25, 75, 150, 225 rem). Protracted experiments with primates are also being conducted in the US. A great deal of attention is constantly being given to more precise definitions of radiation effects on humans, from available therapeutic data and data from radiation accidents [172].

The second problem of biologic effects of heavy ions can be evaluated partially from experiments with accelerated heavy particles at ground level, and partially by verifying the results of these experiments. Establishment of two linear accelerators in Berkeley and New Haven in 1958 made possible the first biologic experiments with low-energy heavy ions [147]. In 1967, low-energy accelerated ions with atomic numbers greater than 18 first became available to radiobiologists at Dubna. Heavy ions of nitrogen and oxygen were accelerated to energies of more than 1 billion eV at Princeton and Berkeley in 1971 [77, 187]. At current rates of technical progress, perhaps within the next few years, it may become possible through the use of accelerators to study the biologic effects of a significant part of the primary cosmic ray spectrum. So far, only limited data have been obtained from spaceflight simulation in the laboratory.

Space radiobiology has thus accumulated extensive material for study in a relatively short time. This experience will allow judicious evaluation of the degree of hazard present in cosmic radiation and will allow us to outline a series of tasks which will require mandatory study in long-term space flight.

COSMIC RADIATION—EVALUATION OF POSSIBLE RADIATION EXPOSURE

Flight duration, trajectory, and other parameters determine the evaluation of the limits of possible exposure to space radiations and of the corresponding radiation hazard to the crew on a given flight. Radiation hazard from the following sources of ionizing radiation will be discussed: galactic cosmic radiation; solar flares; and the Earth's radiation belt.

The radiation hazard from artificial on-board isotope sources, from atomic propulsion installation sources, and from other sources specific to each mission must also be considered.

Another source of artificial radiation is atomic bomb testing. Certain types of radiation from such tests become trapped in the Earth's geomagnetic field (the so-called artificial radiation belts of the Earth), creating an area of high radiation which can persist for several years. During landings on other planets, radiation from natural radioactive ores, and, in certain cases, induced radioactivity, may also act on the crew of spacecraft.

Characteristic of manned space flights, all factors essential for thorough evaluation of possible radiation effects are not simultaneously available. Such factors include spatial and temporal distribution of dose [6] in the body, and linear energy transfer (LET) distribution to each part of the body. Even the LET distribution is not always sufficient for this evaluation; theoretically it would be better to have information on the distribution of cosmic ray particles by atomic number, mass, and velocity.

Instead of the detailed information outlined above (which, even if available, would consist of so many numbers that computer handling of the information would be necessary), simplifications and approximations in regard to space radiation quality and dose are more usually encountered.

For example, it may be possible to measure the "exposure" dose outside the body and to identify the source of radiation, thereby learning about its LET distribution. If exposure is a result of radiation caused by solar flares, something may be known of the magnetic rigidity spectrum of the particles, and the amount of their absorption in tissue may be estimated. The presence of shielding creates additional complexities: (a) as a consequence of unequal distribution of shielding mass at the ship's surface, local dose magnitudes

[6] The unit of dose is the rad. One rad corresponds to 100 ergs absorbed/g tissue.

at various points in the ship will differ significantly; unequal spatial distribution of absorbed dose in the astronaut's body will be observed; (b) the shielding may provide a source for secondary particles and quanta [11, 19, 56, 142].

The varying nature of dose distributions encountered during a flight can be approximated by the introduction of models in which biologic objects may be placed in situations simulating space flight. But extrapolation of the results obtained from experimental animals, when applied to man, leads to special problems which are not always possible to resolve.

Various dose criteria are used to evaluate radiation hazard, because of the complex radiation environment in space. For low-energy radiations, the surface dose is the most suitable criterion. Radiations of this type may be encountered when low-energy protons from solar flares are present, or if an astronaut leaves the spacecraft in the region of the electron layer of the Earth's radiation belt. Under such conditions, the skin, and lens and retina of the eye may be considered critical organs. For high-energy radiation exposure in the presence of spacecraft shielding, exposure to man may be considered uniform, and the concept of mean tissue dose is appropriate. A typical case is exposure to high-energy protons of solar flares with high magnetic rigidity. In these cases, the bone marrow appears to be the critical organ. There are intermediary situations where one may be guided by the absorbed dose to a particular critical organ. This occurs when astronauts are exposed to protons from the lower radiation belt or to solar flares of medium magnetic rigidity. Examples of such correlations are shown in Table 1.

TABLE 1.—*Influence of Type of Radiation and Thickness of Shielding on Choice of Dose Criteria in Evaluation of Radiation Hazard*

Type of radiation	Thickness of shielding in g/cm²	Dose criteria
Galactic cosmic radiation	≥ 1	Mean tissue dose; dose to the bone marrow [1]
Solar flares	≤ 1	Surface dose
	1 ÷ 5	Absorbed dose in critical organ [2]
	5 ÷ 10	Mean tissue dose; dose to the bone marrow and gonads [3]
Earth's radiation belt (protons)	≤ 2	Absorbed dose in a critical organ
	≥ 2	Mean tissue dose
Earth's radiation belt (electrons)	≤ 1	Surface dose; dose to skin and eyes [3]

[1] Special consideration must be given to the effects of individual heavy primary particles on nonregenerating tissues such as certain parts of the nervous system.

[2] Acute exposures to large solar flares are considered. Doses from small flares on long space journeys to other planets must be considered as protracted exposures.

[3] In orbiting spacecraft, chronic exposures must be considered.

Galactic Cosmic Radiation

Galactic cosmic radiation is made up of protons (~85%), α particles (~13%) and heavy nuclei (~2%) [34, 189]. Heavy nuclei include nuclei of elements with atomic numbers greater than 2 up to and including the iron group ($Z=26$). Galactic cosmic rays also have a "*super*heavy" component consisting of particles of very high atomic number up to and including that of uranium ($Z=92$). The possibility that transuranium atoms also may occur is being investigated. Although extremely heavy particles are quite rare, they must be taken into account, since *each* of these arriving in a sensitive region could have serious effects. A large fraction of the dose can be attributed to nuclei with a charge greater than 3. The dose delivered by the heavy particles at constant velocity is proportional to the square of their atomic number (Z^2), which accounts for their significance in producing biologic effects [34]. Table 2 shows estimates of dose contribution for various heavy particles. In addition to dose, the distribution of linear energy transfer (LET) is very important. Figure 1 presents integral number LET spectra for galactic cosmic rays.

It is essential to take into account the dose contribution from secondaries arising from nuclear interactions of galactic cosmic radiation with shielding materials, human tissues, and the spacecraft itself. Estimates are that such interactions may contribute as much as 50–100% to the total absorbed dose from galactic primaries.

The intensity of galactic cosmic radiation near the Earth is not constant. In a period of minimum activity, it increases. Depending on the phase of the 11-yr cycle of solar activity, the intensity of galactic cosmic radiation may vary from 2 to 4.5 particles/cm^{2}s^{-1} [182]. The angular distribution of galactic cosmic radiation in free space away from any planetary influence is assumed to be isotropic. Dose distribution within the astronaut's body will be almost uniform.

TABLE 2.—*Primary Galactic Cosmic Radiation Dose Rates at Solar Minimum Outside the Earth Magnetosphere*

Dose rate		Contribution to the dose depending on atomic number (Z)	
Annual	Daily	Z	Percent of total dose
12.6 rad/yr	34.5 mrad/24 h	1	37
		2	28
		6–9	15
		10–14	10
		26–28	10

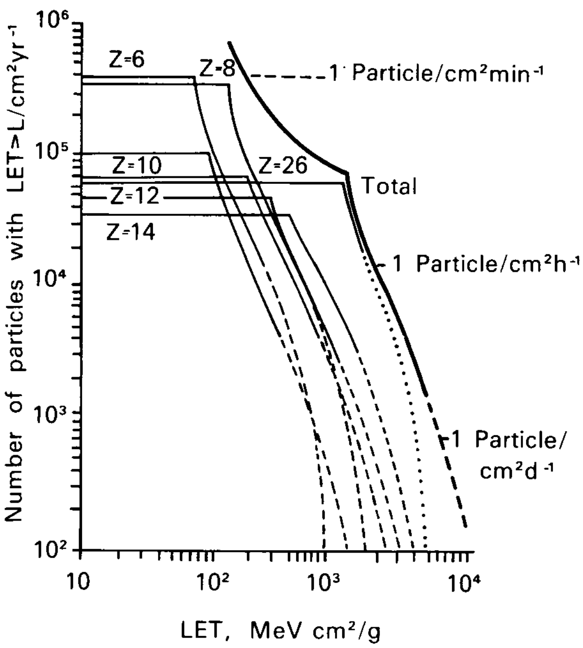

FIGURE 1.—Integral LET spectrum for primary cosmic rays during minimum solar activity, without shielding. LET spectra for particles of various atomic weights are also shown. The dotted line is obtained by assuming an abrupt decrease in the spectrum for iron ions with threshold energy less than 100 MeV/nucleon. The dashed lines represent areas where data are lacking.

Near the Earth, the dose of galactic cosmic radiation is considerably lower because of the shielding effect of the Earth's magnetic fields and of the Earth itself. For orbits at an altitude up to 250–300 km, at a 65° angle to the plane of the equator, the dose rate is 8–10 mrad/d. These results agree quite well with data from direct measurements obtained during flight on the spaceships Vostok, Voskhod, Gemini, Soyuz, and Apollo (see Table 3).

Radiation from Solar Flares

Mainly protons of various energies and a small percentage of helium ions constitute radiation from solar flares. The spectra of proton radiation of solar flares may differ radically with each event, depending on the magnetic rigidity spectrum. Considering that solar flare spectra represent decreasing functions of particulate energy, considerable reduction of absorbed dose to various parts of the body with relatively thin shielding is possible (see Tables 4 and 5) [11, 149, 150, 151].

The magnitude of solar events has been divided into four classes, based on astronomic and radiation parameters. So far, an extremely large flare has not occurred during a manned space flight.[7] Consequently, dose calculations are often based on incomplete measurements of momentum spectra. Extrapolations regarding the ends of the spectra, assumptions regarding charge distributions of the particles, and corrections with respect to shielding from the Earth's magnetic field are usually entailed.

In Table 6, calculations are based on the 10 largest solar eruptions during the 19th solar cycle. One important point is that the largest flares are

[7] In early July 1974, a large flare occurred during a Soviet manned space flight. However, most of the flare radiation was deflected by the Earth's magnetic field and the cosmonauts, within a low orbit, were protected. Had they been outside the Earth's magnetic field, they might have received a large dose.

rather infrequent but are capable of delivering a dose of several hundred rad to the skin surface as well as to the bone marrow. Furthermore, the data in Table 6 show that absorbed dose depends largely upon the configuration of shielding, placement of the crew in the spacecraft, and similar factors. For example, shielding of the Apollo ships varies from 2.75 g/cm² to 212 g/cm² [151], with the thickest portions of the shielding located at the back of the spacecraft. Although very large solar flares are rare (about one every 4 years), the dose from such events can be considerable. During a major solar eruption, the astronaut may receive a dose to the skin of the upper torso of 350–800 rem, to the eyes of up to 180 rem, and to the blood-forming organs of 3–12 rem. Superficial parts of the body receive a larger number of stopping particles (protons, α-particles, and heavy ions), and an astronaut in open space, without the protection of the ship, may receive a significant dose to the skin from high-energy electrons. Figure 2 shows amounts of absorbed dose from solar radiation during the July 10–17, 1959, events.

The contribution of solar radiation to the dose received by astronauts is also dependent upon duration of the space flight. During a short-term flight, of 15 days for example, the probability that the crew may receive a dose of 20–30 rem, with shielding of 3.5 g/cm², is very small and equal to only 0.01–0.02% (see Table 7).

The absence of linear dependence of total dose of proton irradiation on length of flight is an important consideration in evaluating radiation hazard from solar flares.

As duration of the flight increases, the probability of exceeding a certain arbitrary dose

TABLE 3.—*Average Dose Absorbed by the Astronauts, According to Thermoluminescent Dosimetry Data*

Spaceship [1]	Av. absorbed dose (mrad)	Spacecraft [1]	Av. absorbed dose (mrad)
Vostok	2.0	Gemini 3	23.0
Vostok 2	11.0	Gemini 4	46.0
Vostok 3	62.0	Gemini 5	176.0
Vostok 4	46.0	Gemini 6	25.0
Vostok 5	80.0	Gemini 7	164.0
Vostok 6	44.0	Gemini 8	10.0
		Gemini 9	19.0
Voskhod	30.0	Gemini 10	720.0
Voskhod 2	60.0	Gemini 11	28.0
Soyuz 3	85.0	Gemini 12	20.0
Soyuz 4	70.0		
Soyuz 5	62.0	Apollo 7	156.0
Soyuz 6	70.5	Apollo 8	150.0
Soyuz 7	63.0	Apollo 9	202.0
Soyuz 8	72.5	Apollo 10	468.0
Soyuz 9	323.5	Apollo 11	173.0
		Apollo 12	577.0
Salyut	870.0	Apollo 13	237.0
		Apollo 14	1142.0
		Apollo 15	300.0
		Apollo 16	500.0
		Apollo 17	600.0
		Skylab	2500–3500

[1] Inclination of orbit for Vostok and Voskhod spaceships = 65°; for Soyuz ships = 52°; for Gemini craft = 33°; for Apollo craft = 31–33°.

TABLE 4.—*Calculated Dose with Various Thickness of Shielding During Solar Events, May 10, 1959*

Dose criteria	Dose (rad) with shielding thickness 1.0 g/cm²	Dose (rad) with shielding thickness 7.0 g/cm²
External dose	8000	260
Surface dose to skin	5400	140
Mean tissue dose	270	33
Dose to critical organ:		
lens	1800	80
gonads	800	60
bone marrow	55	10

TABLE 5.—*Calculated Surface Dose (D_s) and Dose Along the Midline (D_{mid}) in a Phantom of Man Located Behind Gemini Shielding During Various Solar Events*

Trajectory	Solar flare 6/14, 1959		Solar flare 11/12, 1960		Solar flare 2/23, 1956	
	D_s	D_{mid}	D_s	D_{mid}	D_s	D_{mid}
In free space	145	2.5	128	9	92	16
In orbit; trajectory = 400 km, 60°	17	0.4	17	1.7	13	4

TABLE 6.—*Radiation Dose Received for 10 Largest Flares During 19th Solar Cycle Behind Shielding of Various Thicknesses* (g/cm² Al)

Date of flare event	Dose to the surface of the body (rad)			Dose in tissue, at 4 cm depth (rad)		
	1 g/cm²	2 g/cm²	10 g/cm²	1 g/cm²	2 g/cm²	10 g/cm²
February 23, 1956	280	180	48	73	64	30
March 23, 1958	148	54	2.1	6.4	4.5	0.66
July 7, 1958	150	54	1.93	6	4.3	0.59
May 10, 1959	470	260	15.6	38	29.3	6.4
July 10, 1959	420	210	24.5	50	40	11.5
July 14, 1959	650	273	19.5	48	36	7.5
July 16, 1959	382	191	22.3	46	36	10.5
November 12, 1960	484	263	43	75	62	20.8
July 18, 1961	128	63	7.2	15	12	3.3
November 15, 1970	288	151	20.5	39.6	31.7	10.1
Mean	361	165	21	40	32	10

level due to a combination of small and large flares increases nonlinearly. This is illustrated in Figure 3. During lengthy space flights, as on a 1-year flight to Mars, it is quite likely that at least one large solar flare will be encountered.

Considering the varying spectral makeup of each solar flare, the possibility exists that, even with thick shielding, a considerable dose will be received. For example, with the crew located in a specially constructed cubicle with wall thickness of 30 g/cm², the mean dose for 600 flight days could add up to about 20 rad.

For evaluation of radiation hazard on long flights, then, it is reasonable to expect several proton flares, each with its pattern of attenuation within the spacecraft shield. Conceivably, a model could be devised for dose attenuation from all possible types of solar flares occurring on a long flight, making it feasible to calculate the risk of exceeding established doses.

Such calculations of probable dose incurred on

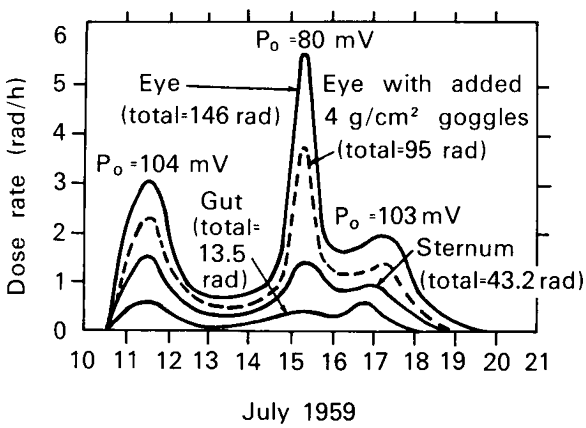

FIGURE 2.—Doses to the crystalline lens, breast, and intestines from solar flares, similar to that which took place between July 10 and 17, 1959. It is assumed that the subject is located in the center of a spherical aluminum shield of 4 g/cm². The dashed line represents decrease in dose as a result of use of goggles which create additional protection of 4 g/cm². Total dose is calculated from integral flux value and a flux-weighted average for each flare.

TABLE 7.—*Probability of Occurrence of Solar Flares and Corresponding Absorbed Dose for a 15-Day Flight*

Solar events & dosage		Dates			
Date of solar flare		2/23/56	11/12/60	5/10/59	10/3/60
Class of solar flare		I	II	III	IV
Dose (shield = 3.5 g/cm²)		34 rem	20 rem	14 rem	0.3 rem
15-day period	Probability of solar events occurring	0.01	0.02	0.02	0.32
	Expected number of solar events per 100 flights	1	2	2	32

a lengthy flight, for example, of 100–1000 d, have already been made on the basis of data from the most characteristic solar flare events in each class, i.e., from the solar flares of February 23, 1956; May 10, 1959; October 31, 1960; and November 12, 1960. However, the calculations did not take into account the dose buildup from secondary radiation produced within the shielding [56]. Possible effects from the large flares in August 1972, and July 1974, have not yet been analyzed.

The aim is to keep the dose from solar flares for a given thickness of shielding below a predetermined dose level. In this connection, the concepts of *risk of exceeding allowable dose* and of *reliability of shielding* will be introduced. If, for example, length of flight is equal to 600 d and thickness of shielding equals 20 g/cm², the risk of exceeding a dose of 50 rem is about 10%, and the probability of exceeding a dose of 100 rem is on the order of 0.1%.

Figure 3 gives values for dose to the eye lens per week of space flight under conditions similar to those prevailing during the maximum of solar cycle 19 with additional consideration for varying thicknesses of shielding [47].

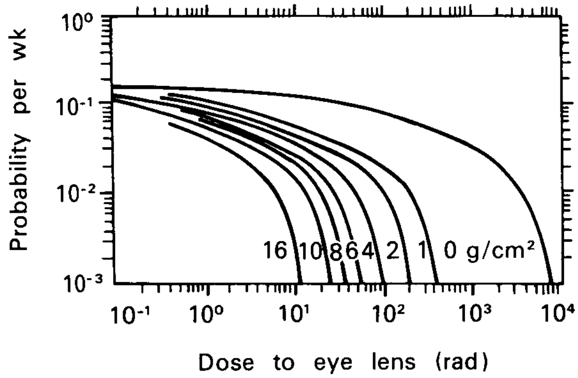

FIGURE 3.—Probability that the lens will receive a given dose (in rads) per week from solar-flare protons during the maximum of Solar Cycle 19. It is assumed that subject is located in the center of a spherical aluminum shielding of various thicknesses ranging from 0 to 16 g/cm².

Radiation Belts of the Earth

The radiation belts of the Earth may be divided hypothetically into inner and outer belts. The inner radiation belt consists of high-energy protons producing a dose essentially dependent upon the location of the trajectory, the length of passage of the spacecraft through the belt, and thickness of shielding.

During brief passage through the inner radiation belt (for example, 10–20 min), the dose will not exceed several rem [19]. Calculations show that traversing the outer radiation belt in a command module of the Apollo type increases that dose by less than 1 rad [47]. With additional consideration of secondary radiation, the astronaut may receive a total superficial dose of 10–20 rad/h. Knowledge of the contribution of protons in the Earth's radiation belts to total dose is essential for investigation of the possible use of space shuttles and space platforms, when transferring from an orbit near the Earth to an interplanetary trajectory. For example, when a ship remains in an equatorial orbit for 30–60 d with shielding of 30 g/cm², the dose received is calculated at 50–100 rem [189].

The outer radiation belt consists of fluxes of electrons and low-energy protons. The electrons of the outer belt have little penetrating capability. At the center of the belt, with shielding of 1 g/cm² aluminum, for example, the dose rate to the surface of the body equals about 40 rem/d. A shield of about 5 g/cm² is sufficient to decrease the dose from electrons to acceptable levels [19].

Artificial (Manmade) Sources of Radiation

Future investigations and the conquest of space are inseparably connected with the use of atomic energy. Atomic reactors and radioactive isotopes will be used on spacecraft in various combinations of equipment [141].

In 1962, a hydrogen bomb equivalent to 1.4 Mt dynamite was exploded at an altitude of 400 km over the Pacific Ocean. As a result of β-decay of isotopes, about 10^{27} electrons were released, a portion of which was captured by the Earth's magnetic field, thereby forming an artificial radiation belt of high intensity. The central part of this belt appears to be situated about 3000–6000 km from the Earth in the plane of the Equator. The intensity of electrons at the central part of this belt exceeds 10^9 electrons/$cm^2 \cdot s^{-1}$. An electron flux of about 10^8 to 10^9

electrons/cm^2 · s^{-1} corresponds to a dose rate of 5 to 50 rad/d.

Thus, the absorbed dose during a long space flight will come from various sources—galactic cosmic radiation, solar flares, radiation belts of the Earth, and various on-board artificial nuclear sources. Landings on the Moon or on other planets could introduce the additional factor of natural radioactivity into calculations for absorbed dose.

BIOLOGIC EFFECTS OF PROTONS AND HEAVILY IONIZING PARTICLES

From the point of view of radiation hazard, the most important component of particulate radiation in space is fast nuclei. These occur in galactic cosmic rays as well as in flare emanations from the Sun. For radiobiologic investigation, it is convenient to divide particulate radiation into light nuclei, which include protons and helium ions, and heavy nuclei, which usually include all those elements with atomic numbers greater than 2. The majority of particles found in galactic cosmic radiation and in solar flares belong to the first, light nuclear group, while the quantity of heavy nuclei is relatively small. Contribution to dose from heavy ions is considerable, however.

The biologic effect from high-energy light nuclei differs only in minor ways from that caused by other types of radiation, i.e., x-ray and γ-radiation. Heavy particles and stopping light nuclei, however, seem to cause more profound and often irreversible changes. The biologic effect of heavy particles has not yet been sufficiently investigated, because of great technical difficulties confronting the researcher.

A single parameter, i.e. dose (usually measured in rad), is not sufficient for quantitating the biologic effects of heavy particles. At least one, and probably two, additional parameters are required, particularly linear energy transfer (LET), a quantity which is also known as the "rate of energy loss" and which is related to the older term, "specific ionization." The LET of heavy particles generally increases as the particles slow down from very high velocities to an eventual collision. Figure 4 provides a quantitative idea of the behavior of these particles in tissue. The figure shows range and energy relationship of particles in water, which may be regarded as approximately equivalent to soft tissue in its ability to stop particles from passing through. In bone, which contains phosphates, calcium, and other organic and inorganic compounds in addition to water, the range of each particle is approximately 0–40% less than in tissue-equivalent aqueous material.

The LET of heavy particles in tissue can be shown as a function of energy and atomic number (see Fig. 5.). In most biologic studies, the effectiveness of each particle increases rapidly with its LET. Prior to the advent of space flight, biologic effects were explored in detail primarily for LET values below 100 keV/μm. LET domains above this value are the subject of most current studies.

When cosmic rays are simulated in the laboratory, it is usually convenient to use parallel monoenergetic beams of component particles. Since the number of collisions and interactions of such particles vary statistically, different types of particle beams exhibit characteristic depth ionization. This concept was originally demonstrated by Sir William Bragg in 1912; he described the track produced by α-rays emitted by natural radioactive isotopes.

Figure 6 provides an example of depth ionization curves produced by two types of accelerated beam: the 900-MeV, helium-ion beam obtained at the 184-in. cyclotron in Berkeley (California), and the nitrogen-ion beam recently accelerated at the bevatron, also in Berkeley. When biologic

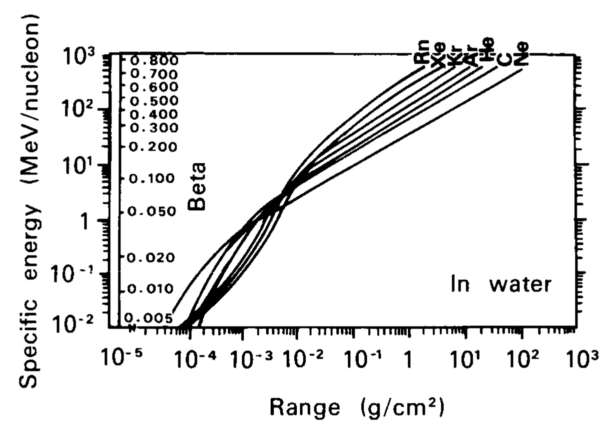

FIGURE 4.—Energy versus range of various ions in water.

objects are placed in the path of these beams, the effect is potentially greater at greater depth. Biologic survival of mammalian cells in culture has been measured by passing such beams through appropriate phantoms. Recent data on the nitrogen beam show that the same beam (for which the Bragg curve is shown) which allows survival of about 40% of cells when entering tissue, will allow only about 0.1% survival at depths expressed in terms of the Bragg peak [167], and indicate that slow, heavily ionizing particles have a greater biologic effect than fast particles of the same charge. Results are similar from recent research on protons by Wainson et al [186].

In free space, particles arrive from various directions with mixed energies, which makes it necessary to evaluate the effects of mixed energy as well as monoenergetic beams. In initial experimental approaches to this problem, measurement of the effects of monoenergetic proton beams in various situations was attempted. Later it became essential to provide mixed-energy beams in the laboratory to simulate conditions in space. Certain technical difficulties arise, since particles accelerated in a cyclotron are usually accelerated only at a single energy. A simulated solar flare spectrum has been obtained at Berkeley using helium ions and ridge-filter type absorbers, a technique initially pioneered in Sweden with the use of proton beams.

Figure 7 shows the dose distribution of a solar flare spectrum simulated at the Berkeley cyclotron in comparison with an actual solar flare

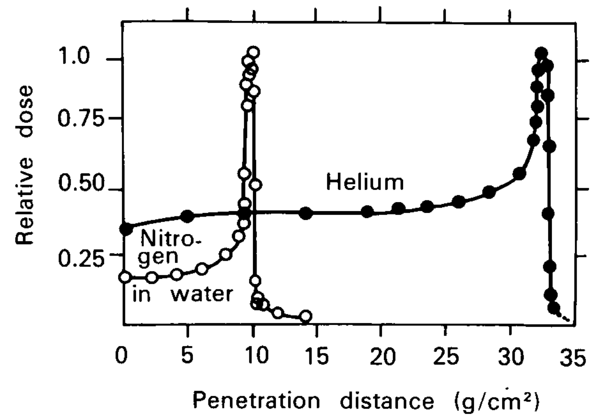

FIGURE 6.—Range of nitrogen ions (270 MeV/nucleon) as measured in water and 910-MeV helium-ion beam as measured in Lucite.

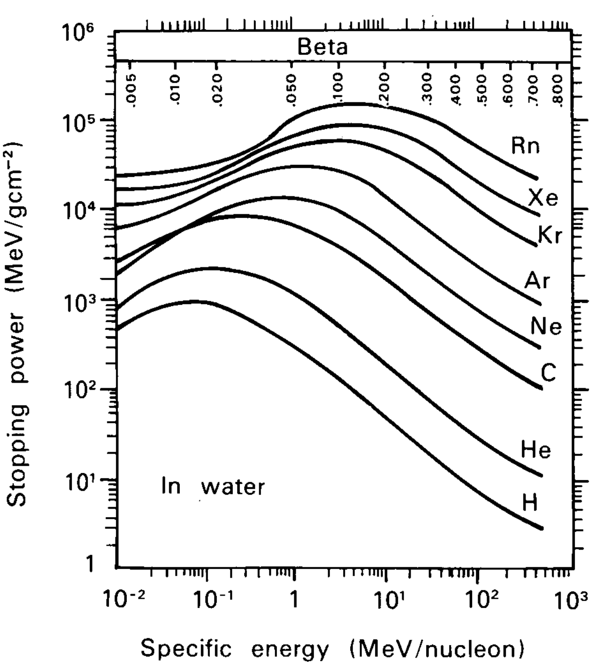

FIGURE 5.—LET versus specific energy of various ions in water.

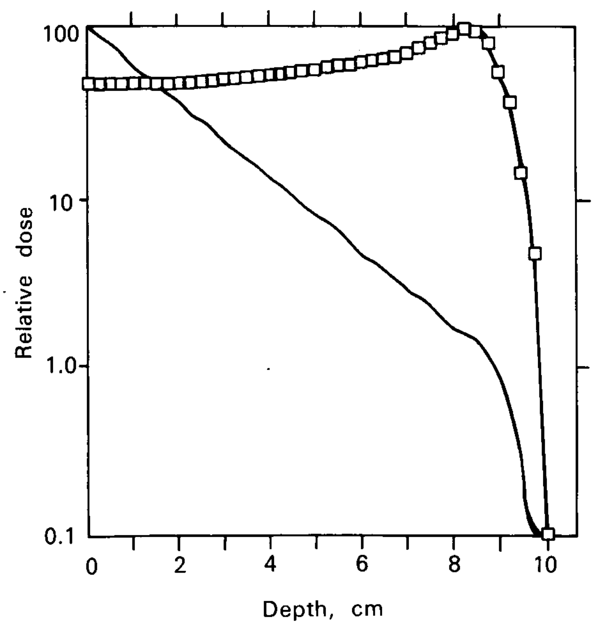

FIGURE 7.—A helium-ion Bragg curve, experimental data (open squares), and a computer calculation of the transformation of the Bragg curve, via a ridge filter, to a simulated "solar flare depth distribution."

spectrum measured by Lyman et al [111]. In the future, it might be desirable to simulate not only dose distribution, but also LET distributions in various types of space radiations.

The problem of heavy-ion effects is further complicated by such particles producing secondary particles, some of which are also heavily ionizing, when colliding with atomic nuclei. Furthermore, light cosmic ray particles in collision, e.g. mesons, can also produce nuclear events that have high LET. Complete absorption of the heavy components of galactic cosmic rays does not generally appear feasible in spacecraft. In fact, with practical shield thicknesses, the secondaries produced by heavy particles passing through the spacecraft wall are more inclined to increase rather than decrease the dose. Before this complex area can be fully understood, a rather complete physical study must be conducted of the fragmentation properties of heavy nuclei and the nature of secondary fragments produced. It will also be necessary to ascertain the special biologic effects of nuclear stars and multipronged nuclear events. At relativistic velocities, some nuclear collisions have been observed which produce a significant amount of secondary particulate radiation, such as nuclear stars. Relatively little data are available on radiobiologic investigation of the effects of pi-meson stars produced in tissue.

Simulation of the effects of protons and helium ions in space is relatively well in hand at a number of different accelerators in various countries. The acute effects of high-energy protons have been well-explored at various particle energies up to 730 MeV; experiments have been conducted recently at the Serpukhov accelerator with high-energy protons up to 70 GeV (see Table 8).

The question of simulation of heavy-ion effects from cosmic rays is more complicated. It has been shown that, in order to reproduce a hazardous dose that might be received in space flight, orbital flights would have to be simulated with radii of 5000 km or more and of several months'

TABLE 8.—*Particle Accelerators in Use for Biologic Research*

Place	Type of particle	Energies
Synchro cyclotron, Dubna, USSR	protons	25 to 730 MeV
Isochronosis cyclotron, Dubna, USSR	heavy ions including xenon	to a few MeV/ nucleon
Synchrotron, Serphukhov, USSR	protons	70 BeV
184-in. Synchro cyclotron, Berkeley, USA	protons	745 MeV
	helium ions	900 MeV
	deuterons	450 MeV
	also pi-mesons	
88-in. cyclotron, Berkeley, USA	helium ions	120 MeV
	protons	60 MeV
	nitrogen	140 MeV
Heavy Ion Linear Accelerator (HILAC), Berkeley, USA	heavy ions	to 7.5 MeV/nucleon
Bevatron, Berkeley, USA	carbon, neon, nitrogen and oxygen	280 MeV/nucleon
BEVALAC, Berkeley, USA	heavy ions	to 2.8 GeV/nucleon (up to Z = 26)
Cyclotron, Howard University, USA	protons	180 MeV
Cyclotron, Texas A.&M.U., USA	protons	55 MeV
Cyclotron, University of Chicago, USA	protons	400 MeV
Synchro cyclotron, Cern, Geneva, Switzerland	protons also pi-mesons	600 MeV
Cyclotron, Uppsala, Sweden	protons	185 MeV
Cyclotron, Langley, Virginia, USA	protons also pi-mesons	300 and 600 MeV
Cyclotron, AERE, Harwell, England	protons	150 MeV

duration. This would be a very expensive and difficult project. Suggestions have also been made for simulating heavy-ion effects through the application of very intense proton or electron beams. It is not technically feasible, however, to produce in this way the instantaneous energy densities that occur in the core of individual heavy-particle tracks.

Most biologic exploration of the effects of heavy ions has been conducted at low energies of only a few MeV. For some time, at the Berkeley Heavy Ion Linear Accelerator (HILAC) and more recently at the cyclic accelerators of heavy ions at Dubna, nuclei with atomic numbers up to argon have been accelerated, but only to energies with a particle range sufficient to transverse a few living cells. During 1971 and 1972, however, the situation changed radically, since at the Princeton and Berkeley accelerators, nitrogen, oxygen, and neon particles were accelerated at energies with sufficient range to penetrate deeply into mammalian tissue.

The BEVALAC (bevatron and linear accelerator) project has recently been implemented at Berkeley; this project will extend the bevatron by coupling it with the HILAC [76]. This should allow reproduction of most nuclei up to and including iron, with range penetration equal to, or greater than, the thickness of the human body. Available energies should then reach 2.8 GeV/nucleon[8]. A similar development has taken place at the Dubna accelerators, so that in the near future we can expect simulation of the radiation effects of cosmic heavy ions at ground level on a much wider scale than was previously possible.

Biologic Effects of Protons, Deuterons, and Helium Ions

In accordance with the concepts that dose and LET are radiobiologically important variables, the biologic effects of protons, deuterons, and helium ions would be equivalent if their LET were the same. Initial studies of these particles were not oriented to space radiation biology. Their possible application to cancer was assessed instead. They have also been used for studies of radiation effects on the brain. Since 1947, high-energy deuterons have been used in Berkeley for such purposes, and by 1952, the acute lethal effects of these particles were established [168]. Since 1955, accelerated ions have been used in human pituitary radiation therapy; they have since been used to treat other tumors as well [171].

The systematic study of the relative biologic effectiveness of protons was begun in 1961 with information concerning the mortality of small laboratory animals, the characteristics of hematologic effects, the behavior of certain radioprotectors, the results of investigating mutagenic effect of protons, and other related subjects [63, 104, 126]. Cyclotron 185-MeV protons have been used in radiobiologic studies since 1956 [100], and the development of techniques in radiobiologic observations was of considerable assistance later in space-oriented studies. Significant success in exploration of space has now sharply stimulated the development of radiobiologic investigations in the area of space radiation biology.

The continuing study of radiation safety in space flight is being pursued in these areas:

> Simulation of the conditions of proton irradiation, imitating as closely as possible the actual conditions of irradiation of man in space;
>
> Investigation of the peculiarities of biologic effects caused by protons of different energies, determination of the coefficient of relative biologic effectiveness, and the study of factors influencing radiosensitivity to such proton radiation in terms of biologic effects;
>
> Investigation of late effects of proton irradiation in animals.

Terms for proton irradiation of various biologic objects, including laboratory animals (dogs, monkeys), were worked out. The proton dose field and the spatial and depth distribution of the absorbed dose of protons in the bodies of animals and other biologic objects have become subjects for investigation [66]. Various methods of proton dosimetry were worked out, and the contribution of secondary radiations to the biologic dose was further clarified.

[8]In August 1974, carbon and neon particles were successfully accelerated to 2.1 GeV/nucleon in this machine.

Biologic objects at different levels of organizational development were used in experiments. In investigations with animals, mortality was studied, as well as functional and morphologic changes in such physiologic systems as the cardiovascular and hematopoietic systems. Functions of the vestibular system and of various internal organs and tissues were analyzed. Particular attention was paid to investigation of various cytologic effects in bone marrow cells, the cornea, the small intestine, and the kidneys [58, 70].

The course of acute radiation illness, reaction of peripheral blood and bone marrow to single and repeated total irradiation with protons of 510 and 126 MeV were studied in dogs [63, 66]. It was shown that in the postirradiation period, the expression of hematologic changes and hemorrhaging syndrome was somewhat greater in animals irradiated with protons of 510 MeV, than in those exposed to Co^{60} γ-rays. Protons of 240 and 126 MeV and Co^{60} γ-rays all induced quantitatively equivalent effects, however.

Numerous publications have been devoted to the study of genetic and cytogenetic effects, in particular, to the investigation of frequency of dominant lethal cases in irradiated rats and mice. A considerable number of radiobiologic studies have been made on "model biologic systems:" populations of mammalian, bacterial, and yeast cells, and biochemical systems [58, 63, 126]. An explanation of the mechanisms of proton action was sought in a series of experiments on factors such as oxygen effect, temperature, and certain radioprotectors, which modify radiosensitivity in biologic systems during proton irradiation at various energies. The results did not show any radiation damage properties specific to protons. The effects, as expected, were similar to those of x- or γ-rays and to helium ions [126].

Similarity of response to irradiation with high-energy protons and with γ-rays was discovered during investigation of the influence of dose rate on response. Change in dose rate from 0.35 to 35 rad/s during irradiation of lysogenic bacteria with both 660-MeV protons and Co^{60} γ-rays did not alter either the radiosensitivity of this system or the coefficient of proton RBE (relative biologic effectiveness) [63]. These findings are highly significant since they point to the similarity of early radiobiologic effects produced by two completely different types of radiation. While the existence of qualitative similarities in these radiation effects is recognized, data are also being collected that indicate the probability of certain peculiarities specific to proton damage. Thus, in experiments with both instantaneous and repeated irradiation of dogs, a somewhat more pronounced hemorrhaging syndrome was revealed [70].

By means of immunologic identification, substances with different immunologic properties were produced in tumor cells irradiated with x-rays and 640-MeV protons [163]. Certain qualitative differences in the action of protons were also observed by other authors [63, 137].

With regard to quantitative peculiarities of proton action on biologic systems, the analysis of data concerning immediate and delayed responses to irradiation in experimental animals, mammalian cells, and bacteria (Table 9) seems to suggest that the relative biologic effectiveness of protons with energies of 50–660 MeV is equal or nearly equal to 1 [15]. However, with further decrease in energy, a tendency toward a certain increase in this coefficient can be noted. This increase in RBE up to 1.8 is clearly marked when mouse corneas are irradiated with 25-MeV protons [63]. Mice irradiated with 55-MeV protons yielded an RBE equal to 1 for cataract formation [33, 176]. Similar results have been obtained with 665-MeV protons [91]. The RBE for stopping deuterons and helium ions in rabbit eyes varies from 2.5 to 5 [185].

In experiments with mice, the acute effects of high-energy protons (730 MeV) and helium ions (900 MeV) were compared with those of 250-keV x-rays [9]. RBE values were found to be between 0.73 and 1.0 for acute lethal effects. At high doses of a few hundred rad/min, the percentage of animals dying from intestinal injury was greater than in situations where lethal doses were delivered over a protracted period of a few hours. The effects of protons and helium ions were found to be rather similar to those of x-rays with regard to fertility and production of dominant lethal reactions in mice.

TABLE 9.—*Relative Biologic Effectiveness of High-Energy Protons According to Data from Soviet Experiments*

Proton energy	Conditions of irradiation	Biologic object	Effect studied	RBE	Author
660 MeV	Single dose	Rats	LD 50/30	0.7	Avrunina, G. A. (1962)
660 MeV	Single dose	Mice	LD 50	0.7	Avrunina, G. A. (1962)
660 MeV	Single dose	Mice	LD 50	0.67	Konoplyannikov (1965)
660 MeV	Single dose	Mice	LD 50	0.8	Shashkov, V. S. (1964)
660 MeV	Single dose	Mice	Degeneration of bone marrow cell	0.9	Shmakova, N. N. (1965)
660 MeV	Single dose	Mice	No. chromosomal aberrations in bone marrow cells	0.9	Shmakova, N. N. (1965)
660 MeV	Single dose	Mice	Atrophy of testes	0.8	Gaidova, E. S. (1965)
660 MeV	Single dose	Mice	Atrophy of testes	0.6	Pomerantseva, M. D., & Ramaiya, L. K. (1964)
660 MeV	Single dose	Mice	Dominant lethal cases	0.85	Pomerantseva, M. D., & Ramaiya, L. K. (1964)
660 MeV	Single dose	Mice	Dominant lethal cases	0.45	Pomerantseva, M. D. (1964)
660 MeV	Single dose	Mice	Suppression of mitotic activity of bone marrow cells	0.64	Pomerantseva, M. D. (1964)
660 MeV	Single dose	Mice	Suppression of mitotic activity of bone marrow cells	0.85	Shmakova, N. L. (1965)
660 MeV	Single dose	*Drosophila*	No. recessive sex-linked mutations	1.0	Rappoport, I. A. (1962)
660 MeV	Single dose	Haploid yeast cells	No. recessive sex-linked mutations	0.9	Rybakov, N. I. (1967)
660 MeV	Single dose	Lysogenic bacteria	No. recessive sex-linked mutations	0.9	Rybakov, N. I. (1967)
660 MeV	Single dose	Lysogenic bacteria	Phagoproductivity	0.9	Rybakov, N. I. (1967)
660 MeV	Single dose	Lettuce (seeds)	No. chromosomal aberrations	1.3–2.6	Nevzgodina, L. V. et al (1967)
660 MeV	Single dose	Potato	No. chromosomal aberrations	2.8–3.7	Nevzgodina, L. V. et al (1967)
660 MeV	Single dose	Cabbage	No. chromosomal aberrations	1.0–3.8	Nevzgodina, L. V. et al (1967)
660 MeV	Single dose	Carrot	No. chromosomal aberrations	5.0–5.5	Nevzgodina, L. V. et al (1967)
660 MeV	Single dose	Potato	Yield	1.9–2.5	Gertsuskiy, D. F. et al (1967)
660 MeV	Single dose	Potato	No. tubers on plant	1.5–2.2	Gertsuskiy, D. F. et al (1967)
660 MeV	Single dose	Potato	No. chromosmal aberrations	0.7–3.5	Gertsuskiy, D. F. et al (1967)
510 MeV	Repeated dose	Dogs	Lethality	1.0	Ryzhov, N. I. et al (1967)
510 MeV	Single dose	Dogs	Lethality	1.2	Ryzhov, N. I. et al (1967)
510 MeV	Single dose	Rats	LD 50/30	0.8	Ryzhov, N. I. et al (1967)
510 MeV	Repeated dose	Rats	Lethality	0.8	Darenskaya, N. G. et al (1964)
240 MeV	Single dose	Dogs	Lethality	1.0	Ryzhov, N. I. et al (1967)
240 MeV	Single dose	Rats	LD 50/30	0.7	Ryzhov, N. I. et al (1967)
240 MeV	Single dose	Rats	LD 50/8	0.8	Ryzhov, N. I. et al (1967)
240 MeV	Single dose	Mice	LD 50/30	0.8	Ryzhov, N. I. et al (1967)
126 MeV	Single dose	Dogs	Lethality	1.0	Ryzhov, N. I. et al (1967)
126 MeV	Repeated dose	Dogs	Lethality	1.0	Ryzhov, N. I. et al (1967)

TABLE 9.—*Relative Biologic Effectiveness of High-Energy Protons According to Data from Soviet Experiments*—Continued

Proton energy	Conditions of irradiation	Biologic object	Effect studied	RBE	Author
126 MeV	Repeated dose	Rats	Lethality	1.0	Ryzhov, N. I. et al (1967)
126 MeV	Repeated dose	Rats	No. neoplasms	1.0	Ryzhov, N. I. et al (1967)
126 MeV	Repeated dose	Rats	Av. lifespan	1.0	Ryzhov, N. I. et al (1967)
126 MeV	Single dose	Rats	No. nucleus-containing cells in bone marrow	1.0	Seraya, V. V. et al (1967)
126 MeV	Single dose	Rats	No. chromosomal aberrations in bone marrow cells	0.9	Govorun, R. D. et al (1967)
126 MeV	Single dose	Mice	LD 50/30	0.7	Ryzhov, N. I. et al (1967)
126 MeV	Single dose	Mice	LD 100/30	0.9	Ryzhov, N. I. et al (1967)
126 MeV	Single dose	Mice	LD 50, no. chromosomal aberrations in epithelial cells phagoproductivity of the cornea	0.8 0.67	Shashkov, V. S., (1964) Mastryukova, V. M. et al (1964)
126 MeV	Single dose	Lysogenic bacteria	Phagoproductivity	0.9	Rybakov, N. I. et al (1967)
50 MeV	Single dose	Rats	No. chromosomal aberrations in bone marrow cells	1.0	Govorun, R. D. (1968)
50 MeV	Single dose	Mice	LD 100/15	1.2	Grigor'yev, Yu. G. et al (1969)
50 MeV	Single dose	Mice	No. chromosomal aberrations in epithelial cells of the cornea	1.0	Vorozhtsova, S. V. et al (1969)
50 MeV	Single dose	Amniotic cells in man	No. chromosomal aberrations in epithelial cells of the cornea	1.0	Ryzhov, N. I. et al (1969)
50 MeV	Single dose	Lysogenic bacteria	Phagoproductivity	1.0	Ryzhov, N. I. et al (1969)
34 MeV	Single dose	Amniotic cells in man	No. chromosomal aberrations	1.0	Grigor'yev, Yu. G. et al (1969)
10 MeV	Single dose	Mice	No. chromosomal aberrations in epithelial cells of the cornea	1.8	Grigor'yev, Yu. G. et al (1969)

A number of experiments using monoenergetic protons of various energies including 32-MeV, 55-MeV, 138-MeV, and 400-MeV protons have been carried out on primates [35–42, 81, 97, 106, 121, 188]. Radiations of 138 and 400 MeV may be regarded as equivalent to whole-body exposure. The RBE for acute lethality in the animals was equal to about 1. Hematologic effects, vascular effects, weight loss, and metabolic changes were similar to those with γ-irradiation, but gastrointestinal symptoms were more severe following proton irradiation, and more hemorrhagic deaths occurred. The 55-MeV proton exposure was not uniform. At high doses of several thousand rad, the neurologic syndrome was strongly marked. Protons of 32 MeV penetrated to a depth of only 1 cm below skin surface. In some ways, effects resembled those induced by external β-irradiation. $LD_{50/80}$ consisted of 1595 rad—almost three times higher than the $LD_{50/80}$ for uniform whole-body irradiation. Death occurred many weeks postirradiation; the course of postirradiation lethality from cutaneous damage was similar in many ways to the effects of third degree thermal burns.

Study of the effects of skin irradiation is of some importance since solar flare ionizing radiation and protons from the Earth's radiation belt deposit a significant dose to the skin. In a study with primates, it was indicated that increased capillary and/or lymphatic permeability and hypoalbuminemia are related to the development of late edema. Studies on mice demonstrated that a dose of 200 rad of helium ions to the outer 500 μm of the skin caused decrease in longevity in the irradiated animals [103]. It was shown in experiments with 10-MeV protons and with helium ions that these particles have greater potential to induce skin cancer than β-rays. Delayed appearance of skin tumors was greater than normal with doses of helium ions as low as 150 rad. Radiation-induced skin carcinogenesis may be related to radiation damage in hair follicles [2, 7].

Few publications are devoted to the investigation of late effects of proton irradiation in animals. Work with dogs, however, shows the presence of irreversible damage in many internal organs (kidneys, heart, spleen). Nonspecific sclerosis of the vessels of these organs takes place as well as degenerative change indicating development of precocious aging processes [52, 63].

Investigation of the blastomogenic effect of protons and γ-rays in rodents did not reveal essential differences in histologic structure, nor in localization of tumors [155]. Analysis of the material on the incidence of neoplasms presented in Table 10 is noteworthy, making it apparent that, after a single acute exposure to protons with energies of 645 MeV, the incidence of tumor development was lower than after exposure to γ-rays. Tumors mainly of the mammary gland developed.

Massive local neoplasms emerged in rat intestinal tracts following deuteron exposure [20]. Pituitary deuteron irradiation of 945 rad led to great increase in various pituitary tumors in young rats [178]. Late gliomas developed in the brains of three of five primates surviving 55-MeV proton irradiation [83]. These preliminary findings indicate the need for further quantitative information concerning late effects of proton, deuteron, or helium-ion exposure.

Experiments with split doses of 55-MeV protons gave evidence that recuperation in primates following proton irradiation is more than twice as slow as that following γ-ray exposure [106].

To summarize experimental studies with accelerated protons and helium ions, there is substantial evidence that acute whole-body irradiation produces lethality and acute syndromes in a manner similar to γ-rays. The RBE for both types of radiation is equal to 1. There are, however, more severe gastrointestinal and hemorrhagic syndromes with protons.

Large doses of protons administered to the skin caused delayed lethal effects with a pathology similar to thermal burns; often edema related to abnormal permeability was observed. Skin irradiation with protons can also cause a shortened lifespan and increased incidence of skin tumors. Stopped helium ions are much more effective in producing skin tumors in mice than low LET radiation [103]. There is evidence that repair following single doses of 55-MeV protons is somewhat slower than that following γ-ray exposure. No proton or helium-ion studies are available that use protracted, continuous exposure. Thus, experiments with the biologic action of protons on various biologic objects show that the coefficient of RBE essentially does not change within a 50-660 MeV energy range and is equal to 1, whereas the RBE increases below 50 MeV. Large, single doses of these particles can cause gliomas.

Biologic Effects of Protons on Plants

The necessity of using plants as one of the links in the ecological system of life support may arise during lengthy space flight. The effect on plants of ionizing radiation, especially protons generated during chromospheric solar flares, is an important problem.

The majority of experiments indicate that protons of a wide energy range have more effect on seeds than γ- and x-rays. Relative biologic effectiveness of protons on seeds of various plants is summarized in Table 11.

An apparently larger RBE for protons was first noted in 1954 in a comparison of the biologic effects of 160-MeV protons with x-rays on irradiated dry barley seeds [48]. Work carried out with fast neutrons also bears on this problem since fast neutrons exert much of their biologic effectiveness because of recoil protons and α-particles. Much higher RBE was noted when dry seeds were irradiated and stored than when moist seeds were subjected to neutron and γ-irradiation [80].

A series of works concerns the evaluation of biologic effect of 600-MeV protons in a wide range of doses. Potatoes, cabbage, radishes, carrots, lettuce, and other plants were used in the experi-

TABLE 10.—*Frequency and Histologic Type of Tumor Developed in Rats Following 645 MeV Proton and Co^{60} γ-Irradiation*

Irradiation and Control	Dose (rad)	No. animals used	No. animals with tumors	No. animals with tumors of mammary gland	Histologic-type mammary gland tumors, %			
					Adenocarcinoma	Adenofibroma	Fibroadenoma	Other malignant tumors
645 MeV Proton	35	40	8	87	28.6	42.8	28.6	—
	100	40	8	87	28.5	14.2	57.3	—
	200	100	30	86	23.0	38.6	11.5	26.9
	400	120	35	82	27.6	24.1	41.4	6.9
Co^{60} γ-ray	35	40	7	86	16.8	33.4	49.8	—
	100	40	4	100	25.0	50.0	25.0	—
	200	40	17	94	31.2	25.0	37.6	6.2
	400	120	56	87	14.3	36.9	30.7	18.1
Control	—	100	4	100	—	50.0	50.0	—

TABLE 11.—*RBE with Proton Irradiation of Various Plant Seeds*

Protons (energy)	Plant	Criteria for RBE evaluation	RBE	Reference
50 MeV	Lettuce *(Lactuca sativa)*	Chromosome breaks	1.4–1.6	[130]
100 MeV	Lettuce *(Lactuca sativa)*	Chromosome breaks	1.4	[130]
160 MeV	Barley *(Hordeum vulgare)*	No. mutations; growth inhibition	>1	[49]
380 MeV	Barley *(Hordeum vulgare)*	Decreased leaf growth	1.5–1.8	[28]
380 MeV	Fern spores	Survival	1.6	[28]
20 GeV	Barley *(Hordeum vulgare)*	Growth of sprouts	3.4	[58]
650 MeV	Barley *(Hordeum vulgare)*	Growth of sprouts	2.1	[58]
660 MeV	Pea *(Pisum sativum)*	Chromosome breaks	1.0	[93]
660 MeV	Cabbage *(Brassica pekinensis)*	Chromosome breaks	1.0–3.5	[130]
660 MeV	Pea *(Pisum sativum)*	Chromosome breaks	2.3–6.9	[4]
660 MeV	Lettuce *(Lactuca sativa)*	Chromosome breaks	3.5	[130]
660 MeV	Potato *(Solanum tuberosum)*	Chromosome breaks	3.7	[59]
660 MeV	Cabbage *(Brassica oleracea)*	Chromosome breaks	3.8	[59]
660 MeV	Daucus Carrot *(Daucus carota)*	Chromosome breaks	5.5	[59]
660 MeV	Potato *(Solanum tuberosum)*	Productivity	0.6–2.8	[59]
2.8 GeV	Nigella *(Nigella damascena)*	Chromosome breaks	2.1	[123]
28 GeV	Maize *(Zea mays)*	Chlorophyll mutations	4.4	[172]

ments, and agrobiologic and cytogenic indicators were used to evaluate RBE [63].

Experiments pertaining to the yield and potential height of plants using potato, cabbage, radish, and lettuce seeds gave coefficients for proton RBE of 2.3, 2.5, 3.0, and 2.4, respectively. With irradiation of potato shoots, the coefficients of RBE ranged from 0.5 to 2.3.

In work where aberrant mitosis of various plants from seeds irradiated with 660-MeV protons and γ-rays was studied, maximum proton RBE values of 2.6, 3.7, 3.8, and 5.5, in lettuce, potato, cabbage, and carrot seeds, respectively, were obtained [63]. In similar experiments on seeds of peas, RBE was found to equal 4.3 to 6.9 [4]. A lower coefficient equaling 2.1 was obtained using seeds of *Nigella damascena* irradiated with 2.8-GeV protons [122].

In evaluating the biologic effect of protons on the plant link in the life-support system, it is necessary to include the influence of a number of physical and biologic factors bearing on the coefficient of proton RBE: first of all, the dose level.

In the majority of these works, the direct relationship between RBE and absorbed dose is noted (see Table 12.). In several works, the *lack* of dependence of RBE on dose is indicated for seeds of lettuce, peas, and barley [27, 58, 122]. Certain difficulties arise in comparing the biologic effectiveness of protons and γ-rays and defining, according to agrobiologic criteria, their coefficients of RBE within a wide dose range. Dose-dependence in a given instance describes a complex curve; distinctions become discernible only at very high dose levels [58]. An inverse dependence of proton RBE on dose rate was revealed by the yield of chromosomal aberrations in the seeds of peas [122]. RBE values for 660-MeV protons were found to equal 6.9, 5.2, and 4.3 when γ-ray dose rates were 70 700 and 4200 rad/min, respectively.

The dependence of the magnitude of proton RBE on proton energy is a study of great interest for radiation biology in general as well as for solution of radiation safety problems in manned space flight. At present, however, work on this problem is inadequate. Barley seeds were irradiated with protons of various energies, i.e., 20 GeV, 600 MeV, [57] and 380 MeV [27]. In each case, initial leaf growth was the criterion for evaluation. Proton RBE at 20-GeV, 600-MeV, and 380-MeV irradiation equaled 3.4, 2.5, and 1.4. A similar dependence was observed on lettuce

TABLE 12.—*Dependence of RBE on Dose with 660 MeV Proton Irradiation of Various Plant Seeds* [64]

Plant	Criteria for evaluation	Dose of 660 MeV protons (krad)	Coefficient of RBE	Reference
Lettuce	Cells with chromosomal aberrations	5	2.0	[64]
		8	2.2	
		10	2.6	
Potato	Cells with chromosomal aberrations	5	1.0	[64]
		10	2.4	
		12	3.2	
		15	3.7	
Cabbage	Cells with chromosomal aberrations	10	1.0	[64]
		25	1.0	
		50	1.8	
		100	3.8	
Bean	Sprouts with lateral rootlets in 3 d	0.7	1.0	[64]
		6.8	0.9	
		9.6	1.4	
		11.0	1.9	

seeds irradiated with protons at 600-, 100-, and 50-MeV energies for RBE values of 3.5, 1.6 and 1.6 [129]. In sprouts irradiated with energies of 660 and 50 MeV, the RBE coefficients were equal to 2.3 and 0.5.

Proton RBE values vary, depending on whether immediate or long-term effects of radiation in plants are considered. Several works are devoted to determination of proton RBE, both immediately following and some time after irradiation, under various storage conditions. The effect of storage on pea seeds irradiated with protons was far less than in seeds irradiated with γ-rays [92]. Lettuce seeds irradiated with protons of 100 and 630 MeV and stored at room temperature for 8 to 30 months showed a lowering of the mean value of the coefficient of RBE from 1.6 to 0.5, and from 2.2 to 0.9. In cabbage seeds, the mean value of the coefficient of RBE immediately postirradiation was 1.9, whereas, following 18 months' storage, it was 1.0 [131]. Roughly the same values were obtained for proton RBE with lettuce seeds stored at a temperature of +30° C and relative humidity of 56%. The coefficients of proton RBE decreased immediately postirradiation from 2.4 to 1.3 for 30 d following irradiation [139]. In resting spores of ferns irradiated with protons of 380 MeV and stored for 301 d after irradiation, a decrease in proton RBE from 1.7 to 1.1 was noted [27].

Proton RBE also depends upon the criteria used in evaluating the biologic effect of radiation. For instance, the results of investigations performed according to agrobiologic criteria, i.e., productivity or growth, differ from data obtained from a count of cells with chromosomal aberrations. Conditions of postirradiation cultivation are also highly important in the determination of proton RBE. Lower RBE values were obtained with cultivation of irradiated plants in the field rather than under hothouse or luminostat conditions [1].

Data on the biologic effect of protons and γ-rays on active metabolic systems, i.e., sprouts, deserve attention, although such data are limited in the literature. Experiments on *Vicia faba* revealed that 185-MeV proton irradiation of lettuce sprouts produced a lower percent of anomalous metaphases than x-ray irradiation [99]. The proton RBE value in this case was 0.7. Low RBE values, i.e., 0.5–0.6, were obtained for 50-MeV proton irradiation of lettuce sprouts [129].

Experiments have been carried out on *Chlorella* with proton and α-particle irradiation. *Chlorella* is a radioresistant culture, and LD_{50} with γ-irradiation was equal to 13 krad. Protons of 660 MeV were 1.6 times more effective, while LD_{50} equaled 5 krad with α-particle irradiation [181].

The study of quantitative characteristics of the effects of 50–60 MeV protons in plants has shown RBE values considerably higher than 1. This differs markedly from all data obtained earlier in irradiation of experimental animals, microorganisms, yeast cells, and other model systems. Additional experimentation is needed to explain the considerable increase in biologic effectiveness with high-energy proton irradiation.

Biologic Effects of Multi-GeV Protons

Preliminary experiments at the Serpukhov accelerator by Akoyev and others indicated a high (from 1.2–6 times higher) effectiveness for secondary radiation from 35-GeV neutrons in comparison with Cs^{137} γ-rays. Criteria for evaluation were: recovery and number of mutations in phage T_4F; recovery in bacteria *Escherichia coli;* recovery, weight decrease, and length of primary root sprouts as well as chromosomal aberration in *Vicia faba.*

According to a series of indicators, RBE increased from two to five times when dose was reduced. A significant discrepancy in the various experimental values for RBE apparently reflects the extreme nonhomogeneity of dose distribution due to creation of secondary particles, in the form of multicharged ions and antiprotons [6].

Biologic Action of Heavy Ions

Heavy ions are generally more effective than lightly ionizing radiation in producing biologic effects at the cellular level. The hazard from heavy ions might be completely different from that of protons and helium ions. When administered in sufficient dose, helium ions will primarily

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affect tissues which proliferate rapidly and which are essential to maintenance of normal bodily functions. Such tissues include bone marrow, epithelial and reproductive organ tissues. Heavy ions might, on the contrary, be quite effective in producing specialized biologic effects in nonproliferating tissues at extremely low dose rates, so that an effect may be produced by only a single heavy particle. The effect on proliferative tissues, which have great recuperative properties, does not appear significant; in this respect, the effect on nonregenerating tissue is more interesting. Nonregenerating tissue includes portions of the central nervous system, in particular, certain cells of the sense organs, and other specialized cells such as those in the eye lens.

The Nature of Heavy-Ion Lesions

A characteristic of the biologic effects of heavy particles in contrast with low LET radiations is: a single heavy particle can cause an important effect at the appropriate place within the cell. In order to obtain the same effect with low LET radiations, it is often necessary for several particles to hit the cells either simultaneously or very closely spaced in time. This relationship can be experimentally expressed by the so-called multiple-hit survival curve for cellular cultures and tissues. When the dose-effect relationship is exponential, description of the events and the quantitation of efficiency of these events can conveniently be translated into terms of interaction cross section. This concept of interaction cross section, representing a probability factor, is similar to that used in nuclear physics. However, in many instances of biologic study, the cross section for biologic interaction of heavy ions is not different from the projected cross section of the cell nucleus.

Figure 8 summarizes the data obtained at Berkeley on inhibition of cell division and the killing effect of heavy ions up to accelerated argon on various biologic specimens, including enzymes, phage particles, bacteria, yeast cells, and mammalian cells in culture. In mammalian cells, it is quite obvious from this treatment that each accelerated heavy ion can be approximately a thousand times more effective than its lightly ionizing counterpart with low LET. When this is translated into terms of relative biologic effectiveness, the general effectiveness of high LET irradiation for acute inhibition of cell division and colony formation in mammalian cells can reach values up to 8. Figure 9 presents a number of mammalian cell survival curves for various heavy ions (from Todd [173]).

With the particles mentioned so far, the magnitude of the cross section may reach the same value as that of the cell nucleus. However, indications are that at very high linear energy transfer of argon and heavier ions, the cross section transcends the size of the nuclear cross section [173]. In experiments with high LET argon particles, Madhvanath et al have shown that lymphocyte cultures from rat tissues were so sensitive to argon ions that the cross section appeared to be equal to, or greater than, the entire lymphocyte cell in size [112]. The lethal effect observed in the lymphocytes due to heavy-ion hits was not similar to that usually observed in in vivo cell culture

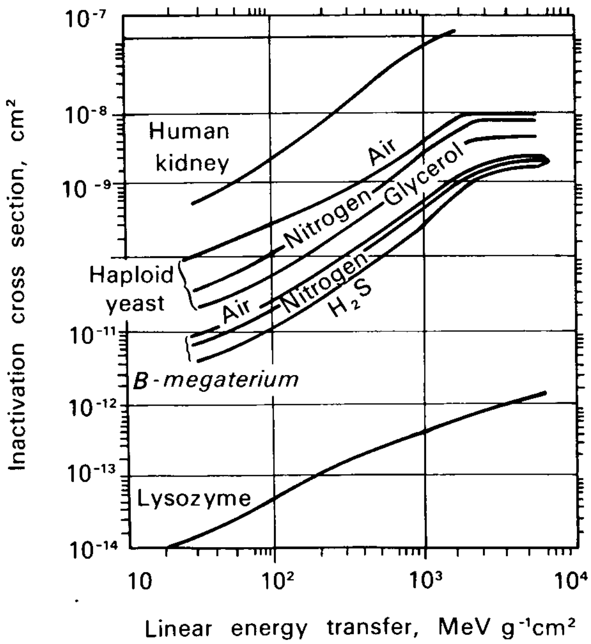

FIGURE 8.—Inactivation cross sections as functions of linear energy transfer. The figure summarizes data obtained at Berkeley on inhibition of cell division and the killing effect of heavy ions up to accelerated argon on various biological specimens including enzymes, bacteria, yeast, and mammalian cells.

experiments. Usually, lethality is observed as associated with cell division.

Lymphocyte death initiated by heavy ions is interphase death, and may relate to damage to the membranous structures of the cell. There are preliminary indications that heavy ions can cause irreversible changes in the structure and biosynthetic activities of nondividing cells such as neurons in tissue culture. The changes observed have not been conclusively quantitated. However, nuclear pyknosis and lipofuscin particles observed in the cytoplasm of neurons are believed to relate to radiation-induced aging processes. Since neurons do not divide in the adult human body, and since the uninhibited function of the nervous system is essential to ensure the performance required of astronauts, minor changes in neurons caused by heavy ions must be studied in more detail for their possible hazard to the crew during long-term space flight.

While the biologic effectiveness (RBE) of heavy ions on living cells is greater than that of low LET radiations, this relationship is reversed when protein enzymes are analyzed. Heavy ions are less effective in activating enzymes than low LET irradiation [31]. For this reason, several investigators have related heavy-ion effects to the special changes which they can produce in nucleic acids, particularly in DNA (deoxyribonucleic acid). It was clearly demonstrated by Christensen et al that single heavy ions can produce double-strand breaks in bacteriophage and that such breaks invariably lead to inability of the phage particles to reproduce. In contrast, single-strand breaks are caused predominantly by low LET irradiation; more than one single-strand break is necessary in the DNA to cause irreversible damage in the phage.

Since the production of DNA lesions parallels the production of biologic effects, even in cells

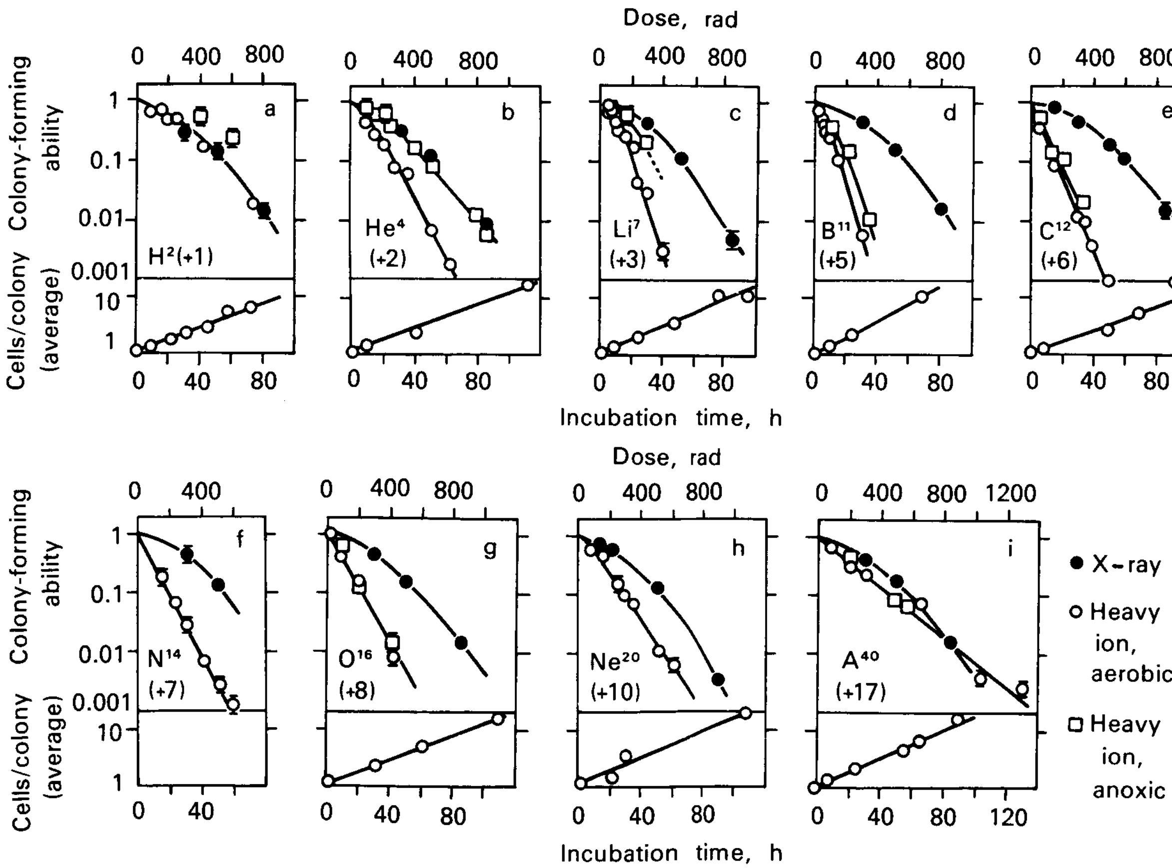

FIGURE 9.—Response of the colony-forming ability of TI cells to irradiation with heavy ions of equal velocity. The ion and its average charge state is indicated on each plot.

that have more DNA than the phages, it is tempting to conclude that much of the heavy-particle effect in eukaryotic cells is also due to double-strand breaks in the DNA. However, this conclusion has not been proved since we do not completely understand the manner in which DNA lesions occur and heal in mammalian cells. It has recently been shown that the application of even lower LET x-rays to mammalian cells results in multiple chromosomal breakage followed by rejoinings, and that there is a great deal of DNA fragmentation which then repairs itself. It is possible that heavy-ion effects on mammalian cells are more complex than the mere production of DNA double-strand breaks. Since the nuclear membrane appears to be intimately involved with submicroscopic distribution of nucleic acids and their biochemical functions, it is quite possible that heavy-ion irradiation can eventually be related to combined membrane and nucleic acid lesions.

Radiation lesions in most cells, including mammalian cells, can repair during the postirradiation period. With bacteriophage, it has been shown repeatedly that single-strand lesions are especially reparable. Single-strand lesions, it is assumed, are produced either by direct single ionization events or by the action of free radicals produced in the cytoplasm which later interact with, and cause alterations in, DNA. The same lesions that are reparable are also susceptible to the modifying action of chemical substances, such as sulfhydryl and aminothiol protectors. As a general rule, the known chemical radioprotectors against x-ray effects become less and less effective as LET increases, and are completely ineffective against very high LET particles (certain alcohols are an exception). If repair occurs in the postirradiation period, such repair can usually be demonstrated by the fact that fractional delivery of radiation exposure produces nonadditive effects. If the dose is delivered in two installments and if a portion of the effects of the first exposure has repaired by the time the second exposure takes place, then the overall effect of both is less than if the entire dose were administered at once.

Although not many experimental results are available in this field, studies made with mammalian cells and bacteria clearly demonstrate that the radiation effects of heavy ions are additive [16]. This is important for radiation protection, since the protective factor due to postirradiation repair which appears to be present when low LET radiations are delivered at a low dose rate, appears to be entirely absent with heavy-ion irradiation. Consequently, at present, high LET radiation must be regarded as completely additive in its effects; it follows that heavy-ion effects are independent of the dose rate.

X- or γ-irradiation produces chromosomal aberrations in the cells of mammalian tissues; however, the aberrations disappear from the irradiated tissues in a few weeks. Grigor'yev and others noted that cells of mammalian liver, exposed to carbon particles, retained chromosomal aberrations for several months [75].

Stable changes in the incidence of aberrant mitosis in mouse cornea epithelial cells following irradiation with carbon ions have been observed at Dubna (see Table 13). It is noteworthy that a low dose of 25 rad of carbon ions produced 30% aberrant mitosis.

Radiation Effects on the Retina

One of the most interesting radiation effects documented in detail by Apollo 11 astronauts was in the form of light flashes and streaks seen about every 2 or 3 min on lunar journeys outside the Earth's magnetic field. Chapman reported (in 1972 [28]), that approximately 15 astronauts on five separate flights to the Moon had seen such light flashes after having reached some degree of dark adaptation. Since these visual events could be seen with the eye either open or closed, this posed the problem of where the light flashes originated and whether the brain or retina was involved [169, 170]. Experiments have clearly demonstrated that heavy ions are capable of producing a sensation of light flashes and streaks if they cross the dark-adapted human retina. It appears that this interaction is an effect created in the visual sensing elements of the retina, probably the retina rods.

Streaks and flashes can be seen if the rate of energy loss is higher than about 10 keV/μm. Consequently, most of the fast and slow cosmic ray particles of nitrogen and higher atomic number elements might be seen by the astronauts, but high-energy cosmic protons and helium ions would not cause such phenomena.

Visual sensations caused by ionizing radiation are not surprising; we have known for more than 70 years that x-rays from secondary light quanta can cause visual effects either directly or indirectly. An additional theory proposed by Fazio et al [51], is that Cerenkov light contributes to light sensation from particles moving with relativistic velocities (> 350 MeV/nucleon). McNulty et al recently described experiments with relativistic nitrogen particles [119]. Much data have already been obtained on such physiologic effects by studying the retina and corresponding changes in bioelectric activity of the brain during ionizing irradiation [61].

Visual observation of streaks by astronauts during space flight to the Moon has indicated the need for better understanding of biologic effects arising along tracks of single-charged particles. Three studies on heavy-ion effects in the retina are currently in progress at Berkeley. It is clear from preliminary observations by Zeevi et al [193] that outer segments of the retinal rods in *Necturus maculosis* are altered by a dose of accelerated nitrogen ions on the order of 1 rad. Similar observations (unpublished) are available on irradiation experiments with mice, rabbits, and primates. The observations indicate that the initial disturbance might be related to a disturbance in the synthetic function of the visual cells, thus producing new visual disks and photo pigments. A 1973 study on primates by Bonney and coworkers demonstrates that retinal lesions caused by several hundred rad of oxygen ions cause severe pathological effects during 9 months as well as important effects on blood vessels [21].

Search for Effects Within the Brain

Exceedingly low fluxes of heavy particles directed toward the human occipital lobe have not caused subjective observation of light flashes. A search has been underway for a number of years for histologic effects that might be produced in the nervous system by heavy cosmic ray primaries. Biologic effects in three primates flown in balloons to an altitude of about 37.5 km (120 000 ft) for 24 h were investigated by Taketa et al [165]. Subsequent histologic studies have uncovered regions in the primate cerebellum showing that a number of cells were disturbed as though a track had been formed in the wake of a passing particle. However, the controls which remained at ground level also showed a number of tracks, although these appeared histologically older than tracks in the brains of animals flown to high altitudes. Peculiar capillary extravascular deposition of iron has also been noted and might

TABLE 13.—*Change in Number of Aberrant Mitoses in Epithelial Cells of Mouse Cornea Following Carbon-Ion and 180 kV x-Ray Irradiation*

Type of irradiation	Dose (rad)	Aberrant mitosis, %			
		Fixation periods, h			
		24	72	240	480
180 kV x-ray	50	14.9±0.5	7.8±0.4	2.8±0.3	2.5±0.3
	100	22.5±0.5	15.6±0.8	4.2±0.5	4.5±0.6
	250	41.5±2.1	34.2±0.3	13.2±0.7	11.1±1.1
	500	59.3±2.9	61.7±0.6	24.4±0.4	14.8±1.6
	Control	0.7±0.1	1.0±0.1	0.9±0.1	1.0±0.2
Carbon ion	25	20.5±0.6	29.6±0.7	24.9±0.5	29.6±0.7
	50	35.5±0.8	46.7±0.5	35.5±0.6	33.6±0.7
	100	52.1±1.0	60.3±0.8	42.8±0.5	41.4±1.8
	250	78.6±0.9	73.9±1.0	67.9±1.0	67.1±0.5
	500	80.3±1.1	—	—	—
	Control	0.8±0.1	0.8±0.1	0.8±0.1	0.7±0.1

be related to heavy-ion effects. In the Apollo 16 flight of 1972, five pocket mice were flown with the intent of obtaining further data on neuropathologic effects of heavy ions. These observations have clearly been hampered by low dose rate during balloon and satellite flights and should be repeated using the beams of heavy-particle accelerators.

Skin Effects

A number of balloon flights in the 1950s used C57 black mice [30]. Their hair pigmentation is genetically controlled—normally there is only about one white or gray hair in each 500 black hairs. Hair development in these experiments was set at the appropriate stage for plucking old hair from animals that had been prepared for flight. The animals were then flown to an altitude of about 25 km (85 000 ft). During the postflight period, many gray hairs developed; it is likely that heavy particles in cosmic rays caused this change in hair color. In some instances, gray hairs were arranged in a straight line, indicating the possibility that one particle had caused a change in pigmentation in several hair follicles found in its path. Recently, similar experiments were repeated with similar findings.

A number of C57bl mice were exposed to intensities ranging from about 10^3 to 10^5 particles/cm^2, using an accelerated nitrogen beam. When the nitrogen ions traveled tangentially to the skin of the animals, the number of white hairs that developed following exposure was significantly higher than in the controls. Leith et al [102] obtained evidence that a single heavy nitrogen particle passing by a hair follicle could change the pigmentation of the hair developing from it (Fig. 10). The indicator chosen, hair color in this instance, does not permit measuring the degree of hazard. However, it seems apparent that hair color in hair follicles is determined by the joint action of about six to eight pigment cells within the follicle. Whatever the mode of action of the heavy particle, it seems to have been simultaneously extended to more than one cell at a time. In animals kept for 6 months or longer, a more general graying effect was noticed as a result of nitrogen-beam irradiation, even at quite low doses. This type of experiment indicates that individual heavy particles can affect single cells or groups of cells, not only in the nervous system, but also in other body areas characterized by rapid proliferation and regeneration. The hair depigmentation effect observed can serve to indicate the presence of heavy particles; in the future, hopefully, some of these observations can be extended to groups of animals flown in orbit for extended periods.

The effectiveness of lithium ions at the Bragg peak in producing skin erythema in rabbits has also been assessed by d'Angio [43]. The conclusion based on these data is that there is no "threshold dose" for deleterious effects produced by high LET radiation in skin whereas there is such a threshold dose for protons, deuterons, and low LET radiations.

Effects in Plants

Several years ago, two different groups of investigators carried out a preliminary study on maize to scan the effect of cosmic, heavy-ion radiation on seeds. *Zea mays* seeds with appropriate genetic constitution were flown in a satellite in near-equatorial orbit by H. Smith [158]. Slater and Tobias exposed maize in a balloon kept at an altitude of 28.5–37.5 km (95 000–125 000 ft) for more than a day [157]. The orbiting experiment indicated only a few abnormalities but the experiment using balloons showed a surprisingly large number of slits and white streaks in the second and third embryonic leaves of plants that developed from exposed seeds. Abnormalities on this flight were about 6% and the estimated total cosmic ray dose was about 50 mrad.

In two different laboratories, similar work was carried out recently with heavy nitrogen particles after earlier attempts with high-energy helium ions failed to produce results similar to those in the balloon flights. Figure 11 shows developing maize after a dose of accelerated oxygen ions. Nitrogen ions at the Princeton synchrotron in Todd's experiment [174], and oxygen and nitrogen ions at the Berkeley bevatron used by Heinze [84], produced a statistically significant number of developmental abnormalities in maize following exposure of its seeds to low fluxes of slow ions. At Princeton, the seeds were presoaked and wet, while those at Berkeley were dry. Interpretation of this type of experiment is still in doubt. Todd et al assumed that the effect of the particles is exerted on several embryonic cells simultaneously. This is clearly not indicated by the data at Berkeley; it is quite possible that only a single cell is affected by the heavy particles as they cross the embryo, and that developmental abnormalities result from death or injury to that particular cell which is essential for providing the developing structure. In dry seeds, the damage caused by heavy ions is stored for many days; in this respect, seed behavior resembles that of plastics and certain special materials (such as mica) that preserve radiation injury following exposure to heavy particles either by artificial means or in space. When LET reaches about 100 keV/μm or more, the core of the rapidly moving particles produces irreversible damage. This damage can later be developed by means of sodium hydroxide to produce microscopically visible holes in the plastic material.

Experiments were conducted by Hirono on dry *Arabidopsis* seeds using heavy ions of He^4, Li^7, C^{12}, O^{16}, Ne^{20}, and A^{40}. According to the criteria of lowering dry weight of the plants and induction of somatic mutations, RBE varied from 11.5 to 25, depending on which particle was used [89].

With irradiation of *Chlorella* by heavy ions of B^{+2}_{11}, C^{+6}_{12}, Ne^{+4}_{22} and A^{+8}_{10}, and with LET ranging from 3 to 26 000 MeV/gcm^{-2}, various types of curves for recovery were obtained: S-shaped for lightly ionizing radiation, and exponential for heavily ionizing. Coefficients of RBE attained

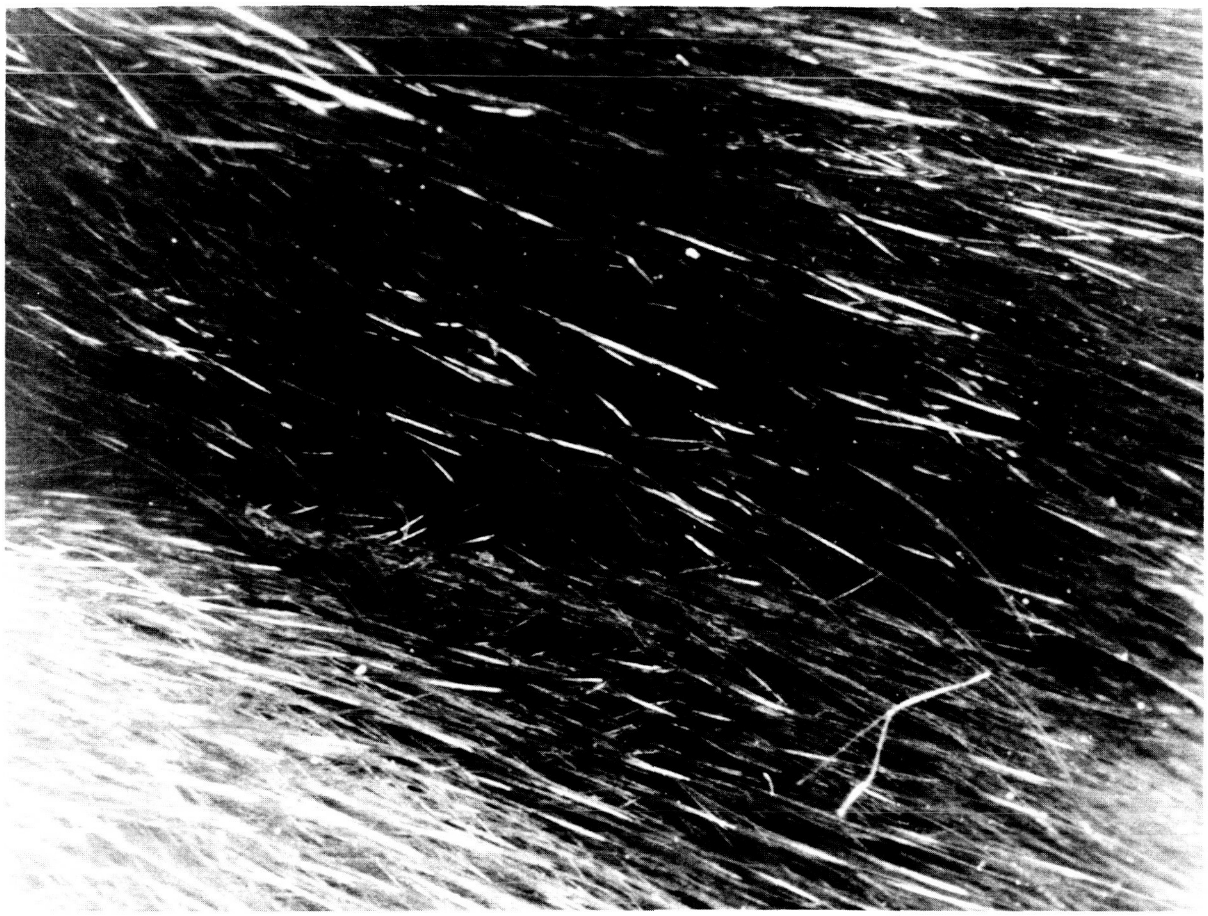

FIGURE 10.—Photograph of regrowing mouse hair 13 days after irradiation. Distinctly white hairs are visible. The animal received approximately 4.14 × 10^4 nitrogen ions.

maximum value at low doses and minimum value at high doses for ions with dE/dx of from 1000 to 5000 MeV/gcm^{-2}. The maximum value of 8 for RBE occurred during irradiation with carbon ions [180].

Tumorigenesis and Changes in Longevity

Available data are extremely scant concerning the possible effects of heavy ions on tumor induction. A preliminary experiment in this area has been performed by Smith on *Arabidopsis* [88]. When seeds of this plant were exposed to accelerated carbon, neon, and argon ions, as well as to helium ions and x-rays, the RBE for tumor induction in plants grown from the irradiated seeds was very high—between 35 and 50. From this finding, the authors feel that further studies should be made on the blastomogenic effects of heavy particles. Studies have been devoted to the effects of heavy ions on longevity. Heavy-ion irradiation of the hypothalamic region of the brain in small rodents resulted in a shortened lifespan. Curtis demonstrated that 500 rad of deuterons directed to the brains of mice can cause shortening in lifespan [134].

Modification of Effects by Radioprotective Agents

While the usual sulfhydryl radioprotective agents are not effective against heavy-ion irradiation, in experiments with yeast cells performed by Manney [114] at Berkeley, it was discovered that large concentrations of glycerol gave dual protection from both heavy ions and low LET radiation. Independent experiments conducted by Grigor'yev and Krasavin at Dubna on intestinal bacteria [75, 95] indicate that glycerol and inositol also exhibit some degree of protective action (see Fig. 12).

By contrast, in analogous experiments using the sulfhydryl drugs, cysteine and cystaphos, as radioprotectors, radioprotective effects were not noted. The precise mechanism of the protective action of polyhydric alcohols is not clear. However, it has been proposed that these alcohols exhibit dehydrating action when mixed with water molecules on the surface of the critical

FIGURE 11.—The leaf of a maize plant, grown from a seed exposed to accelerated oxygen ions.

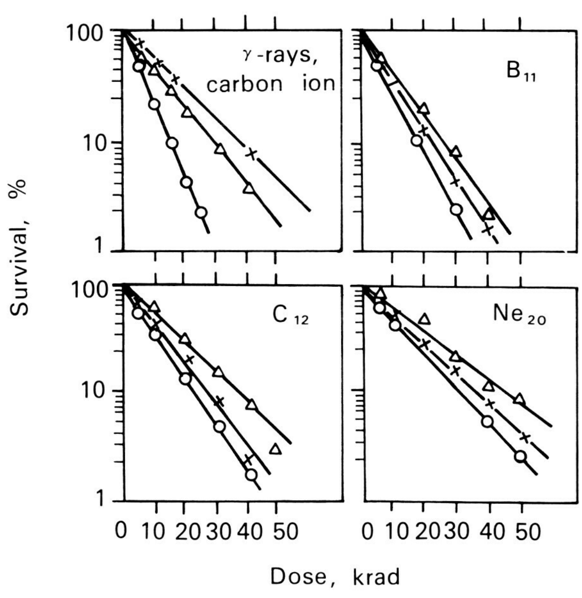

FIGURE 12.—Survival of *E. coli* B. after irradiation with carbon-ion gamma rays and accelerated ions of boron, carbon, and neon in a 1 M solution of glycerol and 0.05 M solution of cystamine. Buffer, —○—○—; glycerol, —Δ—Δ—; cystamine, —×—×—.

macromolecular cells, at the same time decreasing the dimensions of the cell nuclei [95]. Unfortunately, to use alcohol for protection of persons from the action of heavy ions in cosmic radiation is impractical, since concentrations of alcohol needed for protection would be extremely toxic to the human organism.

Summary and Outlook

Single, heavy-accelerated ions and single cosmic ray primaries can cause the sensation of light flashes, retinal pathology, changes in hair pigmentation, and developmental abnormalities in plants grown from exposed seeds. Beams of such particles greatly enhance tumor induction in plants. When directed to mouse and rat brain, decrease in longevity was noted. In liver and corneal tissues, abnormal mitosis and chromosomal aberrations produced by heavy ions persisted for many months. There are only fragmentary data on the biologic action on the intact organism by heavy ions.

Besides the fully verifiable experiments described, which indicate that a single, heavy-accelerated particle, or a particle in cosmic rays, can cause macroscopically significant damage, many other experimental findings have not yet been explained, which may be due in part to the action of heavy ions. One such set of data obtained by Oster [135] shows an abnormal quantity of chromosomal breaks in germ cells of the genital organs of irradiated *Drosophila* on Biosatellite II. An analysis of these data indicates that the results were unexpected even for large doses of radiation at low LET. So far, these findings have not been explained. However, passage through the gonads of one or several very heavy particles at very early stages of development, when proliferation of cells is still taking place, could perhaps explain the high number of chromosome recombinations. It has been shown that, in certain types of plants, for example in *Arabidopsis*, mutagenic action of heavy ions is significantly higher than the action of standard radiation [55].

The results of biologic experiments completed during space flight and the data gathered from satellites, presented in other sections of this chapter, indicate that in certain types of organisms an extremely high number of chromosomal aberrations, dominant and regressive mutations, and anomalous mitoses occur in comparison with Earth controls. A number of factors in space flight could cause the events noted. In the future, it will be necessary to determine the possible role of primary cosmic radiation in creating similar effects.

Clearly, there is great need to extend such observations and to quantitate possible deleterious effects of heavy cosmic ray particles. Such studies are needed for adequate health protection of astronauts on long space flights. New achievements in space and the construction of accelerators will allow us, in the near future, to extend biologic research on heavy ions.

INFLUENCE OF SPACEFLIGHT CONDITIONS ON RADIOBIOLOGIC EFFECT

Man and the living creatures accompanying him, having reached beyond the limits of the Earth's atmosphere, will enter new *space environments* which are characterized not only by a high radiation background, but also by simultaneous action of a number of factors—isolation, weightlessness, changed gaseous medium, vibration, acceleration, and so on. The human organism reacts delicately to small changes in the surrounding environment, especially to such changes that are only rarely present in existence on Earth.

When Selye proposed his general adaptation theory in 1949, he turned the attention of researchers to the general mechanisms of an organism's reaction to a broad spectrum of external irritants. The volume of knowledge on the combined action of factors present in space flight is limited; it does not permit formulating, at present, a complete hypothesis on the possible consequences of interaction of radiation and nonradiation effects during long-term space flight. If there is synergism between the action of radiation and other physical factors, this has importance for the evaluation of hazards in space flight. Certain nonradiation environmental factors can probably alter the radiosensitivity of an organism.

A series of experiments by Yang et al [191] with the flour beetle, *Tribolium confusum*, on the interaction of radiation effects (weightlessness, gravity compensation, temperature, oxygen tension, and magnetic field) in the environment point to generalizations which may also be valid for other organisms. Briefly summarized, they are:

(1) There is usually an optimum value for each organism for environmental variables acting simultaneously. These optimum values are not always known. For example: What proportion of oxygen combined with carbon dioxide should be present in the optimal atmosphere?

(2) Most organisms can adjust to a range of values for any given environmental parameter, due to the presence of the homeostatic system. For example, an organism may have a characteristic "normal" temperature range; when the temperature changes beyond normal limits, the homeostatic mechanisms lose control.

(3) Interaction between two environmental agents is most marked when the organism is stressed near the limits of tolerance by one of the agents. For example, radiation effects in *Tribolium confusum* are more severe near both upper and lower limits of the organism's temperature tolerance. Conversely, the temperature sensitivity of *Tribolium* is increased when it has received a near-lethal dose of radiation.

(4) Several environmental agents acting simultaneously can alter each one's normal range of tolerance. Usually, tolerance decreases, except when one agent acts as "protector" from the effects of another. For example, anoxia may partially protect an organism from radiation injury.

Many published works are devoted to the study of the combined effects (measured on Earth) of ionizing radiation and other stress factors. For example, investigations have been performed on the immediate or subsequent action of radiation and thermal burns, ionizing radiation and mechanical trauma, ionizing radiation and effects on blood. These works have, undoubtedly, an important independent value, but are not necessarily relevant to the problem of evaluating complex radiation effects that may be present in space flight.

The external factors of space flight may be divided into two groups. To the first may be assigned the immediate conditions of flight (for example, vibration, acceleration, and noise, especially at takeoff and landing). These factors act over relatively short periods.

The second group of spaceflight factors acts over longer periods, among which are the near-weightless conditions during inertial phases of space flight. Other long-term factors which depend on the interaction of man with a closed environment include: effects from accumulation of waste products; alteration of immunity to an autoflora of microorganisms; and long-term responses to various ambient temperatures, gases in the environment, nutrition, and to visible and ultraviolet light. These long-term effects are of particular interest when in combination with radiation exposure.

Weightlessness and Hypokinesia

A special problem arises in considering long-term adaptation to spaceflight conditions. The effects of radiation during long-term space flight accumulate, although man has a capacity to adapt to such flight factors as weightlessness, at least up to 2 weeks, and to hypokinesia over a more extended period. It has been demonstrated that, in organisms which survive a regimen of radiation exposures, some residual radiation injury remains; and that the residual portion of radiation injury is greater after high LET radiation exposure than following exposure to "standard" types of radiation. Evidently, an organism with such residual injury may respond to various stressful factors in space flight in a manner differing from that of nonirradiated individuals. In most orbital flights, astronauts have lost significant amounts of weight; on some longer flights, they also exhibited mild anemia, lowered body water content, and some decalcification in bones. In some situations, the astronaut's vestibular system was stressed nearly beyond limits. While most of the changes described might be considered normal physiologic shifts in response to lowered gravitational stress, it is believed that significant doses of radiation would probably enhance these effects and produce pathologic reactions.

As astronauts spend longer intervals in inertial flight, the interaction of weightlessness and other environmental factors will be more likely to produce deleterious effects. It would be desirable to know more about these synergistic effects in biologic test systems in space and on the ground, to avert human emergencies.

Biorhythms and Radiation Sensitivity

Another aspect of the problem of the combined effect of spaceflight factors (not yet discussed) is the relationship between biorhythms and radiosensitivity. Annual changes of radiosensitivity in animals have been established experimentally. An analysis of *dose-effect* curves, using the criterion of survival, has enabled Druzhinin [65] to postulate that differences in survival for animals in groups irradiated for various periods within 24 h reach 50%. The value for change in radiosensitivity during 24 h can be correlated to rhythmic changes of temperature in experimental animals [80]. It is currently believed that two peaks of radioresistance occur every 24 h, probably connected with many factors (for example, distinct waves in mitotic activity). Thus, the mitotic index in mouse skin reaches maximum at about 4 a.m. and again at 4 p.m. Several attempts have been made to connect circadian rhythms with the biochemical activity of the pineal gland which, in turn, depends on light-dark cycles. One of the most outstanding features of diurnal and nocturnal change in radiosensitivity may be the corresponding changes in the abundance of blood-forming cells in bone marrow. Diurnal radiosensitivity can also be correlated to the accumulation of peroxide compounds in the spleen.

During long-term space flight, desynchronization of the circadian rhythms of astronauts may take place if stability in circadian rhythms on Earth is determined by subconscious perception of weak geophysical rhythms [22]. Work conditions in space probably will require the creation of rhythms for work and rest that are different from those on Earth; this might, of course, lead to a certain degree of inner desynchronization, phase shift, and possibly resynchronization to the applied rhythm.

In experiments with desynchronization of circadian biorhythms, radiosensitivity was observed in rats converted to a shortened 24-h period of 6 h light and 6 h darkness. Note that with daily rhythm shifts on Earth, diurnal/nocturnal radiosensitivity remains one of the most stable biorhythms. Moreover, average daily level of radiosensitivity increases at the beginning of the period of transfer to a new light regime. Diurnal/nocturnal rhythms in radiosensitivity have a complex form, perhaps due to the many-faceted influence of radiation on the organism. The character of change in diurnal/nocturnal radiosensitivity, corresponding to the criteria of survival in animals during the course of 30 d, was close to sinusoidal in inbred rats, using two periods during the course of 24 h. The difference in survival in animals irradiated by a dose of 800 rad with 11 or 25 d of 6L+6D light regimes was, respectively, $94.7 \pm 2.6\%$ and $92.0 \pm 0\%$, with death of $65.9 \pm 3.1\%$ in the control group of animals, which were kept in a regime 12L+12D [67].

These experiments are complicated by radiation exposure itself causing a change in synchronization. Moreover, it is believed that any change leading to a new distribution in timing of cell division pattern also changes the radiosensitivity pattern.

Effects of Accelerations and Radiation

Data obtained show that acceleration of mammals before or following exposure to radiation decreases the radiobiologic effect [108, 145]. Other experimenters have concluded that the combined action of acceleration from 3 to 20 g and irradiation does not change the radiobiologic effect significantly [194].

Partial analysis of data in the literature [145] on the influence of immediate factors present in flight on the course of radiation damage in animals points to the probability of a lessening in radiation effect, or at least, to absence of synergism rather than to increase in the effectiveness of radiation effect in the given combinations.

Exposure to linear and angular accelerations can lead to vertigo and symptoms of motion sickness. Ionizing radiation acting on the mammalian organism can produce radiation sickness with symptoms somewhat similar to motion sickness-dizziness, loss of appetite, nausea, and even vomiting. There are indications that, in an organism that has received acute doses of whole-body irradiation, the reaction to angular accelerations alters [69]. Some authors suggest that the vestibular canal and associated structures are quite radioresistant, and that several thousand rad delivered locally are necessary to cause modification in function.

Sveshnikov investigated the sensitivity of reaction of the vestibular analyzer in animals during the combined action of irradiation and vibration, lowered atmospheric pressure, and noise. Irradiation at a dose of 200 rad lowered the sensitivity and reactivity of the vestibular analyzer [164]. With synergism of each of the above factors, irradiation-threshold sensitivity was normal when the vestibulograms were compared with the control. Most of the radiation effects on vestibular function arise from direct or indirect effects on proprioceptors distributed in various regions of the body. Various measurements of radiation effects on vestibular functions do not agree very well, so that more studies are needed in this field.

Interesting pharmacologic problems arise in relation to orientation: How do pharmacologic agents that ameliorate motion sickness modify radiation responses? Can drugs used in radiation protection alter G-tolerance and motion tolerance?

Body Temperature and Radiation Effects

Animals with artificially lowered body temperature are protected somewhat against radiation delivered in single doses. This effect, verified by various investigators, is probably due to tissue anoxia developing from reduced blood circulation in deep hypothermia. This fact has no practical value at present; the degree of hypothermia necessary to produce significant radiation protection would render astronauts unable to perform their tasks. However, research on hypothermia has potential value for the future when long-duration space flight will be undertaken.

There is disagreement about the interaction of artificially induced hyperthermia and radiation sensitivity.

Radiation as a Modifier of Susceptibility to Infection

Acute doses of radiation lower immunologic defense mechanisms and hasten infection from the microbial autoflora present. Similarly, long-term isolation in a closed system can also lead to infection. On some past US and USSR space flights, impressive increases in microbial contamination of the spacecraft have been noted. There is not sufficient data to know whether or not the relatively low ambient cosmic ray and flare dose could significantly increase the chance for autoinfection on long space flights.

Radiation Biology Experiments on Satellites

Special radiation studies with mammals and bioexperiments with various organisms in space flight are beginning to yield valuable information. Reasonably successful bioexperiments have been carried out, particularly on Cosmos 110, Cosmos 368 [65, 71], Apollo 15, and Apollo 16 [24], and Biosatellite II [146]. The latter was specially designed to test the effects of weightlessness in combination with radiation. Such experiments are quite elaborate since many controls are required. Theoretical considerations have led to the suggestion that the effects of weightlessness might be negligible in a living cell less than 10 μm in size, because vigorous thermal motion is present.[9] Optimum conditions for observing weightless effects require that an organism be actively metabolizing and perhaps in the growing stage. Effects observed

[9] However, recent theoretical developments indicate that the size limit might be much smaller. Tobias, C. A., J. Risius, and C. H. Yang. Biophysical considerations concerning gravity receptors and effectors including experimental studies on *Phycomyces blakesleeanus*. *In*, Sneath, P. H. A., Ed. *Life Sciences and Space Research XI*. (Proc., COSPAR XVth Meet.), pp. 127–140. Berlin, Akademie, 1973.

as a consequence of space exposure in dormant organisms (e.g., dehydrated seeds or spores) are probably due to radiation, vibration, or acceleration, rather than to weightlessness. However, the spacecraft must be submitted to vibration for only a short time.

An analysis of the materials obtained yields the information that all spaceflight factors acting together influence the radiobiologic processes to a relatively small degree, if at all. Accordingly, it is expected that the effects due to near-weightlessness would become more important on space flights of long duration.

Radiobiologic experiments have been conducted on macromolecular systems, plant seeds, lysogenic and hydrogen bacteria, yeast cells, parasitic wasps, flour beetles, and *Drosophila*. These biologic objects have been exposed to radiation of various doses before, during, and following space flight. Evaluation of the effect of spaceflight factors on radiobiologic effect was determined according to a series of physiologic, genetic, and cytogenetic indicators.

Certain questions connected with the study of effects of nonradiation factors on radiosensitivity are more conveniently resolved in experimentation with pre- and postirradiation of biologic objects exposed in satellites launched in a quiet period of solar activity and in an orbit below the Earth's radiation belts. In addition to their comparative simplicity, in such experiments, great possibilities for variation in the conditions of irradiation present the possibility of differentially analyzing the effect of a complex of other environmental factors on the various stages of development of radiation damage.

Cosmos 368

In this connection, results of experiments on the artificial satellite Cosmos 368 deserve attention. Conditions and basic results of these radiobiologic experiments have been published in a special number of the journal, *Space Biology and Medicine* [65].

Diploid and haploid yeast cells, hydrogen bacteria, and lettuce and barley seeds were used in the experiments. These biologic objects, with the exception of hydrogen bacteria, were studied from a radiobiologic standpoint. They were placed in small metallic containers within the satellite. An assembly of several thermoluminescent dosimeters was stored in each container next to the biologic objects. The temperature at these points varied from 19°–23° C; pressure inside the capsule was 760–820 mm. Length of flight was equal to 6 days. Within half an hour after landing, the containers of biologic objects were taken from the satellite and delivered on the following day to the laboratory. Objects in dormant and resting states (dormant seeds of plants, cells in a stationary phase of growth) or in a state of partially suppressed metabolism created by depletion of the nutrient medium and limitations of oxygen diffusion in the air (aqueous suspension of microorganisms in ampules) were tested. Prior to placement on-board the spacecraft, the plant seeds were stored at room temperature, and the microorganisms at the temperature of melting ice.

Parallel to the basic experiment, duplicate samples, or "transport" controls, were placed in similar containers located alongside the experimental ones until just the moment of loading the satellite; subsequently, these were returned to the laboratory and stored at a temperature approximating that of the satellite.

In plant seeds with a phase shift of 5 d, a synchronous experiment was also conducted in a special room simulating spaceflight conditions with identical temperature, pressure, humidity, and makeup of the gaseous medium. For microorganisms in the laboratory, temperature conditions were also simulated, with samples in growth chambers completely isolated.

Irradiation of biologic objects up to, and following flight, was conducted with γ-rays at dose rates of 71.8 and 6.7 rad/s, delivered up to the moment of setting up the containers and following return of the samples to the laboratory.

The data introduced in Table 14 make it evident that, prior to and following radiation exposure, spaceflight factors do not exert marked influence on radiobiologic effects [65]. The majority of indicators suggest absence of changes in radiation damage or, extremely insignificant changes, probably caused by indeterminable factors not connected with the flight.

TABLE 14.—*Influence of Cosmos-368 Spaceflight Conditions on Radiation Effects in Yeast, Lysogenic Bacteria, Lettuce, and Chick-Pea Seeds Irradiated Before or Following Flight* [66]

Organism	In-flight maintenance conditions	Radiation effect	Preflight irradiation		Postflight irradiation		Notes
			Dose (krad)	Influence of flight factors	Dose (krad)	Influence of flight factors	
Diploid yeast cells	Water suspension	Inhibition of ability to multiply indef. (form normal colonies)	20	Small decrease	20	Absent	
			40	Absent	40	Small decrease	
			80	Absent	80	Absent	
			120	Small decrease	120	Absent	
			160	Absent	160	Absent	
		Inactivation after 1–4 division cycles	20	Absent	20	Absent	
			40	Absent	40	Small decrease	
			80	Absent	80	Small decrease	
			120	Absent	120	Absent	
			160	Absent	160	Absent	
	Agar	Inhibition of ability to multiply indef.	—	—	20	Small-decrease	
			—	—	40	Absent	
			—	—	80	Absent	
			—	—	120	Absent	
			—	—	160	Absent	
		Inactivation after 1–4 division cycles	—	—	20	Absent	
			—	—	40	Absent	
			—	—	80	Decrease	
			—	—	120	Decrease	
			—	—	160	Decrease	
Haploid yeast cells	Agar	Inhibition of ability to multiply indef.	—	—	1.5	Absent	
			—	—	3.0	Absent	
			—	—	6.0	Absent	
			—	—	10.0	Absent	
		Inactivation after 1–4 division cycles	—	—	1.5	Absent	
			—	—	3.0	Absent	
			—	—	6.0	Absent	
			—	—	10.0	Absent	
Hydrogen bacteria	Water suspension	Inhibition of ability to multiply indef.	0.5	Absent	—	—	
			1.0	Absent	—	—	
			2.0	Absent	—	—	
			4.0	Absent	—	—	
			6.0	Absent	—	—	
Chick-peas	Air-dried seeds	Chromosomal aberrations in cells of sprouts	5.0	Absent	—	—	
			5.0	Absent	—	—	
			10.0	Absent	—	—	
		Appearance of bridges in cells	5.0	Absent	—	—	
			10.0	Absent	—	—	
			5.0	Absent	—	—	
			10.0	Absent	—	—	

TABLE 14.—*Influence of Cosmos-368 Spaceflight Conditions on Radiation Effects in Yeast, Lysogenic Bacteria, Lettuce, and Chick-Pea Seeds Irradiated Before or Following Flight* [66] – Continued

Organism	In-flight maintenance conditions	Radiation effect	Preflight irradiation		Postflight irradiation		Notes
			Dose (krad)	Influence of flight factors	Dose (krad)	Influence of flight factors	
Lettuce	Air-dried seeds	Chromosomal aberrations in ana- & telophase	10.0	Absent	—	—	With prior storage of seeds for 6 d @ 10° C
		No. aberrations in 1st aberrant cell	10.0	Absent	—	—	
		Chromosomal aberrations in ana- & telophase	10.0	Increased suppression	—	—	With prior storage of seeds for 6 d @ 30°C
		No. aberrations in 1st aberrant cell	10.0	Slight increased suppression	—	—	
		Stimulation or suppression of growth processes in part of plant above ground	1.0 5.0 10.0	Absent Increased suppression	1.0 — 5.0 10.0	Absent — Absent Absent	
		Stimulation of growth processes in part of plant below ground	1.0 5.0 10.0	Absent Absent Absent	1.0 5.0 10.0	Slight increased stimulation Slight-increased stimulation Slight increased stimulation	
		Activation & suppression of enzyme action in vegetative plants:					
		a) polyphenyl oxidases	1.0	Absent	—	—	
		b) catalases	10.0	Decreased activation	—	—	
			1.0	Absent	—	—	
			10.0	Increased suppression	—	—	
		c) peroxidases	1.0	Absent	—	—	
			10.0	Absent	—	—	
		Formation of anomalous metabolites in 30-d-old plants	1.0 10.0	Decrease Increase	1.0 5.0	Decrease Increase	

A series of other indicators which did not change were also analyzed for chosen doses of irradiation: rate of germination, germinating power of seeds, mitotic index in sprout cells, and other indices. Nor did these indicators undergo change following flight; conditions of flight evidently did not promote the appearance of latent radiation damage.

In an experiment on diploid yeast cells, an attempt was undertaken to clarify the influence of flight conditions on postirradiation recovery (yeast is extremely suitable for study of this process). The effect of nonradiation factors in flight was studied, not only on still nonirradiated cells, but at times when repair processes were operative under conditions of weightlessness in irradiated cells. In each instance, changes in the repair process were not revealed.

It is possible to conclude that, in "resting" organisms with a low level of metabolic processes, change in radiosensitivity under the influence of the dynamic factors of flight and weightlessness over a period of 6 d either were not generally observed or occurred to a nominal degree.

Discoverer 17

In an effort to obtain better information on the influence of weightlessness on radiosensitivity and formation of radiation damage, radiobiologic experiments with irradiated biologic objects during initial flight were set up. An attempt was made to use natural sources of radiation in space. The satellite, Discoverer 17, was put into orbit within 7 hours after the beginning of intensive solar flare activity. Biologic objects were irradiated at a dose of 30–35 rad. Cultures of human tissue were placed in the satellite along with various preparations of human and animal blood, bacterial spores, and algae. However, no conclusive data were obtained on the general radiobiologic effect [26].

On the space flights, fertilization and development of frog eggs were studied [192] since these eggs respond to disorientation of the gravity vector by abnormal development. Fertilization of frog eggs in space must be conducted by means of a special apparatus which automatically injects sperm into the eggs. The eggs which developed were normal in all respects. A low level of cosmic radiation apparently has no effect.

Cosmos 110

Biosatellite Cosmos 110 passed in a polar orbit inside the radiation belt of Earth (height of apogee was about 904 km). The length of flight was 22 d and the total dose to the bioobject amounted to 10.5 rad.

Two dogs were placed aboard the satellite along with an assembly of bioobjects: yeast, lettuce seeds, tomatoes, beans, radishes, carrots, Chinese cabbage, onion bulbs, garlic bulbs, and a suspension of *Chlorella* [71].

On completion of the 22-d flight, experimental and control specimens of seeds and bulbs were analyzed under vegetative and laboratory experimental conditions by agrobiologic, cytogenetic, microbiologic, and biochemical methods. In the higher plants, a lowering in capacity and rate of seed growth, dynamics of sprout and plant growth, their yield and biochemical makeup were determined. Damage to the chromosome at anaphase and telophase of initial mitosis was also studied; counts were made of the number of chromosome bridges and fragments of various types, and the mitotic index determined. Survival of *Chlorella* cells was studied as well as change in the dynamics of initial sporulation and appearance of mutation.

A distinct stimulation in seed and bulb growth of onions was noted. Experimental plants surpassed controls in all basic elements of evaluation of yield. Thus, plants grown from lettuce seeds flown on Cosmos 110 surpassed controls in height (15%), in width of leaves (14%), and in quantity of leaves (22%). As a result of productive yield, the biomass of experimental plants increased by 50% compared with controls. Rootlets of lettuce sprouts, leafy cabbage, radishes, carrots, and onion bulbs were exposed to cytologic experiments. The resultant data indicated absence of real differences between experimental and control plants in quantity of chromosomal aberrations in the cells of rootlets (Table 15). In all experimental plants, increase in mitotic index was observed, an indication of the stimulating effect of spaceflight factors.

On the basis of the influence of spaceflight factors, it might be assumed that small doses of radiation lead to marked effects in stimulation. On the other hand, it is probably more correct to conclude that the criteria used for evaluation are inadequate to explain the effects of cosmic radiation [71].

A series of experiments with different strains of *Chlorella* produced data indicating absence of any real differences between experiment and control specimens, with respect to both survival and to quantity of mutant cells. Consequently, duration of combined action of the factors present in space flight did not affect the vital activity and mutation process in experimental strains of *Chlorella*. An insignificant effect of these factors on radiosensitivity and postirradiation repair was noted in resting yeast cells [71].

In experiments with lysogenic bacteria, certain activation of prophage and lysogenic bacteria (*E.coli* K–12 (γ)) was established [71, 195]. Research on the content of peripheral blood and bone marrow of dogs, quantitative indicators in sperm, and evaluation of the capacity of these animals to reproduce offspring disclosed no specific radiobiologic effects of cosmic radiation [71].

Gemini 3, Gemini 11, and Biosatellite II

In order to ascertain biologic effects clearly due to radiation, it has been proposed that an artificial source of radiation be used on board the satellite or spacecraft [146, 154]. Such experiments were set up on Gemini 3, Gemini 11, and the satellite, Biosatellite II. On the inner side of the right door of Gemini 3 an experimental aluminum container was mounted in which two portions of blood from two healthy subjects were placed. The blood was irradiated with the aid of a β-applicator with P^{32}. Irradiation was begun 50 min after takeoff and was completed within 20 min. The full period of weightlessness lasted approximately 4.7 h. Suspensions of human leukocytes and the bread mold, *Neurospora*, in millipore filters were placed on board Gemini 11. The human leukocytes were irradiated with the help of a plastic plate loaded with radioactivity, but the intensity of the radioactive source was less, since exposure which was begun 67 h after takeoff lasted 70 h. Specimens of the mold, *Neurospora*, were located in the same area as the leukocyte suspension [13, 14, 152].

Ten different biologic types of organisms were placed on Biosatellite II [146]. A capsule similar except for weightlessness, was set up as ground-based control. The microclimate in this control capsule was similar to that of the flight capsule, and the organisms received similar doses of radiation. Biosatellite II was in orbit for 45 h. An on-board source of radiation, Sr^{85}, was opened 1 h after launching and covered upon return (within 43 h after takeoff). Both spaceflight and Earth capsules were constructed so that one section (the nose) was exposed to radiation at the same time that another section (the stern) was protected from Sr^{85} irradiation. The gaseous composition, temperature, and relative humidity were controlled during the entire flight. Temperature was held at about 20° C for all experiments except those conducted with flour beetles, for which the temperature was held at about 30° C. Relative humidity was kept within the limits of 55–66% for the entire flight. Vibration, acceleration, and noise also were controlled during the entire flight, and recreated in the independent control experiments on Earth [146].

Aberrations observed in chromosomes as single or multiple breaks were counted in metaphase stage, and the results compared with those counted in identical controls on Earth which had received the same radiation dose. Although the results of Gemini 3 did not show significant differences between flight and Earth specimens expressed in chromosomal aberrations with multiple breaks, the number of aberrations with single breaks was significantly higher in flight specimens (see Table 16). In experiments on Gemini 11, significant changes were not noted, either in single breaks or forming dicentric chromosomes.

The most striking findings were in an experiment on larva of *Drosophila melanogaster* on Biosatellite II. Reproductive cells of the larva showed a high number of flight-connected lethal mutations, crossovers, and multiple chromosome breaks leading to translocations [136]. This effect was not connected with the on-board source of γ-irradiation, inasmuch as flight con-

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TABLE 15.—*Effect of Spaceflight Factors On-Board Cosmos-110 on Yield of Cells with Chromosomal Aberrations and Quantities for Mitotic Index in Plant Roots* [12]

Plant	Experiment	Cells with chromosomal aberrations, %	D	Mitotic index	D
Garlic	Expt'l / Control	0.6±0.1 / 0.4±0.4	0.5	9.05±0.7 / 8.06±0.9	0.9
Chinese cabbage	Expt'l / Control	0.4±0.4 / 0.3±0.3	0.2	5.1 ±0.4 / 3.9 ±0.3	2.5
Radish	Expt'l / Control	1.0±0.4 / 1.0±0.5	0	5.8 ±0.4 / 4.2 ±0.3	3.2
Carrot	Expt'l / Control	0.3±0.2 / 0.6±0.4	0.8	5.8 ±0.3 / 6.6 ±0.4	2.4
Lettuce	Expt'l / Control	1.7±0.5 / 1.9±0.6	0.2	9.4 ±0.3 / 5.1 ±0.2	10.8

trols also exhibited the same changes. Therefore, it could have been caused either by a few heavy primary particles in cosmic radiation or other unknown factors of space flight.

Other genetic experiments produced less striking results, i.e., a somewhat higher quantity of certain types of recessive and dominant lethals [23]. Postflight vibration control suggested that vibration could also be a cause of these mutations.

A number of careful genetic experiments on insects (wasps—*Habrobracon*) were conducted, and again, genetic changes appeared that might have been mutations created by ground-level vibration. When irradiation was combined with weightlessness, females laid more than the expected amount of eggs. In space flight, their fecundity increased; after return to Earth, their lifespan was longer than expected [184]. The males showed abnormal mating behavior for a period after the flight was completed.

Several hundred pupae of the flour beetle, *Tribolium confusum*, were placed on Biosatellite II [25]. Stages of development of these organisms were selected so that they remained in the pupal stage during launching and attained adulthood during weightlessness. Each stationary pupa was placed in a separate cubicle of shockproof construction. Vibration effects were observed in control specimens which had been exposed to the influence of vibration on Earth. The end point studied in this experiment was the frequency of radiation-induced wing abnormality. The group flown and irradiated in space developed significantly greater wing anomalies than control groups. The cause for this is unknown, but this type of effect would be expected if the enzymatic

TABLE 16.—*Results of the Analysis of Chromosomal Aberrations According to Data from Gemini 3 and 11* [14, 15]

Dose received (rad)	Single chromosome breaks per cell		Ring and dicentric chromosomes in one cell	
	Earth	Flight	Earth	Flight
Gemini 3:				
4	0.008	0.008	0.003	0
49	0.015	0.035	0.013	0.003
94	0.033	0.070	0.033	0.040
139	0.080	0.120	0.108	0.065
184	0.113	0.220	0.090	0.120
Gemini 11:				
10 (Earth)	0.030		0.063	
8 (flight)		0.025		0.020
76	0.087	0.060	0.045	0.050
145	0.158	0.173	0.139	0.123
216	0.221	0.210	0.218	0.190
283	0.355	0.265	0.245	0.303

repair mechanism usually operating on Earth failed under conditions of space flight. More recently, the effects found in space flight were reproduced in a clinostat in which gravity compensation was combined with radiation [190]. These effects were observable at 30° C, the temperature in the Biosatellite II capsule, but were readily seen at 37° C. Future experiments are proposed with mutants lacking the capacity for repair.

Sparrow et al [161] carried out an experiment on Biosatellite II with the higher plant, *Tradescantia*, designed to determine the effects of weightlessness and other spacecraft environmental conditions on spontaneous and radiation-induced mutation rates and on cytologic changes. Thirty-two young plants were arranged in a plastic housing so that the flower buds were exposed to 223-rad γ-rays, and the roots, immersed in nutrient solution, were exposed to radiation levels from 116 to 285 rad. Thirty-two additional plants were flown in a package shielded from the radiation source.

An enhanced deleterious effect in the flight samples was noted in the mitotic spindle mechanism in microspores, megaspores, and root tip cells. A spindle malfunction was independently observed by Delone and associates on Vostok 5, 6, and Cosmos 110 [45]. Thus, these two groups agree that weightlessness affects the spindle mechanism during cell division.

No effects were observed on spontaneous levels of somatic mutation, pollen abortion, stamen hair stunting, embryo sac abortion, and chromosomal aberration. Radiation-induced somatic mutation rates were, in general, unaffected by flight factors, with the exception of a pink stamen hair cell mutation which exhibited antagonistic response to spaceflight factors. Enhanced interactions between radiation and spaceflight factors were observed in pollen abortion, micronuclei frequency in pollen, and stamen hair stunting. These observations suggest increased injury during more sensitive stages of meiosis and mitosis. Table 17 shows the portion of the results dealing with spindle aberrations.

Lysogenic bateria, both irradiated and nonirradiated, were used for judging the influence of weightless conditions on their growth, structure, and mechanisms regulating induction of latent viruses [117]. No significant influence of weightlessness on radiosensitivity was established.

The bread mold, *Neurospora crassa*, was also flown on Gemini 11 and Biosatellite II [46]. Two types of specimens were sent into flight—microspores on porous filters and spores in liquid medium. Mutants with disorders in purine biosynthesis were studied (two component heterokaryon heterozygotes), with genes which control two different subsequent stages in purine biosynthesis genetically marked. Doses of radiation on Biosatellite II were equal to 884, 2055, and 3116 rad, and on Gemini 11, to 9, 76, 145, 216, and 283 rad. In spores which were in a metabolically inactive state, no differences were found in radiation-induced mutation rates between ground-level controls and spaceflight specimens. In another set of spores suspended in liquid medium and in a highly active state of metabolism, marked radioprotective features, specifically, of survival and induction of recessive lethal mutations, were observed in spaceflight specimens. It was shown that possible anoxia in the liquid medium could not completely account for the observed effect.

Salyut

Material touching on the influence on radiobiologic effect of long-term weightlessness is of great value. In this connection, data from radiobiologic experiments aboard the Soviet orbiting scientific station, Salyut, deserve attention [130]. The flight of this space station lasted 73 days, April 19–June 30, 1971. Total dose received in flight did not exceed 2 rad. Dried lettuce seeds (*Lactuca sativa*) were tested at various levels of spontaneous mutagenesis: some seeds had a normal number of cells with chromosomal aberrations (0.4%), and some 2.0% aberrant cells. Prior to flight, the seeds were irradiated at a dose of 10 krad. Cytogenetic analysis of the cells with chromosomal aberrations in the first mitotic cycle was conducted. On a lengthy flight, an increase in the spontaneous mutation process from 2.0 to 3.9% and from 0.4 to 1.4% took place. An increase in induced radiation mutations also occurred, from 84.9% in Earthbound irradiated controls to 97.4% in irradiated flight specimens. With the aim of establishing the possible de-

TABLE 17.—*Summary of Computed Peak Aberration Rates ± Standard Error for Various* Tradescantia *End Points from Biosatellite* II *and Nonflight Tests Showing Effects Indicated*

End points	Biosatellite II				Simulated flight (phase C)				Component test	
	Flight (301)		Nonflight (201)		301 vehicle		201 vehicle		Clinostat	Erect
	Irradiated	Non-irradiated	Irradiated	Non-irradiated	Irradiated	Non-irradiated	Irradiated	Non-irradiated	Irradiated	Irradiated
	Enhanced flight effects									
Loss of reproductive integrity (stunting)/100 hairs	26.9 ± 1.3	9.60 ± 3.8[1]	11.6 ± 0.73	7.26 ± 0.70[1]	14.8 ± 1.5[4]	13.2 ± 1.5[4]	18.9 ± 1.8[4]	10.7 ± 1.4[4]	11.1 ± 1.6	
Pollen abortion, %	69.5 ± 2.4	36.5 ± 2.2[1]	49.6 ± 2.5	41.0 ± 2.5[1]	69.2 ± 2.5	47.0 ± 2.1	58.8 ± 3.0	47.1 ± 1.9	90.0 ± 2.7	83.8 ± 3.1
Micronuclei/100 pollen	24.1 ± 1.4	4.47 ± 0.44	12.1 ± 1.1	3.0 ± 0.3	33.3 ± 15.6[4]		22.9 ± 10.0[2]			
Flower production, 26-d total	227	244	162	191	221	229	243	261	333	328
Disturbed spindles, % cells:										
Roots[3]	0.55 ± 0.08	0.25 ± 0.05	0.06 ± 0.03	0	0.08 ± 0.03	0	0	0	0	0
Microspores[3]	All aborted	27.5 ± 0.92	0.3 ± 0.09	0.18 ± 0.07	0.93 ± 0.21	0.50 ± 0.11	0.15 ± 0.06	0.12 ± 0.05		
Megaspores[2]	6.2 ± 1.3	4.48 ± 0.9	1.2 ± 0.68	1.94 ± 0.86	1.39 ± 0.79	0.50 ± 0.50	1.54 ± 0.88			

[1] Average of 4 days around peak day of corresponding irradiated sample.
[2] Average of daily observations over extended postflight scoring period (no distinct peak rate).
[3] Observations of single postflight tissue collection.
[4] Average of daily observations over extended posttreatment scoring period of phase B test.

TABLE 18.—*The Effects of Spaceflight Factors on Spontaneous Mutagenesis in Lettuce Seeds (Criterion—Cells with Chromosomal Aberrations)* [131]

Cosmos-368				Zond-8				Salyut			
Seeds with normal level of spontaneous mutagenesis		Seeds with increased level of spontaneous mutagenesis		Seeds with normal level of spontaneous mutagenesis		Seeds with increased level of spontaneous mutagenesis		Seeds with normal level of spontaneous mutagenesis		Seeds with increased level of spontaneous mutagenesis	
Flight	Earth	Flight	Earth	Flight	Earth	Flight	Earth	Flight	Earth	Flight	Earth
1.6 ± 0.2	0.4 ± 0.2	3.3 ± 0.5	1.3 ± 0.2	1.2 ± 0.2	0.4 ± 0.2	3.1 ± 0.4	1.3 ± 0.2	1.4 ± 0.1	0.4 ± 0.2	3.9 ± 0.4	2.0 ± 0.2
D = 4.0		D = 4.0		D = 4.0		D = 3.4		D = 4.2		D = 5.0	

Difference between variants is significant for D ≥ 3.

pendency of the effect on duration of weightlessness, a comparison of materials was conducted by means of cytogenetic analysis of seeds exposed on Cosmos 368, Zond 8, and Salyut over a period of 7 and 73 days. The data introduced in Table 18 indicate the increase in spontaneous mutagenesis notwithstanding its initial level or the length of flight. In all three experiments, an increase in radiation-induced mutagenesis in the seeds was observed.

Biostack and Cosmos-605 Pocket Mouse and Rat Experiments

On lunar flights Apollo 15 and 16, various biologic specimens were flown by Bücker, Pfohl, and others [24, 85, 90, 139, 143] in an attempt to assess biologic effects of heavy cosmic ray particles. The tracks of individual heavy particles were followed by photographic and silver chloride methods in the hope that biologic effects could be correlated with individual tracks.

On Apollo 17, five pocket mice were exposed to heavy cosmic ray particles by Haymaker et al [82]. Each animal had a piece of clear plastic embedded subcutaneously over the cerebrum. Individual tracks are being developed and measured by Benton [17]. The aim of this experiment is to search for heavy-ion-induced brain damage. Similar experiments were carried out on rats flown on-board the satellite Cosmos-605.

Summary of Satellite Bioexperiments

Weightlessness under certain conditions can produce abnormal spindles in meiosis and mitosis, and radiation can increase abortive cell division in plant cells during space flight. Additional observed effects include an abnormally high number of chromosomal rearrangements in reproductive cells of *Drosophila* larva, and increased developmental and behavioral abnormalities in *Habrobracon.* Spaceflight conditions have increased the germinating capacity of a variety of seeds and have yielded an increased number of chromosomal aberrations. Many experiments remain inconclusive or of borderline significance. For example, it remains a matter of conjecture that cosmic radiation can increase the number of dominant lethals in the fruit fly or chromosomal deletions and crossovers in human cells. More experiments must be conducted in space flight to clarify these potentially important points; it will be necessary to correlate all the observed effects with duration of exposure of bioobjects to weightless conditions. It will be important in the future to include satellite experiments directed toward research on biorhythms and change in radiosensitivity under weightless conditions. The assessment of inflight radiobiologic effects caused by heavy cosmic ray primaries is another important topic.

TOWARD THE ESTABLISHMENT OF ALLOWABLE DOSE LEVELS

It is necessary to evaluate each type of space radiation from the point of view of its hazard to a particular individual or a particular population. The usual procedure in relation to professional exposure to radiation is that permissible dose levels are established, which set practical limits of radiation at levels where risk can be considered acceptable for the individual and for the population as a whole.

However, the evaluation of radiation hazard during space flight and the establishment of allowable levels of radiation exposure for the crew of spacecraft present special problems. Consideration must be given to these circumstances:

1. Spaceflight missions represent very elaborate and large-scale efforts. It is essential to insure not only the safety of astronauts, but also that their performance not be impaired by radiation exposure.
2. There are great spatial, temporal, and qualitative variations in space radiation.
3. Extreme environmental stresses on astronauts act simultaneously with radiation.
4. The astronauts are a special group of highly trained and carefully selected individuals.

Evaluation of radiation hazards in such complicated situations must rely on knowledge accumulated during many years of experience with x-rays and γ-rays and on experiments that deal with quantitative comparisons between x-ray effects and those of other radiations. In the US, the evaluation usually is a two-part process: first, a committee of experts studies the problems and makes a scientific report;[10] later, those responsible for each mission set permissible exposure limits based on the scientific report and other pertinent considerations.

In this discussion, we shall follow methodology used by Grigor'yev et al [74], which is similar in many respects to American procedures [98].

For each situation the aim is to derive a *Dose Equivalent* (DE). This is the dose, delivered to an individual's whole body, of 200 keV x-rays that would be equivalent to a particular exposure to solar and cosmic radiation. Thus: DE[rem] = D[rad] × QF × DF × TF × SF [74, 98].

QF (Quality Factor) is the coefficient that accounts in a generalized manner for relative biologic effectiveness (RBE). This depends on the distribution of linear energy transfers (LET), and sometimes also on particle velocities and dose levels.

DF (Distribution Factor) is the coefficient of partial-body irradiation; it describes how the effects of nonuniform radiation differ from uniform whole-body exposure.

TF (Time Factor) is the protraction coefficient; it indicates the relative effectiveness of protracted (uninterrupted or fractional) irradiation in comparison with a single dose of irradiation.

SF is the **(Space Factor)** coefficient. The specific conditions of space flight (weightlessness, hypodynamia, acceleration, and others) demand the introduction of SF, characterizing the combined action of radiation and of other factors in space flight.

Instead of *Dose Equivalent*, a special term has been introduced in the USA [98]: *Reference Equivalent Space Exposure* (*RES*), expressed in special units, *reference equivalent units* (*reu's*) instead of rem.

In a general form: RES (reu) = $\bar{D}$ (rad) × QF × ($f_1 \cdot f_2$ . . . . f_n), where the factors f_1 have nearly the same meaning as the factors in the expression for dose equivalence above [98].

In setting permissible levels for spacecraft crews, we seek exposure levels which do not impair the astronaut's performance capability when carrying out flight tasks and will not cause major expressed somatic changes. The possibility of developing late effects is, of course, also considered.

For short-term flights lasting only a few weeks, the greatest hazard is presented by proton and helium-ion radiation from solar flares. Early consequences of this type of radiation are expressed in the form of prodromal reactions, skin reactions, and reduction of activity of the blood-forming organs. It is also necessary to calculate the significance of changes in the nervous system and in particular, the vestibular system, for the astronaut's performance.

Allowable Dose Levels

In the Soviet Union, the dose standards for short-term space flights up to 30 d have been calculated as:

(1) Allowable dose = 15 rem
(2) Dose of justified risk = 50 rem
(3) Critical dose = 125 rem

The dose of justified risk considers the definite probability of a powerful solar flare developing during flight. If a critical dose of 125 rem is attained, the question of possibility of continuing the flight must be resolved [70]. A permissible dose was set at 25 rem for the crews of the Apollo flights. For evaluation of the possibility that the flight might be terminated, a maximum operating dose was established equal to 50 rem.

For interplanetary space flights of 1- to 3-yr duration, there will be three components of radiation exposure: solar flares that may occur at random intervals; dose from nuclear reactors used for propulsion or for on-board source of power; and light and heavy nuclei of galactic cosmic rays [159].

The most hazardous form of radiation in interplanetary flight might be heavy ions from galactic cosmic radiation which probably can cause serious, irreversible changes. Unfortu-

[10] An example is the report prepared by Wright Langham and a committee of the NAS (National Academy of Sciences). Space Science Board, *Radiobiological Factors in Manned Space Flight* [98].

nately, at present, there are not sufficient data available for evaluating this hazard [59].

Part of the radiation damage in long-term space flight is caused by low LET components. Radiation damage will not accumulate proportionally to dose, but a portion of it will be repairable. With the passage of time during a long flight, the amount of damage repaired increases gradually. Calculated "effective doses" do not increase proportionally to the duration of the flight, estimates for which are in Table 19 for flight durations of 1 to 3 yrs. In calculating values for the table, the assumption was that the irreversible component consists of 20–25% and the rate of repair equals 0.1%/d. Such calculations are especially tentative since no experimentally well-founded constant exists for recovery and irreversible damage under the complex conditions of mixed space radiations.

Estimates have been obtained for the "expected" radiation exposure from trapped solar radiations, galactic cosmic rays, and nuclear reactors on long-term orbital and interplanetary flights. Figures 13 and 14 indicate the dose inside an aluminum cylinder as a function of its wall thickness.

TABLE 19.—*Calculated Levels of Effective Dose for Lengthy Space Flights* [75]

Length of flight (yrs)	Absorbed dose (rad)	Effective dose at end of flight (rad)
1	100	77.5
2	200	125.0
3	300	142.5

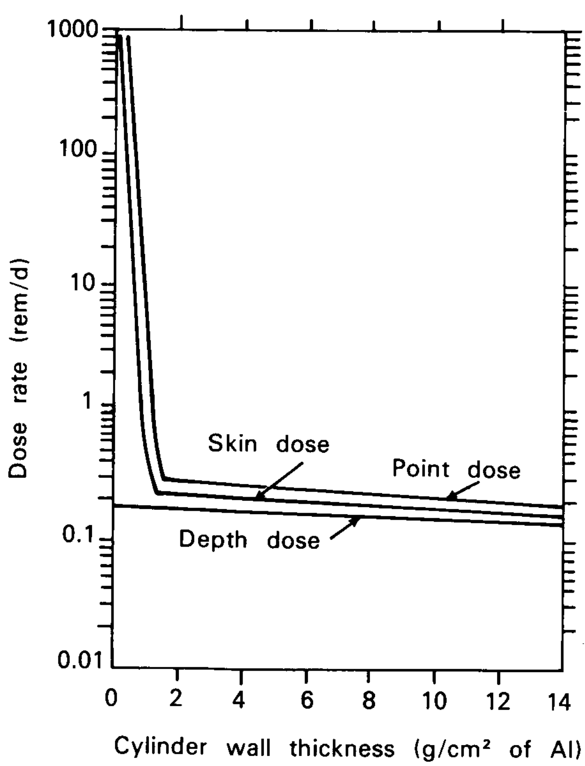

FIGURE 13.—Total daily dose versus wall thickness of an aluminum cylinder for various dose points for 200- and 270-nautical mile orbits. Point dose ignores shielding provided by astronaut's body, i.e. is dose received at a point in space (no phantom). Skin dose is calculated at 0.07 mm depth; depth dose calculated at tissue depth of 5 cm.
(Redrawn from White, Robbins, and Hardy, MSC Doc. No. MSC–00183)

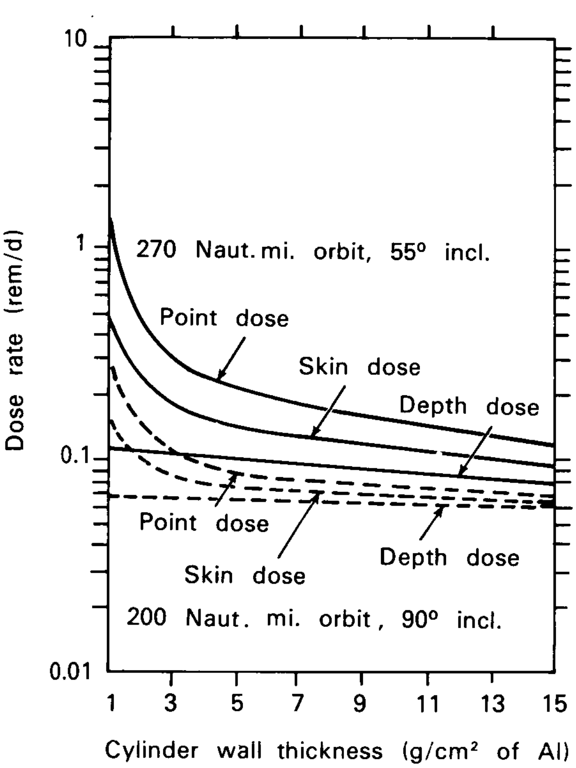

FIGURE 14.—Total daily dose versus wall thickness of an aluminum cylinder for same dose points described in Fig. 13 for a synchronous altitude orbit.
(Redrawn from White, Robbins, and Hardy, MSC Doc. No. MSC–00183)

If shielding is at least 2 g/cm², then these graphs give a depth dose of about 100 rem/yr.

Solar flare events are highly variable. However, the annual dose contribution from all but the largest flare events, behind a wall shielding estimated as 2 g/cm² aluminum, is less than 100 rem/yr. Very large flares during a long-term mission constitute a special hazard, and the possibility of constructing special personnel shelters on-board interplanetary craft should be considered.

For individuals older than 35 on long-term space flights, the preliminary estimates of maximum allowable dose recommended are: for 1 yr, 200 rem; for 2 yrs, 250 rem; and for 3 yrs, 275 rem [70]. Recommendations sometimes differ significantly among various authors. A dose of even 300 rad/yr of flight has been recommended, for example [133].

Clinical Manifestations of Radiation Damage

When the peculiarities of radiation conditions in space are considered, it becomes important to direct attention to the dose-dependence of clinical effects which can arise in man when exposed to external radiation.

Four variants of radiation exposure can arbitrarily be considered:

(1) acute irradiation (uniform whole-body as well as local) of a few days' duration;
(2) protracted irradiation of 3-mo duration;
(3) acute repeated irradiation against a background of cosmic ray particles;
(4) chronic irradiation lasting 1 yr or more.

The character of manifestations and duration of radiation damage is different in each category.

With acute irradiation to a limited area of the body at doses on the order of a few hundred rads, localized radiation damage can develop without any kind of general clinical symptoms. With whole-body irradiation or irradiation of a relatively large surface, at doses significantly less than those used in localized irradiation, severe radiation sickness can arise. For acute radiation sickness, rather precise periods of duration of sickness, as well as its dependence on length and degree of severity of radiation dose are characteristic. In the pathogenesis of severe radiation sickness, damage to the blood-forming organs, to the gastrointestinal tract, and to the nervous system are significant.

For evaluation of radiation effects in man, we are limited to material from radiation therapy clinics, to studies of accidents in reactors and in other professional situations, and to data based on the study of people exposed to radiation from atomic bomb explosions in Japan, as well as injuries from radioactive fallout following experimental atomic bomb tests [3, 10, 79, 98, 109, 144].

Although there is general agreement on the description of various aspects of radiation illness, there are differences in terminology and interpretation among various laboratories. The available human data usually relate to x- or γ-rays and acute exposures. Knowledge of the effects of protracted low doses is meager and human data on the effects of whole-body exposure to protons or heavy ions are not available.

The lack of consistency between figures and tables reproduced here indicates the range of existing uncertainty.

In man, external acute exposure to x- or γ-rays at doses of 100–1000 rad [79] leads to the development of "typical" forms of acute radiation sickness. Rather definite time-dependence and the dependence on dose of severity of illness are characteristic.

An early symptom complex in radiation pathology of acute irradiations is the so-called "primary" or prodromal reaction, for which the most frequent manifestations are anorexia, nausea, and fatigue. Particularly unpleasant for the astronauts are vomiting, general weakness, dizziness, headache, apathy, disturbance of sleep, and diarrhea.

Four degrees of severity in radiation sickness can be distinguished by clinical progression:

First-degree reaction. General symptoms of the reaction in the individual at barely perceptible level of slight weakness, headache, lowering of appetite, light dizziness, and so forth; performance is not disturbed.

Second-degree reaction. Symptoms leading to certain loss of performance during the first days such as general weakness, persistent nausea, vomiting once, expressed anorexia, olfactory and gustatory (taste) disturbances, headache, dizziness, and interrupted sleep.

Third-degree reaction. Symptoms causing expressed loss of performance in the first days following irradiation: strong general weakness, absence of appetite, acute nausea, repeated vomiting, apathy, expressed disturbance of taste and smell, acute dizziness, severe headache, sleeplessness or somnolence.

Fourth-degree reaction. Symptoms indicating irradiation in very large doses, which appear similar to third-degree reactions but include also, diarrhea, rigor, cramps, and prostration.

The primary or prodromal reaction develops in the first hours following irradiation and can continue from several hours up to 1–2 days. The probability of development, time of appearance, duration, and severity of symptoms depend basically on two factors: radiation dose and individual variations in radiosensitivity of the irradiated organism. With increase in the radiation dose, individual variations gradually disappear.

The dose-dependence in development of primary reaction has been systematized in a series of observations developed primarily from studies of a large quantity of clinical material on irradiation of oncologic patients [70, 79, 109]. The data give information on periods of onset and duration and development severity for symptoms of prodromal reaction, taking into consideration variations in individual peculiarities of the organism.

At the Oak Ridge National Laboratory, a large amount of clinical data was collected (on 2100 patients) in relation to radiation therapy of advanced cancer, with the aim of evaluating radiation hazard during Apollo spacecraft flights.

Although there is some dispute on the most suitable statistical method for analysis of this clinical material, dose-dependency of appearance of clinical symptoms in 50% of persons irradiated can be presented [110]:

82 ± 32 rad produce anorexia;
136 ± 36 rad produce weakness (during 42 d);
138 ± 20 rad produce nausea;
173 ± 18 rad produce vomiting;
194 ± 19 rad produce diarrhea.

Clinical observations of patients at doses on the order of 25–50 rad indicate the presence, in some, of very high sensitivity to prodromal effects. This points to the desirability of special choice of candidates for space flight. However, at present, criteria are not yet known for choosing an individual who is not particularly sensitive to development of radiation illness. Elaborate medical programs have been established for choosing extremely healthy persons to become astronauts, for which a special training program is mandatory.

It is of essential importance in the evaluation of radiation hazard to determine dose-dependence for the incidence of the most hazardous prodromal symptoms. An attempt will be made to obtain statistically reliable data on that dose which produces particular signs of primary reaction during whole-body irradiation, with the probability of symptoms occurring at 10, 50, and 90% respectively for anorexia, nausea, and vomiting (see Table 20) [98].

TABLE 20.—*Absorbed Dose with Acute Whole-Body Irradiation, Causing Symptoms of Primary Reaction at Various Probabilities* [99]

Symptoms	Absorbed dose (rad) causing reaction with probability		
	10%	50%	90%
Anorexia	40	100	240
Nausea	50	170	320
Vomiting	60	215	380

In the first days following acute radiation exposure during space flights, primary reaction can create a serious hazard. In this period, disturbance of the capacity of the crew to perform its task is possible, which in turn can influence successful completion of the flight program.

The prodromal reaction is followed by a latent or "false well-being" period, the length of which is determined (similar to the prodromal reaction itself) by severity of radiation damage. In this period, the general state of the irradiated subject improves, but certain neurologic symptoms and changes in peripheral blood appear.

At the height of radiation sickness, a distinct complex of symptoms arises, including general weakness, increase in body temperature, drop in white blood cell count, erythema, epilation, and internal hemorrhage typical of general sepsis. In a light form of radiation sickness, functional changes may occur in the nervous system, while in a severe form, organic changes are possible. In this period, inhibition of hemopoiesis is marked. The degree of suppression of hemopoiesis and the severity of symptoms depend on the amount of radiation received.

The less the radiation dose, the earlier the recovery. It can continue for a month or more, and in some instances may not be complete. Improvement of general condition, normalization of body temperature, weight increase, and improvement of the state of peripheral blood are the first signs of recovery.

Some investigators assume that in healthy persons, the threshold dose for development of a mild form of radiation sickness is equal to 100 rad [79]. With doses of 100–250 rad, acute radiation sickness of first-degree severity develops; at doses of 250–400 rad, second-degree; and at doses of 400–1000 rad, third-degree.

In general, such dose-dependence for the development of radiation pathology in man occurs when acute whole-body uniform irradiation is applied. With nonuniform exposure, a great variety of clinical manifestations of radiation damage is possible; these depend upon the size of irradiated area, its localization, absorption of dose by the critical organs, and other similar factors.

Analysis of certain clinical causes indicates that shielding comparatively small portions of the bone marrow allows preservation of life following doses which, in instances of whole-body irradiation, undoubtedly would lead to mortality [79]. These observations agree well with experimental studies [73, 145].

Under conditions of protracted irradiation for several months with attainment of a larger total dose than with single doses of irradiation, a "subacute" form of radiation sickness with indeterminate periods of progression may occur.

Almost no studies characterize clinical effects of protracted irradiation (up to 3 mo); available data are concerned with isolated accidents for which either the magnitude of radiation exposure has not been precisely determined or irradiation was not uniform. On the basis of these data, it is difficult to express quantitatively the radiation pathology of protracted exposures. The most valuable data can be found in the materials on fractionated total-body and partial irradiation in radiotherapy clinics. For purposes of analysis, information has been used concerning 97 oncological patients exposed to partial fractionated x-ray irradiation (single doses of 15–50 rad, totaling up to 250 rad in the series). Irradiation occurred daily or at an interval of 1–3 d [44, 70].

Early primary reaction with fractionated, daily irradiation increases gradually as total dose increases and disappears only after cessation of irradiation. At first, irradiated individuals complain of a general weakness, rapid fatigue, and anorexia; with degree of increase in total dose, nausea, olfactory and taste disturbances, headaches, disturbed sleep, dizziness, and vomiting can occur.

It is apparent that, with fractionated and protracted irradiation, precise periods of radiation damage are not observed. The symptoms of primary reaction somehow become transformed into those of actual radiation illness (general weakness, rapid fatigue, sleep disturbance, headaches, dizziness, lowering of blood pressure, and the like). Changes in peripheral blood occur as a result of radiation exposure in the form of leuko-, lympho- and neutropenia.

On the basis of available radiobiologic knowledge and clinical observations, it is assumed that the symptoms of prodromal reaction and radiation damage, both with fractionated whole-body irradiation and protracted irradiation, occur to a lesser degree than with acute irradiation at corresponding doses. The less the dose rate of protracted irradiation, the slower and less expressed is the development of radiation pathology. This is only true for low LET radiation, however.

With radiation exposure for the duration of 1 yr or more at dose rates exceeding many times the maximum allowable dose for occupational irradiation, chronic radiation sickness can develop, most characteristic of which is the slow development of symptoms of radiation damage without definite periods of illness.

In summarizing the existing material on clinical characteristics of the illness and on individuals working in radiation fields, three groups of affected individuals can be distinguished, depending on accumulated total dose of relatively uniform external radiation [12, 70, 78, 79].

Group 1: Dose of 30–50 rem for 5–10 yrs. There are no clinical signs of illness, but certain functional changes in distinct organs are revealed through special clinical and physiologic research methods.

Group 2: Total dose of 50–150 rem for 10–15 yrs. The clinical picture takes on the aspect of instability with possible symptoms of neurocirculatory disturbances of a hypotonic type. This is sometimes accompanied by hypofunction of the secretory activity of the stomach and some depression in hemopoiesis. At doses of more than 100 rad, a light form of chronic radiation sickness is possible in individual situations. Changes arise slowly and regress within 2–5 yrs after cessation of irradiation.

Group 3: Dose of 150–400 or more rem for 20 yrs or more. Chronic radiation sickness of first and second degree severity can appear. The asthenic syndrome develops, which is associated with lowering of functional capabilities of higher levels of the central nervous system; increased mental fatigue with loss of attention and memory; disturbance of diverse analyzers; symptoms of functional disturbance in the digestive tract, cardiovascular, and endocrine systems; more expressed and stable alterations on the part of the hemopoietic organs can also appear.

This division into groups of clinical symptoms of radiation illness is extremely tentative, since the symptoms of functional disturbance and slight decrease in hemopoiesis develop only gradually with radiation exposure. The later and more severe symptoms of chronic radiation illness are characterized by organic damage to the central nervous and cardiovascular systems, and by aplasia of the bone marrow.

Chronic radiation exposure in space presents a hazard in long-term space flight when the crew is constantly being bombarded with galactic cosmic radiation. In calculating the dose rate of galactic cosmic radiation at 10–15 rad/yr, the analysis of clinical material on the irradiation of humans at total doses up to 150 rem (i.e. *Group 2*) is of special interest, if it is assumed that the quality factor for cosmic rays is 10 to 15. In this group, all enumerated pathologic changes in the organism develop slowly over several years. Therefore, for a flight of 1-3 yrs, development of symptoms characteristic for the given group is highly improbable. Following cessation of irradiation, functional disturbances are repaired, although slowly, during 2-5 yrs. There is no experimental evidence at present for the biologic effectiveness of primary cosmic ray particles.

Chronic radiation sickness can develop from acute radiation exposures against a background of chronic exposure to ionizing radiation, and, following periods of acute exposure, there can be symptoms of acute radiation sickness with development of prodromal reaction. This variant of radiation sickness has not yet been sufficiently studied and requires further experimentation; however, it can be postulated that a background created by chronic radiation activity can change the severity of symptoms normally observed with acute irradiation. Acute irradiation, on its part, can alter the development of chronic radiation sickness.

Evaluation of Late Effects

The problem of late effects is extremely important and complicated for the evaluation of hazard to man from the action of ionizing radiation. Late effects of radiation are called somatic if discovered in the irradiated individual, and inherited if they influence his progeny. Among late somatic effects are leukemia, malignant tumors, cataracts, skin damage, decrease in fertility and, possibly, "nonspecific aging." As a rule, it is exextremely difficult, even impossible, to relate these effects to the action of radiation in individual cases.

The question of revising allowable exposure limits for professional workers should not be decided solely on the basis of risk of development of somatic effects, without wider consideration for genetic effects and effects on future populations. For evaluation of radiation hazard to astronauts, only somatic effects have significance, because of the extremely small contribution of irradiation of astronauts to the general population dose.

Committees of the US National Academy of Sciences and the United Nations (the Scientific Committee for the Effects of Atomic Radiations) have recently considered, independently, questions of leukomogenesis and carcinogenesis of radiations [3]. These groups have argued that, for health protection, a linear dose-effect relationship should be assumed, since this yields more reliable values for protection, while the actual dose-dependence is possibly nonlinear.

It has been clearly established that radiation exposure causes leukemia in humans at doses greater than 100 rad. An open question remains: whether or not there is a lower threshold dose at which leukemia does not arise. The existence of a threshold dose would eliminate the hazard of malignant illness arising at doses not exceeding that threshold. For health protection purposes, the relationship is usually represented as linear; leukemia incidence after high LET particle irradiation is not known. It is estimated that leukemia arises within several years following irradiation.

Calculations show that, for a dose of 100 rad or more of low LET radiation, the risk of leukemia is one case/10^6 individuals irradiated rem^{-1} yr^{-1} [3]. Leukemia has an average natural occurrence of 50 cases/10^6 people yr^{-1}.

In evaluating the risk of development of leukemia, it is imperative to take into consideration the age factor; it should also be kept in mind that the probability of development of leukemia by local irradiation or by irradiation of half the body is approximately twice lower than by whole-body irradiation.

It has been demonstrated that certain types of leukemia are associated with specific types of chromosomal aberrations: high LET radiations cause chromosomal aberrations with high frequency and are suspected of being more effective in causing leukemia.

Substantial data have been accumulated on the development of various forms of cancer through the action of ionizing radiation. Analyses of this development have been made on the basis of international data and data presented to the Atomic Bomb Casualty Commission at Hiroshima and Nagasaki [10].

The Japanese data, based primarily on illness in adults, indicate that the doubling dose for cancer of the thyroid gland is about 100 rad, or an increase in the number of tumors of the thyroid in the population of 1% for each rad of irradiation.

It was also established that the doubling dose for thyroid gland cancer is between 5 and 10 rem for children in the USA. This means a 10–20% increase in risk of cancer of the thyroid gland in children for each rad of irradiation per year. Thus, with a group of children (USA) and adults (Japan), the degree of increase in cancer of the thyroid gland in a year/rad of irradiation will be within a range of 1–20%.

According to data in Japan and the USA, a doubling dose of 175 rad has been determined for cancer of the lung, or 0.6% increase in lung cancer in the population/rad yr^{-1} [10].

In summarizing the incidence of radiation-induced cancer (including leukemia) from existing data, it becomes apparent that, for widely varying organs and systems, the range of values for doubling dose is very small (see Table 21) [3]. The overall incidence of all kinds of cancer and leukemia combined may be assumed to be 4×10^{-6}/rem yr^{-1}. The thyroid gland is apparently the only organ for which there exists a higher radiosensitivity for induced radiation cancer in young people.

Genetic effects appear in the descendants of individuals exposed to irradiation. It is extremely

TABLE 21.—*Rate of Induction of Various Types of Neoplasms, Assuming a Linear Dose-Effect Relationship* [3]

Neoplasm	Incidence at 1 rem/yr[1]
Leukemia	1/10^6
Lung cancer	1/10^6
Stomach cancer	1/10^6
All other forms	1/10^6
Overall tumor incidence	4/10^6 rem^{-1}. yr^{-1}

[1] Incidence of thyroid cancer when children are exposed is higher.

difficult to evaluate the genetic effect, especially since this risk has not been evaluated for other circumstances. It was proposed by an International Atomic Energy Agency Committee that the risk be quantitated as 0.5×10^{-6}/rem yr^{-1} [3].

Thus, to summarize the risk from late effects, it is possible to present it as:

Leukemia:	1×10^{-6}/rem yr^{-1}
Other types of tumors:	3×10^{-6}/rem yr^{-1}
Genetic effects:	0.5×10^{-6}/rem yr^{-1}
All tumors and genetic effects combined:	$< 10 \times 10^{-6}$/rem yr^{-1}

The results from experiments in relation to lifespan following low-level irradiation exposures in humans provide conflicting information. It is not clear from a statistical standpoint whether or not there is significant shortening in the lifespan of radiologists compared with specialists who have not been exposed to professional irradiation. A definite effect of large doses of daily irradiation on the length of life appears in mammals exposed to irradiation at various daily doses. Assuming that it makes sense to extrapolate the annual data of lesser daily doses, and that the results are valid for man, then it can be concluded that chronic irradiation of man causes shortening in his lifespan. Such an effect may be explained as a speeding up of the natural process of aging.

The probability of lifespan shortening is 1×10^{-4} for the average lifespan/rad. For the average lifespan of 70 yrs, the shortening due to whole-body irradiation can consist of 3 d/rad. However, it should be emphasized again that the given evaluation of risk is extrapolated from data on small mammals and may be inaccurate.

The Critical Organs

In the past, allowable doses of irradiation have been expressed either as dose in air or as surface dose. For more precise measurement of radiation hazard in connection with dissimilar radiosensitivity of tissues and organs and their special functional significance, it appears necessary to know the dose actually received by the most radiosensitive (critical) organs since their selective damage may condition the development of irreversible changes in the organism.

The majority of authors consider the blood-forming organs, sex glands, retina, skin, lens of the eye, and certain others as critical organs. It is also necessary to point out that, for space flight, as numerous experiments indicate, shielding the area of irradiation, and unequal distribution of absorbed dose to the body of the astronauts all help determine the role of an organ as critical.

On the basis of an extensive series of experiments, it is also advisable to consider the vestibular system as a critical organ. The normal functional activity of the vestibular system is of great importance for man's successful completion of space flight [61, 62, 69].

Under spaceflight conditions, the vestibular system is exposed to a series of adverse stimuli that include weightlessness, acceleration, and vibration. Other stresses, such as changed gaseous medium, temperature variations, hypokinesis, disturbance of biorhythms, and others can also provide adverse stimuli. Radiation action against this background, even at small doses, can call forth serious disturbances in the function of the vestibular system, which can, in turn, complicate completion of flight tasks by the spacecraft crew.

A series of experiments on irradiation of the vestibular system, with special reference to space flight, was completed at the beginning of the 1960s [128, 153].

Threshold radiosensitivity for vestibular malfunction was studied in more than 500 rabbits and 50 dogs. Single doses of irradiation consisted of 50, 100, 200, 500, 600, 800, 1000, 1600, 5000, and 10 000 rad. The initial reaction of the vestibular system to radiation exposure was evaluated (mainly in rabbits exposed to single doses of radiation), as well as the dynamics of vestibular disorders during the course of all stages of radiation sickness. After low doses (50–100 rad), there was depression in some cases, and in others increased excitation of the vestibular system. With increase in the dose of radiation, depression of the vestibular function became more pronounced (see Table 22). Single doses of whole-body exposure in the first hours following irradiation lead to sharp depression in the function of the vestibular system: (a) by lowering excitability, expressed by an increase in thresholds for angular acceleration perception and Coriolis acceleration as recorded by nystagmus, and (b) by lowering reaction of the vestibular system to angular and Coriolis accelerations [8, 68].

In this manner, the influence of ionizing radiations on vestibular function with whole-body irradiation of animals is expressed as a significant lowering in the response of the system to the action of adequate stimuli. Other physical factors also contribute, for example, Coriolis acceleration created as a result of continual slow rotation of the cabin [8], the conditions of hermetically sealed quarters [68], and vibration [115].

The data introduced above permit consideration of the probability of similar trends in the effects of certain environmental stimuli on the function of the vestibular system. However, this feature can change under conditions of the combined action of radiation and certain other stimuli.

Other workers who attempted to evaluate the effects of radiation in smaller groups of animals found that significant effects began at 500 rad, and the effects were transient. There was also a training or habituation factor [118].

The vestibular system under spaceflight conditions appears to be a critical organ not only in terms of complications in fulfilling spaceflight tasks on the part of the crew, but also in evaluating radiation safety in space. The study of reactions of the vestibular system to irradiation exposure combined with other spaceflight factors, and the study of reactions of an organism in a state of vestibular disorder, make evident the significance of the vestibular functional state for calculating allowable doses of space radiation.

The nervous system is of special interest, particularly the visual pathways and the retina. Damage caused by heavy primary cosmic ray particles might be expressed most clearly here [59]. Indications are that single heavy ions might cause degeneration of rods in the retina [193]. At large doses, heavy-accelerated oxygen ions have proved more effective than x-rays in producing irreversible damage to circulatory and neural components of the retina [21]. Radiations are also efficient in producing DNA strand breaks in the cerebellum [105]. A great deal of radiation sensitivity in functional response of various parts of the nervous system has been shown [61, 64, 93, 101, 107].

TABLE 22.—*Changes in Radiosensitivity of the Vestibular Analyzer During the First Hours Following Whole-Body Irradiation at Various Doses* [129, 154]

Dose (rad)	No. rabbits in series	No. rabbits in which changes in radiosensitivity appeared		
		Increased radio-sensitivity	Decreased radio-sensitivity	Total deviation
50–100	66	19	18	37(56%)
500–800	62	2	56	58(95%)
5000	20	2	18	20(100%)
10 000	10	0	10	10(100%)

Effective Dose

An important feature of radiation in space appears to be its duration. The necessity of calculating this feature to evaluate the radiation hazard on long flights cannot be doubted.

Protracted radiation, in an overwhelming majority of cases, shows less damaging effect than acute irradiation. With increase in duration of exposure there is decrease in the appearance of clinical symptoms of radiation. For quantitative characterization of this type of effect, the concept of *effective dose* has been introduced. The term relates mainly to the process of recovery in the irradiated organism versus the irreversible part of the damage.

Under the heading of effective dose with protracted irradiation, it should be understood that a dose of acute irradiation would produce the same effect as a given protracted dose. For calculation of effective dose, mathematical models are used which are based on the dynamics of recovery from exposure to radiation [4, 18, 162]. A series of mathematical models has been proposed for calculating effective dose, based on experimental data obtained under various conditions of protracted and chronic irradiation [33, 113, 116, 127, 175]. Several authors have also attempted to introduce mathematical models for calculation of processes of premature aging or shortening of lifespan [18, 60, 162].

Data have been compiled giving evidence that the dynamics of recovery from radiation damage, through split-dose irradiations, have more complex character than was assumed in earlier models, and thus demand further study [5, 40, 50, 160]. The study of reversible and irreversible portions of radiation damage has indicated that, in determining constants for recovery, these conditions of irradiation should be considered: dose level, time factor, type of radiation, distribution of absorbed dose in the body, and extent of shielding. Other considerations are the organism's individual recovery capabilities including age. From these premises, a more protracted regime of irradiation can be recommended for astronauts aged 22 to 25; astronauts from age 35 to 37 should probably be exposed to the maximum allowable dose for shorter intervals [140].

For evaluation of radiation hazard on short-term space flights, allowable dose is usually derived from total absorbed dose without consideration for degree of recovery from radiation damage. However, for standardization of radiation dose on lengthy space flights, such an approach is not acceptable. Under these conditions, it becomes necessary to calculate effective dose. Thus, for example, the maximum value for dose of justified risk is calculated at 215 rem for a long space flight on the basis of an effective dose of justified risk of 50 rem [94].

Individual Radiosensitivity and Selection of Astronauts

Methods for evaluating radiosensitivity in man prior to radiation exposure do not exist at present, although extremely hypothetical opinions on this question can be formulated.

It has been established that, during irradiation of humans with small doses, bioelectric activity of the brain can change [61]. Furthermore, it has been shown that in rabbits irradiated with small doses, changes in bioelectric activity of the brain do not occur. Subsequently, they prove to be more radiosensitive than animals in which there are such bioelectrical changes. Evaluation of possible changes in bioelectric activity of the brain might prove valuable for preliminary evaluation of radiosensitivity. Results of experiments indicating the presence of a particular dependency between functional state of the vestibular system and the character of its reaction to low doses of radiation on the one hand, and radiosensitivity in irradiation of animals with large doses on the other hand, deserve attention [50].

The question of the possibility of prior determination of radiosensitivity by means of irradiation of autogenic cell cultures taken from the astronaut before flight demands further consideration. This problem is closely related to the question of initial increase in radioresistance of spaceflight crews. Data indicate that the initial action of a series of stress factors can have an important effect on increase in radiostability of spaceflight crews.

Many scientists do not accept the idea that individuals in a population have a specific sensitivity, although a small change in sensitivity to lethal dose seems to accompany age. Other complicating factors are the known diurnal variations in radiosensitivity, that chemical substances can alter sensitivity, and that cells have different responses in different physiologic states. However, sensitive and resistant mutants do exist in microorganisms, which can be differentiated by their various abilities to repair radiation damage. Genetic strains differing in radiosensitivity have also been found in mice.

Summary

Evaluation of radiation hazard for short-term and long-term space flights and determination of allowable doses of radiation for astronauts are difficult. However, there are many known facts concerning biological peculiarities of the effects of solar and cosmic radiation in its various forms and energy spectra as well as its spatial and temporal distributions.

The problem of biologic effects of heavy ions on astronauts deserves special attention. Methods for correct evaluation of this hazard have still not

been defined. Only extensive radiobiologic research in space with accelerator experiments using heavy ions will permit solution of the problem. A thorough evaluation of the combined effects of ionizing radiation and other factors of space flight is demanded. At present, it is not known how long-term exposure of man to weightlessness will influence his radiosensitivity, in what way radiation damage under conditions of weightlessness will develop, and, finally, the reactions of an irradiated organism to the influence of other spaceflight factors.

Considerations of the development of space science, the realization of long-term space flights, and the possible use of atomic energy for propulsion and on-board power sources, pose the problem of reliable shielding for the crew and life-support systems. From this perspective, the possibility of creating electromagnetic and electrostatic protection and the partial shielding of critical organs and systems are being studied.

The possibility of shielding the crew from cosmic radiation by using fuel reserves and provisions, machinery and various apparatus on-board the spacecraft, should also be considered.

Drugs for pharmacologic protection from radiation would be desirable. However, the use of radioprotective chemicals presents special problems: they must be effective against various types of radiation at low dose rates; be marked by low toxicity even with repeated applications during a short time; and not lower the general functional capability of the organism. Research on the development of such drugs is still in process.

For success in obtaining radiation safety in space flight, future availability of a complex of special additional instruments and methods is envisaged. These would include systems of on-board and individual dosimetric devices for astronauts, continuous monitoring of the conditions of radiation in space, and radiation prognosis, especially prognosis of solar activity. However, even precise dosimetric information concerning absorbed dose on-board the spacecraft is not always sufficient for making the decisions to take prophylactic measures, since the range of individual responses in man can be extremely wide. The necessity might arise on long-duration flights for working out criteria and methods of evaluating some aspects of the degree of radiation damage directly on-board the ship. The chosen criteria must be marked by specificity, high verifiability, and maximum suitability for characterizing the astronaut's condition.

Thorough analysis at ground level of all medical information received from the spacecraft, including the search for indications of radiation effects, is envisaged. Data must be obtained in-flight which characterize the condition of the most radiosensitive systems of the organism. To this group of data, information might be added on the quantitative state of peripheral blood, the presence of disorders of the alimentary tract, or the state of blood clotting.

The development of special tests, particularly if biochemical, would probably be worthwhile. Some authors think that a method to determine substances in urine containing deoxyribose would be extremely valuable. Successful tests to evaluate immunologic states of an organism also deserve attention. The criteria and choice of methods to evaluate radiation effects in astronauts on-board the ship will probably be based on new developments in experimental radiobiology.

Radiations emanating from planetary surfaces and from the Moon, including the radioactivity of surface dust, must also be studied in detail before the prolonged stay of humans can be considered safe.

Thus, with further exploration of space, the realization of long-term space flight, and the projected establishment of manned bases on other planets, new problems are continually being raised which await solution.

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Part 4

PSYCHOPHYSIOLOGICAL PROBLEMS OF SPACE FLIGHT

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Chapter 13

BIOLOGICAL AND PHYSIOLOGICAL RHYTHMS

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Chronobiology, the branch of science concerned with the cyclic phenomena in living organisms, has contributed in various ways to biomedical planning for human space travel. This chapter brings together biomedical data obtained in space ventures, with emphasis on the sleep/wakefulness rhythm. Certain effects of space flight and those of transmeridian flight are similar, so that the latter type flight is given brief consideration. Adaptational changes in human physiologic rhythms are also discussed. To aid in the preparation of this chapter, compilations of the chronobiologic literature were made.[1] Recent reviews [4, 5, 17, 18, 25, 38] of the European and American human chronobiologic literature were also consulted.

The circadian rhythm of sleep and wakefulness or rest and activity is one of various biologic and physiologic rhythms discussed in this chapter. It is a dominant topic of the International Society for the Study of Biological Rhythms (founded in 1935) which deals with the entire spectrum of this phenomenon found in plants, animals, and man [11, 13, 19, 31, 39]. The human circadian rhythm came increasingly into the focus of scientific and general public interest with the development of jet-propelled airplanes, which permitted the crossing of a greater number of time zones in a matter of hours, thus producing a considerable phase shift of the circadian rhythm [46, 48, 54, 55]. This physiologic "time zone effect" in the higher levels of the first aeronautical speed (below Mach 1) may become more drastic in the realm of supersonic speed or the second aeronautical speed (beyond Mach 1).

Westward or eastward travel in jet aircraft over many time zones, by causing disruption of psychologic and physiologic rhythms, can be considered an analogue of space flight. Studies of persons involved in transmeridian flights have, therefore, provided insight with regard to desychronosis[2] and adaptation to unaccustomed temporal stimuli.

Chapek [15] used 4-h serial determinations to evaluate circadian rhythms for body temperature, pulse rate, pulse pressure, and cardiac minute volume for 105 members of flight crews during and following eastward and westward flights, which were made at different times of day over 6 to 7 time zones. He also evaluated motor activity, higher nervous activity, and electrical sensitivity of the eye. A team of German scientists [12, 28, 29, 30, 59] investigated physiologic and psychologic effects of transmeridian flights of 6- to 8-h duration, bringing out relationships

[1] B. S. Alyakrinskiy, who compiled the Russian chronobiologic literature, drew material from publications dating back almost 100 years, and found this topic very broad in scope.

[2] "If a term related to medical language is needed to designate the psychophysiological effect of cycle desynchronization, *desynchronosis* would be an appropriate one, and the individual could be described as *desynchronotic*" [55].

to flight direction, flight duration, time of day, and amount of previous flying experience. Eastward and westward flights were differentiated on the basis of alterations in oral temperature, oxygen consumption rate, reaction time, and psychomotor performance. Pilots who were highly experienced, whose performance in a flight simulator showed circadian variability during a preflight period, showed aberrance in this respect on the first day after a westward transatlantic flight. Resynchronization, judged by performance in the flight simulator, required 9 days. For complex psychomotor performance, readjustments continued to 10–12 d respectively after westward and eastward flights; but for simple performance skill, restabilization required 6–9 d, respectively. Adrenocortical resynchronization after westward and eastward flights required 5–8 d, respectively. On the basis of rectal temperature rhythm, resynchronization was found to require 11–12 d after westward flight and 14–15 d after eastward flight.

With the development of rocket propulsion, the first astronautic or cosmonautic velocity in near-Earth space (8 km/s) was reached on October 4, 1957 (Sputnik I); with this achievement, aerodynamic flight advanced to controlled celestial mechanics. The flight vehicle itself became a satellite orbiting around the Earth. In orbital flight in near-Earth space, a completely novel situation is faced: the customary geographic day-night cycle is replaced by a short, sunlight-shadow cycle.

Within the relatively radiation-safe altitude range from 200 to 800 km, below the Van Allen radiation belt, the orbital flight periods last from about 90 to 140 min. About 40% of this time—depending upon the orbit's inclination—is satellite night, or Earth shadow time. This external light-shadow or photoscotic[3] cycle in orbital space flight is not longer than 1/10 the 24-h day-night cycle on Earth. Furthermore, it is modified by earthshine and moonshine with a permanently velvet-black sky in the background. This is a brief statement about the physics of the cyclic photoecologic environment in orbital flight in new Earth space.

MANNED ORBITAL FLIGHT

Manned orbital flight was preceded by a short dog-and-monkey phase (Laika, Sam, Ham, Strelka, and Yelka). It became a reality with the flight of cosmonaut Yuri Gagarin in Vostok I, on April 12, 1961, followed by astronaut John Glenn in Mercury Atlas 6, on February 20, 1962. This historic achievement of man's advance on the vertical frontier brings him beyond the Earth's time zones. Nevertheless, in the short periodic, photic environment encountered during orbital flight in near-Earth space, the astronaut remains bound to the temporal patterns of sleep, rest, and activity of his inborn circadian rhythm [3, 24, 27]. This is dictated by his physiologic clock which is a psychoneurohormonal system with a tendency to maintain near constancy—rhythmostasis.[4] Like thermostasis, rhythmostasis must be considered a part of homeostasis [14].

Before manned space flight began, doubts were voiced occasionally about the possibility of sleep under condition of weightlessness. In order to obtain a complete picture of the actual situation, let us examine certain physiologic variables of astronauts and cosmonauts who have been in near-Earth space for 1 day or longer, and the telemetric recordings of physicians who were in charge of the medical control of the flight.

Although various types of biomedical data were collected in the Mercury, Gemini, and Apollo flights, the within-day (circadian) cycles were not studied extensively. Weil-Malherbe and colleagues [60] studied the seven Project Mercury astronauts, by means of urinalyses, during stress-free baseline periods, stressful training periods, and suborbital and orbital flights. On the basis of urinary catecholamine values, these men were judged highly adapted to stress and to have normal day-night variability with respect to sympathoadrenomedullary activity during stress-free periods. Flight-induced elevations in urinary catecholamines (evidence of sympathoadrenomedullary stimulation) occurred during the fourth manned orbital flight (MA–9), the duration of which was 34 h 20 min. There was

[3] Photoscotic: Greek, photos = light, scotia = darkness.

[4] Rhythmostasis: the tendency of the body to keep its rhythms nearly constant.

also cyclic change which suggested that preexisting entrainment acted as a basic factor throughout the flight. Superimposed upon the entrained rhythms were displacements, which obviously relate to flight stressors.

In the earlier manned space flights, sleep was recorded by means of the electroencephalogram (EEG) which requires electrodes on the head. This method has been abandoned for the sake of comfort; the recorded heart rate, respiration, and blood pressure now serve as sleep indicators.

The personal experiences of orbiting space pilots and telemetered data will be discussed according to the chronologic order of those flights which lasted longer than 1 day.

Sleep and Wakefulness in Space

The first "cosmic slumber" of the second Soviet cosmonaut, Gherman Titov, in Vostok 2 (17 orbits, 25 h 18 min, August 6–7, 1961), was not without interruptions. After seven orbits he felt a definite state of fatigue. When he flew over Moscow at 6:15 PM, he prepared for sleep, according to schedule, by releasing special belts from the side of the seat, strapping his body to the contour seat, and adjusting the seat to the bed position. He promptly fell asleep, but awoke much earlier than scheduled, during the eighth orbit. When he opened his eyes, he saw his arms dangling weightlessly, and his hands floating in the air.

> "The sight was incredible," Titov reports [56]. "I pulled my arms down and folded them across my chest. Everything was fine – until I relaxed. My arms floated away from me again as quickly as the conscious pressure of my muscles relaxed and I passed into sleep. Two or three attempts at sleep in this manner proved fruitless. Finally I tucked my arms beneath a belt. In seconds I was again sound asleep." Titov states further: "Once you have your arms and legs arranged properly, space sleep is fine. There is no need to turn over from time to time as a man normally does in his own bed. Because of the condition of weightlessness there is no pressure on the body; nothing goes numb. It is marvelous; the body astoundingly light and bouyant . . . I slept like a baby."

He awoke at 2:37 AM, Moscow time, a full 30 min behind schedule because of oversleeping. He immediately started the required morning calisthenics. Thereafter, he carried out all scheduled assignments, and during the 17th orbit prepared both the rocket and himself for the "baptism of fire" – atmospheric reentry. Titov's sleeping period coincided largely with nighttime over the USSR, which was also the experience of the other Soviet cosmonauts.

During NASA's Mercury project (Mercury Atlas 9–22 orbits, 34 h 20 min, May 15–16, 1963), astronaut Gordon Cooper found that even early in flight, when he had no tasks to perform and the spacecraft was oriented so that the Earth was not visible from the window, he dozed off easily for brief naps. During the scheduled sleep period, he slept only in a series of naps lasting no more than 1 h each; his total sleep time was about $4^1/_2$ h. If another person had accompanied him to monitor the systems, he could have slept for longer periods, he stated; also that he slept perhaps a little more soundly than on Earth, according to NASA's mission report.

Valerey F. Bykovskiy in Vostok 5 (76 orbits, 119 h, June 16–19, 1963), slept four times for periods of 8 h, alternating with 16-h periods of wakefulness.

The first woman in space, cosmonaut Valentina Tereshkova, had a similar sleep experience during her 70 h 50-min flight in Vostok 6 (45 orbits, June 16–19, 1963). With regard to these two orbital flights, Parin and associates [45, 47] stated, ". . . the diurnal periodicity of physiological functions changed only during the first and last days of the weightless state, which was most probably associated with the emotional strain." During phases of wakefulness, brief rest periods were usually scheduled for times when the spaceship was not over the Soviet Union. "It should also be noted that at night, during sleep, nearly all cosmonauts displayed a greater reduction in pulse rate than that recorded during the same hours in earlier space-simulated flights."

The three-man team, Vladimir M. Komarov, Konstantin P. Feoktistov, and Dr. Boris B. Yegorov in Voskhod I (15 orbits, 24 h 17 min, October 12, 1964), rested and slept in shifts during their 24-h flight [47].

In two 1965 flights of the Gemini Project—Gemini 4, James A. McDivitt and Edward H. White (62 orbits, June 3–7), and Gemini 5, Gordon Cooper and Charles Conrad (120 orbits, August 21–29)—special attention was given to the sleep and wakefulness cycle. According to Dr. Charles Berry, Chief of Medical Space Operations and Research, NASA Manned Spacecraft Center, Houston, Tex. [10], "The GT-4 and 5 crews (4 and 8 day missions) have reported no difficulty in performance related to the 45 minute darkness and daylight cycle created by orbital flight."

"The GT-5 crew had a long sleep period, each programed in conjunction with nighttime at Cape Kennedy. They, too, had intermittent spacecraft noise irritants interfering with sleep, and found themselves tending to retain their ground-based, day-night cycle. It appears best to provide a joint long sleep period related to normal sleep time at the Cape." This was Dr. Berry's proposal in 1965.

Wakefulness/Sleep Schedules

Further insight into desynchronosis and adaptation to new wakefulness/sleep schedules has been gained from experimental studies. Stepanova [49] has postulated that humans cannot adapt to a day shorter than 12 h or longer than 52 h. This hypothesis holds as the basic point that there is a daily "information-energy cost" which is determined by an individual's occupation. With any increase in the length of the daily cycle, the hourly information-energy cost must decrease; conversely, decreased hourly cost is essential when the cycle is shortened. Stress results when the cost is improperly regulated. When applied to space flight, this hypothesis (and the formula for computing curves describing human adaptability to days of different duration) indicates that disorders of wakefulness/sleep rhythms can be prevented by lengthening the period of the daily cycle when physical and intellectual demands are low. When psychic loads become high, disorder can be avoided by shortening the cycle.

There has been worldwide interest in the phenomenon of adaptation to "time displacement;" consequently, a great variety of wakefulness/sleep schedules (as well as a great variety of bodily rhythms) has been studied. Litsov [37] studied electroencephalography (EEG), pulse rate, breathing rate, and body temperature in men who, at different times, used dissimilar work/rest schedules, each of which allowed three 3-h periods of sleep in each 24-h period. Adaptation rates varied with schedules. Stepanova [50, 51] did not find evidence of adaptive change in pulse rate rhythm during a 16-calendar day test period in which 11 h wakefulness were regularly followed by 5 h sleep. Dushkov et al [20] found that adaptation proceeded slowly when the schedule required 6 h work, followed by a 6-h rest period in which there could be 4 h sleep. Adaptation was greatly accelerated by adding factors such as regular calisthenics, lively music, vitamin supplementation, between-meal candy, and hourly cold-water washing of face and neck. This facilitation was evident in cardiovascular, neuromuscular, and psychic functions.

In a study of human adaptation to simple inversion of the wakefulness/sleep schedule, Litsov [36] found evidence of a three-stage restructuring. Old rhythms for pulse rate, breathing rate, and body temperature were retained for 1–3 d ("latent stage"). Next, the stage of "apparent restructuring" lasted for 2–7 d. Finally, there was the stage of "deep restructuring." Simple motor responses and the EEG adapted readily, whereas psychomotor performance, pulse rate, breathing rate, and body temperature adjusted less readily. In day-night inversions, Lugovoy [40] found that restructuring proceeded rapidly when prolonged sleep deprivation was a "priming" factor. Baranov [6] found that individuals varied greatly in speed of adjustment to energy expenditure rhythm when there had been day-night inversion; some subjects showed full adjustment on the first day, while others required as much as 13 d.

Although immediate phase restructuring of the rhythm for cardiac rate was observed by Kukishev [34] after day-night inversion, certain of his subjects experienced desynchronosis for as long as 10 d, showing sleepiness during working hours, performance decrement, faulty coordination, irritability, nycturia, et cetera. The effects of day-night inversion on urinary excretion of potassium, sodium, and calcium were studied by Krotov and Lugovoy [33]. Potassium excretion rhythms were well-defined, but not those for sodium and calcium. There was gradual development of normal temporal relationships for potassium, but aberrancy on the 25th day indicated that adaptation was incomplete. In a study of the effects of 72-h sleep deprivation, Zykova et al [61] also found high individual variability, some subjects showing phasic change and others decreased amplitude. According to Chernyakova [16] and Koreshkov [32], persons who have unstable circadian rhythms of cerebral bioelectric activity adapt readily to time displacement.

During the longest American orbital flight in Gemini 7 (14 d, Dec. 4–18, 1965), the two astronauts, Frank Borman and James A. Lovell, had no significant sleep difficulties during 206 orbits. The inside of the spacecraft was artificially darkened by covering the windows. Thus, they had a microenvironmental day and night of their own and kept in tune with the day/night cycle at Cape Kennedy [10].

Endocrine-Metabolic Evaluation

Serial urine specimens collected during the approximately 14-d Gemini 7 flight enabled endocrine-metabolic evaluation [41]. Day-to-day changes were studied, not the within-day variation. Still, the findings seem pertinent to the present discussion, since they suggest that this prolonged flight, unlike the shorter MA-9 flight, altered endocrine-metabolic rhythms, producing de-entrainment (internal desynchronization). Evidence is that the two astronauts demonstrated dissimilar patterns of change in urinary sodium, chloride, and calcium. Both men showed progressive increases in urinary inorganic phosphate for 9 d, with subsequent reversions to preflight levels.

This long-term response to space travel evidently indicates adaptation. Urinary sulfate remained unaltered, but potassium excretion followed a biphasic pattern of change, falling during an early period and rising subsequently. Magnesium output increased after a lag of 1 week. Increased excretion of aldosterone was accompanied by decreases in urinary 17-hydroxycorticosteroids (17-OHCS) and nonprotein nitrogen (NPN). The latter changes strongly suggest adaptation. Transient increases in epinephrine occurred both at the start and at the end of the flight.

Data collected from both Vostok and Gemini crewmembers formed the basis for Halberg et al [26, 57] concluding that circulatory rhythms persisted during prolonged periods in space. As evidence, the phase relations for a set of circulatory functions for the men in space showed close agreement with those for men who, while remaining on Earth, experienced simulated weightlessness. Prolonged bed rest was used to simulate weightlessness.

Evidence of adaptation was obtained from Apollo 15 crewmembers who were evaluated by means of pre- and postflight blood and urine analyses [35]. Specifically, postflight plasma potassium and cortisol levels were relatively low, urine aldosterone values were relatively high, and plasma and urine sodium values clearly indicated homeostasis.

In a discussion on the importance of circadian rhythms for space biology and medicine, Mikushkin [44] emphasized neuroendocrine and metabolic aspects, noting that stress tolerance depends upon complex couplings of rhythmic functions. It is especially important that both physiologic adaptability and wakefulness depend to a considerable extent upon some common mechanisms.

During the wakefulness phase of a typical day, healthy persons exhibit stress tolerance superior to that demonstrable in the alternate phase. Disruption of the wakefulness/sleep rhythm results in mismatching of physiologic rhythms, a condition termed internal desynchronization or desynchronosis, manifested by malaise, confusion, psychomotor decrement, anorexia, and relatively low tolerance to stress. Adaptation to a new activity-sleep schedule requires restructuring of the entire set of bodily rhythms. This author also considers preadaptation an appropriate procedure for space flight, suggesting that it be accomplished by use of unusual degrees of illumination, with crewmembers following self-selected activity-sleep schedules. It would be expected that weak illumination would promote development of rhythms with periods greater than 24 h, while strong illumination would act oppositely. After attainment of a stable state, further modification could be accomplished by means of programed activity to include physical exercise.

The group flight program of Soviet Soyuz-6, -7, and -8 in October 1969 included 8 h sleep daily, i.e., within 24 h. However, the cosmonauts slept only 6 or 7 h and subjectively regarded this as fully adequate, feeling refreshed and fit for work. The sleep time was kept more or less in tune with nighttime at the launching area (near the Ural Mountains). In contrast, the two cosmonauts in Soyuz-9 (17 d, 17 h record flight in January 1970), had to shift the sleeping cycle of 12 h because their spaceship passed over the USSR at night and they had to land in early morning [42]. They slept during daytime and worked at night. "Our sleep in flight was normal. After the sleep we felt refreshed and quite efficient," according to the Commander, cosmonaut Andrian Nikolayev.

Principles that are applicable to formulating work/rest schedules for space flights have been worked out by Alyakrinskiy [1, 2]. He points out that desynchronosis merely represents the alarm response of the general adaptation syndrome. Physiologic rhythms differ in sensitivity toward a given disrupting influence; hence there is phase mismatch of rhythms which are normally coupled. Adaptation to a new activity-sleep schedule, like adaptation to any stressor, involves stereotyped changes in neuroendocrine systems. Restructuring the entire set of coupled rhythms is necessary for complete adaptation, but there is an intermediate stage: latent or compensated desynchronosis. In this stage there is subjective normalcy, along with normalization of cardiovascular and respiratory rhythms. However, at this time there are still mismatched endocrine-metabolic relationships, along with relatively low stress tolerance. Obviously, chronobiologic techniques are advantageous, for they can bring out vulnerability which would be undesirable immediately before space flight.

The recorded and reported sleep-and-wakefulness time patterns in orbital space flight reflect the physiologic circadian rhythm of 24 h, by and large. But, the Earth's surface time zones are environmentally meaningless for the astronauts, since they cross one time zone in only a few minutes. Their basic guiding time is Greenwich mean time (G.m.t.) or universal time (u.t.). Nevertheless, their body clocks have to run more or less isochronous [5] with their natural circadian rhythms and for flight operational reasons, it is also very desirable to remain synchronous with the local time of the Mission Control Center on Earth to which they were adapted during the prelaunch period. Parin and Gazenko made an interesting neurological comparison concerning sleeping in the state of weightlessness, which in presatellite times was considered difficult. During the weightless state, the parasympathicus is dominant (parasympathicotonia). The same is true during sleep. This can be considered as beneficial for sound sleep during the weightless condition in space flight, if the sleep facilities are adequate and comfortable.

FUTURE SPACE STATIONS

In the years ahead, we can expect *space stations* for the purpose of meteorological, geological, astronomical, and biomedical studies [22]. Such a "manned orbiting research laboratory," called Skylab (a project of NASA), kept three crewmen on-board. In the future they will be ferried by means of a reusable space shuttle to the space station and back to Earth in intervals of 4 or 8 weeks. A cooperative docking operation of Apollo and Soyuz spacecraft is planned for the mid-seventies, which will allow crew transfer between the two craft. At the moment of such an international link in space, the time of alert wakefulness of both teams must be in synchronization.

The Skylab is the predecessor of a larger permanent *Space Station* that can accommodate a staff of 12, including crewmembers, scientists, and experimenters. The duty-and-sleep regimen of professional personnel in charge of the flight operation will require a rotating shift which will

[5] Isochronous: taking place at equal intervals of time.

be possible because of more comfortable sleep facilities. But switching this shift within the operational team is not advisable, which would be an additional stress to their delicate duties. The researchers, too, will sleep in special soundproof sleep compartments in order to remain fresh and alert during the hours devoted to their exploratory tasks.

The Space Station clock time will be about the same as that in the Control Center on Earth. There is no question that time regulation will be a decisive factor for successful research work in these coming space-bound scientific "institutes."

MISSIONS TO THE MOON

The circadian rhythm during flight to the nearest celestial body, the Moon, will now be discussed following the material on orbital flight in near-Earth space. Flight to the Moon requires an escape velocity of 11.1 km/s from the Earth's gravisphere. The photic environment en route to the Moon includes permanent sunshine, earthshine, moonshine, and a velvet-black sky. It takes only about 3 d from an Earth departure orbit to a circumlunar parking orbit. This relatively short duration of the trans-Moon trajectory requires a carefully planned sleep-and-duty regime for the three-man team of the lunar astronauts [53].

The sleep-work regimen of the crewmembers of Apollos 7, 8, 9, 10, and 11 has been described in detail by Berry [7, 8]. Statements follow about sleep, work, and rest cycles of the teams of Apollos 7 to 15, published in the respective NASA Apollo mission reports.

Apollo 7

This was the first flight of Apollo spacecraft, with Walter H. Schirra, Jr., Donn Eisele, and R. Walter Cunningham, October 11–22, 1968.

Work/rest cycles. "Based on previous flight experience, a medical recommendation was made to program simultaneous crew rest periods during the mission, referenced to the crew's normal Cape Kennedy sleep cycle. Flight plan and crew constraints, however, precluded simultaneous sleep. The ac electrical bus failure, which occurred unexpectedly and required immediate action, demonstrated the wisdom of having at least one crewman on watch on the first flight of a new spacecraft. The large departures from the crew's normal circadian periodicity caused problems during the mission.

"The crew reported poor sleep for about the first 3 days of the flight and experienced both restful and poor sleep after that period of time. The Command Module Pilot reported that fatigue and exhaustion caused him to fall asleep once on his watch and that he took 5 mg of d-amphetamine on another occasion to stay awake during his work cycle." The amount of sleep each crewman obtained was indeterminable.

Apollo 8

On this first manned flight around the Moon, the astronauts were Frank Borman, James Lovell, Jr., and William Anders, December 21–27, 1968.

Work/rest cycles. "The very busy flight schedule precluded simultaneous sleep and resulted in large departures from normal circadian periodicity, thus causing fatigue. The Commander experienced a 'practical shift' of 11 hours before to 2.5 hours later than his assumed Cape Kennedy sleep time. Real-time changes to the flight plan were required because of crew fatigue, particularly during the last few orbits before the transearth injection maneuver."

Apollo 9

Docking with lunar module were James A. McDivitt, David R. Scott, and Russell L. Schweickart, March 3–13, 1969.

"This mission was the first in which all three men slept simultaneously. A definite improvement over the previous flights was observed in the estimated quantity and quality of sleep. Lack of postflight fatigue was correspondingly evident during the medical examination on recovery day. It should be further recognized that crew workload during the last 5 days of flight was significantly lighter than on previous missions.

"The flight plan activity for the first half of the mission resulted in excessively long work periods for the crew, and the time allocated

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for eating and sleeping was inadequate. Crew performance, nonetheless, was outstanding. Departures from the crew's normal circadian periodicity contributed to some loss of sleep during this time. The crew experienced a shift in their sleep periods, which varied from 3 to 6 hours from their assumed Cape Kennedy sleep time."

Apollo 10

The descent to within 9 miles of the Moon in the Lunar Module was made by Thomas P. Stafford, John W. Young, and Eugene A. Cernan, May 18–26, 1969.

"The three crewmen were scheduled to sleep simultaneously, and in general, they slept very well during the nine periods. Estimates of the quality and quantity of sleep were based entirely on subjective reporting by the crew. In post-flight debriefings, the Commander commented that the sleep stations and sleeping bags were satisfactory."

Apollo 11

The event of the first landing of men on the Moon involved Neil A. Armstrong, Michael Collins, and Edwin E. Aldrin, Jr., July 16–24, 1969. Total stay time was 21 h 36 min.

"It is interesting to note that the crewmen's subjective estimates of amount of sleep were less than those based upon telemetered biomedical data. By either count, the crewmen slept well in the command module. The simultaneous sleep periods during the translunar coast were carefully monitored, and the crew arrived on the lunar surface well-rested. Therefore, it was not necessary to wait until after the first planned 4-hour sleep period before conducting the extravehicular activity. The crewmen slept very little in the lunar module following the lunar surface activity. However, the crewmen slept well during all three transearth sleep periods."

Apollo 12

The second manned exploration on the Moon was made by Charles Conrad, Jr., Richard F. Gordon, Jr., and Alan L. Bean, November 14–24, 1969. Total stay time was 31 h 31 min.

"Sleep periods during translunar coast began approximately 7 to 9 hours after the crew's normal bedtime of 11 p.m. The crew reported that they had no particular trouble in adapting to the shifted sleep periods. However, the first flight day was extremely long, and the crew was thoroughly fatigued by the time the first sleep period began 17 hours after lift-off.

"The crewmen slept well in the command module during the translunar and transearth coast phases, and the Lunar Module Pilot took at least two unscheduled naps during transearth coast. However, they reported their sleep periods were longer than necessary, since they would invariably awaken about 1 hour ahead of time and would usually remain in their sleep stations until time for radio contact.

"The lunar module crew slept only about 3 hours on the lunar surface prior to the second extravehicular activity period. In the next sleep period following rendezvous and docking, all three crewmen in the command module slept only 3 or 4 hours, which was less than desirable.

"Biomedical monitoring during sleep periods was very limited. The crew complained that it was inconvenient to hook up to the biomedical harness while in the sleeping bags; hence, very little data were received."

Apollo 13

The landing mission was aborted because of oxygen tank failure; astronauts were James A. Lovell, Jr., John L. Swigert, Jr., and Fred W. Haise, Jr., April 11–17, 1970.

"The crew reported sleeping well the first 2 days of the mission. They all slept about 5½ hours during the first sleep period. During the second period, the Commander, Command Module Pilot, and Lunar Module Pilot slept 5, 6, and 9 hours, respectively. The third sleep period was scheduled for 61 hours, but the oxygen tank incident at 56 hours precluded sleep by any of the crew until approximately 80 hours.

"After the incident, the command module was used as sleeping quarters until the cabin temperature became too cold. The crew then attempted to sleep in the lunar module or the docking tunnel, but the temperature in these areas also dropped too low for prolonged, sound sleep. In addition, coolant pump noise from the lunar module and frequent communications with the ground further hindered sleep. The total sleep obtained by each crewman during the remainder of the mission after the incident is estimated to have been 11, 12, and 19 hours for the Commander, Command Module Pilot, and Lunar Module Pilot, respectively."

Apollo 14

The third manned landing on the Moon was made by Alan B. Shepard, Jr., Stuart A. Roosa, and Edgar D. Mitchell, January 31–February 9, 1971. Total stay time was 33 h 31 min.

"The shift of the crew's normal terrestrial sleep cycle during the first four days of flight was the largest experienced so far in the Apollo series. The displacement ranged from 7 hours on the first mission day to 11½ hours on the fourth. The crew reported some difficulty sleeping in the zero-g environment, particularly during the first two sleep periods. They attributed the problem principally to a lack of kinesthetic sensations and to muscle soreness in the legs and lower back. Throughout the mission, sleep was intermittent; i.e., never more than 2 to 3 hours of deep and continuous sleep.

"The lunar module crewmen received little, if any, sleep between their two extravehicular activity periods. The lack of an adequate place to rest the head, discomfort of the pressure suit, and the 7-degree starboard list of the lunar module caused by the lunar terrain were believed responsible for this insomnia. The crewmen looked out the window several times during the sleep period for reassurance that the lunar module was not starting to tip over.

"Following transearth injection, the crew slept better than they had previously. The lunar module crewmen required one additional sleep period to make up the sleep deficit that was incurred while on the lunar surface.

"The crewmen reported during postflight discussions that they were definitely operating on their physiological reserves because of inadequate sleep. This lack of sleep caused them some concern; however, all tasks were performed satisfactorily."

Apollo 15

The fourth lunar landing witnessed the first use of the lunar roving vehicle, with astronauts David R. Scott, Alfred M. Worden, and James B. Irwin, July 26-August 7, 1971. Total lunar stay time was 66 h 55 min.

"Very little shift of the crew's normal terrestrial sleep cycle occurred during the translunar and transearth coast phases of this mission. As a result, all crewmen received an adequate amount of sleep during these periods.

"Displacement of the terrestrial sleep cycle during the three lunar surface sleep periods ranged from 2 hours for the first sleep period to 7 hours for the third sleep period. This shift in the sleep cycle, in addition to the difference between the command module and lunar module sleep facilities, no doubt contributed to the lunar module crewmen receiving less sleep on the lunar surface than was scheduled in the flight plan. However, the most significant factors causing loss of crew sleep were operational problems. These included hardware malfunctions as well as insufficient time in the flight plan to accomplish assigned tasks. During the first sleep period, the crewmen went to sleep 1 hour later than planned and had to arise 1 hour early to fix a cabin oxygen leak. The crewmen again were an hour late in getting to sleep for the second lunar surface sleep period. The final sleep period was changed so that the beginning of the period was 2½ hours later than originally planned. The period, which had been planned to last 7 hours, was terminated after 6½ hours to begin preparations for the final extravehicular activity. Lengthening the workdays and reducing the planned sleep periods on the lunar surface, coupled with a significant alteration of the lunar module crewmen circadian rhythm, produced a sufficient fatigue level to cause them to operate on their physiological reserves until they returned to the command module."

Lunar Sleep

The recorded and reported sleep and wakefulness time patterns in the Apollo flight series reflect, by and large, the inherited rhythmostatic nature of the astronauts in terms of the circadian time scale. But it must be integrated into the fixed flight schedule.

At this point, a personal communication from Dr. W. R. Hawkins, Chief of Flight Operations, NASA, Houston, is in order. It summarizes the factors influencing the astronaut's clock during both orbital and lunar flights.

"The primary factors that contributed to the fact that inflight sleep was less than that obtained on Earth were (1) cyclic noise disturbances resulting from such events as thruster firings, communications, or movement within the spacecraft; (2) staggered sleep periods; (3) significant displacements of the astronauts' normal diurnal cycle; (4) the so-called command pilot syndrome; (5) the unfamiliar sleep environment; and (6) excitement.

"During the Apollo program, no new sleep problems have been encountered. Apollo missions are necessarily tailored around an operational trajectory which, by nature, is highly inflexible and constraining. The astronaut must be integrated into this fixed mission plan in the best possible way. That is, man is required to accommodate to the mission and not the converse."

A mission to the Moon requires a fixed time schedule comprising more astronautical actions than in orbital flight: after insertion into an Earth orbit, injection into the trans-Moon trajectory, insertion into a lunar orbit, separation of the lunar module from the command module, and similar. This makes the programing of the sleep-and-duty cycle more complicated.

During a longer stay on the Moon—such as in a future *lunar research laboratory*, which, since 1965, has been the objective of the Lunar International Laboratory (LIL) Committee of the International Academy of Astronautics (under the direction of F. J. Malina)—the sleep-activity cycle will be completely independent of the 27 terrestrial days-long light/dark cycle of the Moon. During the light phase of the cycle, solar illuminance [6] on the Moon amounts to 140 000 lux,[7] the same as that above Earth's atmosphere. There is also periodically earthshine, which is 75 times stronger at "full Earth" than is moonshine on Earth at full Moon. Such is the general photorama on the Moon.

In a broader sense, the sunrise-sunset cycle on the Moon does not provide a time cue or Zeitgeber [8] comparable to the 24-h dark/light cycle on Earth. There are about 2 terrestrial weeks of sunshine followed by a night of the same duration. Therefore, the selenonauts inside the Lunar Station must schedule their sleep and activity rhythm in terms of the terrestrial circadian pattern. This must be arranged in shifts between the members of the operational team, to keep in constant radio contact with the manned Moon Ship Control Center on Earth. Communication is possible, of course, only when the Control Center is on the "near side" of the rotating Earth, as seen from the Moon.

Generally, sleep on the Moon might be better than on Earth due to its lower gravitational force which is only one-sixth that on Earth. A hypnogram, or actogram [9] of a sleeping selenonaut probably will show fewer of the occasionally sleep-interrupting body movements, because pressure between the body and the bed would be greatly reduced. Thus, sleep could be indeed more refreshing in the gravitational arms of Luna, the goddess of the night.

MANNED MARS MISSION

The first planetary target for a manned mission will be the planet Mars, envisioned for the mid-eighties by Wernher von Braun [58]. A flight to the Red Planet requires a complete escape velocity from the gravisphere of Earth (11.2 km/s—the second astronautical velocity). If based on a minimum energy trajectory, this interplanetary journey would take about 8 months to reach the martian gravisphere. From a medical point of view, this time spent in interplanetary space is too long; it should be shortened to less than 20% of this duration. This will be achieved by novel methods of propulsion such as nuclear propulsion [54].

[6] Illuminance: the intensity of light coming from a light source, measured in candela per sq. meter (cd/m^2) or lux (lx).

[7] Lux: unit for measuring the intensity of illumination; 1 lx = 1 mcd.

[8] Zeitgeber: time cue for entraining sleep and wakefulness.

[9] Actogram: device attached to the mattress of a bed to record the body movements during sleep—hypnogram.

The photic space environment en route to Mars, when the spaceship with a team of six to eight martianauts reaches a distance of 1300 million km, is beyond the shadow of Earth: consequently there will be constant sunshine and a velvet-black sky. In this exotic, nonperiodic environment along the trans-Mars trajectory, the occupants of the spaceship must arrange their sleep, rest, and activity regimen corresponding to the temporal pattern of their physiologic circadian rhythm on Earth. It cannot be that which is called in the science of biorhythmology a "free-running cycle" [11], because it will be telecontrolled by the control center on Earth. Six to 8 hours' sleep have been found adequate, with occasional catnaps every 24 h, in space simulator experiments lasting several months [43, 48].

It is encouraging to learn from these reports related to orbital and Moon flights that space sleep poses no difficulties if intracabin conditions are adequate. This is a prerequisite for the martianauts' health and maintenance of high performance capability. Furthermore, exercise necessary to prevent a certain observed physiologic deconditioning (such as orthostatic hypotonia of the muscles and veins, and decalcification of bones), will automatically contribute to a sound pattern of sleep and wakefulness.

As soon as the Mars ship comes within 0.5 million km to Mars, it enters its gravisphere and can be inserted into a circum-martian orbit for the preparation of the landing maneuver. If an altitude of 100 km is chosen, the martianauts will observe a cycle of sunshine and Mars shadow of about the same duration as in the departure orbit in near-Earth space.

On the Red Planet Mars itself, the day-night cycle is only 37 min longer than that on Earth. The daytime sky is dark bluish in color, except in regions occasionally covered with thin, whitish clouds. Solar illuminance on the martian surface at noon may reach one-third that on Earth (about 60 000 lx). Thus, the dark/light alternation on Mars offers a Zeitgeber sequence familiar to terrestrial visitors for entraining their sleep and activity phases, and, with a gravity of 0.38 g there should be no sleep difficulties in a martian station.

If there should be native life of lower order on Mars, it would be active only during some 5 daylight hours. At night, such life would become dormant or hibernate due to the extremely low temperature (cyclocryobiology).

Mars will probably be the only target for a manned landing mission, which can be concluded from the observations and recordings of modern ground-based astronomy. The results of the US Mars probes, Mariners 4, 6, 7, and 9, and of the USSR Mars 2 and 3, are very promising. All other planets are not accessible to terrestrial visitors because of extreme hostile environments in terms of terrestrial environmental medicine. They are either too hot, such as Venus, or too cold, as are the outer planets. Venus' rotation takes 293 terrestrial days in retrograde direction. The slowly rotating planet Mercury, closest to the Sun, combines both temperature extremes; it is too hot on the sunlight side and too cold on the opposite side. Nevertheless, whatever the future interplanetary manned missions will be, the physiologic clock, running in telecontrolled terrestrial circadian rhythmicity, will play a vital role in the maintenance of health and performance capability of man in his potential conquest of space.

INTERSTELLAR FLIGHT

Some billion kilometers beyond Pluto in interstellar space, solar illuminance drops below the light minimum for reading and color vision. This is a realm of eternal night, with the Sun attaining a stellar magnitude not very different from that of other stars. In interstellar flight, which requires the third astronautical velocity (the escape velocity from the gravitational field of the Sun, in which a velocity in higher fractions of the speed of light is required), the sleep and wakefulness rhythm of interstellar space travelers must be imagined as projected against the phenomenon of time dilation [10] or prolongation [23]. Its duration might be many times longer than on Earth, but there would be no awareness

[10] Time dilation: prolongation of time. According to Einstein's theory of relativity, time would slow down for occupants of a spaceship moving at velocities approaching the speed of light.

of this because at speeds approaching that of light,[11] molecular movement slows down. This factor would affect all body functions, including the physiologic clock of interstellar travelers. Interstellar flight is still a matter for science fiction, at least in this century, whereas manned interplanetary flight as far as Mars is in the realm of reasonable, realistic science vision.

[11] Speed of light: 299 792 km or 185 971 mi/s.

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Chapter 14

PSYCHOPHYSIOLOGICAL STRESS OF SPACE FLIGHT[1]

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The term "stress" (tension) was introduced into the literature by Hans Selye. It was a designation for a nonspecific adaptive reaction in higher living beings to sufficiently strong and unusual effects of the environment: physical, chemical, biological (infection), and psychological. In a comparatively short time, use of this term began in a wider sense, independent of whether or not the stress was accompanied by classical changes in the hormonal system. Today, the term stress is used for a state of high working capacity, and an expedient mobilization of the organism's resources where factors acting on the organism potentially threaten man's working capacity and his endurance.

Psychophysiological stress is a term customarily applied to a state of stress with objectively recorded characteristic symptoms; it is evoked by factors which are not energetic, but rather *informational*. As distinct from cold, hyperthermia, penetrating radiation, infection, and other such actions, in this syndrome there is no direct intervention of "stressors" in the biophysical and biochemical processes. Signals that are insignificant in their physical characteristics carry information concerning events which are significant for man and only indirectly, through a change in the state of the brain, exert powerful effects on various functions of the organism. This definition of psychophysiological stress is in need of refinement, perhaps only the expression "significant event," inasmuch as—depending upon the facts and the personal state of the subject—an extremely wide range of environmental phenomena can become pertinent. In the first approximation, an action is termed significant which alters (reinforces or satisfies) any human need, be it hunger, thirst, self-preservation, curiosity, a striving to conform to certain ethical norms, and the like. When psychophysiological stress is caused by a shift in physical conditions of the vital activity (weightlessness, hypodynamia, acceleration), it is not the direct action of these factors on the organism which is important to reckon, but that specific "addition" to the action of weightlessness and hypodynamia induced by the brain in response to altered impulses from the internal organs and systems.

The state of psychophysiological stress is characterized by two principal features. First, as a rule, it is accompanied by involvement of the neural apparatus of the emotions. Developing

[1] Translation of Psikhofiziologicheskiy Stress Kosmicheskogo Poleta, Vol. 2, Part 4, Chapter 1, 63 pp., *Osnovy Kosmicheskoy Biologii i Meditsiny* (*Foundations of Space Biology and Medicine*). Moscow, Academy of Sciences USSR, 1972.

For the preparation of this chapter, in addition to available publications, surveys were used which were compiled for this publication by F. D. Gorbov, D. B. Lindsley, D. F. Lindsley, and R. C. Dillehay; the author extends sincere thanks to them.

well-reinforced skills in an uncomplicated situation also requires mobilization of the intellectual and physical resources of the operator, but it would be difficult to term this state "stress."[2]

Second, work on the human emotions by Lindsley [35] and other investigators made it obviously correct to speak of psychophysiological stress only in the presence of its objective symptoms in the form of shifts in the electrical activity of the brain, and in the motor and vegetative functions of the organism. Emotional stress without these objective signs does not exist in nature, no matter how vividly the subject might describe his "most powerful inner experiences."

Experience accumulated by Soviet and US astronauts during the first 10 years of the space era indicates that space flight is accompanied by clear signs of emotional stress. The various manifestations of this state, similar to the factors which cause it, have been described in adequate detail by the cosmonauts [16] and factually investigated by scientists [36]. The task before us is not essentially to summarize the available literature, but to attempt a theoretical analysis of the genesis of emotional stress, the specific characteristics of this state in cosmonauts, and methods of dynamically controlling and preventing the untoward sequelae of space stress.

PSYCHOPHYSIOLOGICAL MECHANISMS OF EMOTIONAL STRESS–EFFECT ON COSMONAUT ACTIVITY

The onset of emotional stress depends, to the greatest extent, on two factors: presence of an adequately strong need (motivation), and an estimation by the brain of the probability of its satisfaction, which were noted by Pavlov. He linked the first with inborn, unconditioned reflexes and the second with the formation and disruptions of the dynamic stereotype. Pavlov based his posture on the results of Asratyan's experiments [6], a study of the principle of systematization in the functioning of the cerebral cortex, and on the work of other coworkers. Pavlov formulated a hypothesis concerning the dynamic stereotype—a stable system of response reactions which form under the influence of a stably maintained system of internal and external signals. In his report to the International Congress of Psychologists in Copenhagen, Pavlov stated, "The processes of establishing the stereotype, of completing the establishment of it, and of maintaining the stereotype and its disruptions are subjectively varied positive and negative feelings" [43]. This concept was the starting point for an entire series of subsequent modifications.

In Hodge's opinion [25], emotions arise at the moment when the higher brain centers cannot provide an adequate response to a situation which they have perceived, or when there are doubts or fluctuations relative to the possibility of a successful response. The strength of the emotional reaction is inversely proportional to the capabilities of the higher centers of the brain to adequately respond to a given situation. The emotions, Hodge asserts, always represent unsuccessful integration at the level of the cerebral cortex [25].

Hebb [24] later developed similar theoretical propositions based on the example of activation of the nervous mechanism of fear. This mechanism is involved in the process of behavior, when the situation proves strange—partially familiar and partially unfamiliar—and not entirely comprehensible. The reaction of fear is based more on enduring a period of disagreement than on actual sensory perception of the real situation as it develops. Results of systematic experiments involving the destruction of various structures belonging to the so-called "limbic system" allowed Arnold [5] to assert that emotions appear under the influence of activating commands from the neocortex, where a "fusion of expectation with the sensory representation of a situational evaluation" occurs.

The "biological theory of emotions" of Anokhin [1] is organically linked with his general concepts concerning the functional organization of adaptive actions. The signal to involve the nervous

[2] The active state of the operator, without signs of emotional tension, has been factually investigated by the A. N. Leont'yev School at the Moscow State University (O. V. Ovchinnikova et al).

apparatus of the negative emotions is the fact of disagreement of the "acceptor of action"—an afferent model of the expected results—with afferentation concerning the real results of the adaptive act. Coincidence of the "acceptor of action" with the afferentation concerning achieving the goal leads to the occurrence of positive emotions. Incidentally, disagreement can also lead to activation of positive emotions ". . . if a reverse afferentation which signals a biologically negative effect is absent" [2]. It is not difficult to perceive that this concept, which satisfactorily explains the genesis of negative emotional stress, encounters difficulty during an analysis of the mechanisms of the appearance of positive emotions. The reason for these difficulties lies in the concept of the "acceptor of action" which assumes a prediction by the brain of only one *semantics* of the goal, i.e., that it must in fact be obtained as the result of adaptive effects. With this concept, there is no implication of predicting the *probability* of achieving the goal; consequently, the possibility of achievement exceeding expectation is ruled out.

According to Pribram, "the emotions express a relationship between perception and action. . . . The emotions are linked with the informational processes and the mechanisms of control. . . . On the basis of experience, emotions arise each time as soon as the probability of reinforcing actions seems low" [47].

Probability of Reinforcement

In the process of forming new habits, the probability of reinforcement is evaluated by the brain not only according to the quantity of reinforcements, but also by means of estimating the degree of perfection of the motor reactions on which the reinforcement depends. Demonstrative data to this effect were obtained when developing the conditioned defensive reflex in man [60].

The test subjects were given the task of pressing a button 20 s after hearing a brief tone. If a man pressed the button earlier than 19 s or later than 21 s following the tone, his forearm skin was given a painful electric shock—a discharge from a capacitor on the order of 60–90 V. The true reaction time was reported to the subject following each test run. The degree of emotional stress was evaluated according to change in heart rate. Simultaneously, the galvanic skin reflex was recorded.

By grouping those segments of the experiment which contain an equal number of sequential test runs and an equal number of painful stimuli, the resulting total deviation in heart rate from the background in these sections varies. Consequently, it does not depend merely upon the number of reinforcements. The experiments showed that the total increase in heart rate is proportional to the total deviation in time of the motor reactions from the assigned value, i.e., the degree of perfection, accuracy and stability of the conditioned defensive reflex. This rule holds true for those cases where the limits of errors (but neither their number nor the number of reinforcements) increased together with the increase in pulse and where, consequently, the dynamics of the vegetative shifts cannot be explained by habituation to the painful stimuli proportional to the increase in the total number of test runs.

The fact that the brain estimates, on a prediction basis, the probability of reinforcement according to the degree of perfection of the instrumental motor reactions is also indicated in experiments performed on animals. Preobrazhenskaya [46] elaborated a conditioned defensive reflex in dogs where raising the forepaw to a specific level and keeping it there for 10 s prevented painful stimulation of the opposite hindleg. An arbitrary sound signal was turned on 10 s prior to onset of painful stimulation by the current.

The result was the beginning of combinations of the sound stimulus with action of the current prior to appearance of conditioned motor reactions, accompanied by a sharp increase in the regularity of the θ-waves in recordings from the dorsal hippocampus, and increase in the amplitude and percentage makeup of the θ-rhythm in the total voltage spectrum of the bioelectric activity.

A quantitative analysis allowed observation of a positive correlation between changes in the total voltage of the θ-rhythm in the dorsal hippocampus (according to the readings of the integrator) and the heart rate. Both symptoms became noticeably milder proportional to the strengthening of the motor habit, which reliably frees the animal from pain. Any difficulties in accomplishing movement lead to an increase in the θ-rhythm. Preobrazhenskaya's experiments [29] are convincing, that the degree of expression of the hippocampal θ-rhythm depends not on the presence of motor activity itself, but on the degree of effectiveness of the motor acts attained in the sense of their influence on the probability of reinforcing the adaptive actions of the animal.

Informational Theory of Emotions

Based on the results of experiments which revealed the dependence of emotional stress on the probability of reinforcement, as well as on analysis of a great deal of data in the literature, an "informational theory of emotions" was formulated. According to this theory, the emotions of higher animals and man form a special cerebral apparatus which reflects the magnitude of a need and the probability of its satisfaction at a given moment [46, 61, 62]. The degree of emotional stress (E) quantitatively depends on the strength of the need-inclination, upon motivation (M), as well as on the differences between the information which is predicted to be necessary for satisfying this need (I_n), and the information which the subject has or receives (I_r). The rule under discussion can be represented in the structural formula:

$$E = -M(I_n - I_r)$$

Use of the term "information" takes into account its pragmatic meaning, which can be determined as a change in the probability of achieving a goal, thanks to obtaining a given item of information [28]. Hence, information in our case is actually the whole sum of habits and skills necessary for achieving a goal. Without doubt, the formula idealizes and simplifies the realistic complexity of the phenomena. The existence of a linear dependency of emotional stress on the magnitude of the need and the deficit (or increase) of pragmatic information is only a partial case of the possible relationships. A time factor also participates here, as well as the individual (typological) features of the subject and many other factors (including unknown factors). Finally, it must be remembered that the frequent coexistence of several needs can create a complex gamut of simultaneously arising emotions.

Nevertheless, the information theory of emotions turns out to be extremely productive in solving a whole series of disputable and contradictory problems. The relative independence of the nervous mechanisms of motivations, emotions, and estimation of the probability of achieving a goal permits a discussion of their mutual influence. Activation of the nervous apparatus of emotion strengthens the need, while an increase in the deficit or accretion of information weakens it, inasmuch as $M = E/(I_n - I_r)$. On the other hand, a change in the degree of emotional stress and in the magnitude of the need influences the estimation of probability of achieving the goal, inasmuch as $(I_n - I_r) = E/M$. Experiments [58] indicate that the distribution of reactions according to the objective probability of their reinforcement is observed only at a certain level of motivation. An increase in the need entails transition to an optimal strategy, to a predominant reaction, to a more frequently reinforcing stimulus. Hence, the formula predicts complex interrelationships between the emotional and intellectual components of human behavior.

Dependent upon the character of the motivation, whether the self-preservation instinct, or concern for comrades' lives, as well as for the equipment entrusted, or striving to fulfill a responsible assignment, or other motivation, the occurrence of emotional stress during a *deficit* of pragmatic information (when I_n is greater than I_r) determines its negative character: alarm, fear, anger, despair, and the like. Positive emotions such as happiness, delight, and inspiration arise in situations when newly received information increases the probability of achieving a goal (of satisfying a need) in comparison with the earlier prediction, i.e., when I_r proves greater than I_n.

For the occurrence of negative emotions, the lack of coincidence of the semantics of the goal (according to the terminology of various authors: the "acceptor of action," the "nervous model of stimulus," "establishments," "model of drive of the future," etc.) is quite adequate with the actually obtained results. For a positive emotional reaction, it is necessary to predict the probability of achieving a goal [15]; in this case only can positive disagreement occur, i.e., the attained exceeding the expected. It is not the satisfaction of a need (with a satisfied need any of the emotions fade away, being maintained for a certain time only due to the memory apparatus), but the presence of a need with simultaneous increase in the probability of its satisfaction leads to a positive emotion which is actively maximized by the subject. It is precisely this which actively stimulates higher living beings to disrupt their homeostasis and to strive toward unsatisfied needs and situations in which actual reinforcement can exceed its predicted probability.

The information theory of emotions allows clarification of a very important moment in the mechanism of competitive needs (motives) during the formation of goal-directed behavior. Factually, it is precisely the emotions, not the motives or an estimation of the probability of achieving a goal, which have the functions of the mechanism capable of subordinating a predominant need to real time, and orienting behavior to its immediate satisfaction [59]. Inasmuch as the informational component of one emotion can exceed the informational component of a second significantly more than the second need exceeds the first, behavior is oriented to satisfying the original weaker need: "a bird in the hand" takes precedence over "two in the bush." Such a property of emotions must be compensated for by a special cerebral apparatus which counters the emotions and offsets their negative influence. Such an apparatus actually developed in the process of the long evolution of living beings. At the level of the human higher nervous activity, it is the physiological mechanisms of the will.

Freedom Reflex

The "freedom reflex" described by Pavlov serves as the phylogenetic precondition of willed behavior. In opposing the animal by limiting his motor activity, Pavlov saw considerably more than a single variety of the protective reaction. The freedom reflex is an independent form of behavior for which an obstacle serves as no less an adequate stimulus than food does for the food-obtaining search, or pain for the defensive reaction, while it is a new and unexpected stimulus for oriented behavior. "If it did not exist [the freedom reflex]," wrote Pavlov, "any of the smallest obstacles which the animal would encounter in its path would completely interrupt the entire course of its life" [42].

The presence of a genetic component, doubtless, does not diminish the vast significance of ontogenetic influences of education which are capable of significantly developing, strengthening, or, on the other hand, suppressing the will qualities of a personality. The dependence of will upon a motive which primarily initiated conduct shows that will, as such, does not have a self-contained social value inasmuch as this value is determined by the essence of motives which drive man.

The activity of the mechanisms of will in man require reactions to "internal interference" (for example, competing motives), as well as the participation of consciousness, which perceives freedom as a cognitive necessity. Deviation from this recognized necessity is perceived by the subject as non-freedom and activates mechanisms of willful effort.

Hence, with the presence of a need, an obstacle in the path of its satisfaction activates two independent cerebral mechanisms: the nervous apparatus of the emotions and the structures of the "surmounting reaction," which, on the human level, form a cerebral mechanism of will. In the organization of goal-directed behavior, these two mechanisms play significantly different roles. The positive significance of the emotions is included in the hypercompensatory mobilization of the energy resources, as well as a transference to those forms of reaction which are oriented to a wide circle of probably significant signals (dominant reactions). Generalizing the search for an escape from the situation, the emotions contain the danger of deviating from the goal, the danger of a blind groping at variants by the method of trial and error. In this regard, the will compensates for the vulnerable aspects of emotional stimulation, preventing it from making a disorganizing generalization and enabling maintenance of the basic goal. On the other hand, willful conduct can be a source of positive emotions even before the final goal can be achieved, as a result of satisfying the drive to overcome obstacles itself. For this reason, a strong will combined with an optimal level of emotional stress proves the most productive for human activity.

Compensatory Function of Emotions

The informational theory of emotions permits an answer to the question of the role of emotions in the organization of goal-directed behavior. The occurrence of emotions in a situation of pragmatic uncertainty indicates the compensatory significance of the emotional states. It should be emphasized that an emotion is not and cannot be a source of new information. Liquidating the information deficit occurs in the process of searching actions, in reexamination of memory cells, and in learning. The role of emotions is, in fact, included in compensation, in an urgent substitution for missing knowledge. This compensatory function of the emotions takes place in varied forms:

1. In connection with a lack of clarity in the prediction concerning the real amount of energetic provision for upcoming actions, activation of the vegetative functions, as a rule, has an excessive character.
2. For emotional stress, a presumable reaction to signals whose probability of reinforcement is slight is characteristic. In a state of fear, a man frequently responds with the defensive reaction to any environmental changes, including response to stimuli encountered for the first time in his life.
3. Many emotions are accompanied by a transition to imitative behavior. When the subject does not have data or time for an independent and thoroughly thought-out decision, he must base his behavior on the example of other group members. Signals of the emotional state serve as additional means of communication between members of a society. It is not by chance that human speech becomes more emotional as the logical arguments of the speaker become less effective.
4. Activation of the higher brain regions during emotional stress hastens formation of conditioned reflexes and makes coupling possible, even when there is a single combination of an indifferent stimulus with a reinforcing effect.

The chief significance of the positive emotions for the organization of behavior consists of the fact that the positive emotions stimulate man to strive for unsatisfied drives and the pragmatic uncertainty. Thus, during satisfaction of the food drive the stimulating role of the negative emotions disappears at the moment of satiation. The positive emotions require variety in food, and force a search for new varieties and new combinations of foodstuffs. Specifically, the positive emotions serve as a powerful developmental factor in the conquest of new spheres of reality. The negative emotions, on the strength of their nature and mechanisms of occurrence, cannot principally fulfill these functions; they are subordinated to the rule of drive reduction.

The distinguished Soviet psychologist, Vygotsky, stated ". . . The path of determinations and classification, which has been made by psychology over the course of several centuries, has led to a situation in which the psychology of the feelings is the most fruitless and boring of all the areas of this science" [67]. The informational approach to the problem of the emotions, having had its beginning in the Pavlovian principle of systematics in the function of the cerebral cortex, opens hopeful perspectives in its development.

From the viewpoint of the informational theory, space flight includes all the conditions capable of causing quite powerful positive and negative emotions to appear, primarily related to the cosmonaut's high degree of motivation. Many motives of responsibility—for success, a thirst for knowledge, a striving to achieve the assigned goals, and in certain cases, care for the safety of the crew and the favorable completion of the flight—serve as a natural basis for emotional stress. On the other hand, unavoidably inherent in space flight are the elements of pragmatic uncertainty, novelties, the necessity to make alternate decisions, i.e., that "informational component," which is important for the genesis of emotional states.

That the effectiveness of accomplished work is dependent on the degree of emotional stress has been established by experimental investigations. According to the Yerkes-Dodson rule, for each type of activity there is an optimal level of stress during which this activity occurs most successfully. In emotional stress, both an increase, and a decrease (indifference, loss of interest, sleepiness) lead to a worsening of results. In addition to the quantitative characteristics of stress, a vast role is played by the sign of the emotion as well as by the nature of the drive (motivation), on the bases of which the given emotional state appears. Unfortunately, the dependence of the effectiveness of actions on the qualitative aspect of emotional stress has received less detailed study than the dependence on its strength. At present it can only be pointed out that of all the known states, the most productive has been found to be the positive stimulus, brought about by interest in the very process of the work being accomplished and linked with satisfying a drive for creativity, in a nontrivial solution of even the most common assignments.

Emotional Stress Levels

An optimal level of emotional stress is also necessary for the formation of new conditioned-reflex connections and for recognizing signals which already have pragmatic significance. The systematic investigations of Gershuni and others [18, 23] have established that in the presence of a stimulus which has the value of a signal, there is an increase in the sensitivity of the analysor systems. This sharpening of sensitivity is characteristic only for certain degrees of activation, because both a decrease and an increase in stress are accomplished by an increase in thresholds, particularly when there is concern with recognition of complex (including verbal) numerical symbols [41].

The presentation of words having emotional significance for the observer, with an increasing brightness of illumination or gradual increase in exposure, has shown that the threshold of identification of these words, as a rule, is higher than with that of neutral words. Inasmuch as accurate experiments have established the possibility of vegetative (for example, galvanic skin) reactions appearing only following identification of a signal, this instance cannot be termed the so-called subsensory reaction. Delaying the spoken response to an emotionally significant word, apparently, should be interpreted as a "psychological defense" from signals which are unpleasant to the observer. In this regard, the data of Kostandov [30] are quite interesting; in an experiment he found both an increase and a decrease in the thresholds of reproduction of emotionally colored words in comparison with indifferent words. Since in normal subjects the thresholds of directing aural signals associated with painful stimulation of another man are, on the average, significantly lower than thresholds of detecting signals for oneself [66], a hypothesis can be stated relative to Kostandov's results.

When the emotionally significant word is addressed to the drive for self-preservation and produces the emotion of fear, it is in keeping to expect phenomena of "psychological defense," consequently, an increase in the thresholds of reproducing this word. On the contrary, when the analogous word activates a socially determined sense of responsibility for the partner, a lowering of the thresholds is obtained. The example of experiments with identification of speech signals is convincing of the need to take into account the motivation at the base of the given emotional state.

When an inadequate level of activation negatively affects the effectiveness of actions, deteriorating perception and recognition of significant signals, leading to distraction of attention and drowsiness, extreme emotional stress disorganizes the goal-directed activity of man.

Emotional stress interacts uniquely with other flight factors: physical stress, effects of weightlessness, accelerations, and similar conditions. There is reason to surmise that the exhaustion of Alan Shepard and Edgar Mitchell following completion of their lunar descent from Apollo 14 was caused not only by physical stress, but also by prolonged emotional stress during their approach to the crater Cone. Whereas during training in the centrifuge a man comparatively easily endures acceleration of 6-g, during actual flight he can lose consciousness with G-loads on the order of 4-G [57].

Hence, for productive activity, an optimal level of emotional stress is necessary. Both the breaking of stereotypes, which disorganizes man, and the depressing monotony of automatic actions equally decrease the cosmonauts' working capacity. Thus, a study of the genesis of emotional stress during flight and developing methods of objective monitoring of a man's state, as well as the means of prophylaxis of the untoward sequelae of emotional stress, comprise one of the pressing problems of space psychophysiology and medicine.

SPACEFLIGHT FACTORS CAUSING NEURO-EMOTIONAL STRESS

Motivation

The conduct and state of a man during space flight are determined by a complex system of motivations which alternate or coexist [64]. Numerous facts indicate that the emotions of a cosmonaut cannot be reduced to a sense of self-preservation, which is natural for man, but far from the only feeling and not the dominant one. The brilliant presence of mind of Lovell, Haise, and Swigert during the emergency flight aboard Apollo 13, of Leonov during the first egress, and of Belyayev during the first manual landing of Voskhod-2 have forced a reexamination of the reasons for emotional reactions during flight. The idea arose that in many cases the reason for an increase in pulse rate and appearance of θ-rhythm in the electroencephalogram (EEG) should be sought sooner in curiosity and in recognition of the historic significance of the events occurring, rather than in a (conscious or unconscious) fear for one's life. The feeling of responsibility and the striving for achievement of socially significant goals are developed so strongly in man that they lead to emotional stress, even when there is no threat to the well-being and life of the operator. For example, during launch of Lunokhod from the landing field, and at the very onset of steering it on the Moon, the pulse rate in members of the groundcrew reached 130–135 beats/min, while respiration was delayed 15–20 s.

During the ground training of cosmonauts, as a rule, they clearly accomplish their program. Radio communications are terse, strictly according to procedure, and are carried out using only the correct call signs. An analysis of the frequency spectrum of speech does not detect signs of emotional stress. The pulse increases somewhat, but this is linked with physical efforts, inasmuch as the cosmonauts are forced to perform under conditions of terrestrial gravity. The "egress" situation was perceived as a routine, although complicated training task.

Accomplishing the same program in real flight conditions proceeded against a pronounced emotional background. A delay was observed in the activity compared with the program. In radio communications the stereotype of radiogram construction is violated, and in place of call signs personal names are used. Jokes appear in the radio conversations, which are not in keeping with the situation. In spectral analysis of the words from these joking statements, a high degree of emotional stress is detected. Pulse rate at certain times reaches 160 beats/min. In contrast with the ground training, in real flight there is an increase in responsibility for completed actions in connection with difficulty, and occasionally with the impossibility of duplicating them. A man becomes increasingly perceptive to everything which seems important to him. He processes ancillary information (noise, vibration), and occasionally has a distorted concept of the situation.

Life has been convincing, many times, that of all the fundamental motivations, the most fruitful is personal orientation "to one's work." Korolev stated that the cosmonaut's perception of the upcoming flight as an achievement and act of self-sacrifice indicates his inadequate preparation. A man should have a concept of the flight as a difficult and responsible job which requires maximal mobilization of professional skill, and a creative approach to solving the tasks before him. An orientation to one's work does not, to any extent, diminish the cosmonaut's high civil incentives, his bravery, and pride in being a pioneer. But these fine ambitions must be assimilated by the satisfaction which will give the expert free reign on his professional skills and enable him to reveal his creative strengths. All experience accumulated by aviation psychology indicates that the greatest successes are achieved by a man who has experienced positive emotions from the very process of overcoming difficulties

In the genesis of the emotional state of the cosmonauts, an important role is played by motives which are linked with the assignment of roles in the vital activity of the crew as an integral social system. This relationship is clearly manifested where maximum professional responsibility and the role of the leader alternately transfer from one crewmember to another. Such a situation took place during the flight of Voskhod-2 during egress of the copilot into outer space.

The material obtained indicates that in the 7 min prior to opening the hatch of the airlock and A. A. Leonov's familiarization with outer space, his pulse rate fluctuated within the limits of 87–90 beats/min, not exceeding the value which was recorded at the same stage in the thermal pressure chamber. However, immediately following the hatch opening, the pulse rate of the cosmonaut began to increase and in 6 min rose by 60 beats/min, reaching 147–162 beats/min. As soon as A. A. Leonov returned to the airlock and closed the hatch door, his heart rate in 1 min decreased from 160 to 138 beats/min, after 2 min to 117 beats/min, and after 4 min to 91 beats/min (his preflight norm).

Another example of the physiological reactions at this same flight stage was observed in the spacecraft commander. P. I. Belyayev recorded the highest heart rate in the 7–10 min prior to opening the hatch, which coincides with the most responsible stage of his work as the crew commander. Following the opening of the hatch and A. A. Leonov's exit into space, notwithstanding that P. I. Belyayev followed his state and supervised his activity, Belyayev's pulse rate began to decrease and after 5 min reached the level noted in the pressure chamber during the accomplishment of similar operations: 94 beats/min [4]. This observation coincides with data on pulse rate increase, and increase in amplitude of finger tremor in only one of the two pilots who is actually making a difficult landing. The difficulty of the situation and the degree of risk are evaluated by both pilots at approximately the same level [40].

Estimating Probability of Achieving a Goal—Pragmatic Uncertainty in Predicting Degree of Risk

The psychophysiology of space flight clearly illustrates the informational theory of emotions. Many observations indicate a weakening in the objectively recorded signs of emotional stress proportional to formation of the dynamic stereotype of actions, and of these signs likely appearing each time the previously formed stereotype requires changes.

A number of investigations have established the dependence of the magnitude of vegetative shifts on the probability of appearance of a meaningful signal. According to Zingerman's data [71], heart rate was maximal at a probability of 1:4. It must be emphasized that the source of emotional stress does not serve as a formal uncertainty, but rather a pragmatic uncertainty, on which the effectiveness of performed actions depends. Pragmatic uncertainty predicted by the subject generates emotional stress, even under those conditions where ongoing activity is carried out in precise correspondence to the program, and where any physical stress is practically absent. Prior to his entry into lunar orbit, Borman's heart began to beat at 130 beats/min, while at the moment of the

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Moon landing, Armstrong's pulse reached 150 instead of its usual 77. In this regard, the stage of 5-min crew preparation before launching is quite characteristic. The degree of emotional stress which develops in connection with an up-coming space flight is demonstrated in Table 1 (derived from Yazdovskiy et al [70]).

TABLE 1.—*Heart Rate/Min*

Cosmonaut	Absolute numbers			Percent original value (8 d)	
	8 d preflight	4 h	5 min	4 h	5 min
Yu. A. Gagarin	64	65	108	101.5	168.7
G. S. Titov	69	69	107	100.0	155.0
A. G. Nikolayev	64	72	112	112.5	175.0
P. R. Popovich	58	56	117	96.5	201.7

The successful flight of Yu. A. Gagarin decreased the degree of emotional stress in G. S. Titov; however, a report on certain unpleasant sensations experienced by Titov had an effect on the functional state of A. G. Nikolayev. A significant heart rate increase in P. R. Popovich was related to his individual characteristics: his emotional lability and his tendency to bradycardia. In the cosmonauts who were launched alone, the pulse rate, on the average, during the 5-min preparation period, increased by 84% with respect to the initial background, while in members of multiman crews it was 34%.

An examination of the dynamics of the emotional state of crewmembers of Soyuz-6, -7, and -8 (launched on consecutive days) reveals that all crewmembers (7 men) went through practically identical training, had similar flight assignments and habitability and equipment conditions. The only difference was that the Soyuz-8 crew had participated in a previous flight. These crewmembers had decreased pragmatic uncertainty relative to the first minutes of launching, actions of G-loads, and the craft's entry into orbit as well as the transition from G-loads to weightlessness.

An analysis of pulse rate indicates that the first and second crews in the first revolutions of the flight showed significant increase in pulse rate (in comparison with preflight), and by the sixth to seventh revolutions of the flight these indicators approximated the postflight data. Heart rate in crewmembers of Soyuz-8 did not undergo sharp changes. This same crew, in the flight of Soyuz-10, demonstrated exceptional accuracy in fulfilling the unique assignment of docking with the first space station, the Salyut. The cited facts confirmed that in the genesis of emotional stress in representatives of the new profession of cosmonaut, the role of the *informational component* is extremely great.

The objective symptoms of emotional stress become even more obvious with the presence of any complicating factors in the course of the spaceflight. Yankelevich [69] modified our formula for emotional stress, introducing a coefficient which characterizes the probability of an unfavorable outcome of the situation from the viewpoint of the pilot. The Yankelevich coefficient is the ratio of the number of accidents known to the pilot to the total number of flights of the given type. At the instant of descent in the lunar module of Apollo 10, the pulse rate of Cernan increased twofold and reached 129 beats/min. Heart rate in crewmembers of Apollo 12 was, prior to launch, ~80–90 beats/min, at the moment of launch nearly 120 beats/min, and at the moment of malfunction of the power supply system, 130–140 beats/min. These data demonstrate convincingly that the pulse rate (one of the objective measures of emotional stress) can, indeed, be the sum indicator of the functioning of the *astronaut-spacecraft* system as a whole, clearly reflecting events occurring in this system, including its technical branches.

During flight of the Voskhod-2 spacecraft, similar to preceding flights of Vostok and Voskhod spacecraft, the program provided for automatic orientation of the spacecraft and automatic switch-on of the retrorocket installation. However, at the concluding stage of the flight, at the end of the sixteenth orbit, Belyayev discovered malfunction in the automatic landing system and reported this to Earth. He decided to manually guide his spacecraft from orbit and requested permission to land manually on the eighteenth orbit. Permission was granted.

An analysis of the physiological information of this period provides interesting data concerning the emotional state of the Voskhod-2 crew. A sharp increase in the commander's pulse rate, noted after 8 h 54 min, was linked to discovery of the malfunction in the automatic landing system. At the same time, the copilot's pulse rate fluctuated within the limits of 68–72 beats/min, i.e., remained practically unchanged. The possibility of making a manual descent was foreseen aboard the spacecraft; in the course of ground training, it had been worked out by the cosmonauts. The crew commander was also forced to make decisions which had not been foreseen in training conditions. Following permission to make a manual landing, the stress in Belyayev decreased somewhat (pulse rate 85 90 beats/min), and he began to orient his spacecraft.

When the commander had oriented the spacecraft and was convinced of the accuracy of his orientation, he did not hurry to select the moment for switching on the engine. The manual landing system had not yet been tested in actual flight conditions. Belyayev decided to fire his retrorockets at the beginning of the segment of the orbit passing over the territory of the Soviet Union. Notwithstanding the absence of pronounced physical stresses in this period, Belyayev's heart rate was at its highest (129 beats/min). With the firing of the retrorockets, his pulse rate decreased, although at that moment, in Belyayev's words, the crew had been actively working. It is known that the stage of atmospheric reentry, which is linked with the presence of G-loads, had been characterized by an increase in pulse rate in all cosmonauts who had previously flown.

The liquidation of emotional stress as the result of optimal actions (the craft moves toward the Earth, the engines are working normally) completely offset the physical influence of the G-loads: Belyayev's pulse rate decreased, at the same time Leonov's heart rate increase was normal for the given state of flight [4]. Hence, in the case cited, the primary condition of eliminating emotional stress was a correct and well-founded choice of actions in a complex situation. For this reason, training actions of cosmonauts during equipment malfunctions, in the most probable emergency situations which can occur in space flight, should be viewed as the most important aspect of their professional training and the most effective method for prophylaxis of neuro-emotional stress.

The working out of skills should reach a degree of perfection so that the very action being performed serves as a guarantee of optimal behavior in the ongoing situation, and does not require constant monitoring for approval by outside signals. This was well-expressed by cosmonaut Ye. Khrunov:

> Sometimes it happens that a man does everything completely correctly, but he is forced to seek confirmation that this is true. If there is no such "feedback," he becomes confused and begins to make mistakes. Another, however, does not require such "support." This, the confident one, is the future spacecraft commander.[3]

A partial case of an increase in pragmatic uncertainty is an informational excess, making it necessary to perceive signals against a background of noise which, in characteristics, is similar to the useful signal. An excessive number of requests, recommendations, and commands from the control point is also capable of complicating decisionmaking. It has been shown experimentally that in conditions of informational oversaturation, reactions to stimuli have little informational value [27], and overloading of one of the analysor systems leads to decreased sensitivity in the other analysors. These objective principles of the brain's activity must be taken into account when organizing the work of cosmonauts and during communications with the spacecraft.

Specific Characteristics of Afferentation During Space Flight

Informational (Sensory) Deprivation

In the Soyuz and Apollo flights with durations of up to 3 weeks, the astronauts encountered

[3] *Lit. Gazz.* 32 : 11, 1972.

practically no hardships of sensory deprivation. However, it can be assumed that a decrease in the influx of external stimuli and limited motor activity will be important factors in longer space flights.

Experiments at the Pavlovian school performed on animals with simultaneous exclusion of the most important analysors (sensory organs) provide a basis to predict, during sensory deprivation, a sharp decrease in the tonus of the higher regions of the brain and almost uninterrupted sleep. However, the first experiments involving participation of man have demonstrated a direct contradictory effect in the obvious signs of neuroemotional stress. The theoretical key to an understanding of the sequelae of sensory deprivation is the biphasic motivational theory of Schneirla [53], according to which living beings strive to avoid inadequate motivation as actively as they avoid extremely motivational stimuli.

Man endures with great difficulty maximum limitation of ordinary stimuli with the aid of opaque glasses, a constant auditory background, rubber silencers, seals, and immersion in warm water. After several hours, a dozing state occurs and loss of capacity to concentrate attention; there are hallucinations, eidetic images, and signs of depersonalization. After 3–4 days, subjects categorically refuse to continue such an experiment [11, 31, 73, 75].

Less strict conditions of isolation allow extension of the period of solitude. As a rule, the state of the subjects in the first 2–3 days is characterized by symptoms of emotional stress: increase in the content of 17-ketosteroids in the urine and a decrease in the α-index on the electroencephalogram (EEG). On the 6th to 8th day, a feeling of fatigue appears, with attempts to make contact with the experimenter. Secretion of 17-ketosteroids in the urine decreases. Slow waves and a long trace exaltation of the α-rhythm are recorded on the EEG following the action of light stimuli. The latent period of motor reactions increases [20]. Frequency of appearance on the EEG of the α-rhythm of the occipital region decreases proportionally to the increase in the degree and duration of isolation; there is also an increase in the θ-activity of the temporo-occipital regions. There are data concerning the presence of a correlation between frequency of appearance of the α-rhythm on the EEG and the effectiveness of the subject's activity [72, 74].

A basic source of emotional stress during deprivation is loss of contact with reality, mixing memory traces with actual sensations, an increased self-analysis, and disorientation in space and time. The test subjects cannot successfully concentrate, their clarity of reasoning decreases, and they have difficulty in organizing their thoughts. Memory and the capacity for analysis are disrupted to a lesser degree. There is relative preservation of the indicators for thinking capacity and processes of decisionmaking. There is a deterioration to the greatest extent in accomplishing those assignments which require imagination and estimation of the situation as a whole [55, 65, 76].

The influence of sensory deprivation significantly depends upon the individual prediction relative to duration of isolation, and on the degree to which the subject has been informed concerning the symptoms which appear in conditions of sensory deprivation: hallucinations, eidetic images, and the like. In subjects who expected 7 days of deprivation, the decrease in frequency of the EEG on the 7th day was more strongly pronounced than in the group of subjects who expected 14 days isolation [65]. There is evidence that repeated isolation leads to elaboration of adaptive habits, which, however, pertain primarily to the behavioral manifestations of sensory deprivation and involve the vegetative sphere to a lesser degree [75].

The primary means of overcoming sensory deprivation is the cosmonaut's activity in controlling the spacecraft, fulfilling the program of scientific investigations, and in processing their results. Investigators correctly note that the basis of pathologic deviations consists not as predominantly in decrease in afferentation, as in limitation of the number of significant signals having adequate value content [9]. It should be recalled that the measure of a signal's significance can be a change in the probability of achieving a goal, occasioned by receiving a given piece of information [28]. To combat sensory (informational) deprivation, a simple influx of supplementary stimuli is not adequate; information is necessary which maintains interest in the flight, also communication with fellow servicemen on Earth [51].

Organization of the cosmonauts' leisure time requires attention—time free from duty and scientific work. The orbital station Skylab has books, musical recordings, playing cards, and a dart board. Experience in training Soviet cosmonauts in the isolation chamber has shown that sensory deprivation is well compensated by artistic creativity: creating stories and verse, sculpturing, making models and toys [16].

Influence of Hypodynamia and Weightlessness

The influence of *hypodynamia* will also be examined only in its psychophysiological aspect, not in the general medical aspect. The minimal living space for each crewmember must be 6–7.5 m^3 (200–250 ft^3), the recommended volume, 9.8–11 m^3 (350–400 ft^3), while the desirable space during long-term space flights is 16–19 m^3 (or 600–700 ft^3) [14]. Such space for working and living quarters will make it possible to avoid extreme limitation of motor activity with its characteristic deterioration in mental activity, and the accompanying decrease in frequency of the α-rhythm on the EEG. Only 30-min daily exercise during 7 days of sensory deprivation and hypodynamia averted working-capacity disorders, and a lesser decrease in the frequency of the α-rhythm compared with a control group that had not participated in physical exercise [74]. In later Apollo flights, 1/2 h/d was alotted to physical exercise with an expander. Questions of on-board physical training of cosmonauts have received a great deal of attention in the Soyuz-Salyut and Skylab programs, experience which will doubtless be used in planning longer space flights.

The physiology of weightlessness can serve as a significant example of the nonspecific adaptation of living beings to conditions of probability of a changing environment. In the 20th century, we have witnessed twice the encounter of living beings with factors against which they could not form mechanisms of specific defense in the process of their evolution:

the effect of large doses of penetrating radiation
the state of weightlessness

It is astonishing that in both cases animal and man have proved not completely defenseless. Mechanisms of compensation developed under the influence of other environmental factors have been effective during exposure to factors not encountered in the phylogenetic past. Infrequent and short-term cases of partially altered gravitation (swimming, jumping from heights, and so forth) can scarcely be compared with minutes, hours, and days of total weightlessness. In this regard, serious warnings were expressed on the eve of the orbital flights. Human and animal organisms have coped with weightlessness substantially more successfully than we could have imagined a few years ago.

The material available shows that the physiological effects of weightlessness cannot be attributed to the influence of the absence of gravitation on any one organic system or to any reflexogenic zone. An extremely complex disorder of spatial analysis is involved, which builds up under the influence of altered impulses from the otolithic apparatus, a decrease in skin and proprioceptive reception, and relative predominance of afferentation from the semicircular canals of the labyrinths [17]. Humans can be divided into two basic groups according to the character of their reaction to weightlessness. At the beginning of the period of weightlessness, the first group experiences feelings of falling and fear, suddenly replaced by feelings of happiness, uncontrolled gaiety, and euphoria. In a majority of those observed, these emotional reactions weaken following a few periods of weightlessness, while after 5–20 training flights aboard aircraft, they practically disappear. In this category specifically, disorders of the visual functions appear later [29]. The electrical resistance of the skin decreases in the period of awaiting weightlessness and increases after the state of weightlessness becomes obvious [54].

The switch of emotions in weightlessness is of great interest to the physiologist. The feeling of fear when sensing a fall is innate in character. Three innate emotional reactions have been successfully recorded in the neonatal infant, one of which is the reaction of fear during equilibrial disturbance. The emotion of happiness is of a more complex nature. It appears as the result of a partially conscious comparison of prediction (falling, throughout the entire course of evolution, was the forerunner of a blow, injury, and death) and actual security, when the subject becomes convinced following a few seconds of weightlessness. The informational theory of emotions (which has already been described) in this case postulates the appearance of a positive emotional state which is also observed in the flight experiment.

In the second group of observed subjects, the acute feeling of falling, emotions of fear and happiness are absent; however, these subjects experience spatial illusions of flying upside down, or to one side, and similar effects which are accompanied by vegetative disorders of the seasickness type. Signs of similar illusions and symptoms of motion sickness were recorded in G. S. Titov. In the process of training, vegetative reactions (nausea, vomiting) diminish after the 20th to 30th periods of weightlessness and, as a rule, disappear after the 40th to 50th periods [29].

Once again, this indicates the high plasticity and compensatory capabilities of the central nervous system, although in certain persons adaptation does not appear. Occasionally, those resistant to motion sickness on Earth endure weightlessness well, and vice versa. To predict the reaction of a particular individual to a long term in weightlessness is difficult. The majority of cosmonauts evaluate the state of weightlessness as subjectively pleasant, if abrupt movements are not present. They state that on the surface of the Moon a man feels better than he does on Earth.

Weightlessness does not prevent accomplishment of the higher psychological functions. In a genuine emergency situation (when propellers became loose), pilots evaluated the situation in 2 seconds and made the correct decision [7]. In accomplishing tasks that require oculomotor coordination, subjects very quickly compensate for absence of the force of gravity. Although subjects affirm that it is easier to work in weightlessness, the speed and clarity of the motor reactions are more strongly disrupted than during moderate G-loads. Disorder of the normal interaction of the analysor systems leads to characteristic errors when accomplishing coordinated acts. If a man does not see his finger, it will strike lower than the intended target (the illusion of target movement downward). During acceleration on the order of 2-g, the target is struck above the intended point. When a man draws a horizontal row of figures with eyes open or closed, in a state of weightlessness he displaces this row downward. The enumerated illusions are absent in professional flyers, which again indicates the perfection of the compensatory mechanisms of motor functions in sharply altered conditions. It has been assumed that the actions of man in weightlessness will take twice as much time as on Earth. However, this time is diminished proportionally to the cosmonauts' adaptation to new work conditions. In comparison with conditions on Earth, the time for carrying out operations on the Moon increased 30%, while the duration of intricate operations accomplished using the fingers increased 50–70%.

In summarizing this section, it can be said that man's encounter with long-term (several days) weightlessness was a triumph of nonspecific adaptation and evidence of the great plasticity of the central nervous mechanisms. This does not mean that months of the influence of weightlessness will not promise us any unexpected phenomena or any principally new physiological effects. Thus, further study of weightlessness is one of the more pressing problems of space physiology.

During space flights, man encountered sensory effects unknown to him on Earth, such as flashes of light reminiscent of the discharge of lightning in clouds, which are linked hypothetically with the effect of cosmic particles. Observing flashes does not depend on the eyes being closed or open.

Identical light flashes have been successfully observed under terrestrial conditions using high-energy neutrons [8]. It was reported that monkeys exposed to cosmic rays suffered brain damage. A plan was made to place mice with dosimeters mounted on their skulls in the cabin of Apollo 17 to compare the particle tracks with histological changes in brain tissues. An investigation of the direction and density of fluxes of heavy nuclei in the helmets of astronauts aboard Apollo 8 and Apollo 12 permit the assumption that the degree of brain damage in long-term flights will be insignificant [10]. Nevertheless, this phenomenon requires further careful study.

Influence of Neuro-Emotional Stress on Duration and Quality of Sleep

In flights so far, disorders of sleep have depended upon many causes, including uncomfortable position of the cosmonaut, crowded conditions, weightlessness, and others. Even so, emotional stress remains one of the leading factors that influences the duration and inner structure of sleep.

In addition to cosmonauts' reports of their sleep before flights, their preflight sleep can be analyzed according to the electrooculogram (EOG), EEG, and ECG; during flight—according to the ECG, EEG, and respiration; and in the lunar module according to the ECG. No correlation has been observed between the stages of sleep as diagnosed according to the EEG, EOG, and heart rate. Nevertheless, recording the pulse provides an indication of calm or agitated sleep, and the general character of sleep compared with that of the preflight period. Subjective sensations of the duration and quality of sleep, as a rule, coincide with pulse changes.

Difficulty in falling asleep in certain cases forced Soviet and American astronauts to use soporifics. It is assumed that in space flight, change is not predominantly in the total duration of sleep, but in its internal structure: there is an increase in the duration of slow sleep, and periods of rapid sleep are diminished. A systematic study of sleep was planned for the mission of Skylab, to make multiple recordings of the EEG and EOG in the three crewmembers.

PSYCHOPHYSIOLOGICAL PROBLEMS OF CREWMEMBERS' JOINT ACTIVITY IN LONG-TERM FLIGHT

The task of an optimal and scientifically based makeup of crews for long flights is dictated by increased interest of specialists in problems of social psychology of small groups, and has led to a new subdiscipline termed *social space psychology* [12, 22, 50, 56]. This discipline is presently still in the developmental stage but has already succeeded in premature formalization. The fact is that, the concept of "group" might not be abstract from the essence of motive impelling the group members and goals for which people unite for joint activities.

For this reason, concern for agreement of motives (drives) of group members is the basis for the so-called psychological compatibility determined by purely empirical means. However, defects in our actual knowledge concerning human drives, and absence of reliable methods of objectively diagnosing them, do not leave any other approach besides attempts to explain the relationships between people by means of observing their joint activity preflight.

At the *Third International Symposium, Man in Space*, in Geneva in 1968, I. F. Kubis suggested that lie-detection methods be used for revealing latent ill-will among prospective flight participants. Emotionally significant questions cause strong reactions if they are asked in the presence of a person who inwardly is not favorably disposed toward the candidate being examined.

Experience has shown that an important factor for successful crew activity is agreement between formal and informal leadership. Specific work in space does not allow it to be structured on formal discipline, which is adequate, for example, for military units where unquestioning subordination to the commander is ensured by a sense of duty and by regulations. The presence of two leaders in a small group can significantly complicate its activity. With the goal of revealing the informal leader and the number of leaders in a single group, Gorbov developed an experimental methodology which has been successfully used in the field of space psychophysiology [19, 21].

To clarify relationships among crewmembers under prolonged isolation, a useful, objective method was continuous recording of attempts to make contact, whether by word, touch, or smiling. The experiment, at the McDonnell Douglas Co., did not detect correlation between the number of such attempts and the content of 17-ketosteroids in the urine of the subjects, in addition to the high correlation between these indicators and the potassium and sodium equilibria in the blood.

In recent years a great deal of attention has been paid to the problem of "personal space," necessary temporary isolation from other crewmembers and from observation from Earth. With these goals in mind, the orbital station, Skylab, had three isolated cabins for sleep, with no television cameras. Decreased interpersonal contacts and the related emotional stress are provided by steady work-rest cycles—some crewmembers work and others rest [13]. However, too firm a shift schedule throughout the entire flight is undesirable since it could lead to formation of isolated subgroups within the cosmonaut collective. A cosmonaut already adapted to an altered circadian rhythm, when paired with a rookie, will permit the rookie to adapt to the new working conditions.

The principles of social psychology are applied to the relationships between the spacecraft crew and the ground support group. It has proved expedient to bring the cosmonauts themselves to the control points for work, particularly those who are personally close to the crewmembers making the flight.

Commands from Earth, their content, tone, and emotional coloring, have great significance for those for whom they are intended. As a rule, preference is for brief, business-like recommendations rather than long, detailed instructions. At the Manned Space Flight Center, Houston, all conversations with the spacecraft are carried out through one man—an astronaut by profession, but the supervisor of each specialized group can join a separate conversation with the crew from another room. The location at the press center for all conversations occasionally creates difficulties for discussing specific medical problems with the crew.

Man's natural desire to shine in the eyes of his colleagues on Earth in a specific manner again indicates the necessity of objective monitoring of the state of the cosmonauts.

MONITORING AND PROPHYLAXIS OF NEURO-EMOTIONAL STRESSES IN COSMONAUTS

The best indicator of a cosmonaut's flight readiness, stability, and reliability remains the results of preflight professional activity; accuracy and time of fulfillment for operations, expenditure of fuel, and the like. Nevertheless, the necessity of predicting the cosmonaut's reliability for a long flight has required special methods of selection.

The ability to withstand pain, sex, the inclination to concentrate on external or internal stimuli, have not proved satisfactory criteria of stress resistance [39]. More informative is measurement of behavioral and physiological reactions when unfavorable occurrences are expected [68], or at the moment of the experimental occurrence itself.

The state of confusion that is accompanied by bradycardia, a slowing in EEG frequencies, general hyperhidrosis, arterial hypotonia, and a decrease in the venous tone are unfavorable signs and a basis for negative expert decision.

Among the varied objective indicators of stress resistance, the data of electroencephalographic investigations attract attention. Comparing individual EEG characteristics with the characteristics of numerous persons examined by psychological tests has allowed a preliminary conclusion to be made that predominant β-activity makes possible an increase in emotionality, stress, and feelings of alarm and uncertainty. On the other hand, persons with a pronounced α-rhythm, as a rule, are characterized by activity, absence of stress, and confidence in their own strengths and capabilities [32]. The results of clinical investigations show that a dense EEG is characteristic of patients with neurotic symptoms, with phenomena of emotional instability. Persons with a pronounced monorhythmic α-rhythm also have more full homeostatic reactions (for example, to adrenaline) in comparison with patients whose EEGs record polyrhythmic α-rhythms [33]. It is assumed that subjects with dense, low-amplitude and mildly pronounced α-rhythms are poorly suited for aviation, although this is a sign, but not to be viewed as the only one [49].

The author concludes that:

Electroencephalographic data can actually be taken into consideration only in combination with other indicators of a person's individual characteristics, primarily during a comparison with the results of tests which are most adequate to the specifics of space flight. The characteristics of the morale and will qualities of a man also have great significance. In answering a question such as suitability for being a cosmonaut, social and physiological evaluations do not compete but complement each other, which has been tested and substantiated by the entire practice of preparing man for flights in space.

Professional selection and training, in its full significance, cannot replace dynamic diagnosis of the state of the cosmonaut in the process of a long-term flight with the goal of preventing sudden and unforeseen diminution of his functional capacities. Evaluating the state of the cosmonaut according to the results of his ongoing activity cannot be recognized as sufficiently effective, inasmuch as compensating mechanisms frequently enable a man to maintain a high level of working capacity up to the moment of a critical decrease in his reliability as a controlling link. For this reason, particular attention should be given to the objective analysis of involuntary vegetative and electrophysiological indicators, which allow timely diagnosis of undesirable shifts in the state of the cosmonaut, and making a decision in regard to replacing him with a standby or an auxiliary automatic device in the control system.

Monitoring the state of attention according to skin resistance to an electrical current, which would increase during fatigue and drowsiness but decrease with interest in the surroundings [34], has been suggested. A change in respiration is one of the most reliable signs of transition from a state of calm wakefulness to active attention. Although in a state of calm an extended inhalation is combined with brief exhalation, while the ratio of the inhalation phase to the exhalation phase exceeds 0:5, intense attention, on the other hand, is characterized by sharp inhalation with slow exhalation. The ratio of the phases of the respiratory cycle is less than 0:5. There is special interest in a correlational relationship between the average duration of the respiratory cycle and the average rate of processing visual information in binary digits (bits per second). The coefficient of correlation for the indicators mentioned was 0:8. In regard to changes in the surface lead of the EEG, the transition from passive observation of visual signals to active differentiation and counting [of them] is accompanied by a broadened spectrum of the α-rhythm (the predominant frequency becomes less pronounced), in addition to a stabilization of the total energy of the entire α-band according to readings of the band integrator [38]. In experiments involving differentiation of complex visual images, there was deterioration in assignment accomplishment preceded by a reliable decrease in δ-activity of the EEG and smoothing of the interhemispheric asymmetry along the θ- and α-components [48].

Recording the EEG is less productive for diagnosing emotional stress. The spectrum of the α-rhythm expands proportionally to the increase in emotional stress, while the degree of expression of the frequencies dominant in a state of calm noticeably decreases. With low degrees of stress, exaltation of the α-rhythm rather than depression is frequently observed. The spectral peak in this case does not fall, but increases, although it is displaced into the region of higher frequencies. Hence, dependent upon the degree of emotional stress both suppression of the α-rhythm and its enhancement can be observed, which has been noted by a number of authors. Comparison of changes in the α- and θ-rhythms in the same subject has shown that with adequately high stress, the θ-rhythm is capable of increasing against a background of depressed α-rhythm. It is highly probable that this is explained by a simultaneous increase in the activating and synchronizing influences on the higher regions of the brain.

A number of objective indicators were used for estimating the emotional stress of cosmonauts at segments of the flight varying in complexity and significance. The objective indicators are:

- a psychophysiological analysis of the cosmonaut's behavioral and professional reactions [26],
- state of cardiovascular and respiratory systems [3],
- intonational (spectrographic) characteristics of speech.

For control material, reports were used which were sent to the flight-control command point by regular radio and television, telemetric data of medical monitoring, and tape recordings of radio conversations between crews and the Earth.

Heart rate proved to be the most informative of the vegetative indicators. This indicator has high resistance to various types of interference of technical origin which appear during the reception of physiological information from space. During use of the cardiac rhythm for objective monitoring of emotional stress, it is necessary to take into account its dependence on various conditions of the human operator's work—dependence on physical, operator, gravitational, and other types of loads.

Analysis of the experimental data shows that with exposure to long-term transversely directed accelerations, neuro-emotional stress is caused by carrying out operator activity. This causes a decrease in the absolute magnitude of the maximal and minimal values of the cardiac cycle intervals, determined at each segment of time equal to the duration of the respiratory cycle; there is also a decrease in the scale of values of the cardiac cycle determined at the same time interval. With an increase in the value of acceleration, there is a tendency for the signal to decrease; with large values of G-loads it decreases to zero. Hence, the cardiac activity can be an indicator of human neuro-emotional stress only in a certain range of G-load action. With a subsequent increase in G-loads, their influence on the cardiac activity masks the neuro-emotional factor.

Analysis of the acoustic characteristics of speech has been used successfully in recent years for estimating the degree of emotional stress [38, 44, 45, 63]. This method has a number of advantages, specifically the absence of contact sensors, the possibility of using ordinary communications channels with the spacecraft, and the hidden nature of the recording. The method of formant frequency [44] allowed correct differentiation of the degree of emotional stress in 85% of all cases, not requiring separation of specific sounds, which is significant in actual conditions, especially in the presence of static interference. A high correlation was noted in shifts in heart rate with voice changes caused by emotional stress during space flight. Dissociation of these two indicators, as a rule, indicates that an increase in pulse rate is related not to the emotions, but to the purely physical load.

The formant method does not permit determination of the character of the emotional stress, which could be positive (enthusiasm, happiness) or negative (alarm, dissatisfaction, fear). Accordingly, additional investigations were carried out regarding the envelope of speech signals at the outputs of five octave filters, which allowed differentiation of positive emotions from negative emotions in 90% of all cases where emotional stress was diagnosed. Supplementing this method with an analysis of the dynamics of the formant maximum in time makes it possible to decrease, and with adequately high degrees of stress—to exclude the influence of voluntary and involuntary speech distortions appearing in connection with a change in its tempo (rapid talking, slow speaking).

The state of attention in the process of operator activity is characterized by stabilization of the spectral components and by a decrease in the probability of displacement of the formant maximum in comparison with the state of operational calm [63].

Methods of prophylaxis of undesirable emotional stress are determined by its dependence on drives and the deficit of pragmatic information. Hence, efficient training of cosmonauts requires, on the one hand, inculcation of the corresponding motives, while on the other hand it requires maximal saturation with pragmatic information by means of acquiring the most varied skills necessary in both ordinary space flight and in emergency situations. An excess of information disrupts the negative emotion from within and leads to its replacement with positive emotions of confidence, presence of mind, and happiness at having overcome the encountered difficulties.

A strong urge to victory in the successful fulfillment of an assignment and a striving to perfect professional skill are factors capable of supplanting such needs as the self-preservation instinct, concern about rank in the group hierarchy, and other secondary motivations, which are the bases for the negative emotions of fear, petulance, and hostility (toward crewmembers). The orientation of personality "to one's work" (already mentioned) is the most productive motivation when accomplishing difficult and responsible assignments. In answer to a correspondent's question concerning stimulative motives for cosmonaut activity, Ye. Khrunov stated, ". . . the cosmonaut is primarily motivated by interest in the new—the possibility of working on new equipment, of solving new tasks—and by natural human curiosity. If, however, we are concerned with ambitions, then it appears that a man who is ambitious should not be entrusted with any responsible assignment."[4]

It can be affirmed confidently that space flights will, for a long time (if not forever), contain inherent significant elements of uncertainty, probability of encountering new unforeseen situations, and an increasing responsibility for the successes of the joint efforts of many individuals. This projection involves the emotions as constant participants in the conquest of space, while the task of monitoring the state of man, developing measures of prophylaxis, and liquidating undesirable emotional stress comprises one of the most important branches of the psychophysiology of space operations.

In the future, the working out of this problem will follow these main trends:

1. A deepened theoretical analysis of the origin of the mechanism of human emotional reactions, of their dependency on motives of activity and its structural (information) organization;
2. A study of the complex dialectical nature of the influence of the cosmonaut's activity (degree of skill, capability to make decisions in unexpected situations, and similar) on the emotional state, in addition to the reverse influence of emotions on the character and quality of this activity;
3. An investigation of questions between group psychology and the psychophysiology of the emotions, including the question of dependence of emotional stress on the degree of leadership, and measure of personal responsibility for the fate of the crew, and the flight as a whole at any stage;
4. Developing systems of automatically evaluating the state of a man with the aim of predicting his reliability, and making timely corrections of undesirable degrees of emotional stress. A diagram of such a proposed system is described in the literature [37, 38] and shown in Figure 1. The basic distinguishing aspect of this diagram from other widely known control systems is a special loop which makes it possible to trace the state of the human operator and controlling factors. During the development of such systems, there is particular value in contact-free objective recording of emotional reactions (speech analysis, the use of television channel).

[4] *Lit. Gazz.* 32:11, 1972.

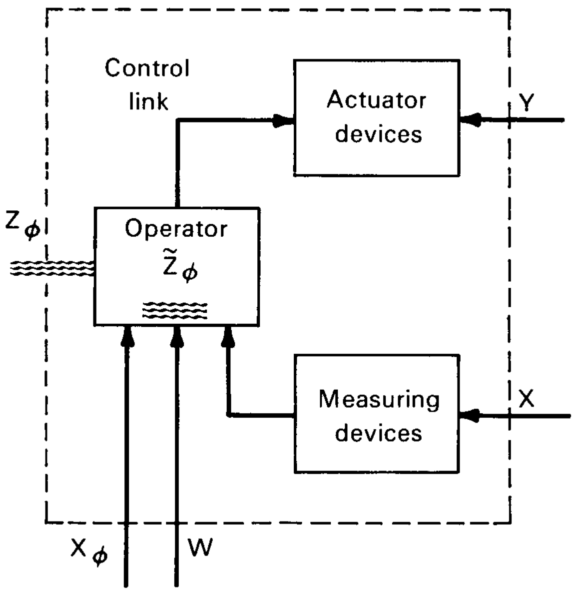

FIGURE 1.—Closed control system. The control link, in expanded form, combines the actuator devices serving to act on the object and the measuring devices designed for transmission of information concerning the state of the object (human operator) performing the operation in correspondence with goal function W. The characteristics of the control link in the presence of a human operator are essentially dependent on the functional state of the operator resulting from perturbations of the external (Z_ϕ) and ininternal ($\tilde{Z}_\phi$) medium [38].

The solution of these pressing problems should be made possible by linking the efforts of representatives from various scientific disciplines and specialists in many nations.

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Chapter 15

PHYSIOLOGY OF THE SENSORY SPHERE UNDER SPACEFLIGHT CONDITIONS[1]

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Manned space flight has made prominent a multitude of questions related to the problem of the physiology of the human sensory sphere. According to the data of Soviet and American astronauts while they were undergoing gravity changes, shifts were observed in the functioning of individual analysors (sensory organs). This was sure to be reflected in the overall resistance of the organism to the complex effect of flight factors, or in the level of work efficiency. A decline in resistance and in fitness for work was noted in most instances, which points to the practical significance of all the studies being performed concerning physiology of the sensory systems during space flight.

There are not, at present, many investigations directed toward a systematic study of the sensory sphere of man during the prolonged influence of a complex of spaceflight factors, including weightlessness. Essentially, we may include from them only reports concerning the results of space experiments carried out in the USSR and the USA. Included in this chapter are information about the isolated influence (for the most part) of certain spaceflight factors on the functional state of the analysors, as well as the results of ground-based experiments where the sensory sphere was studied with simulation of a varied level of afferentation (with limitation of visual information and an unusual working posture).

STATE OF VARIOUS TYPES OF HUMAN SENSITIVITY DURING SPACE FLIGHT

Weightlessness Phenomena

The most valuable information about the changes undergone by the sensory sphere during space flight has been obtained from the astronauts' reports. As early as the first space flight, Yu. A. Gagarin noted that toward the end of his stay in a weightless state there was "a sense of discomfort connected with the absence of pressure of the back and seat of the chair on the human body" [60]. A similar sensation was indicated by other astronauts. Thus, most crewmembers of the Apollo 7 to 11 spacecraft did

[1] Translation of: Fiziologiya sensornoy sfery cheloveka v usloviyakh kosmicheskogo poleta. Vol. 2, Part 4, Chapter 3, *Osnovy Kosmicheskoy Biologii i Meditsiny (Foundations of Space Biology and Medicine)*, 79 pp. Moscow, Academy of Sciences USSR, 1972. The authors wish to express their gratitude to Professor James R. Lackner for his extensive work in compiling the American and other works devoted to the problem of the physiology of the human sensory organs, which greatly facilitated the writing of this chapter.

not feel the weight of various objects and of clothing [19]. Such phenomena are evidently conditioned by a change in the kinesthetic sensations as a result of removal of the stimuli of the tactile mechanoreceptors which are usual for terrestrial conditions. In the more pronounced cases, the astronauts complained of pain in the legs and lower back [20, 21]. The causes are still unclear, but it may be assumed that they were conditioned by the unusual position of the astronauts during sleep (the fetal position), resulting in changes in the kinesthetic sensations.

The longer space flight of Soviet cosmonaut G. S. Titov made it possible to reveal one more type of unusual sensation. During the first minutes of his stay in weightlessness, he experienced a sensation of flying in an inverted position which lasted for about 1.5 min [160]. A. G. Nikolayev, P. R. Popovich, B. B. Yegorov, K. P. Feoktistov, and G. T. Beregovoy [154, 161, 196 206] experienced sensations which were the same in character, but of different duration (minutes or hours). During the transition from G-loads to the state of weightlessness, most US astronauts who participated in the flights of Gemini and Apollo spacecraft noted a feeling of heaviness in the head similar to that in a person on Earth hanging with his head down. The phenomenon was temporary in character, and had no influence on the spatial orientation of the astronauts [19, 20, 21]. Explanations for these phenomena are quite contradictory. They are considered by some to be the result of redistribution of blood, that is, congestion in the head [19, 20]. Others consider them a disorder of systemic functioning of the analysors which reflect space, as a result of change in afferentation from all the mechanoreceptors, and chiefly from the otolithic part of the vestibular apparatus [47, 56, 98, 200]. Both viewpoints apparently are valid to a certain extent, although the latter has certain advantages.

The cosmonauts noted that illusions are intensified during rapid head movements and are analogous to sensations during action of the Coriolis forces [134, 159, 160, 196]. Astronauts who had illusory sensations during flight developed, in a number of cases, the space form of motion sickness. Motion sickness, as a rule, was expressed quite weakly, on the microsymptomatic level, and was not essentially reflected in the level of work fitness [20, 21, 90, 98, 154, 182, 183, 184]. It was observed in four of the 22 Soviet cosmonauts. Disorders of the vestibular function in US astronauts are shown in Table 1.

TABLE 1.—*Vestibular Function in US Astronauts*

Project	No. astronauts	Unpleasant sensations in stomach	Nausea, vomiting	Spatial disorientation, illusion of inverted position
Mercury	6	0	0	0
Gemini	20	0	0	0
Apollo	27	6	2	3

Appetite. Data about changes in appetite were obtained during the flights. G. S. Titov reported absence of appetite, and V. F. Bykovskiy and V. V. Tereshkova mentioned reduced appetite for sweets and a desire for foods of pungent taste. There was substantial change in appetite when the space form of motion sickness developed [19, 20, 21, 159, 160, 161].

The report on characteristics of the sensation of hunger in astronauts under conditions of weightlessness should also be noted [19]. Hunger was the same as under terrestrial conditions, but occurred more rarely, even though less food was consumed. Members of one crew reported that a sensation of fullness in the stomach interfered with consumption of the usual quantity of food and drink. It would seem that the conditions of weightlessness had an effect, to a certain extent, on the receptor apparatus of the interoceptive analysor.

Visual phenomena. Subjectively, the astronauts did not note any essential changes in the visual function. Their visual acuity increased in a number of cases; they were able to distinguish terrestrial reference points—rivers, lakes, roads, cities, automobiles, and groups of people, and at night to identify main streets. Their observations included the wake of moving ships on the water [19, 20, 21, 36, 140, 154, 160, 161].

Hypotheses have been proposed concerning the psychophysiologic mechanisms of the phenomenon described. Leonov and Lebedev [117] consider that an illusory feeling of cognition occurred in the astronauts due to euphoria from a decreased amount of impulses from gravireceptors and proprioreceptors in weightlessness. In the opinion of White [193], improved vision in weightlessness is caused by increased frequency of physiologic tremors of the eyeballs. The more probable hypothesis of Petrov [143, 144] presumes that the high resolving power of vision in astronauts may be caused by two factors: a considerable degree of initial visual acuity, and discrimination of objects according to secondary signs, that is, imagining the objects. For example, seeing the traces of the wake of a ship in an open sea, in the form of an acute angle, an astronaut distinguished the ship as well.

Color. The astronauts, as a rule, in all reports mentioned the broad range of colors observed in flight when they examined terrestrial objects and the sky. However, their descriptions differ. Yu. A. Gagarin reported that the stars seemed to be surrounded by a sky-blue aureole, P. I. Belyayev noted a red halo, and J. Glenn did not see any aureole [156]. There are similar differences in the description of the color of the Earth's halo and the surface of the Moon. Crewmembers of Apollo 10 spacecraft saw the surface of the Moon as tinted primarily with a brown color; F. Borman, commander of Apollo 8, asserted that it was of a gray color, and so forth. Thus, color perception in space is not the identical process as is color perception on Earth. An understanding of its mechanisms requires further study and is probably connected not only with the peculiarities of the physiology of vision, but also with external lighting conditions of the objects at the moment of observation.

Flashes/optical patterns. The astronauts also stated that during flight they observed flashes of light (stripes, dots) at a frequency of 1 flash/2 min, both when eyes were open and closed. The mechanism of this phenomenon is still unclear. Researchers are, for the most part, inclined toward the opinion that the flashes (photopsia) are caused by an external source of radiations, evidently of cosmic origin.

The astronauts' own reports during space flights have been augmented with experimental materials concerning the state of the human sensory sphere. Popov, Boyko [147], and Ivanov et al [85] studied visual acuity and the operative visual work-fitness in cosmonauts V. M. Komarov, P. I. Belyayev, A. A. Leonov, and B. B. Yegorov during space flights by means of focusing patterns in the form of dashed lines, which were pasted into the cosmonauts' on-board log and viewed from a fixed distance of 300 mm. The selection of patterns included 25 focusing patterns with different frequencies of dashes, making it possible to test visual acuity within the limits of 0.3 to 2.2 units. It was found that there were practically no changes in visual acuity.

The level of operative work-fitness was studied by means of a set of the same dash-shaped focusing patterns. In this case, the optical pattern was determined in which the astronaut was able to see not only the direction of the dashes, but also to count their number. The operative visual work-fitness of all the cosmonauts decreased. For working, the cosmonauts selected focusing patterns averaging 20% higher than their threshold of vision, the only exception being B. B. Yegorov. For him, this number was close to 43%. Ivanov et al [85] believe that the cause is discoordination of movements in a group of the oculomotor muscles. These same experiments established that in the cosmonauts, the subjectively evaluated brightness of the colors examined decreased notably: P. I. Belyayev averaging 26% and A. A. Leonov averaging 25%.

Yuganov et al [206] and Volynkin and Vasil'yev [181] reported the results of vestibulometric studies during the flight of the Voskhod spacecraft. The excitability of the vestibular apparatus with respect to a galvanic current was determined. There were no changes of the threshold noted under these conditions. However, the authors note that, because of the small number of measurements, it is not possible to derive final conclusions.

An analysis of the material which has been presented points to the conclusion that changes occur to a certain extent in the sensory sphere when the complex of spaceflight factors is acting on man. However, the limited number of observations and considerable complexity of the flights have made it difficult to obtain the necessary

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information. Ground-based experiments, chiefly simulating individual flight factors, have provided supplementary data about the state of the sensory sphere of man under unusual conditions.

HUMAN SENSITIVITIES DURING SIMULATED SPACE FLIGHT AND ELEMENTS OF ASTRONAUT ACTIVITY

Short-Term Weightlessness Illusions

Several methods are employed at present under terrestrial conditions to study the influence of weightlessness on the organism. Short-term weightlessness is produced in special elevators, swings, in devices of the "Roman tower" type, and so forth [73, 120, 121], also during airplane flights along a parabolic curve [10, 14, 15, 16, 41, 48, 49, 88, 89, 91, 92, 93, 94, 95, 96].

The studies have confirmed the observations of astronauts concerning possible occurrence of illusory sensations during transition to the state of weightlessness. Three groups may be distinguished, according to the character and acuteness of the sensory reactions. The first group includes persons who undergo no reduction in fitness for work and whose subjective state of well-being does not change in the state of weightlessness. They have no illusory sensations, and become well-oriented in space. In the second group are test subjects who have illusory sensations (falling down, turning upside down) which disappear after 12–15 repetitions of weightlessness. The third group consists of those who develop motion sickness quite rapidly and in whom signs of adaptation are observed only after 20–30 exposures to weightlessness [41, 89, 139, 211].

In subsequent studies, refinements were introduced into this classification. It was established that the acuteness of illusory sensations depended on flight experience of the test subjects and positioning of the human body in the working site, and the physiologic mechanisms of the illusion of being turned upside down were discovered [64, 91, 92, 93, 94, 95, 96]. Thus, in the experiments of Kitayev-Smyk with 193 participants (92 were aviators or parachutists), under the influence of weightlessness lasting 21–30 s, in 25% of the persons who lacked flight experience spatial illusions were not observed. In 16%, at the beginning there was a sensation of falling and sinking, accompanied by fear, changing after 3–5 s into a sensation of pleasant lightness, "floating," and happiness. In 52%, the test subjects did not feel the absence of the Earth's attraction but a change in its direction, i.e., they felt that they were lying on their chests, backs, and sides. The illusions continued for as long as 26–30 s with a weak, negative emotional coloring. In 7% of the cases, both illusions of falling and of turning upside down were observed, which evoked strong fear and disorientation in space. In most of those with flight experience, the illusions were insignificantly acute.

Visual illusions. In another series of experiments with 28 participants, test subjects were either in darkness or in daylight. Under conditions of short-term weightlessness, they were shown various figures—in the dark, bright figures; in the light, black figures against a white background. Illusory sensations observed in 19 subjects were:

- increase in dimensions of the figure (12 persons)
- movements of the figure (seven persons)
- distortion of the shape (13 persons)
- appearance of a violet halo around the bright figure (four persons).

As a rule, the illusions appeared during the first seconds of weightlessness.

TABLE 2.—*Frequency of Illusory Sensations in Test Subjects During Flights Producing Short-Term Weightlessness (in Percentage of the Number of a Given Group)*

Group of test subjects	Consecutive number of weightlessness regimen										
	1	2	4	6	8	10	12	14	16	18	20–30
Aviators	82	70	32	12	10	6	2	—	—	—	—
Nonaviators	100	70	54	54	43	30	19	16	14	11	10

Kolosov [96] studied sensory reactions by analyzing subjective accounts and special questionnaires. Forty-one persons (30 were aviators) were examined. In the 950 flights carried out, there were 3010 regimens of weightlessness produced (each regimen was 20–37 s). The frequency of illusory sensations in the test subjects is shown in Table 2.

Labyrinth illusions. The studies of Graybiel and Kellogg [64] aimed to establish conditions under which the illusion of turning upside down occurs. In short-term weightlessness during an airplane flight along a parabolic curve, they compared the indices of sensorimotor coordination in persons with normal and imperfect functioning of the labyrinth, in three variants of the experiments:

position of free floating
position of limited movement
"standing" position with reference to the cabin floor.

The experiments showed that none of the test subjects with imperfect labyrinth functioning experienced illusions of turning upside down, while some of the healthy persons experienced the illusions in all variants of the experiments. The authors consider that the otolithic receptors are responsible for the genesis of the illusions. Head movements in weightlessness lead to a normal but weakened stimulation of the semicircular canals and to completely altered stimulation of the otoliths. In experiments with rabbits, Yuganov et al [213] demonstrated that the ocular musculature tone declines under conditions of weightlessness. Their hypothesis is that movement of the projection of the visual after-image in space under alternating influences of G-loads and weightlessness is determined by vertical displacement of the eyes resulting from reflex influences from the otolithic apparatus.

Later, Miller and Graybiel [131] utilized the specific otolith-function index for counterrotation of the eyes during changes of position in space to make it clear that the duration of otolith stimulation declined as gravitation was reduced. Persons with reduced labyrinthine functioning (deaf-mutes) showed significantly decreased reaction compared with healthy persons. After laboratory simulation of orbital flight, Johnson et al [86] concluded that stimulation of the otoliths during weightlessness, in the absence of changes in linear acceleration, may cause disorientation and illusions during flight.

The literature contains contradictory data on the frequency of sensory disorders. Vertigo was observed in 25 of 47 persons [52], and during parabolic flight, 50–60% of test subjects experienced vertigo and nausea [41]. However, Yuganov et al [211] found unpleasant sensations in only one of 39 test subjects during flights under conditions of weightlessness, which is explained by the participants being absolutely healthy fliers.

Vestibular apparatus illusions. Sufficiently complete information concerning the function of the vestibular apparatus has been obtained in airplane flights along a parabolic curve. Under conditions of short-term weightlessness, the thresholds of sensitivity to galvanic current increased (by 0.5–67 mA), duration of postrotational nystagmus was shortened (by 1–17 s), duration of counterrotation illusion was shortened (by 1-12 s), and the latent period of illusion of rocking was lengthened (by 7–16 s) [204, 210, 212, 217]. It was concluded that under conditions of weightlessness there is a pronounced change in the excitability of receptor formations of the semicircular canals. The hypothesis stated is that such changes are conditioned by inhibiting influences on the semicircular canals from the otolithic apparatus. The authors note that study of the problem concerning interrelations between otolithic and ampullar apparatuses is far from complete. It was possible to show some dependence only by analysis of the vestibulomotor reactions (nystagmus and others). Further studies are necessary, taking into account the vestibular-vegetative reflexes and sensory reactions [202, 204, 205].

Gorshkov [54] determined the sensitivity thresholds of the otolithic part of the vestibular apparatus to linear accelerations, which increased under conditions of short-term weightlessness. While the threshold of sensitivity under terrestrial conditions fluctuated within the range of 0.005–0.01 g, the threshold of electrical excitability was 2.0–4.5 mA, under conditions of weightlessness they were 0.005–0.05 g and 3.5–5.2 mA, respectively. These changes are explained in terms of peculiarities of the intracentral dominant relations. Weightlessness is a minus stimulus [202], which creates such a high level of excitement in the otoliths that the stimulation must be of great strength to evoke an illusion of rolling or movement.

Kopanev and Kolosov [102] confirmed that the excitability of the vestibular analysor decreases under conditions of weightlessness, and at the same time, introduced some refinements. In persons resistant to the weightlessness factor, an increase of the thresholds was regularly observed, while in those not resistant to weightlessness, the excitability thresholds increased only moderately if at all, and in some cases, declined.

Insignificant deviations in perception of a vertical line are observed in humans during a short term of weightlessness [77]. Sasaki [154] found that depth perception decreases during parabolic flights. Careful studies by Kitayev-Smyk [91, 92, 93, 94, 95] showed that visual acuity did not change substantially during short-term weightlessness. At a high level of tone saturation, color sensitivity increased toward red and yellow; at low saturation, chromatic sensitivity declined. Reactions of the eye muscular apparatus varied during short-term weightlessness. In most cases, there was an increase in accommodation capabilities and a decrease in the ability to attain maximum convergence.

The functional state of the motor analysor has also been studied during airplane flights along a Keplerian parabolic curve where short-term weightlessness was produced, and in various high-speed elevators.

Motor Activity and Coordination

Scientists, many years ago, attempted to represent the nature of man's motor activity in weightlessness. In 1883, Tsiolkovskiy [175] pointed out that in "free space" (under conditions of weightlessness) there would apparently be changes in the leg functions as a supporting apparatus. Primarily, they would carry out "grasping movements, like those of tensors to maintain a position" or would serve to "push things away." Later, Haber [7] noted that the absence of weight would seriously change sensorimotor coordination due to destruction of interaction between the visual, tactile, and motor analysors. The possible onset of disorders in the coordination of movements was also indicated [4, 45]; when moving under conditions of weightlessness, man would develop excess energy, corresponding to the terrestrial stereotype of movement but inadequate for new conditions. These disorders would disappear quite rapidly as a result of compensatory reactions. The hypotheses were subsequently substantiated experimentally.

Studies were made in producing weightlessness in a "Roman" tower designed by Lomonaco et al [120, 121], and Gurfinkel' et al [73], in the high-speed elevator of Moscow University. Motor coordination was monitored in 30 healthy persons under the influence of weightlessness for 1.7 s. The test subjects, each at his characteristic rhythm, was required to hit a target 15 cm in diameter with a pencil. In comparison with the control tests, in these subjects a scattering over the entire target was noted, which decreased considerably as the task was repeated in a state of weightlessness. To elucidate the role of stimulations to the vestibular apparatus when precision of the movements varied, the same studies were carried out on five deaf-mutes in whom there was less discoordination of movements. This pointed out the importance of the labyrinth function in the genesis of motor disorders.

In other experiments [73], the test subjects also hit a target, but there were no essential changes in precision. One of the limitations of the experiments described was the short time of weightlessness (no longer than 2 s) which alternated with accelerations. This made it extremely difficult to analyze the material.

Parabolic Flights and Related Experiments

More complete information on the character of motor activity under weightlessness conditions was obtained during parabolic flights. During weightlessness of 15–25 s, Grossfield

[70] and Ballinger [10] observed difficulties the test subjects had in hitting a target with their hands, and failure to do so in individual cases. In other tests [14], the experiment was somewhat complicated. The test subjects, eyes open or closed, drew crosses along diagonal lines from top to bottom in special squares. While the test was entirely satisfactory under terrestrial conditions, the test subjects, without control of vision in weightlessness, in most cases after the third image, deviated from the line they were drawing by 90° toward the upper right corner. Such changes could be explained by domination of the muscle tone raising the arm.

Similar data were obtained by Gerathewohl [50, 51] in studying the accuracy of hitting a target. In a state of weightlessness, the test subjects hit a point approximately 1 cm to the right and above the target. Discoordination of movements was more pronounced at the beginning of weightlessness, and compensation for the disorders began after five or six repetitions. Signaling from the tactile and visual analysors evidently plays a definite role in the development of this compensation.

A more complete study was undertaken by Yuganov et al [196, 210, 212, 213] on the nature of motor activity under conditions of short-term weightlessness. The muscular power of wrists, coordination of movements during writing tests and while working on a special coordinograph, precision with which definite muscular efforts could be maintained, and the bioelectric activity of musculature during static and phasic movements were recorded. Muscular force was determined by a hand dynamometer. The coordination of movements was studied by means of two types of coordinographs, one of which was a device of five clusters (contacts), which the test subjects hit with a metal pencil. The other was a panel with six targets, each target consisting of rings with different resistances. Whenever the electrode (located in the index finger of the glove) hit the target, a signal of corresponding magnitude was transmitted to the recording instruments. The prescribed muscular effort of 750 g was generated and maintained on a special dynamograph. The test subjects, visually monitoring their own actions, squeezed a lever with the right thumb and with eyes closed, maintained the effort throughout the period of weightlessness.

The studies, carried out with 26 test subjects, established that in 82% of the cases, of 266 measurements, the magnitude of the muscular effort declined by 4–22 kg when there was an initial magnitude of 45–65 kg. During flights along a parabolic curve, the decrease in the astronauts' muscular effort was somewhat less: for the right hand, by 6–12 kg, and for the left hand, 4–12 kg [88]. The same general pattern of changes was maintained when the test subjects were fastened to their work sites and when allowed to float freely in the aircraft cabin. The authors explained such shifts in terms of a lowering of the musculature tonic tension, which was confirmed by data on the nature of changes in muscle bioelectric activity. As a rule, under conditions of weightlessness, a decrease was noted in amplitude of the neck muscles and hip flexors and extensors [209, 210, 213].

Data of "writing tests" indicated that short-term conditions of weightlessness have no essential influence on the handwriting of most test subjects. This was explained, in large part, by the test subjects being fastened firmly to their working sites during the flight experiments.

Muscular Efforts

Measurement of precision with which specific muscular efforts could be maintained is shown in Table 3. In weightlessness, only four of 14 persons could maintain the precision of static work practically unchanged; in the remaining 10, an error of 150–1250 g was observed when the given effort was 750 g. Such a phenomenon is considered the consequence of the fact that man does not expend efforts to perform static work to hold up his hand in weightlessness, and in connection with this, the magnitude of the specific effort increases 1.5–2 times in relation to the initial magnitude [211]. Signs of adaptation were revealed during repeated study. During the first seconds of weightlessness, the test subjects were practically unable to reproduce a prescribed effort of 500 g (fluctuations from 0 to 400 g), but after repeated flights, the error in reproduction amounted to approximately 30–40 g [25]. Table 3 shows the state of the time reflex (performance of a time test during 20 s). It became clear that, under conditions of weightlessness, the reflex time is shortened in most of the test subjects (10 of 14).

TABLE 3.—*Test Subjects' Maintenance of Prescribed Muscular Effort (750 g) and Time Reflex (20 s) under Terrestrial and Short-Term Weightlessness Conditions*

Test subject	Muscular efforts (g)			Time characteristics (s)	
	Terrestrial conditions	Weightlessness		Terrestrial conditions	Weightlessness
		Flight 1	Flight 2		
1	750	750	1200	20.8	15.8
2	760	750	—	20.5	19.8
3	750	800	750	21.0	21.7
4	750	850	750	19.1	19.8
5	780	900	1000	19.0	14.4
6	750	1000	—	19.5	19.1
7	750	1000	—	19.0	18.4
8	750	1000	900	18.1	17.4
9	750	1000	900	20.0	17.4
10	750	1200	1200	20.0	19.1
11	750	1200	1000	20.2	20.6
12	750	1300	1200	21.1	17.8
13	780	1700	—	19.0	20.2
14	750	2000	1500	21.0	19.7

Motor Disorders

Animal experiments were performed to clarify mechanisms by which motor disorders develop. With rabbits and dogs as test animals, Yuganov et al [209, 210, 213] studied the bioelectric activity of muscles in animals with intact labyrinths and in those labyrinthectomized. As a rule, the bioelectric activity of the antigravitational skeletal musculature decreased in all intact animals under conditions of short-term weightlessness, indicating changes in the muscular tone, but these changes were insignificant in the labyrinthectomized animals. Other researchers also noted that motor disorders during weightlessness were less pronounced in labyrinthectomized animals [14, 15, 16, 48, 81, 157].

Yuganov and Afanas'yev [203] found that this rule held only when considerable time had passed after labyrinthectomy and the motor disorders caused by removal had been compensated for. When this had not occurred, the animals behaved the same as the intact animals under conditions of weightlessness.

When analyzing data concerning motor disturbances under conditions of weightlessness, it should be remembered that the nature of the motor disturbances depends on the degree to which they are secured. Tsiolkovskiy pointed out that, when not fixed in place, a human being's insignificant movements (even breathing) might bring about involuntary body movement in space, which has been confirmed experimentally. Animals not fixed in place revolve in space in quite a disorderly manner, resulting from the peculiarities of stimulation and interaction of the analysors [14, 81, 196, 198, 209]. Human test subjects behaved approximately the same, which had substantial influence on the nature of their motor activity. In this case, test subjects only moved about in the aircraft cabin by guy ropes, or they would bounce off the cabin wall and essentially be unable to write. Simple operations were carried out with difficulty [196, 211, 212].

The materials cited concerning motor activity under conditions of weightlessness permit the conclusion that motor activity is essentially undisturbed if the test subjects are fastened in position at their working sites. Moderate motor disorders have been observed: discoordination of movements, disturbance of the precision with which they can reproduce specified muscular efforts, and others. The subjects successfully carried out routine work operations which did not require great precision. The results were opposite when they were not secured. When "floating" freely in conditions of weightlessness, subjects would try to maintain the body in a certain equilibrium in relation to the surrounding objects. Clearly, under these conditions it became impossible to carry out more-or-less delicate motor acts because each movement would destroy equilibrium and displace the body in space.

Noise

During orbital space flight, the astronaut is subjected incessantly to noises from operation of various life-support units and systems. Loudness of jet equipment noise reaches super painful values (up to 145 dB) and there is a tendency toward further increase [84]. Roth and Chambers [152] indicate that measures to protect the astronauts from noise are anticipated for modern spacecraft. They feel that noise control at present should be directed basically toward developing protective means for the auxiliary staff on Earth, not for the astronauts. It is hardly possible to agree. During prolonged flight, the uninterrupted noise has an unfavorable effect [111]. In this case, noises, which influence all human analysors, primarily change the function of the auditory analysor.

The action of acoustic stimuli can evoke various response reactions in the auditory analysor, ranging from reversible phenomena to persistent pathologic states. Three types of reactions of the auditory analysor to acoustic stimuli are: adaptation, fatigue, and acoustic trauma. Auditory adaptation is manifested in lowered sensitivity of the analysor and is regarded as a physiologic process continuing during the period of action of noises of low intensity and duration. Fatigue is manifested also in lowered sensitivity, maintained for a considerable period after the influence. During the prolonged action of intense noises, an irreversible process such as hearing impairment or deafness may set in [84, 110, 115].

Organic Changes

The influences of adaptation and auditory fatigue are not the only functional shifts which occur when noise affects the organism. Noise changes the functional state of the central nervous system (CNS). When this happens, test subjects complain of a feeling that their ears are stopped up, noise and ringing in ears, deterioration of hearing, and torpidity, apathy, headache, and loss of appetite. The electroencephalogram (EEG) shows, as a rule, during chronic action of noise, reduction in amplitude and frequency of the α-rhythm, the appearance of slow waves (θ-rhythm). Also noted are: decrease in the stability of clear vision, which is more pronounced the more intense the noise; an increased sensitivity of peripheral vision and weakening of the scotopic vision; decrease in sensitivity of vision toward orange rays, and heightened sensitivity toward blue-green rays [107, 108]. There are changes in the flow of visual afterimages. Noise influences the vestibular analysor: vertigo commences, the body's stability is disturbed [186], and there may be illusory sensations in regard to movement of objects in space [1, 38, 42].

When an acoustic energy with intensity higher than 125 dB acts on the organism, the noise exerts a direct, unfavorable influence on the mechanoreceptors of the skin [215]. The mechanism by which noises influence the organism is quite complex. During the action, the functional state of the higher sections of the CNS changes, primarily the cerebral cortex. Nor can the significance of the function of the reticular substance be ruled out, the activity of which increases during acoustic stimulation [191].

Changes occur in the sensory sphere when the human is subjected not only to "orbital" noise, but also to various factors connected with the specifics of space flight: isolation, hypodynamia, work schedule, rest, feeding, and clothing. When high-frequency noise with an intensity of 74–76 dB acts on the human auditory analysor incessantly for a prolonged period (up to 30 d), this will lead to a feeling that the ears are stopped up and to a decrease in hearing [214]. Such sensations are accompanied by an increase in the auditory thresholds of 20–30 dB and increased readaptation time, 2–3 times the original values. Restoration of auditory sensitivity takes place during 48 h. Analogous data have been obtained by other researchers [106, 195].

On the basis of data cited, it was concluded that high-frequency noise levels with 74–76 dB intensity cannot be recommended as permissible for spacecraft cabins during the orbital phase of flight. Studies were continued to elucidate the characteristics of the human auditory system's reaction to acoustic actions during space flight.

The influence of high-frequency noise with intensity up to 60–65 dB, with exposure up to 60 d, was studied. During the period of many days' exposure to noise, the thresholds of auditory sensitivity changed within insignificant limits (5–15 dB). A comparative evaluation was made of the dynamics of auditory sensitivity thresholds with humans exposed to high-frequency noises of 74–76 dB and 60–65 dB intensities. This evaluation showed that in the first case, change in the auditory thresholds was 1.5–2 times greater than in the second.

The steady increase of hearing thresholds during noise exposure and considerable fluctuations in auditory sensitivity (greater than 20 dB) provide evidence of exhaustion of the adaptative mechanisms and fatigue of the analysors. The stabilization of the auditory thresholds in dynamic audiometry (up to 15 dB) reflects, to a certain degree, persistent compensation [112] and good adaptation. Differences in physiologic reactions of the auditory system during exposure to noises of different intensities may, apparently, have prognostic use also during exposure to other factors of space flight, particularly to conditions of isolation and hypokinesia. Krylov [112] demonstrated that, with favorable tolerance to hypodynamia for 2 weeks, fluctuations of hearing thresholds on different days and at different times of the day do not exceed 10–15 dB. In severe conditions of hypodynamia, fluctuations in auditory sensitivity reach 20–25 dB or more [195].

Vibrations

The astronaut's body is affected by vibrations also during space flight, which may act on the human sensory sphere. It has been established that reactions of test subjects varied from a feeling of discomfort to anticipation of pain as a result of general vertical vibration [23, 53, 119, 133, 170, 187, 192]. Vibrations can be tolerated subjectively more easily when standing than when seated, apparently due to flexing of the legs [82]. For spacecraft flights, the sedentary (semirecumbent) position is more characteristic for crewmembers.

Exposure to vertical vibration causes primary functional changes in higher nervous activity. This is manifested in the development of phasic states and in the appearance of a widespread protective inhibition, which is expressed clinically by feelings of apathy and somnolence. Subsequent changes may occur in vibrational, tactile, and painful sensitivity, as well as disorders of visual, vestibular, and other functions of the organism. Man may develop a neurotic state accompanied by fatigue, various paresthesia, pain, and other unpleasant sensations [84].

Organic Changes

Deterioration of vision is the basic psychophysiologic effect of the unfavorable influence of vibrations in spacecraft [162]. Lowering of visual acuity is directly dependent on the amplitude and frequency of vibration [143, 144]; visual acuity decreases as the amplitude increases. Its greatest changes, reaching 40%, are observed at a vibration frequency of 20 Hz and an amplitude of 1.6 mm. The changes in visual acuity occur after the beginning of vibration and remain at a constant level during the entire period of exposure; aftereffects last several minutes. The mechanism of such vision disorders is conditioned by the mechanical oscillations of the eyeball. The greater decrease in visual acuity at a vibration frequency of 20 Hz is apparently explained by the presence of resonant oscillations, which have not been observed at other parameters of vibrations.

Similar results have been obtained by other researchers. Coermann [35] found that visual acuity deteriorated at frequencies higher than 15 Hz, especially in intervals from 25 to 40 Hz and from 60 to 90 Hz, and in some persons, from 50 to 55 Hz. The deterioration of visual acuity in the interval from 60 to 90 Hz is conditioned by resonance. Dennis [40] believes that the decrease in vision in the interval of 20–40 Hz is explained by movement of the eyes resulting from the resonance of the soft tissues of face and skull.

Prolonged exposure to vibration (4–8 h) does not have a noticeable effect on the state of the auditory function. A change in hearing was observed only with simultaneous exposure to vibrations and noises of 105–110 dB, in which spectrum high-frequency components predominated [126].

When Mikulinskiy [130] used human subjects to study physiologic characteristics of the effect of low-frequency vibrations up to 16 Hz with high amplitudes of 2–16 mm, he observed a unique reaction of the organism which differs from reactions during exposure to high-frequency vibration. Shifts in the body's resistance clearly manifested—a lowering of pain and skin sensitivity, while the vibrational sensitivity remained unchanged.

The physiologic mechanisms of the influence of whole-body vibrations on the human organism are quite complex. The organism's reaction to the effect of whole-body vibration is conditioned by that flow of impulses resulting from stimuli of the peripheral nerve endings, and of the receptors of the displaced organs of the abdominal cavity and small pelvis [2]. Vibration sickness is the result of the onset of a parabiotic state in the CNS, chiefly in the centers of the spinal cord.

Accelerations

Few studies concern changes in functions of the sensory organs upon exposure to transverse accelerations. There are limited data on the functions of vision and of the vestibular apparatus. Vision is highly vulnerable when prolonged overloads of varying magnitudes and directions are acting on the organism [9, 153]. The light sensitivity of the eye and changes in the field of vision have been fully studied.

Depending upon the magnitude and duration of the action of G-loads, in disorders of vision, a number of successive phases is characterized by the appearance of subjective sensations. The earliest phase of visional disturbance is the subjective sensation of fogginess or grayness with weakening of the peripheral vision. At this phase, the sensory sensations which appear are grayout, haze, whitish fog, and seeing through rain or fog. Thereafter, peripheral vision begins to disappear, and central vision weakens. Finally, there is complete loss of vision, the blackout. At this stage, test subjects note complete blackness before their eyes, while maintaining consciousness and hearing. In individual cases, visual disturbances are accompanied by illusory sensations such as the appearance of luminous dots and colored circles of radiance. The phenomena of the grayout and blackout vary widely in individuals. The threshold of their appearance depends on the person's posture with respect to the G-load vector, magnitude and duration of its operation, and functional state of the organism.

Organic Changes

Deterioration of functional capabilities of the visual analysor during exposure to G-loads is observed before the appearance of grayout or blackout. As the magnitude of the influence increases, there is often a reduction in the visual acuity, narrowing of the field of vision, a drop in contrast sensitivity, and an increase in time duration of the response reaction to color signals [11, 104, 177]. Total loss of vision with the body in the optimum position sets in during exposure to G-loads in the range of 14–16 units.

Under actual flight conditions, short-term visual disturbances—grayouts—have occurred in some cosmonauts during Earth-bound descent of Vostok spacecraft [180]. During exposure to G-loads, changes in the functional state of the vestibular analysor are also possible. This is confirmed by change in the excitability thresholds to galvanic current, and by the character and degree of acuteness of the basic indices of caloric and postrotational nystagmus under these conditions [202, 205].

It is presumed that any influence of G-loads of constant magnitude, as well as increase in the magnitude of a G-load, evoke activation of the indices of a nystagmic reaction. The decrease of the G-load is also an external agent leading to inhibition of nystagmus. Such effects are explained in terms of characteristics and peculiarities of the functional interaction between cupular and otolithic apparatuses under conditions of increased positive G (the action of G-loads). From the standpoint of the appearance and acuteness of vestibular-sensory and vestibular-vegetative reactions, the forecast of human working capacity under conditions of increased positive G forces may be recognized as favorable[205].

Spaceflight experience also indicates that in the individual stages of a flight, because of imperfect systems for the craft's orientation and stabilization, astronauts are exposed to the influence of angular accelerations and Coriolis forces of insignificant magnitude [90]. These influences will be more pronounced in spacecraft with simulated positive G forces [57, 203, 207, 216]. A current detailed study concerns the influence, on the functional state, of certain vestibular stimuli analysors, chiefly during rotations when angular accelerations are operative.

Darwin [37] first observed the possibility of sensory disturbances appearing under these conditions, noting that when man is subjected to rotations there is a sensation of apparent self-rotation, depending on the position of the head in space. Mach [122] analyzed sensations during rotation and concluded that there are six types of rotation sensations. Two each of the six sensations are oriented in opposite directions and correspond to stimulation of neural receptors of a definite pair of semicircular canals.

Orientation and Illusory Sensations

The part played by the otolithic section of the vestibular apparatus in the orientation of animals in space was first pointed out by Delage [39], later by Kreidl [109] and others. When the functioning of the otoliths (or in animals, different versions of "otocysts") was disturbed, signs of disorientation in space were observed and illusory sensations of an upside-down position occurred.

Interest in research on vestibular-sensory reactions increased with the development of air transportation, since most aviators experienced vertigo and illusions of counterrolling, rolling, and tail heaviness during flights under complex weather conditions. Studies of 685 fliers (478 flying jet planes and 207 propeller planes) showed that they had vertigo and illusions of counterrolling [18, 168]. In 47% of the fliers, these phenomena were greatly pronounced. Approximately the same findings are reported by other investigators [165, 172, 201, 208]. Sensory disturbances are most frequent in so-called blind flights, i.e., instrument flights.

In fliers experiencing illusory sensations, a maximum of 96% was found according to data of Clark and Graybiel [26], who interviewed 137 fliers with an average 675 h flight experience. Illusory sensations were essentially erroneous ideas of attitude and movement of the plane, such as pitching, diving, and banking; the sensations ranged from one of light banking to flying upside down. Tolokonnikov [172] categorized four groups according to duration of the counterrolling illusion. Individual acuteness of counterrolling illusions was measured in 105 cadets; the illusion was of prolonged duration in most of the unsuccessful cadets [219].

As further progress was made in mastering outer space and as the related sensory disorders were detected, the vestibular-sensory reactions again attracted researchers' attention. Yemel'yanov et al [199] proposed the use of a rocking and rotating seat installed on an unstable support for determining sensitivity to illusions in space of banking and total disorientation. Under these conditions, loss of equilibrium (more than 30 s) with total disorientation for 10–15 s is observed in persons with an inclination toward disorders of spatial orientation in flight.

During and after rotation, thresholds of cutaneous sensitivity increase, as a rule [218], cutaneous temperature drops [137, 150], auditory sensitivity changes [7, 47, 132], light sensitivity decreases [17], and depth vision deteriorates. Grigor'yev [69] studied the cutaneous temperature of human beings under the influence of angular accelerations of various magnitudes (subthreshold, threshold, and superthreshold stimuli). When subthreshold accelerations ($0.05°/s^2$) are used, changes in skin temperature are different in principle from those when superthreshold stimuli are used. With subthreshold accelerations there is an increase in temperature, and a decrease in temperature with superthreshold stimuli.

When test subjects were rotated in a Bárány chair, 84% exhibited changes in the thresholds of auditory analysor sensitivity to sounds of 128 and 2048 oscillations/s, respectively, there was an increase of the thresholds in 45.6%, a decrease in 25.2%.

One of the causes of the adverse influence of ejection is the rotation at high speed around the center of gravity of the body, according to Sperry [163]. When a rotation speed of 120 rpm continues for 3 s, there are headaches which may last for days and be accompanied by disturbance in the equilibrium function ("swinging of the room to right and left").

Test subjects were rotated, either in sedentary positions or lying on their sides, with an acceleration of the order of 65 and 80 min/s^2. The axis of rotation passed through the center of gravity. The G-load in the "pelvis-head" direction amounted to about 18 units. Under these conditions, disturbances of vision (light and dark spots in front of the eyes) were observed [169].

Possible disorders of the sensory sensations during exposure to Coriolis accelerations were first pointed out by Purkinje [148], later by Voyachek [185]. Unlike angular accelerations, Coriolis forces influence both the receptor formations of the vestibular analysor and those of other analysors (proprioceptive, interoceptive, and others). The influence of Coriolis forces on the human organism has been studied by many researchers [3, 22, 44, 101, 102, 116, 127], and significant contribution to the resolution of this problem was made by Graybiel and colleagues from slow-rotation room experiments [31, 62, 65, 68, 129, 135].

During the first stages of the studies, many were performed with rotations not exceeding 24–48 h. Subsequently, the duration was increased; examples of the experiments are shown in Table 4. During these experiments and later ones [68], sensory disturbances were observed in some of the test subjects: illusory perceptions of spatial sensations, vertigo during head movements, and the like. The disturbances were notably intensified when the test subjects were subjected to the forces of rotations exceeding permissible limit values: 14 data speed 36°/s, 7 data speed 40°/s, 4 data speed 60°/s, or when stability of the vestibular analysor was lowered—due to disturbance in the rest schedule, influence of flight factors, and other conditions.

Information on sensory disturbances was obtained in experiments with exposure to oscillations. Motion sickness sharpens the senses of smell and taste, however, the human being cannot endure noise and loses his appetite, vision becomes less clear, and visual uncertainty arises [149, 174, 188]. Information on the clinical treatment of seasickness has been carefully analyzed [188]. The data indicate that when there is motion sickness, apathy occurred in 95% of the cases, loss of appetite in 81%, and headache in 78%.

TABLE 4.—*Experiments on Influence of Coriolis Forces*

Study	Duration of experiment	Rotation speed
Newsom et al [138]	5 d	36°/s
Galle and Yemel'yanov [44]	7 d	10°/s, 40°/s
Graybiel et al [65]	12 d	60°/s
Guedry [72]	2 wk	18°/s uninterrupted

Oscillation Studies

In the literature on the effects of oscillations on the analysors, Lapin [114] studied the effects of oscillations on the olfactory analysors in 11 persons. During oscillations, the acuity of the sense of smell changes, more noticeably toward hyposmia, in the presence of weak stimuli to the otolithic apparatus. Kopanev [100] studied the effect of oscillations on the functional state of the visual analysor. The method of adequatometry, proposed by Makarov [123], was used in the investigations. In most of 79 persons, motion sickness in its latent form reduced excitability and lability of the visual analysor and lowered the speed of adaptation to darkness and the acuity of vision. The decrease in the excitability of the visual analysor was directly dependent upon the duration of exposure to oscillations. Funtikov [43] later studied the excitability of the visual analysor during rolling at sea and drew similar conclusions. Noteworthy studies were carried out by Graybiel, Kitayev-Smyk, and Yuganov on the physiological mechanisms of the oculogyric, oculogravic, and autokinetic illusions which occur under the influence of vestibular and other stimuli [63, 71, 84, 93, 94, 151].

The oculogyric illusion results from stimulation of the vestibular apparatus when the human is exposed to angular accelerations. It is manifested in apparent movement of objects in the field of vision, or in field of vision movement itself.

A test subject was rotated in a chair or a modernized Link cabin for the purpose of reproducing the illusions. The chair was placed in the center of a dark, cylindrical room on a rotating platform. A bright target was installed opposite the test subject; the cylindrical room and the target rotated simultaneously with the chair. The velocity of rotation was 1–25 rpm (up to 20 rev in all) and illumination intensity was varied. The apparent movement of the target depended on the direction and force of rotation of the subject, on the point where his gaze was fixed, and on the position of his head. If the test subject was subjected to powerful rotation, several illusory effects could occur; acuteness of the illusion was greater after rotation. Under conditions of weak illumination, the phenomena occurred with smaller stimuli, corresponding to rotary acceleration of 0.2–0.3°/s^2.

Graybiel et al [61] relate the appearance of the oculogyric illusion to the trace stimuli of the retina during the period of the slow component of nystagmus. This interpretation is validated by the conformity of the sensations of the target movement in time and direction with nystagmus. If the nystagmus appeared in the form of phases (a first positive phase, a first negative phase, a second positive phase, and so forth), the direction of movement of the visual object also underwent corresponding changes. However, a number of authors do not agree. Cawthorne et al [24] observed that the oculogyric illusion can occur in the absence of nystagmus. Other authors note that the oculogyric illusion is observed together with visual afterimages and a stabilized image in the retina [176]; thus they consider the explanation of Graybiel and others insufficient concerning the mechanism of the oculogyric illusion. Obviously, there is still not complete clarity concerning the psychophysiologic causes for the phenomenon.

Oculogyric illusions evidently can occur in flight, especially at night, when sensitivity of the vestibular apparatus to angular accelerations increases. The illusions occur far more easily during rotary motion of an airplane if visual control is also difficult. The oculogyric illusion exemplifies a shift in visual perception beginning as a result of stimulation to the vestibular apparatus. The reverse situation can also occur, when shifts in vestibular sensations can develop as a result of stimulation of the visual analysor—for example, the development of motion sickness during optokinetic stimuli.

An illusion in the auditory sphere is similar to the oculogyric illusion [27]. After being rotated, test subjects made mistakes in identifying the position of a sound source. Apparently they had a persistent tendency to locate the source of the sound they heard in the direction opposite the rotation. The authors called this illusion the audiogyric illusion. These data were later confirmed [5, 171] by demonstrating that when the visual field is rotated around the test subject (who remains immobile), he perceives sounds displaced in the direction of rotation. The audiogyric illusion has been related to the binaural effect and to the head position of the test subject during rotation [113, 118]. It has also been related to the illusory displacement of objects in the field of vision [55, 59, 60, 67].

Oculogravic Illusion

The oculogravic or vestibular-visual illusion is manifested as an apparent motion of a visual reference point, or portions of it, during definite changes of accelerations acting upon the human subject, such as when the power of gravity is decreased or disappears. The illusion begins as a result of simultaneous stimulation of the otolithic apparatus and semicircular canals. The effect of the illusion is that immobile objects acquire an illusory movement in the direction of the resultant force of gravity and the inertial forces when the movement is accelerated.

This phenomenon has been studied extensively. It is presently believed that the oculogravic illusion results from a central integration of the feedback afferent signals from the oculomotor muscles, which were subjected to vestibular tonic influences when the accelerations underwent change [26, 29, 32, 59, 67, 92, 93, 94].

A human subject was rotated on a centrifuge in order to produce the oculogravic illusion. The chair could be fastened in various positions. The experiments showed that at the moment of rotation, the subject determines his position in agreement with the resultant force, which is made up of the centrifugal and gravitational forces. All objects within the subject's field of vision are included in the scheme of orientation. There is direct correlation between the accelerations and the degree of aberration of a bright point which has been purposely fastened in place. As the centrifugal force is increased, the point is displaced upward until it seems to the test subject that he is moving in the opposite direction. When the velocity is decreased, the bright point, on the contrary, is displaced downward. Oculogravic illusions also occur when there is a lack of sensitivity in the semicircular canals to adequate stimuli, but the otoliths retain their function.

The thresholds of the oculogravic illusion were studied by means of special devices which made it possible to produce rotation with the test subjects in different positions (standing up, lying on their sides, or with legs up), with the head fastened in one place [67]. The thresholds of the illusions in the standing position corresponded to a rotating velocity of $1.5°/s^2$ for 75% of the correct replies. When the subjects were lying on their sides, the thresholds increased to $8.9°/s^2$. The studies justified relating oculogravic illusions with the function of the otoliths.

Oculogravic illusions were similar to those in fliers during steep banks. Studies were carried out during flights [28]. The test subject was in the rear seat of a two-seater plane, the instrument panel was concealed, and the visual object was a centrally located bright spot. The experiment was performed in darkness. Head movements were restricted, and in some experiments the head was turned 85° to the left and fastened in position. The values of the prescribed accelerations varied from 1.0004 to $1.0925°/s^2$, and in direction from 1.7 to 23.7°.

From the beginning of the acceleration, 4–6 s passed until the shift of the bright spot. The apparent shift of the visual object had definite relationship to the linear acceleration. When the head was turned to one side, this shift was especially pronounced in the counterclockwise direction at the moment the acceleration increased, and in the clockwise direction when it decreased. Shifts of the visual object were accompanied by movements of the test subject. The subject oriented himself in relation to the resultant of the aerodynamic forces, as a rule, but the apparent movement of the bright spot did not coincide in time with action of the total force. This led to the conclusion that the illusions resulted from stimulation of the otoliths, but not from stimulation of the proprioceptors.

Contrary to the oculogyric illusion, the oculogravic illusion (in Graybiel's opinion) is not related to nystagmus or other eye motions. Causes of the illusion must be sought in the psychophysiological mechanisms. The oculogravic illusion is an example of sensory "cooperation," when visual signals are subordinate to afferent impulses which occur when the resultant force (from combined aerodynamic and gravitational forces) acts upon the test subject. Kitayev-Smyk [94] regards the oculogravic illusion as a portion of the illusory distortion of visually perceived space, which occurs during change in gravitation.

Perception of the oculogravic illusion did not commence immediately, it was observed [29], even though the vector of the operating force attained constant values; rather, a certain delay was noted. The dynamics of the illusions depend on the level of illumination (at a higher illumination, the illusions are less pronounced), on the functional state of the labyrinth (illusions may be absent in deaf-mutes), on the visual stimulation, and on other conditions [32, 33, 34]. Illusory sensations in the auditory function during rotation on a centrifuge were studied and it was found that audiogravic illusions occur [66]. Experiments demonstrated that these illusions are analogous to the oculogravic illusion, except that they are in the sphere of the auditory analysor.

A human has great difficulty in determining his movements and the movements of others in the dark, especially when subjected to the influence of accelerations. The researchers studied this phenomenon in a Link cabin, finding that in addition to effects of vestibular stimuli, a special form of the so-called autokinetic illusion also appeared. This designates a movement of the object in the field of vision when there are no visual supporting points for comparison.

Autokinetic Illusion

The autokinetic illusion is observed when an aviator fixes his gaze on an immobile point outside the cabin against a uniformly colored background, and after a time perceives that the point is moving. The practical significance of such an illusion with relation to a cosmonaut's activity is that it might serve as a precondition or cause of an accident during landing, especially on the surface of other planets [84].

Graybiel and Clark [58] elucidated some of the properties of autokinetic illusions, which they studied under laboratory conditions (with 500 test subjects) and during flight at night. In the laboratory, they used a Link cabin and bright target located 2 m and 10° below eye level, also visual objects of various sizes and shapes, the locations of which varied with reference to the cabin. The test subject was sometimes given the task of moving the cabin in the direction toward which the light spots appeared to be moving. In most test subjects, the illusion that the light source was moving occurred after his gaze had been fixed on it for several seconds. The erroneous sensations continued for 9–12 s (average 10 s) which was approximately half the time the object had been fixed in place.

The movements usually were of small amplitude (3–4°) and slow speed (0.2–0.3°/s), although sometimes the speed and amplitude were greater. Their directions (highly varied) were not taken into account. In general, the visual object did not move far from the original position. Test subjects usually were unable to distinguish the actual movement of the light source from the apparent movement. There appeared to be only limited possibilities of suppressing the phenomenon. An increase in dimensions and number of the light objects led to a decrease in the degree of autokinesis, especially when the illumination was increased. The autokinesis was also inhibited when the visual object moved rapidly, or when attention was fixed periodically on other visual reference points for 10 s.

Illusions of the movement of a single light source during flight in a dark night were, as a rule, slow, had low amplitude, and lasted 10–15 s. When there were two light sources, the illusion decreased; if there were many, the illusion would disappear. It is felt that the optical illusion described plays a role in accidents during night landing. The appearance of the autokinetic illusion during flight is facilitated by: darkness, presence of only a single light of low intensity, prolonged fixation of the gaze on the light source, and fatigue, as well as other conditions.

Movements of Head and Torso

Under normal conditions, inclination of the head or body in an illuminated site does not lead to change in perception of the spatial position of visual objects. However, it was noted that if the head is inclined in a darkened room, the spatial position of bright lines begins to appear to be changing [8]. Later studies indicated that the direction of displacement depends on the degree of inclination of the head; at small inclinations of no more than 60°, displacement in the direction of the inclination is 7–8°, when the inclinations are greater, movement in the opposite direction can reach 40–50° [12, 136]. Similar phenomena were observed when the test subject was returned to the upright position; in this position, when the visual vertical is evaluated, small errors of about 2–3° are assumed [189, 190]. Other investigations showed that when the body is inclined, there are aberrations in identification of the tactile-kinesthetic vertical, localization of auditory stimuli, and evaluation of the spatial position of the body with reference to the postural vertical [13, 113, 125].

It has been proposed that the otoliths and the proprioreceptors of the neck muscles play a role in genesis of the illusion [190] and that kinesthetic information from torso muscles and extremities is significant in reducing illusions [34]. The importance of visual information when determining the visual gravitational vertical has also been confirmed [6, 124].

Influx of Distorted Information Along the Visual Channel

The coordination of movements performed with eyes closed is disturbed substantially if the visual perceptions are "overturned" by means of special optical devices. This was shown at the end of the 19th century [164] and established that a displaced visual field influences and changes sensorimotor coordination; errors in aiming and hitting targets have been observed [80, 194]. After a few days the human subject adapted himself to these conditions, and movements were carried out precisely. Together with sensorimotor changes during the perception of distorted visual signals, shifts in the perception of space were observed in the straight-ahead position [78, 79], as well as changes in coordination of eyes and head [80, 128], and illusory perceptions when localizing a sound source [145, 146].

Adaptation of sensorimotor reactions has been discussed in the literature with an intent to determine whether it results from correcting distorted visual perception or is a byproduct of goal-oriented movements, taking into account the peculiarities of visual perception. Attention was directed to the intercoordinational links of both arms which are of great significance in the process of adaptation [79, 87]. Experimental data point to the importance, for this process, of active movements when a distorted reflection of visual space is perceived [79]. While not denying the role played by active movements, it is believed that there may be adaptation also in the process of carrying out passive movements [83]. Other investigators found satisfactory adaptation in both active and passive movements [158]. Evidently, it may be concluded that movements are not the only condition for adaptation to perception of a distorted visual representation of space. However, active movements lead to adaptation more rapidly than passive movements.

PHYSIOLOGICAL MECHANISMS OF SENSORY DISTURBANCES AND PROPHYLACTIC MEASURES

Sensory disturbances during space flight may be conditioned by numerous causes. A simple movement of head and torso under terrestrial conditions at a lowered illumination brings about illusory sensations. During space flight, however, this phenomenon would apparently be more pronounced.

Two groups of causes for sensory disturbances are: internal and external. The internal are connected primarily with change in the functional state of individual analysors, the external with specific conditions of the external environment and its inherent individual factors. Such a division is quite arbitrary, since these groups of causes act simultaneously with different specific significance for each situation. Both external and internal causes exert considerable pressure on the neural and humoral regulatory mechanisms, for they are forced to act against a changed afferent background. This background is attained in many ways, such as by changing the magnitude of the stimulation force of apparatus receptors in one or several of the analysors. The effect is attained when the magnitude of the stimulus is both increased and decreased. In both cases, changes occur in the correlations which usually exist between the afferent signals from different analysors, for example, the effects of noise and weightlessness. When there is noise stimuli, the primary influence is on the auditory analysor (plus load), and during weightlessness on the mechanoreceptors of a number of analysors (minus load).

At present, there is fairly complete medical knowledge about the physiologic mechanisms of the influence of any given factor on the human organism and the physiologic mechanisms of development of sensory disturbances. Weightlessness is an exception; data concerning the influence of lowered weight in the genesis of sensory disturbances are contradictory.

Physiologic Reactions

Most researchers believe that the physiologic shifts during weightlessness are conditioned by disturbance of the analysor interactions, especially the vestibular and visual [46, 56, 57, 74, 75, 105, 141, 142, 166, 167, 179]. Experimental results plus data in the literature led to opinions on the direct and indirect influences of weight-

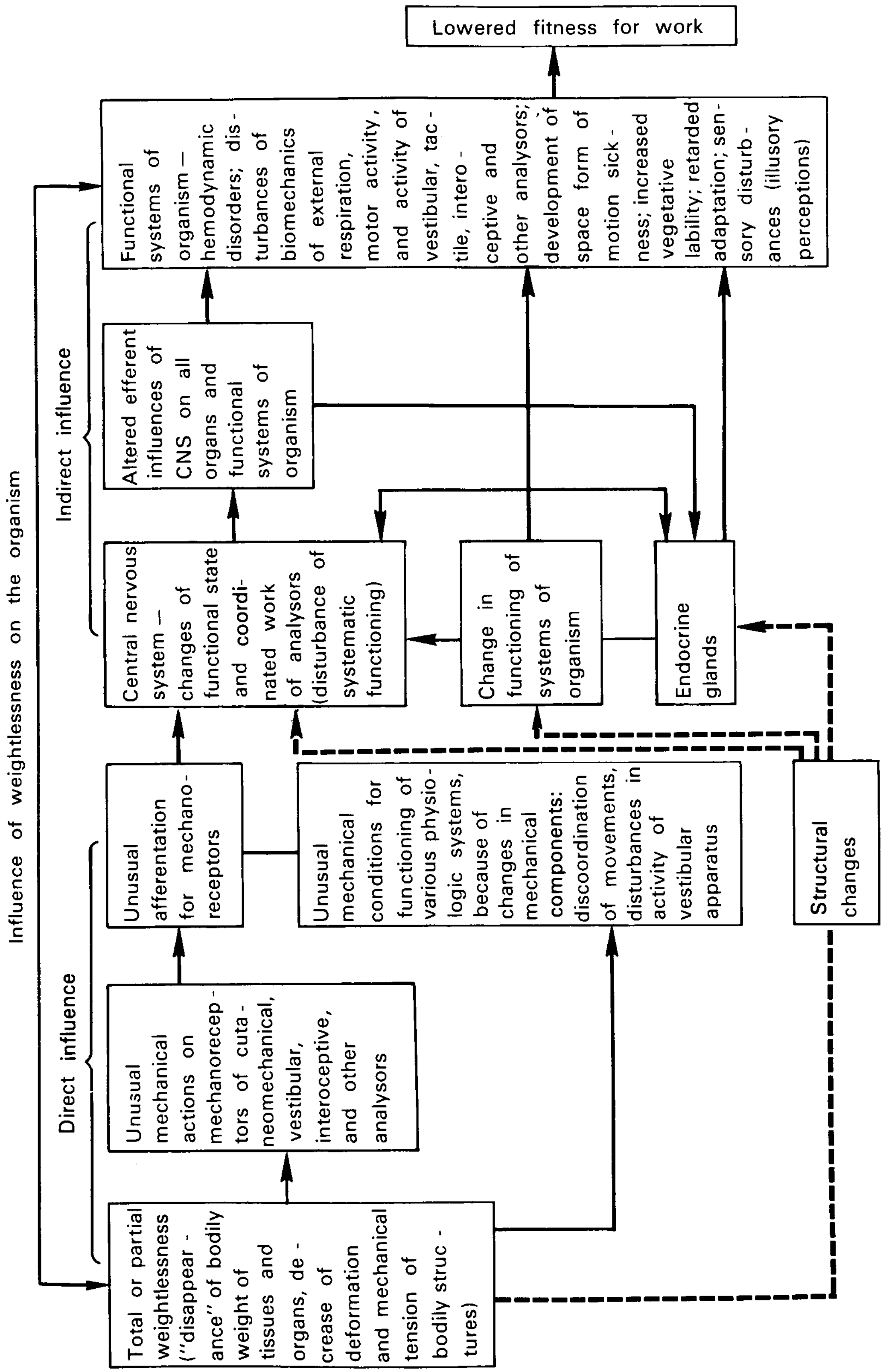

FIGURE 1.—Sensory disturbances observed under weightlessness conditions.

lessness on the human organism [197]. These opinions serve to explain the sensory disturbances which have been observed under weightlessness conditions (Fig. 1). "Direct action" designates the entire complex of reactions determined by decrease in the deformation and mechanical tension of the body structures when the body is in a state of weightlessness (complete or partial). As a result, there are unusual afferent influences from all mechanoreceptors, substantial changes in the mechanical conditions for the functioning of many systems in the organism, and probably structural changes. A possible consequence of the direct influence of weightlessness may be the disturbance (failures) of movement coordination, since movements are completed according to the normal terrestrial stereotype, taking into account the weight of the extremities. The functioning of the auditory, vestibular, and visual analysors may undergo changes to a certain extent, since the weight of the auditory ossicles, otoliths, and eyeballs decreases ("disappears") during weightlessness.

The indirect influence of weightlessness is a comprehensive term. It embraces the entire complex of physiological reactions resulting from change in the functional state of the CNS and coordinated functioning of the analysors—under the influence of unusual afferent impulses from mechanoreceptors of the vestibular, interoceptive, motor, and other analysors, as well as altered hormonal influences. There are resultant disturbances in the systematic functioning of the analysors participating in analysis of spatial relationships and in positioning the body in space; the statokinetic stability is lowered, and space motion sickness develops.

As the organism remains in weightlessness, in most cases it becomes adapted to these unusual conditions. The physiologic foundation of such adaptation evidently is formation of a new systematic function with the CNS functioning on a level adequate for the unusual conditions, the state of weightlessness. The sensory, motor, and vegetative components are integrated on a level sufficient for these conditions.

There is an effort at present to establish the significance of different analysors in the genesis of disturbances observed in test subjects in the state of weightlessness. Investigators [46, 90, 202] recognize the significance of the vestibular analysor in the constellation of analysors reflecting space. In experiments with turtles [14], cats [157], and mice [203], a preliminary destruction of the vestibular apparatus was noted which makes possible better orientation for the animals under conditions of weightlessness. Motor disturbances under conditions of short-term weightlessness were less pronounced in five deaf-mutes than in unimpaired individuals [120, 121].

Vestibular and Otolithic Apparatus Effects

The vestibular apparatus under conditions of weightlessness is evidently the source of altered stimuli which disturbs the coordinated work of the analysors, and removal of the apparatus prevents development of motion sickness to a certain degree. At this level, Yuganov [202] studied the reciprocal interrelations between the otolithic apparatus and the cupuloendolymphatic system. Primarily on the basis of theoretical concepts, a number of investigators think these reciprocal interrelations should be substantially changed under conditions of weightlessness. That is, functions of the otolithic apparatus should be cut off, and sensitivity of the semicircular canals be increased [45, 49, 76, 90, 141, 142, 159, 160, 161].

Yuganov [202] concentrated on determining the excitability of the otolithic apparatus in weightlessness. Studies were carried out by the indirect methods of postrotational nystagmus, illusion of counterrolling, latent occurrence of illusion of oscillation, and threshold time of unbending; and by the direct methods of determining excitability by means of galvanic current. It was established that under conditions of weightlessness, in all subjects there was an increase in the latent period of occurrence of the reactions, a decrease in duration of the counterrolling illusion and postrotational nystagmus, defensive movements were less pronounced, and thresholds for galvanic current increased. The data indicated a decrease in excitability of the semicircular portion of the vestibular apparatus.

It was taken into account that these changes could not have been evoked by the special char-

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acteristics of the influence of weightlessness on the semicircular canals, for weightlessness was not reflected in the inertial properties of the endolymph. Thus, it was concluded that the changes were determined by influences from the otolithic apparatus. It followed that under conditions of weightlessness, the otolith is not turned off; on the contrary, weightlessness is an unusual "minus-stimulus, determining the occurrence of specific vestibular reactions." Experiments showed that the nystagmic reaction depends on the absolute magnitude and direction of weight changes. That is, inhibition of the nystagmic reaction is observed when weight is decreased, and the nystagmic reaction is activated when weight is increased.

There are convincing experimental results on the role of the vestibular apparatus in the genesis of space motion sickness, but this does not apply to the other analysors. Schock indicates the significance of the proprioceptive stimuli impulses in orientation under conditions of weightlessness [157]. He cites the work of Strughold who anesthetized the gluteal muscles, then tested the degree of difficulty of orientation in space under the influence of short-term weightlessness. In experiments on rats and mice [198] it was revealed that during weightlessness, the animals rotated less when in contact with the wall of the container. The implication was that stimulation of the cutaneous-mechanical analysor improved orientation in space, which was substantiated by the experiments of Kolosov [96]. When test subjects were fastened in their work places, statokinetic disorders were less pronounced.

A knowledge of the physiologic mechanisms by which spaceflight factors influence the human organism, and knowledge of physiologic mechanisms in developing sensory disturbances, provide means of planning a procedure in prophylaxis. The procedure may follow two directions: (1) elaboration of means aimed at heightening specific and nonspecific resistance of the organism; and (2) perfecting the spacecraft technically.

Adaptability of the Organism

The functional and compensatory capabilities of living organisms are perfected by conditioning during terrestrial testing, and in airplane flights along the Kepler parabola, by using pharmacologic agents, conditioning the central nervous system, and other means [19, 20, 21, 56, 57, 74, 90, 115, 178, 202]. The physiologic regulatory mechanisms are perfected during this process in regard to altered conditions of the external environment. Thus, during experiments in an anechoic chamber, there was change in the flow of information reaching the central nervous system from the sensory organs, and the habitual coordinated activity of the analysors was disturbed because of the small chamber, limitation of movements, and absence of external stimuli. Sensory disturbances were observed in some subjects. Establishment of new intercentral connections and relations and transition of the central nervous system to a new functional level increased the adaptive properties of the CNS, which is the foundation for more rapid adaptability of the organism to altered conditions of the external environment, in particular to weightlessness. As conditioning continues, illusory sensations occur more rarely, become shorter in duration, and are easily surmountable; this, approximately, is observed with vestibular and other types of conditioning. As a result of these measures, altered signalization from various organs and systems develops. During the process, the neuroreflex mechanisms are perfected, and resistance to spaceflight factors is heightened.

In recent efforts to avert illusions, there has been wide use of astronauts flying in airplanes along the Kepler parabolic curve with simulated short-term weightlessness, as well as training in an aqueous medium. The astronaut becomes acquainted with various illusions and is able to devise means of combatting them, after being exposed to such conditions.

The second direction in combatting sensory disturbances is also important: perfecting spacecrafts technically and creating optimum physiologic and hygienic living conditions in the cabins. Measures which make it possible to decrease sensory disturbances are: removing effects of noises and vibrations; reducing linear and angular accelerations in both magnitude and duration; designing special protective equipment; and improving the working site by developing ways of fastening the astronaut in his working place. Such measures do not, of course, mean the removal of the harmful influences of weightlessness. In spacecraft carrying out prolonged flights, the most effective means will be creating an artificial gravity [57, 207].

In the overall system of biomedical preparation of astronauts, significance is ascribed to the physical training. Experience shows that, by means of reasonably selected exercises and systems of applying them, it is possible to obtain positive results in the prevention of illusions in persons with heightened sensitivity of the vestibular analysor.

Prophylaxis of sensory disturbances is not accomplished only with a program of special training. The entire preflight program of work, rest, and nutrition must also be observed strictly. The creation of optimum living conditions also may be regarded as an important component of the struggle against sensory disturbances.

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Chapter 16

ASTRONAUT ACTIVITY

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Manned space flight evolved from the confluence of two adjacent lines of technology. One line was developed from experience with high-performance and experimental aircraft; the other evolved from experience with rocket-propelled vehicles. The characteristics of manned spacecraft have been derived almost completely from the traditions of aircraft. At the time rocket technology was progressing at a rate that would make manned space flight feasible, high-performance aircraft already were operating at altitudes functionally equivalent to space flight. Control stability over a wide range of dynamic conditions had been studied, and substantial empirical and experimental data about optimum methods of integrating man into the vehicle, both as a control element and as a system and mission manager, had been developed. Major modifications to crew accommodations in the progression from aircraft to spacecraft were: geometric accommodations to the acceleration environments of launch and entry, and to the weightless conditions of orbital flight [6, 42]. Other modifications were induced by the *shiplike* characteristics required for long-duration missions, which imposed system servicing requirements and long-term habitability management on the spectrum of crew duties.

The effects of the space environment on man's sensory and motor performance and on higher order mental functioning could not be predicted with certainty. Therefore, man's role at the beginning of manned spaceflight programs was that of a semipassive passenger whose capability had to be demonstrated and who could act as a backup system if a primary system failed. With continued successful task accomplishment, man's role in spacecraft has evolved to that of mission manager where crewmen supervise highly automated systems and manually execute critical operations. In this capacity, the crewman provides the capabilities to select the systems configuration and modes most suitable for characteristics of the particular mission phase and to reconfigure the systems to influence system performance during off-nominal conditions.

Optimization of the crew-to-spacecraft interface is not a specific objective of any manned spaceflight program. This is important to note in any review pertaining to spacecraft design details influenced by the interface between crew and spacecraft. The design objective is to optimize the achievement of program objectives, not the configuration of the crew compartment, the displays and controls, or the other interfaces through which the crew affects spacecraft activities. In this group of interfaces, as in all other systems, compromises are made to each of the interfacing elements to achieve overall program effectiveness.

The sections that follow describe the characteristics of man pertinent to the design and operation of spacecraft, geometric characteristics of spacecraft that define the degree and type of confinement imposed on the crew, and character of equipment management and housekeeping necessary for hygiene, comfort, and safety. The controls and displays of each spacecraft are described to indicate the degree to which crew functions become integral to functions of the total spacecraft. The last section summarizes the contribution of the crew to system reliability and performance and notes the increasing significance of the crew's role in scientific observation and experiment.[1]

MAN/MACHINE FUNCTIONAL CAPABILITIES

Historically, studies of man/machine interfaces have focused on proper allocation of system operating functions between man and machine [1, 3, 6, 8, 9, 13, 16, 24, 27, 28, 30, 35, 43]. A typical approach has been to analyze task sequences to discover task components and allocate these functions to man or machine, depending upon which would be better at the particular task. Man is able to handle a variety of information processing tasks in which input (sensory) and output (motor) aspects vary widely. He is able to store and recall great amounts of information pertinent to system operation under both normal and emergency conditions. He is able to operate as a decision-maker through his capability to evaluate information and to distinguish between useful and unusable and irrelevant information. He can solicit additional information from the system when necessary, and can estimate probabilities. The human operator can respond to the unforeseen and operate at a level of complexity exceeding any reasonable amount of premission planning and programing of on-board automatic control equipment. So far, man is the only real-time system capable of accepting and operating on asynchronous and nonsequential input data. However, certain functions have been identified where man could be expected to perform more poorly than the machine. His limitations include a relatively low information-handling rate, limited short-term memory, and poor performance in detecting infrequent signals for which the time of occurrence is unpredictable (vigilance tasks).

Recent design practices emphasize a trend toward viewing the human operator as a system component recognizing that optimal use of man may involve a task that a machine could do better, but in which operator performance expected would be adequate to perform the function. In such circumstances, his availability should be exploited when cost effective.

Senses as Information Collectors

In operating a spacecraft, the crewman is required to perform a variety of tasks beginning with gaining information through his sensory apparatus. Vision, hearing, and proprioception are the most important senses for information collection during space flight. The information is processed in various ways, and appropriate control adjustments are made to obtain and maintain the desired state of system operation, correct out-of-tolerance conditions, and achieve new modes of operation when necessary. Research in these processes as they occur in man has been conducted for many years. The information obtained from research is valuable in defining the proper role of man in the operation of manned space vehicles.

Man's capabilities for sensing data have been studied longer and more thoroughly than any other aspect of his performance. Much information is available concerning the basic processes of seeing, hearing, and sensing motion. Significant aspects of man's sensory capabilities are shown in Table 1. Such data are in substantial agreement in US and Soviet handbook compilations.

The most significant sense, vision, has been

[1] The data presented were prepared from material compiled by N. D. Zavalova and V. A. Ponomarenko of the USSR [50], and J. P. Loftus, Jr., R. L. Bond, and R. M. Patton of the US, who prepared reviews and abstracts of the literature in their respective nations and languages.

TABLE 1.—*Characteristics of the Senses*

Parameter	Vision	Audition	Taste and smell	Touch	Vestibular
Sufficient stimulus	Light-radiated electromagnetic energy in the visible spectrum Heavy particles	Sound-vibratory energy, airborne or structural paths	Particles of matter in solution (liquid or aerosol)	Tissue displacement by physical means	Accelerative forces
Spectral range	Wavelengths from 400 to 700 μm (violet to red)	20 to 20 000 Hz	Taste: salt, sweet, sour, bitter Smell: fragrant, acid, burnt, and caprylic	> 0 to < pulses/s	Linear and rotational accelerations
Spectral resolution	120 to 160 steps in wavelength (hue) varying from 1 to 20 μm	~ 3 Hz (20 to 1000 Hz) 0.3 percent (above 1000 Hz)	– –	$\frac{\Delta pps}{pps} \simeq 0.10$	– –
Dynamic range	~90 dB (useful range) for 3×10^{-9} cd/cm² (0.00001 mL) to 32 cd/cm² (10 000 mL)	~ 140 dB 0 dB = 0.0002 dyn/cm²	Taste: ≃ 50 dB 3×10^{-5} to 3% concentration quinine sulphate Smell: 100 dB	~ 30 dB 0.01 to 10 mm	Absolute threshold ≃ 0.2°/s
Amplitude resolution $\frac{\Delta I}{I}$	Contrast = $\frac{\Delta I}{I}$ = 0.015	0.5 dB (1000 Hz at 20 dB or above)	Taste: ≃ 0.20 Smell: 0.10 to 50	$\frac{\Delta I}{I}$ nonlinear and large at low force levels ~ 0.15	~ 0.10 change in acceleration
Acuity	1° of visual angle	Temporal acuity (clicks) ≃ 0.001 s	– –	Two-point acuity =0.1 mm (tongue) to 50 mm (back)	– –
Response rate for successive stimuli	~ 0.1 s	0.01 s (tone bursts)	Taste: ~ 30 s Smell: ~ 20 to 60 s	Touches sensed as discreet to 20/s	~ 1 to 2 s nystagmus may persist to 2 min after rapid changes in rotation
Reaction time for simple muscular movement	~ 0.22 s	~ 0.19 s	– –	~ 0.15 s (for finger motion, if finger is the one stimulated)	– –
Best operating range	500 to 600 μm (green-yellow) 107.6 lm/m² (10 ft-ca) to 2152 lm/m² (200 ft-ca)	300 to 6000 Hz 40 to 80 dB	Taste: 0.1 to 10 % concentration	– –	~ 1-g acceleration directed head to foot

TABLE 1.—*Characteristics of the Senses*—Continued

Parameter	Vision	Audition	Taste and smell	Touch	Vestibular
Indications for use	1. Spatial orientation required 2. Spatial scanning or search required 3. Simultaneous comparisons required 4. Multidimensional material presented 5. High ambient noise levels	1. Nondirectional warning or emergency signals 2. Small temporal relations important 3. Poor ambient lighting 4. High vibration or g-forces present	1. Parameter to be sensed has characteristic smell or taste 2. Changes are abrupt	1. Conditions unfavorable for both vision and audition 2. Visual and auditory senses	1. Gross sensing of acceleration information

studied extensively. The basic operation of visual receptors is reasonably well understood, as are certain mechanisms of color vision, characteristics of depth and distance perception, and conditions under which various visual illusions are produced. In addition to viewing displays inside the spacecraft, other significant tasks involve viewing features outside the spacecraft.

1. Visual reference to the horizon or other external reference criteria for spacecraft heading and spacecraft orientation in pitch, roll, and yaw;
2. Visual observations of a ground plane for reconnaissance or determining spacecraft location;
3. Visual observations in surrounding space for reconnaissance or maintenance of relative position of one spacecraft to another;
4. Stellar navigation and astronomical observation;
5. Observation of external indications of the function or malfunction of components of the spacecraft.

In a spacecraft where the astronaut could assume a variety of orientations during weightlessness, there was concern for possible difficulty in reading instruments designated for viewing from a particular orientation which might increase errors and reading time. It was thought that, either the spacecraft should be designed to provide a consistent visual *up*, or displays be designed for ready interpretation by an observer in any position. Such difficulty has not occurred so far, perhaps because spacecraft built in a gravity field have an inherent *up*, and, although work stations may be at substantially diffierent orientations to each other, each has its own axis of action.

Man's ability to perceive change in either sound level or composition has been widely studied. The sensitivity of the ear to changes in frequency or intensity is quite high; however, ability to assign absolute values to either frequency or intensity is poor. The most useful operational auditory cues are the abrupt, or those with dramatic change in character. Even with such restrictions, there are many uses of auditory cues because they do not require directional focus by the crewman. Mechanical, pneumatic, and pyrotechnic systems are monitored for function or malfunction and alarm signals are used to waken crewmen or direct their attention to appropriate displays when conditions are abnormal.

Interaction between vestibular organs of balance and the vagal nervous system has been studied to find effective palliatives for motion sickness. Great concern had been expressed that such malaise would impact crewmen who were being abruptly placed in the weightless condition after launch acceleration. Discomfort has been reported on several flights but has never precluded successful continuation of the mission. The widely known illusions and disorientation caused by moving the head during acceleration have been experienced by most pilots, but none of the incidents has been forceful enough to interfere with normal operations.

No explicit use was planned for man's ability to detect the condition of systems through taste and smell, although the sensitivity of this capability, recognized as aiding in detection of anomalous conditions, has been used on several occasions.

The greatest value of the astronaut as a system operator is in complex information processing. In performing any operational task, the astronaut must first gather information from a variety of sources, including instrumentation, data transmitted by voice from the ground, and directly observable features of his environment—both internal and external to the spacecraft. He must delete useless or obviously inaccurate information but retrieve necessary information from long-term or short-term memory storage to supplement present information and evaluate its meaning. He must call for more or better information if that which he has is inadequate. Finally, he must decide on appropriate control action.

Information and Decisionmaking Models

The question of how decisions are derived continues to be investigated. Two early models of information processing and decisionmaking (decision theory and information theory) have been used to define man's role in spacecraft operations. Significantly, each model of man is an analog or variation of models used in communication systems or computer design theory. Developments in this field have proved at least partly applicable to the description of human decision processes, and demonstrate the utility of viewing man as a system or system element with operating characteristics analogous to hardware systems. The models also aid in assessing the value of crew intervention.

Decision Theory

Decision theory, developed by Edwards and others [10, 11, 47], concentrates on the risks in reaching a decision. The theory begins by assuming that the individual will always optimize benefits and is never completely informed in advance about the outcome of his choice. In situations of concern, at least two or more alternatives exist, and each has two or more possible outcomes. Two questions arise: the first concerns the probabilities attached to possible outcomes; the second, the utility of each outcome, that is, where each stands on a scale ranging from highly desirable to highly undesirable (+1 to −1). Decision theorists speak of a payoff matrix that specifies attendant gains and losses for each possible choice, both when that choice is right and when it is wrong. Multiplication of utility by probability results in *expected utility* and forms a basis for the choice of one possible course of action over another.

In principle, a fully automated decision system could be computer-implemented. However, this is possible only if all contingencies can be foreseen and all probabilities and utilities stated explicitly. Even if this could be done, there is no adequate strategy that will at all times establish rules to minimize losses and maximize gains to the system for every decision point.

In practice, decision situations are often ambiguous in structural and temporal values, and the information on which the decision must be based may be incomplete, contradictory, or unreliable. The human decisionmaker can often make appropriate choices under such circumstances by assigning what are termed *subjective expected utilities* to the alternatives. Obviously, experience and training enhance judgment in decision situations. Astronaut and cosmonaut selection and training are strongly influenced by these considerations as is the selection of control and display design strategy.

Information Theory

The information theory model was originally developed to study transmission characteristics of communication systems, and has been used to study the rate and accuracy of human information processing [4, 12, 14, 26, 32, 36, 41, 44]. Information has been defined as the aspect of a message that reduces uncertainty; the unit of measurement is the *bit*. One bit of information is defined as the amount that reduces uncertainty by one-half. Thus, in a situation where two alternatives are equiprobable as far as the information receiver knows, one bit of information permits selection of one or the other. The amount of information (usually denoted by the symbol H) is given by the formula $H=\log_2 n$, where n is the number of equally probable alternatives. This formula is used where many alternatives are possible requiring only that they be equally probable.

Where events are not equiprobable, the usual case, information content declines but can be calculated by a somewhat more complex procedure. A formula commonly used is $RT=0.17+0.14\ \log_2 n$, where n is the number of alternatives, and reaction time is used as the measure of uncertainty.

Developments in information theory have enabled measurement of the quantity of information conveyed by one or more stimuli dimensions and the maximum rates for human information processing. In operation, subjects could accurately identify as many as 15 pointer positions on a scale, thus transmitting 3.9 bits. This is an unusually high figure for a single-stimulus dimension; multiple dimensions give improved performance.

Another consideration is the rate at which information can be processed (i.e., human channel capacity). Test results of channel capacity in sequential dial reading and air traffic control tasks indicate that approximately 8 bits/s may be realistic maximum value.

Both theories endeavor to characterize complex human activities in simple mechanistic terms. A man does, on occasion, act in such a simple mechanical manner, but, when simple modes of action are inadequate, he resorts to more complex strategies or processes for which no adequate model exists. Numerous authors have discussed the inadequacy of these theories and models as descriptive of man's decision formulation and information acquisition processes [23, 26, 33, 45]. Others have challenged the relevance of the model variables to design criteria [7, 23, 33]. Although there are real and significant shortcomings to these theories and models, they are of some use in formulating a *figure of merit* which may be used to assess design alternatives in engineering trade studies.

Displays and Controls

In the operation of any complex system, numerous displays and controls are available to the operator for monitoring system status and maintaining or altering that status. A closed-loop tracking system is used to control the attitude and flight path of spacecraft. Given a set of desired vehicle motion characteristics, a system must be developed in accordance with the expected inputs and control characteristics with the characteristic transfer function of the operator linking the two. This human transfer function must account for man's sensory and perceptual processes, reaction and decision times, and accuracy in force and direction of control movements. All these affect his characteristic as a link between display and control.

Closed-loop tracking systems incorporate a means for sensing the system output and presenting a form of error information to the astronaut through a feedback loop, permitting him to adjust controls to minimize error. This process is continuous in tracking tasks.

The control order of a system is determined by the order of the mathematical equation necessary to define the human transfer function. Zero order, or position control, means the operator's control output directly determines the system output; the only concern is the necessary amplification or gain (equivalent to arithmetic multiplication). First order, or rate control, means the operator must perform an operation equivalent to differentiation to perform the task. Second order, or acceleration control, in effect, requires double differentiation.

In general, tasks involving second-order or higher order functions are not suitable for manual systems. There is evidence that humans perform integration better than differentiation, but performance deteriorates if too much such activity is required. These requirements often can be eliminated by designing the machine to perform integrating and differentiating functions and to display the results of these computations to the operator. Such "aiding" of the operator makes integrated flight control displays more effective than the sum of the input data.

Servosystems. In the type of system under discussion, man operates in a manner analogous to a closed-loop servosystem. A basic assumption of

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linearity—that the observed response of a system to multiple inputs equals the sum of the response to the separate inputs—is made in servosystem theory. However, humans are not linear. In practice, functions are developed for particular cases that consist of a linear component and a remnant. The latter includes both systematic nonlinear elements and noise elements that are random and unpredictable.

The ability of pilots to operate manual control systems successfully in response to various forcing functions has been studied extensively. Specification of successful tracking limits of complex functions, such as those that occur in turbulent air, is of particular importance to aircraft designers. Human bandwidth characteristics preclude successful operation at frequencies higher than approximately 3 Hz. Because the operational regimes of manned spacecraft have not encountered extensive regions of such random phenomenon as turbulence, system design has been somewhat simpler.

The inclusion of man in the control system rather than use of a servosystem is desirable because the crewman is inherently adaptive. The pilot is not only adaptive in a gain-varying sense, but also he is adaptive in the sense of imposing purpose. He can operate to varying criteria of precision and time to complete a given maneuver. This is particularly important in spacecraft energy conservation.

The application of knowledge about man's capability to definition of his role in a new system has been assessed in many ways. Walker [48] endeavored to evaluate the benefit of the pilot to the X–15 experimental rocket aircraft program. He concluded that system redundancy in a piloted vehicle gave the greatest potential for mission success, and that elimination of either redundancy or the pilot had comparable impact (an estimated 40% reduction in successful missions, based on an analysis of 44 flights).

In another line of reasoning to define man's role in space flight, the endeavor was to assess his contribution to time-dependent system reliability [19, 20, 31, 38]. With the use of performance data characteristic of systems operational between 1950 and 1960, various studies led to the conclusions that man's contribution to mission success lay in the maintenance of redundant systems, and that for long-term missions, he was cost-effective in this role. Such arguments are highly sensitive to the state of the art in electronic piece parts, and the effect of integrated circuits was not foreseen. Although these study results continue to have force for some electromechanical and mechanical systems, the argument is substantially modified from the early conception of primarily electronic system maintenance.

Stress. In contrast to those considerations that argued for the inclusion of man in space systems, there have been concerns about man's response to the physiologic and psychologic stresses of space flight. Isolation, confinement, and disruption of the diurnal cycle have been studied as significant forms of stress [25, 37, 49, 51, 52]. In general, experimental studies identify performance degradations, such as longer periods required to complete tasks, higher error rates in the execution of tasks, and reduced ability to concentrate.

In the limited number of space flights so far, such performance losses have not been observed. Failure to observe such degradation is attributed to substantial overtraining of flight crews for the tasks they must perform, diverse and interesting stimuli present in the real environment contrasted with minimum stimulation environment in simulations, and stronger motivation in flight crews compared with test subjects. The selection of cosmonauts and astronauts is strongly biased to identify men of superior psychologic stability and stress tolerance. The relevance of sensory deprivation studies to current spaceflight operations seems marginal. Confinement is not frustrating to the crewman's purpose or desire; the flight activities required of him are varied and demanding, not minimal and monotonous. Finally, the crewman is in frequent or continuous voice communication involving both work and social topics. Normal operations of space flight contrast significantly with the conditions that induce isolation symptoms.

Work-rest cycles. The variation of work-rest cycles has been studied intensively because of its significance to productivity and safety. Operator efficiency is highest when a stable 24-h period of work and rest is maintained. The most important benchmark is a consistent time for sleep. Other cycles, such as 4 h work followed by 4 or 2 h sleep, have been studied and are less satisfactory, both physiologically and psychologically, than the customary 24-h day, with an uninterrupted 8 h sleep.

Although the orbital period of the spacecraft may be only 90 min and the track over the ground varies continuously, generally it has been possible to design spacecraft systems and plan flights so crews can sleep their accustomed cycle.

A common argument for the inclusion of man in a system is the use of human judgment; that is, the ability of man to perceive the relevant in novel situations and to improvise and react intelligently to the unanticipated. This argument, although hard to quantify, is applied equally to man's role as a system operator or as a scientific observer and is consistent with historical experience (e.g., Darwin's insight as a function of his voyage on the Beagle).

The role of the crew in manned spacecraft, as it has reflected these theories, considerations, and studies, is discussed in subsequent sections of this chapter.

GEOMETRIC CONSIDERATIONS

The most prominent characteristic of manned spacecraft is orientation of seating so that launch and entry loads are imposed on the crewman transversely, that is, from front to back rather than from head to foot. This orientation maximizes physiologic tolerance to acceleration. Orientation of interior work stations is fixed by this consideration in Mercury, Gemini, Vostok, and Voskhod spacecraft. In the Apollo command module, a second array of interior work stations is oriented at 90° to the launch- and entry-oriented main display console. These stations are used for operation of the navigation optics, food preparation, and other functions. The Apollo lunar module was configured so as to provide maximum visibility with the smallest possible window. Because flight acceleration loads are less than 1 g and the worst-case landing impact loads are small, the crewmen can attenuate such loads with their legs and be positioned upright close to the front of the spacecraft with the window oriented so that they can see down, ahead, and to the sides.

The Soviet Soyuz spacecraft has two habitable modules: the command module, with primary controls arranged in panels accessible from the launch and entry couch; and an orbital module, with stowage compartments and work stations arranged around the periphery of the spacecraft. The Salyut configuration establishes a conventional gravity-oriented architectural arrangement relative to a floor on one side of the spacecraft. This spacecraft has three discrete, though not isolated, volumes: transfer tunnel, console area, and (in the region of maximum diameter) a large working area. Instruments and viewing ports are provided at locations throughout the spacecraft.

The Skylab configuration is controlled by the need to maintain a central-axis transit passage and by the endeavor to achieve a conventional architectural arrangement normal to the major axis of the spacecraft. By all previous standards, the Skylab orbital workshop module is a spacious spacecraft. This configuration is attributable, in part, to its derivation from an existing structure, the Saturn IVB (S–IVB) stage, and in part to the need for assessing the value of greater volume to the operational effectiveness of longer missions. Volume use rate also will be low, reflecting the restrictions of the initial launch weight and the limited payload to and from Skylab that can be accommodated by the Apollo command module. Distribution of volume among so many modules and levels has some disadvantages in the loading and transportation of equipment through the assembly.

The general configurations for each American spacecraft and current Soviet manned spacecraft are shown in Figures 1 to 5.

The relationship of crew size, pressurized volume, and usable volume of each spacecraft is shown in Table 2. The usable volume is defined as that within the pressure vessel not occupied by equipment and that can be used for temporary stowage, movement by the crewmen, or other functions that enhance habitability. The

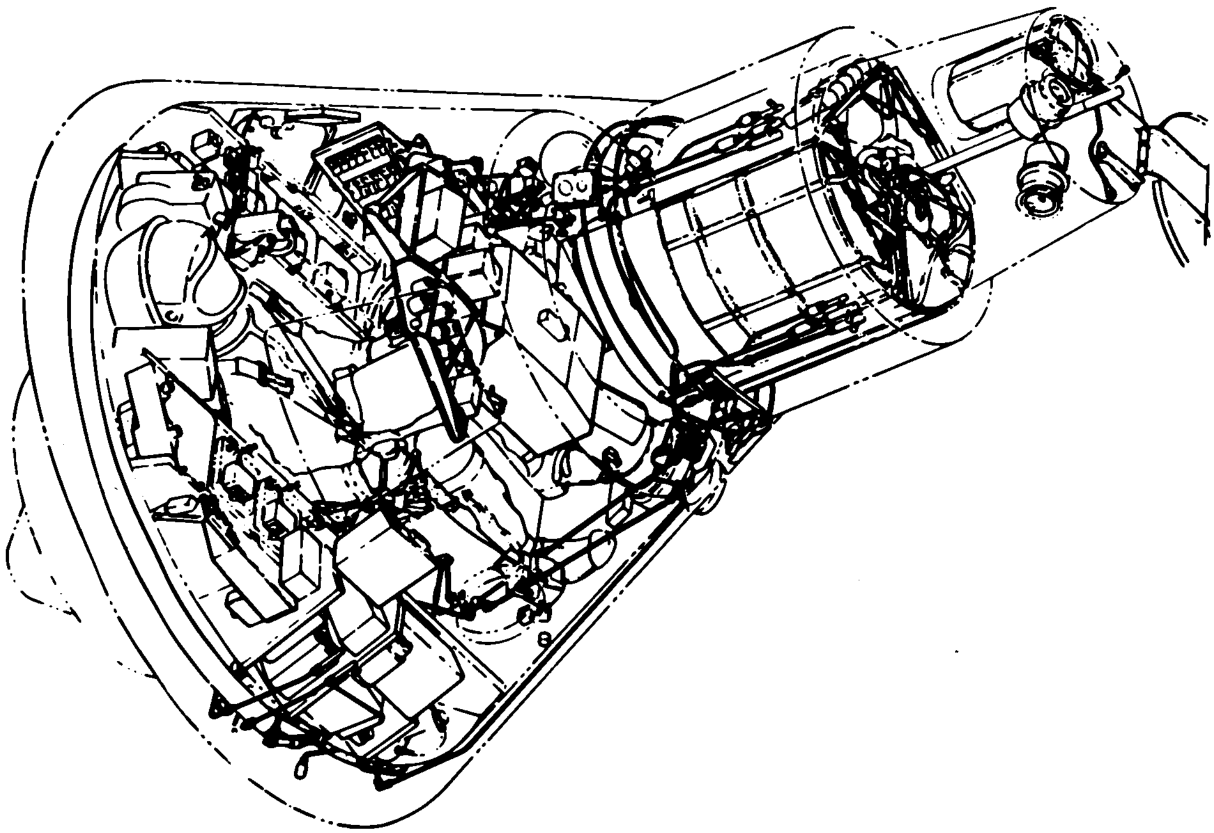


FIGURE 1.—Mercury capsule internal arrangement.

volumes increase noticeably from the first to the present spacecraft configurations. For the Mercury and Apollo command module spacecraft, the relationship of the pressurized volume to effective free volume reflects that most equipment was installed within the pressure vessel. Gemini and lunar module spacecraft had only the crew instrument panels and portions of the environmental control system installed within the pressure vessel. Estimates of the volumes for Soviet spacecraft indicate similar arrangements.

There are relationships of spacecraft volume, mission duration, and crew size to similar values for submersibles and aircraft (Fig. 6). In all vehicles, the pressurized or conditioned volume of the vehicle increases as a function of both crew size and mission duration. Mission duration can be varied extensively for a given vehicle; however, for smaller vehicles, significant stresses may be placed on the crewmen.

Fraser [15], in 1965, reviewed extensively the literature compiled on the effects of confinement. He indicates that motivated and experienced personnel, occupied with meaningful tasks and informed as to the status and duration of the mission, need a volume of 0.7 to 3.5 m^3/man for missions of 7–10 d and that 4.24 m^3/man appears to be adequate for missions as long as 30 d. Present spacecraft are adequate by such standards, which flight experience substantiates. However, more general experience indicates that such cramped quarters are not efficient for larger populations or for small crews subjected to high workloads.

Stresses placed on the crew by limited volume are: lack of movement and exercise that leads to physiological deconditioning; loss of efficiency as two or more crewmen endeavor to pursue their duties without interfering with each other; and sleep disturbance when one crewman's motion disturbs others.

Spacecraft dimensional characteristics become

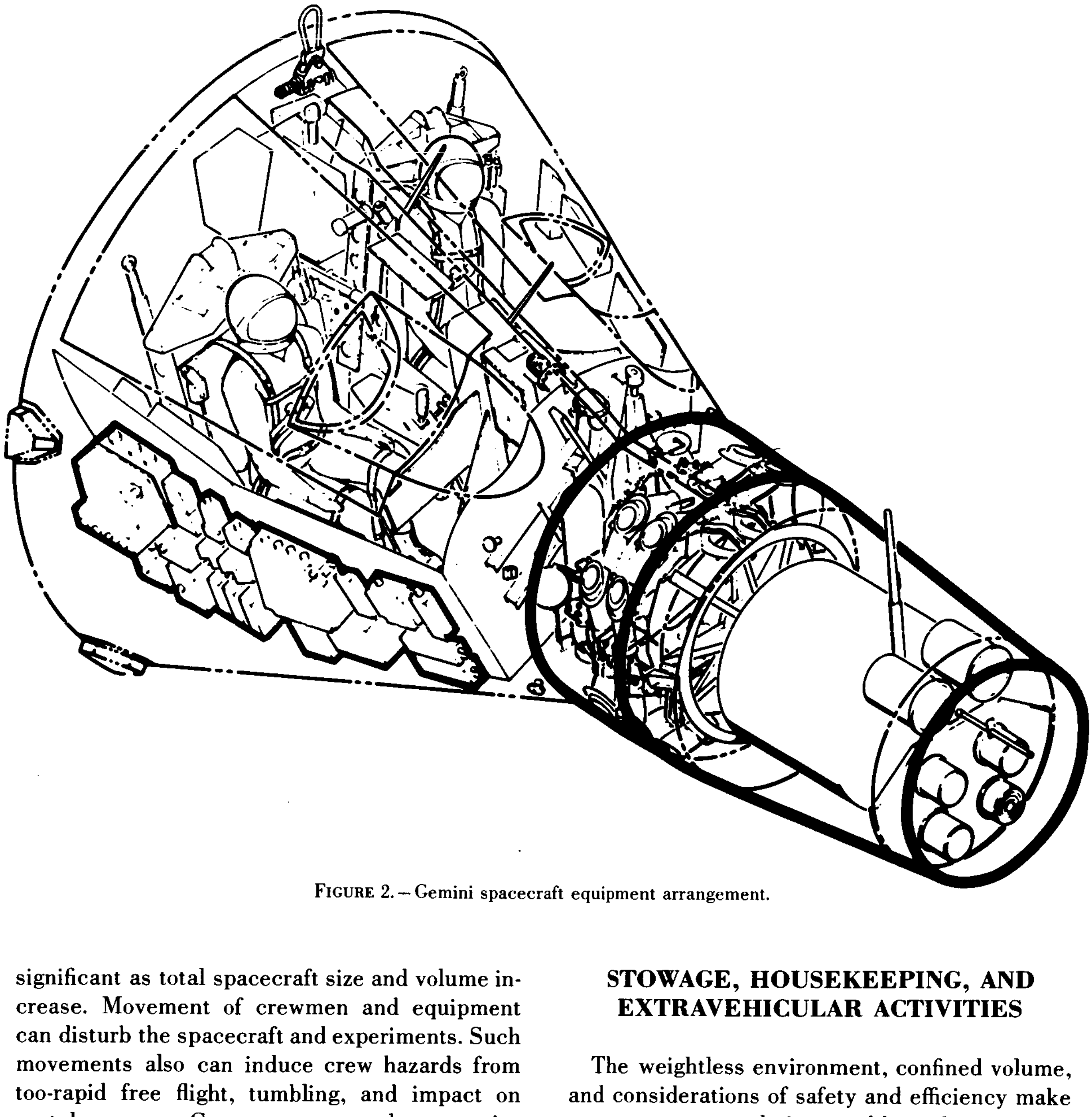


FIGURE 2.—Gemini spacecraft equipment arrangement.

significant as total spacecraft size and volume increase. Movement of crewmen and equipment can disturb the spacecraft and experiments. Such movements also can induce crew hazards from too-rapid free flight, tumbling, and impact on protuberances. Crewmen must also exercise caution in movement to avoid inducing vestibular disturbances.

Crew and medical reports indicate that increased volume of the Apollo spacecraft and opportunity for movement have removed many of the discomforts and debilitating effects of the close confinement characteristics of Mercury and Gemini spacecraft. For future space vehicles with increased performance, more volume for each occupant will enhance both efficiency of operation and habitability.

STOWAGE, HOUSEKEEPING, AND EXTRAVEHICULAR ACTIVITIES

The weightless environment, confined volume, and considerations of safety and efficiency make stowage accommodations and housekeeping procedures a significant part of the crewman's total activity. During extravehicular activity (EVA), safety precautions become even more significant. The dynamics of object movement in orbit are such that items not secured to the spacecraft or to the crewman will separate rapidly; consequently, efficient operation requires orderly procedures and careful stowage and handling of all items. Because of inherent interdependency of extravehicular activities with stowage and housekeeping, these tasks are discussed collectively.

The Mercury spacecraft pilot was restrained by his couch harness assembly and by the spacecraft's interior confines. The spacecraft was designed as a one-man vehicle, with all items necessary for either vehicle control or personal use within reach from the crewman's restrained position in the couch. Only one stowage compartment was available, which was used for flight checklists and other documents. Other equipment items were stowed in bags, pouches, or on specific attachments to the interior structure.

The Gemini Program introduced a spacecraft with a two-place, side-by-side seating configuration (Fig. 2). Quarters were still cramped, and essential cockpit activities again were confined to the approximate reach envelope of the seated crew. However, increasing activity by the crewman in more complex mission operations is evidenced by the increased number of stowed items compared with that of the Mercury spacecraft (Table 3). The advent of several compartments within the cockpit for stowage of specific items generated the need for disciplined management of loose items to make efficient use of space, avoid time lost searching for stowage space for items in use, or recover from stowage items required for anticipated activities.

The increase in the number and scope of Apollo and Skylab mission objectives is indicated by the growth in the number of stowed items. This growth reflects increase in crew size, duration of missions, and emphasis on scientific objectives as operational maturity evolves. An analysis of the information in Table 3 shows that growth is caused primarily by time-dependent operational items (e.g., food and film) and by increased emphasis on scientific and applications experiment activities. The number of items increased, also the di-

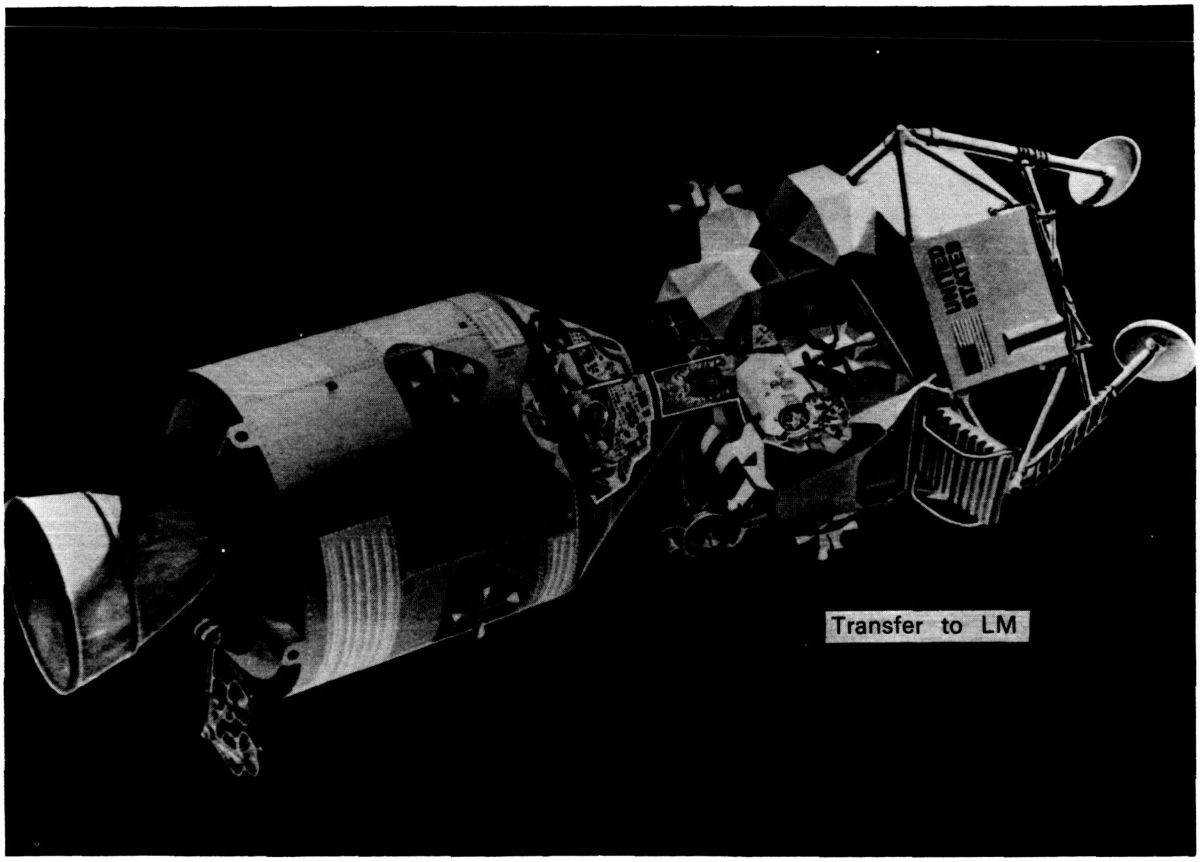


FIGURE 3. – Apollo command and lunar module configuration.

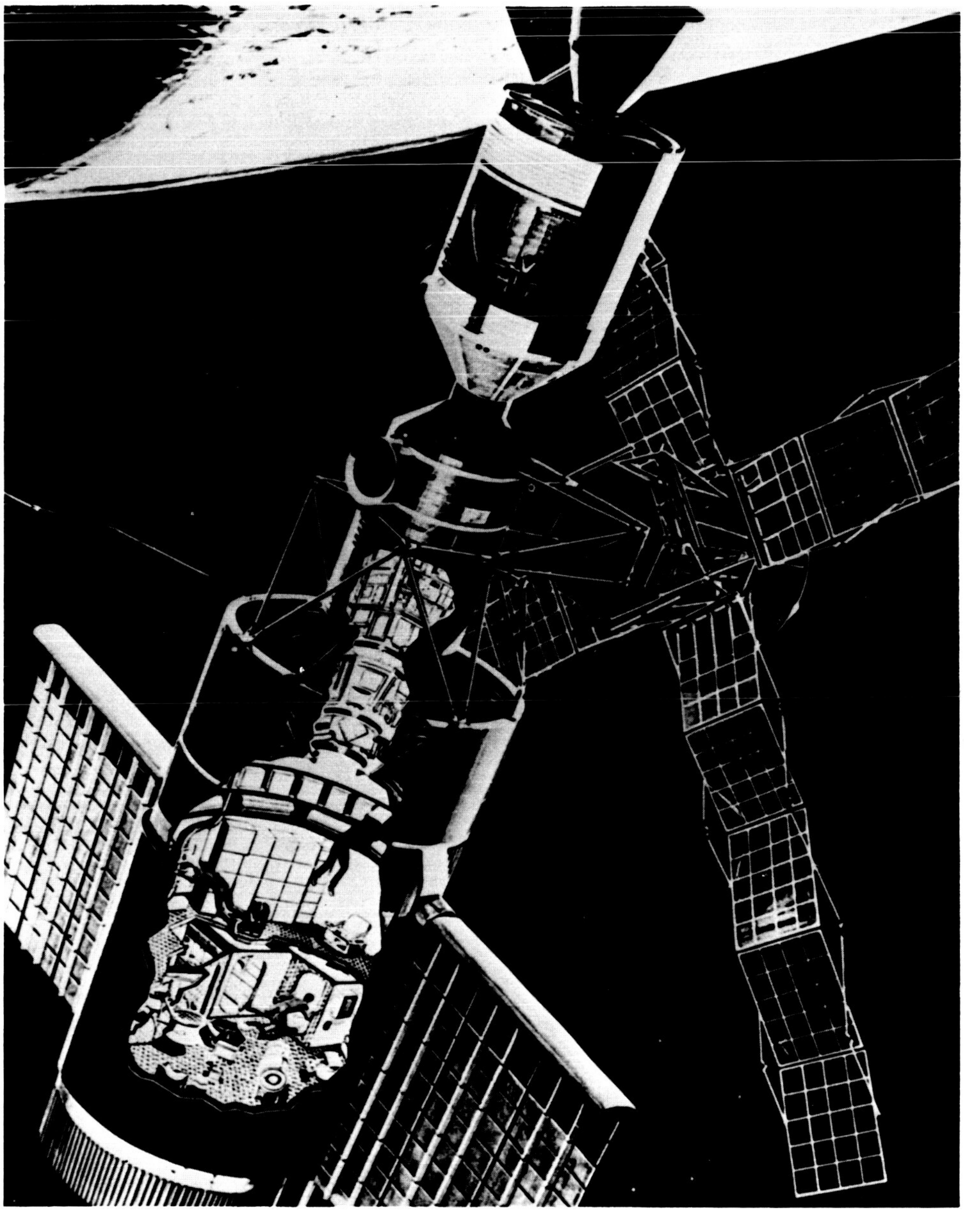


FIGURE 4.—Skylab spacecraft configuration.

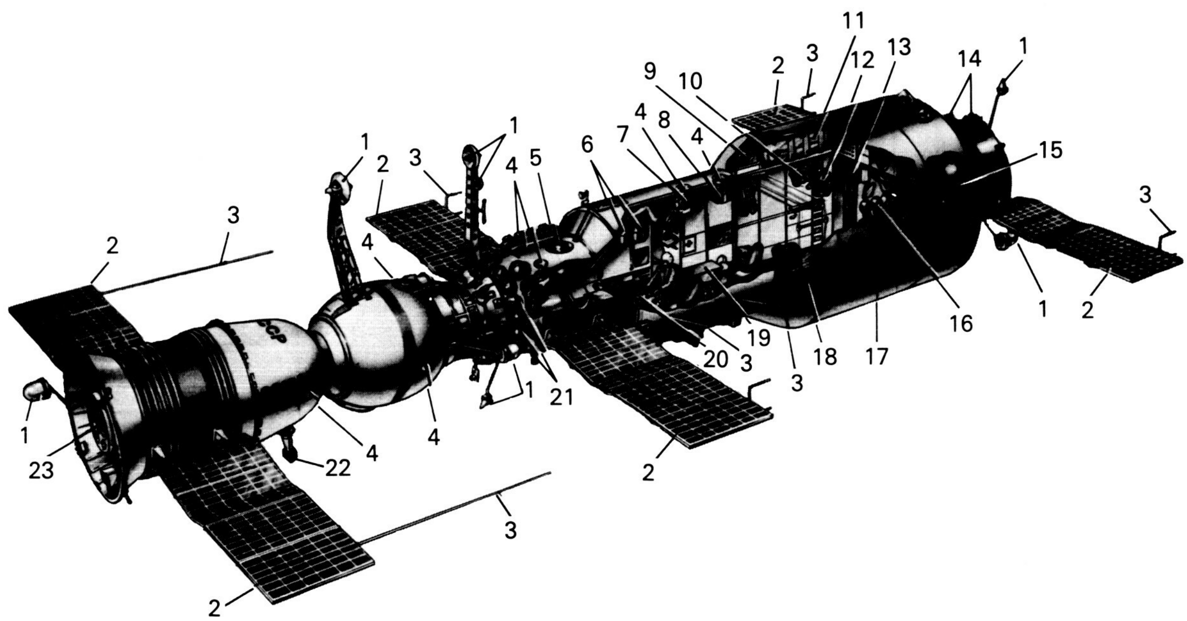
versity and complexity of the items. Table 3 indicates that the number of stowed items increased by a factor of 4, even when the items attributable to more crewmen and a longer mission were omitted.

A problem not apparent in the tabulation of this experience is the demand placed on the crew to become familiar with all equipment manipulations. Each unit is simple in its operation and stowage, but the proliferation of such items places great demands on the crew. To contend with these factors, extensive use of decals and placards with appropriate instructions is required which helps to minimize training requirements and save time during mission operations.

EVA Considerations

Preparation for EVA is one of the most demanding activities for space crews. The cabin to be depressurized must be properly organized, the equipment donned, and its operation tested. In the limited volume of the spacecraft, this requires well-planned procedures, teamwork, and extensive training. The need for such careful simulation and training was established during some of the early Gemini extravehicular activities, when astronauts were not able to complete planned tasks. The simulation of weightlessness by water immersion has been an effective method for developing procedures and training astronauts. The water immersion simulation is augmented by short periods of zero g produced in aircraft.

Both astronauts and cosmonauts report that EVA is pleasant, with no difficulties in orientation [18, 21]. The crewman appears to use his body or the spacecraft as a frame of reference and is not disturbed by his relative location to the Earth and spacecraft. Because vision is the only sense stimulated and because it provides adequate reference, there are apparently none of the illusions



Design outline of the "Salyut" orbiting scientific station

1. Antennas for the rendezvous radiotechnical system
2. Solar battery panels
3. Antennas for the radio telemetric systems
4. Beacons
5. *Orion* stellar telescope
6. Air-conditioning unit
7. Motion picture camera
8. Photographic equipment
9. Equipment for biological experiments
10. Refrigerator for food supply
11. Sleeping berth
12. Water supply tanks
13. Water collectors
14. Motors of orientation system
15. Fuel tanks
16. Sanitary and hygiene unit
17. Micrometeroid registration sensor
18. Treadmill
19. Work table
20. Central control post
21. Tanks for pressure charging system
22. Cosmonauts' sighting device
23. Engine assembly of the Soyuz spacecraft

FIGURE 5. – Soyuz-Salyut spacecraft configuration.

TABLE 2.—*Relationship of Crew Size and Spacecraft Volume*

Spacecraft	No. crewmen	Pressurized volume,[1] m^3	Effective spacecraft interior free volume,[1] m^3	Habitable volume per crewman, m^3
Mercury	1	1.42	0.71	0.71
Vostok	1	2.55	2.00	2.00
Gemini	2	2.27	1.15	.57
Voskhod	2 or 3	4.85	3.68	1.84/1.23
Apollo				
Command module	3	8.95	7.27	2.41
Lunar module	2	6.63	5.25	2.62
Soyuz				
Command module	1 to 3	4.81	3.96	3.96/1.32
Orbital module	1 to 3	6.22	4.53	4.53/1.51
Salyut	3	90.00	81.00	27.00
Skylab				
Command module	3	8.95	7.24	2.41
Orbital assembly total	3	351.17[3]	316.06	– –
Multiple docking assembly		32.57	28.30	105.35
Airlock module	– –	16.99	12.74	– –
Orbital workshop	– –	301.61	279.71	– –

[1] Pressurized volumes are derived from design data for US spacecraft and from reports in literature for USSR spacecraft.
[2] All effective free-volume estimates are based on geometric analyses.
[3] Total volume of all modules of the orbital assembly.

customary when sensory cues conflict. Certain visual illusions are present to a greater degree than when the crewman is inside the spacecraft; bright stars seem closer, and dim stars seem farther away. This illusion appears to some degree in all orbital and in many high-altitude aircraft flights.

The $\frac{1}{6}$-g environment of the lunar surface proved to be both a help and hindrance to crewmen during EVA. Loads heavy and cumbersome in 1 g become quite manageable in $\frac{1}{6}$ g. However, lightweight items reacting readily to Earth gravity tend to respond quite slowly in reduced gravity and can become critical in the development of a proper time line. Lightweight items, such as thermal blankets, have inherent stiffness and must be placed in the specific location desired in the $\frac{1}{6}$-g environment; in a 1-g environment, the mass overcomes the stiffness and items fall into place.

To develop the lunar surface time line properly for a given mission, the crew begins exercises without suits to gain familiarity with all items and progresses through a set of activities wherein each step approximates more closely the actual lunar surface activity in terms of procedural details and time planned. Final practice runs are made in pressurized suits using working models of actual hardware and adhering strictly to time allocations and procedural details.

Adaptation to the $\frac{1}{6}$-g environment has proved reasonably rapid. Movement across the surface averages 0.38 m/s during the first excursion and increases to an average of 0.61 m/s for later excursions.

Despite the extensive training, the activities take almost 30% longer during flight than during training. This additional time is caused, in part, by the extra time required for each movement when moments of inertia are high and control capability dependent upon gravity forces low, and in part by the time required to assess characteristics of the real-time situation.

The EVA experience so far is shown in Table 4. An increasing demand has been placed on lunar mission crews in terms of time allocated to actual surface EVA excursions. As the Apollo program matured, greater confidence was gained in hardware performance, and crew capability was better understood, there was a larger commitment to surface EVA as a function of total surface stay time. The initial Apollo mission committed only 10% of surface stay time to EVA, while subsequent missions committed as much as 30% of total lunar stay time. Most of this additional exploration capability was a function of systematically maturing hardware and procedures.

Orbital EVA proved more predictable as soon as proper techniques were designed. Efficient methods provided for the return of primary image materials to Earth, adding significantly to the lunar science experiments. In Skylab, there were provisions for EVA to recover the film canisters from the Apollo telescope mount. The techniques for this operation included the use of handrails, tethers, and supports similar to those used on Gemini 12, Soyuz, and Apollo spacecraft for extravehicular transfer, and for film recovery from the Apollo scientific instrument module.

Structural failure of the meteoroid shield during launch and subsequent failure during the mission of other equipment led to a great number of excursions and tasks not considered in the original plans. The crew successfully executed repairs and adjustments for which no preflight design

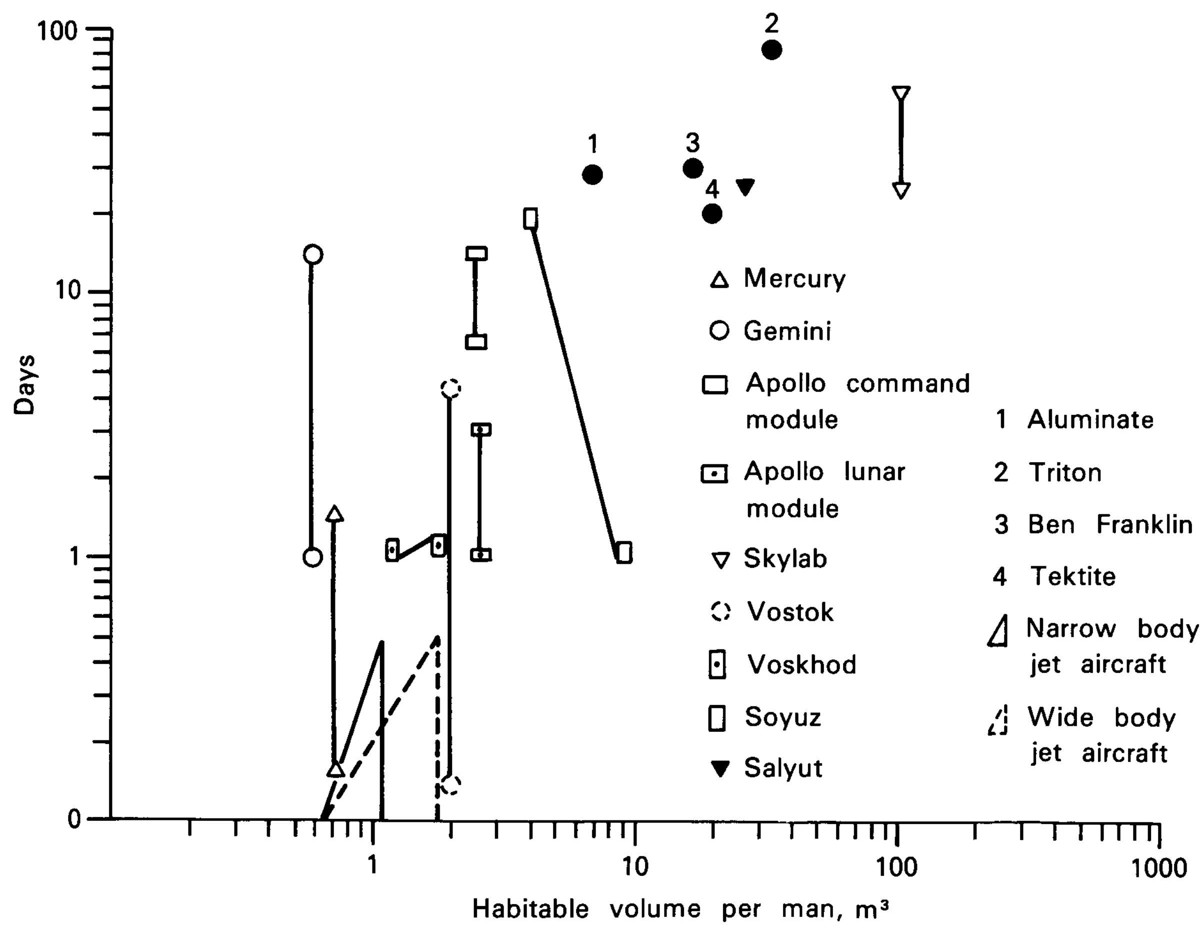


FIGURE 6. — Confinement effect of mission duration and spacecraft size.

TABLE 3.—*Spacecraft Stowage Characteristics*
(All numbers are typical and vary for specific missions)

Class of equipment	Spacecraft								
	Mercury	Gemini	Apollo			Skylab [1]			
			Command module	Lunar module		Command module [2]	Orbital assembly module		
				Ascent stage	Descent stage		Multiple docking adapter	Airlock module	Orbital workshop
Food and hygiene,[3] no. items	10	46	200	40	0	45	0	0	743
Experiment equipment, no. items	16	7	12	4	33	22	192	6	330
Television and photographic equipment, no. items	7	52	40	18	7	35	0	0	254
Extravehicular activity equipment, no. items	0	21	30	62	5	35	1	2	14
Operational equipment, no. items	15	70	230	89	8	285	44	417	455
Total no. of items	48	196	512	213	53	422	237	425	1796
No. stowage compartments	0	13	32	22	8	32	14	8	186
Nominal mission duration, d	$\frac{1}{3}$–$1\frac{1}{2}$	3–14	8–14	1–3		5	– –	140	– –
No. crewmen	1	2	3	2		3		3	

[1] Planned.
[2] For each of three spacecraft.
[3] One unit of food is three meals for one man.

provisions had been made. The success of these endeavors confirms the adequacy of the basic design provisions and the training regimen. Orbital EVA offers no significant difficulty if the crewman has adequate cooling in his life-support system and mounting provisions which allow him to react to forces appropriately.

Increased duration and complexity of missions; increased number, duration, and complexity of extravehicular activities; and forces during launch, spacecraft maneuver, and entry all demand orderly progression of equipment from stowed positions to use positions and to disposition locations. Many hours are spent by crews during preflight training to become thoroughly familiar with stowage provisions for each item and with the sequence in which the item is unstowed, used, and restowed or jettisoned. The precision with which these actions are performed has significant influence on the time allotments provided within the operational time line. Realistic values must be determined during preflight training for the times to be allocated to these activities in the mission flight plan. All astronauts and cosmonauts, during and after their missions, have remarked on the importance of order and discipline in these activities to efficient conduct of the mission. The consistency with which this aspect of each mission is discussed by astronauts and cosmonauts indicates that this aspect of accommodating to the weightless environment is a source of significant stress, where new design approaches might be beneficial. It is noteworthy that only in these housekeeping

TABLE 4.—*Extravehicular Activity Summary*

Mission	Type of EVA	Objective	Remarks	Standup EVA time, h:min	Umbilical EVA time, h:min	Free EVA time, h:min
Voskhod 2	Earth-orbital	Demonstrate feasibility of EVA	First EVA; all objectives satisfied	0	00:12	0
Gemini 4	Earth-orbital	Demonstrate feasibility of EVA Demonstrate maneuvering capability with hand-held maneuvering unit (HHMU)	All objectives were satisfied	0	00:36	0
Gemini 9	Earth-orbital	Retrieve experiment package Demonstrate astronaut maneuvering unit (AMU) Perform experimental star photography	Successfully retrieved experiment package Difficulty in AMU donning and visor fogging led to early termination of EVA	0	02:07	0
Gemini 10	Earth-orbital	Retrieve experiment package Evaluate HHMU Perform star photography	All objectives were satisfied First transfer of tethered crewman between undocked, orbiting vehicles	00:50	00:39	0
Gemini 11	Earth-orbital	Perform simple work tests Evaluate HHMU Perform star photography	Experiment package retrieved EVA terminated early because of metabolic overload of crewman	02:10	00:33	0
Gemini 12	Earth-orbital	Evaluate matrix of simple tasks Evaluate translation and restraint aids Perform experimental photography	All objectives were satisfied	03:24	02:06	0
Soyuz 4	Earth-orbital	Transfer crewman between spacecraft	Transfer successful	0	0	00:15
Soyuz 5	Earth-orbital	Transfer crewman between spacecraft	Transfer successful	0	0	00:15
Apollo 9	Earth-orbital	Demonstrate lunar module to command module transfer capability Demonstrate adequacy of Apollo EVA equipment and procedures	All objectives were satisfied This was first two-man EVA	00:47	0	00:47
Apollo 11	Lunar-surface	Demonstrate lunar-surface EVA capability Gather samples Emplace experiment station	All objectives were satisfied This was first lunar-surface EVA	0	0	02:48 per astronaut
Apollo 12	Lunar-surface	Emplace experiment station	All objectives were satisfied	0	0	07:56 per astronaut

TABLE 4.—*Extravehicular Activity Summary*—Continued

Mission	Type of EVA	Objective	Remarks	Standup EVA time, h:min	Umbilical EVA time, h:min	Free EVA time, h:min
Apollo 12—Con.		Conduct geological traverse and sampling Inspect and recover parts of Surveyor 3 spacecraft				
Apollo 14	Lunar-surface	Perform scientific experiments Emplace an experiment station Conduct geological traverse	All objectives were satisfied	0	0	09:20 per astronaut
Apollo 15	Lunar-surface	Perform scientific experiments Emplace an experiment station Conduct extended traverse using lunar roving vehicle	All objectives were satisfied	00:38	0	18:35 per astronaut
	Trans-Earth	Recover film from service module instrument bay		0	00:39	
Apollo 16	Lunar-surface	Perform scientific experiments Emplace an experiment station Conduct extended traverse using lunar roving vehicle	All objectives were satisfied	0	0	20:15 per astronaut
	Trans-Earth	Recover film from service module instrument bay		0	01:24	
Apollo 17	Lunar-surface	Perform scientific experiments Emplace an experiment station Conduct extended traverse using lunar roving vehicle	All objectives were satisfied	0	0	22:04 per astronaut
	Trans-Earth	Recover film from service module instrument bay		0	01:07	
Skylab[1] 1st visit	Earth-orbital	Deploy failed solar array	Attempt failed	00:35		
		Deploy failed solar array Retrieved and installed film packs Retrieved and installed film pack Deployed samples Repaired equipment	All objectives were satisfied		4:59 per astronaut	

See footnote at end of table.

TABLE 4.—*Extravehicular Activity Summary*—Continued

Mission	Type of EVA	Objective	Remarks	Standup EVA time, h:min	Umbilical EVA time, h:min	Free EVA time, h:min
Skylab [1]—Con.						
2nd visit		Retrieved and installed film packs and samples Mounted experiment Deployed sunshade Repaired gyros and experiment covers Cleaned occulting disk	All objectives were satisfied		13:42 per astronaut	
3rd visit		Installed and retrieved film pack Mounted samples and experiment and experiment apparatus Repaired experiment apparatus Observed Comet Kohoutek Documented spacecraft exterior systems Made atmospheric and contamination observations	All objectives were satisfied		22:15 per astronaut	

[1] Preplanned mission objectives contained 18 discrete tasks and required 14:30 hours of EVA for each of the crewmen. Contingency and mission objective opportunity tasks numbered 51 and extended actual total EVA time to 40:56 for each of two crewmen and an additional 35 minutes of standup EVA.

activities and in the related extravehicular activities does flight performance require significantly longer amounts of time than performance in training simulators.

CONTROLS AND DISPLAYS

The complexity, size, and number of display consoles in spacecraft have increased with more complicated missions and design commitment to the maximum effective use of crewmen. Panel layouts from each US spacecraft are shown in Figures 7–11 and for Soyuz spacecraft in Figure 12. This growth, in terms of types and number of components for US spacecraft, is shown in Table 5. The technology of display and control components grew substantially more sophisticated from Project Mercury to the Gemini program, and this new technology was further refined for the Apollo and Skylab programs. Increased complexity of the displays and controls emphasizes the importance of crew functions on success of the mission; the emphasis is on finding the most efficient means to convey information to the crew.

The Mercury display and control panel is noteworthy for relative simplicity of displays, large number of sequential backup controls, and prominence of sequence and time displays. The instrument panel illustrated in Figure 7, for the last flight (Mercury-Atlas 9), reflects the most complex configuration of the series. The major factors in the derivation of this configuration

TABLE 5.—*Crew Control and Display Characteristics*

Device characteristic	Spacecraft							
	Mercury	Gemini	Apollo		Skylab			
			Command module	Lunar module	Command module	Orbital assembly module		
						Multiple docking adapter	Airlock	Orbital workshop
Panels	3	7	28	12	26	31	58	74
Work stations	1	2	5	2	5	3	4	8
Control elements (total)[1]	98	286	721	378	760	350	694	363
Circuit breakers	(20)[2]	107	264	160	256	19	307	214
Toggle switches	56	123	326	144	372	239	326	88
Pushbutton switches	8	20	13	7	15	12	0	0
Multiposition rotary switches	6	19	21	16	19	50	22	32
Continuous rotary switches	3	0	35	21	36	17	3	9
Mechanical devices	3	13	57	26	57	7	35	18
Unique devices[3]	2	4	5	4	5	6	1	2
Display elements (total)[1]	45	68	131	144	152	222	323	116
Circular meters	16	7	24	6	23	1	0	2
Linear meters	0	25	33	25	33	14	64	42
Digital readouts	3	14	18	13	19	20	1	18
Event indicators	19	16	47	96	68	182	258	50
Unique displays[4]	7	6	9	4	9	5	0	4
Inflight measurement points[1]	100	225	475	473	521	918	521	281
Telemetered	85	202	336	279	365	918	521	230
Displayed on board	53	75	280	214	289	167	129	30
Caution and warning	9	10	64	145	61	97	91	8
Input								
Analog signal	9	10	42	45	33	2	87	2
Discrete signal	0	0	22	100	28	95	4	6
Output	9	10	35	34	35	13	38	8

[1] Numbers for each program vary, depending on particular spacecraft.
[2] Fuses, not circuit breakers, used in Mercury.
[3] Three-axis hand controllers, computer keyboards, etc.
[4] Flight director attitude indicator, computer displays, entry monitor, cross points.

were:

the principle that there would be redundant means available to accomplish all critical functions;

the need to have available both on-board and ground data concerning the status of consumables;

the need, with intermittent communications, to maintain a common time reference with the ground control system to control mission sequences and the retrofire maneuver, which initiates ballistic entry.

To save weight and power, attitude was displayed on a meter with three movements: a horizontal needle moving in the vertical plane for pitch and two vertical needles (one at the top and one at the bottom) moving horizontally to display yaw and roll. Attitude rates were displayed on separate movements arranged around the attitude indicator.

With ground command, the automatic stabilization and control system could perform all the critical flight maneuver sequences; in fact, the system had been used for unmanned flights. On manned flights, as a rule, the crewmen used a rate-command mode to conserve propellants. The simplicity of the system reflects minimal demands on the crewman and simplicity of the mission.

The Vostok and Voskhod spacecraft also had relatively simple controls and displays. Both portholes and a periscope were used for viewing outside the spacecraft. Systems displays were simple, circular meter movements. The most prominent display element was an Earth sphere that provided reference to groundtrack.

The Gemini panel (Fig. 8) was notably more complex than that of the Mercury. The Gemini panel introduced the computer keyboard and digital readout; the integrated display of attitude, attitude error, and rates on the flight director attitude indicator; the comparative display of redundant system conditions; vertical-scale meters; and the extensive use of circuit breakers, not only to protect circuits but also to disarm selected systems during certain mission phases. The panel arrangement was similar to that of aircraft, in that flight-control displays were furnished for each crewman (command pilot and pilot), supporting systems were centrally located and shared, propulsion systems were primarily accessible to the command pilot, and navigational systems were primarily accessible to the pilot.

Increased complexity of the spacecraft and mission objectives resulted in additional subsystems (e.g. the inertial reference unit, the radar system, and the computer) and in greater complexity and redundancy in other systems (e.g. the attitude maneuvering system and electrical power systems). These complexities were reflected in the larger number of display and control

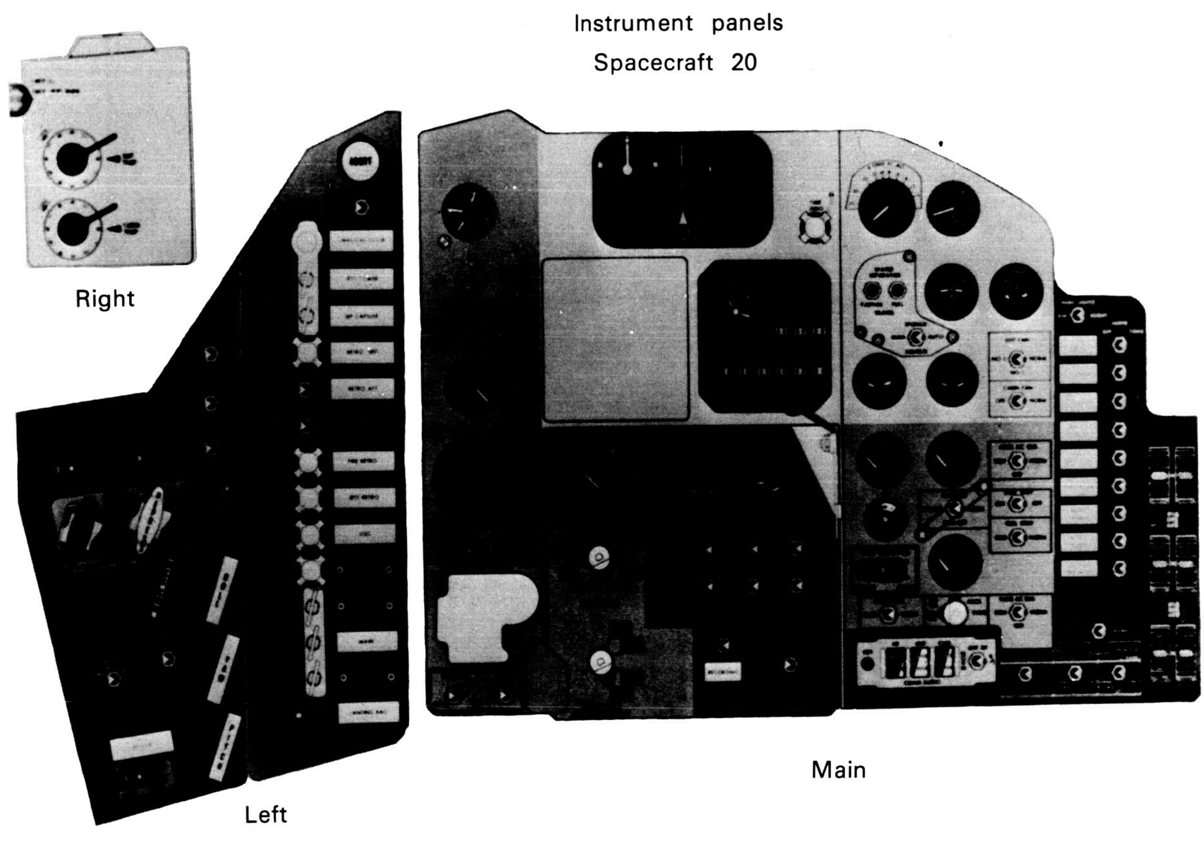


FIGURE 7.—Mercury spacecraft instrument panel.

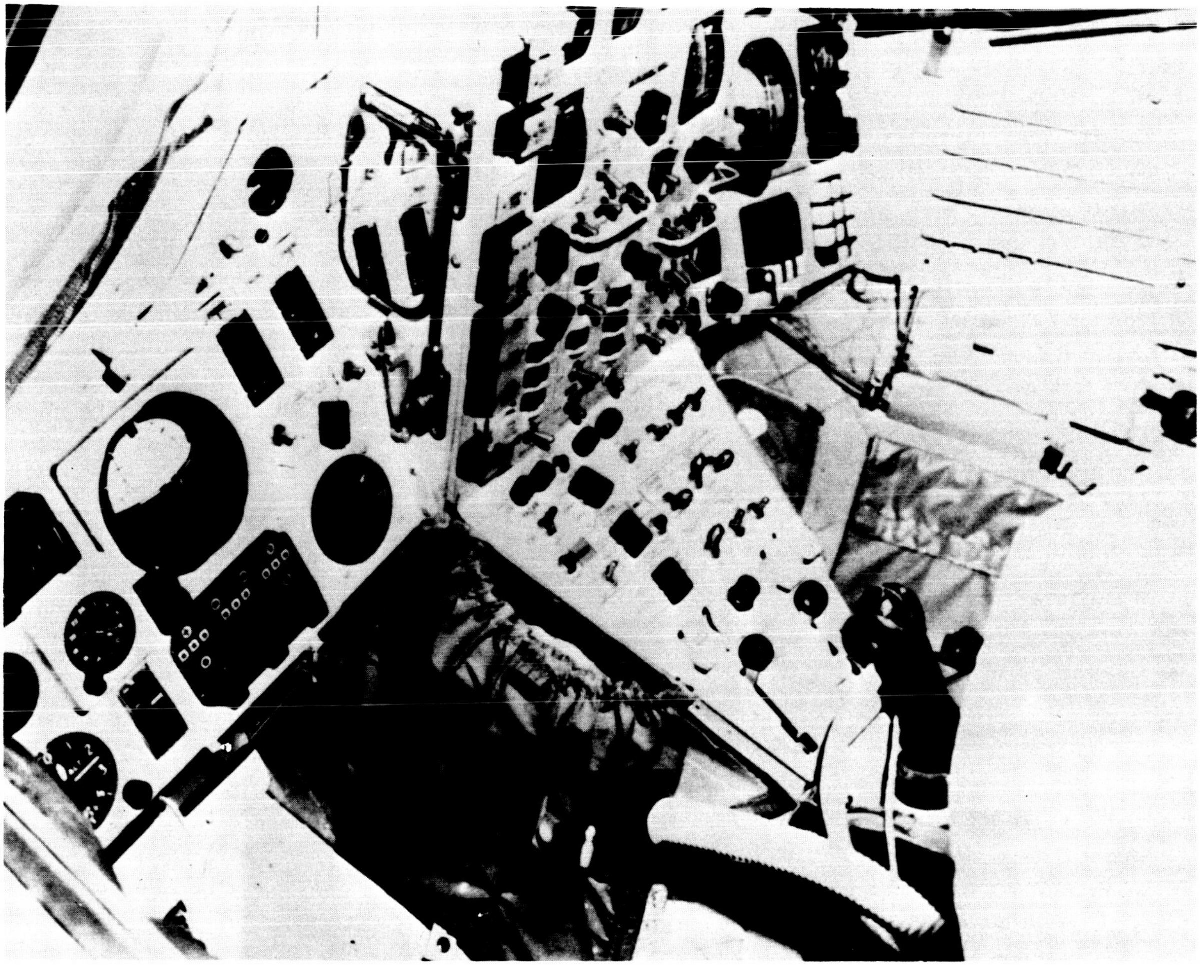


FIGURE 8. – Gemini spacecraft displays and controls.

elements and increased telemetry of data to the ground. To accommodate display requirements, many of the meters were time-shared among several parameters for a subsystem or among redundant systems for a single parameter.

Experience with the display and control system indicated that the integrated display of attitude and rate information on the flight director attitude indicator was superior to the Mercury display. For most flight modes, a local vertical reference was useful; for rendezvous, however, maneuvers were more effectively visualized in a target-centered inertial frame.

The use of vertical-scale meters conserved panel space and provided a more effective cross-check than had been attainable on the Mercury spacecraft with circular meters that were in line only at the 9 and 3 o'clock positions. Similarity of the cockpit to that of high-performance aircraft illustrates the degree to which the crew had been allocated a similar role. With ground assistance in navigation and flight planning, the mission could be conducted from on-board the spacecraft.

The Apollo command module and lunar module display and control panels (Figs. 9, 10) are three to four times more complex than the Gemini panel. The increase in complexity results from additional mission phases and level of system redundancy provided. The Apollo Program includes all the elements of planetary exploration. No previous spacecraft has had more than a

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fraction of this capability; at least a second generation of spacecraft must be developed before another program will require such capability.

The left side of the main panel of the command module (Fig. 9) is arranged for the commander and has the displays and controls for launch, entry, and all propulsive maneuvers. The center section provides access to guidance, navigation, and propulsion functions; the right center and right panels contain primary displays and controls for the sustaining systems (environmental control, communications, and electrical power). In addition to the main panel array accessible from the couch, 17 to 20 other panels are located elsewhere in the command module. The most significant are the guidance and navigation station in the lower equipment bay, where navigational optics are located, and the environmental control system management panel in the lower left equipment bay, where a large number of mechanical controls are located. The other panels have controls and displays for special system functions.

In Figure 9 and in Table 5, several trends are evident in the Apollo console arrangement. Circular meters are used in only a few cases and only for parameters with a limited range of excursion; vertical meters are predominant and are time-shared by switching to display a parameter for several redundant systems; prominence in access and visibility is provided for the flight director attitude indicator, the display and keyboard, and the caution and warning matrix; discrete elements (such as circuit breakers, toggle switches, and event indicators) are used extensively. Discrete controls and displays are used

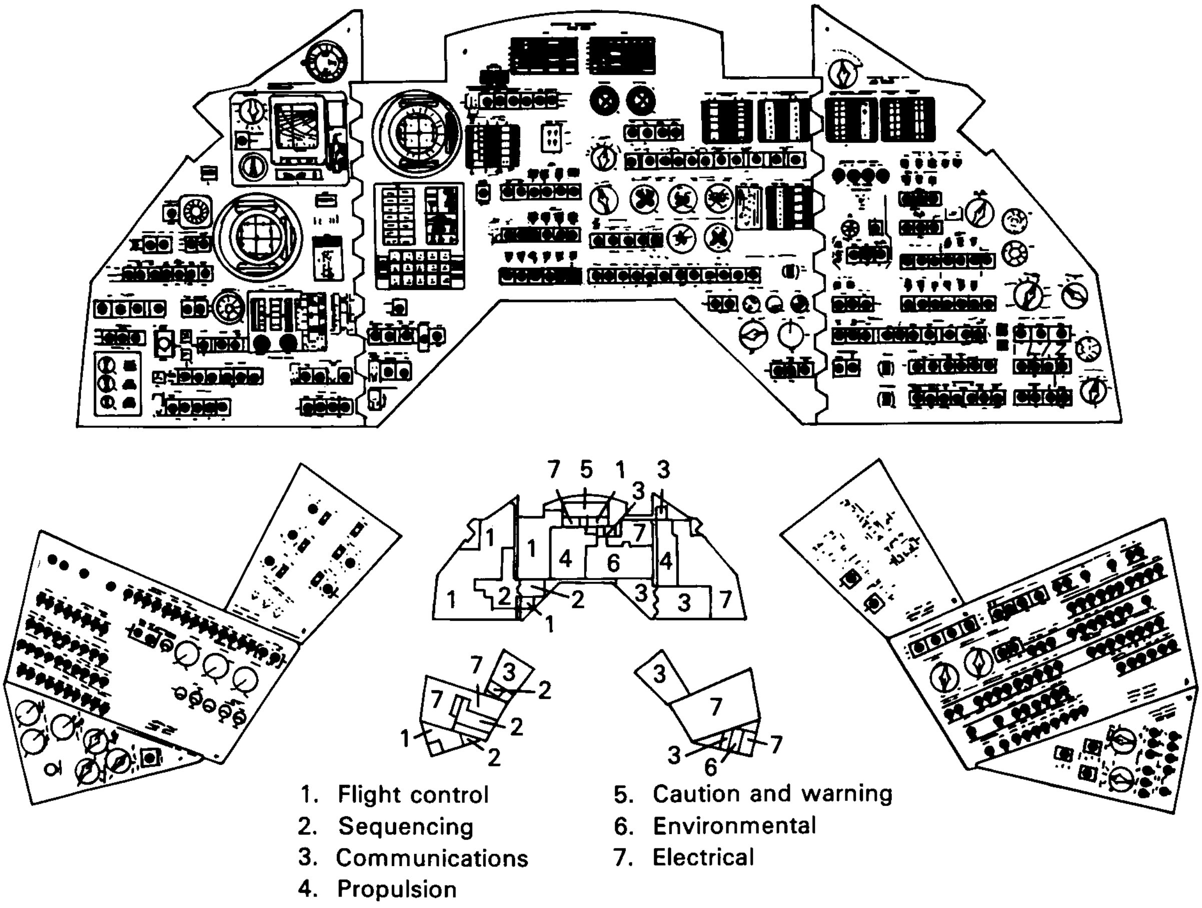
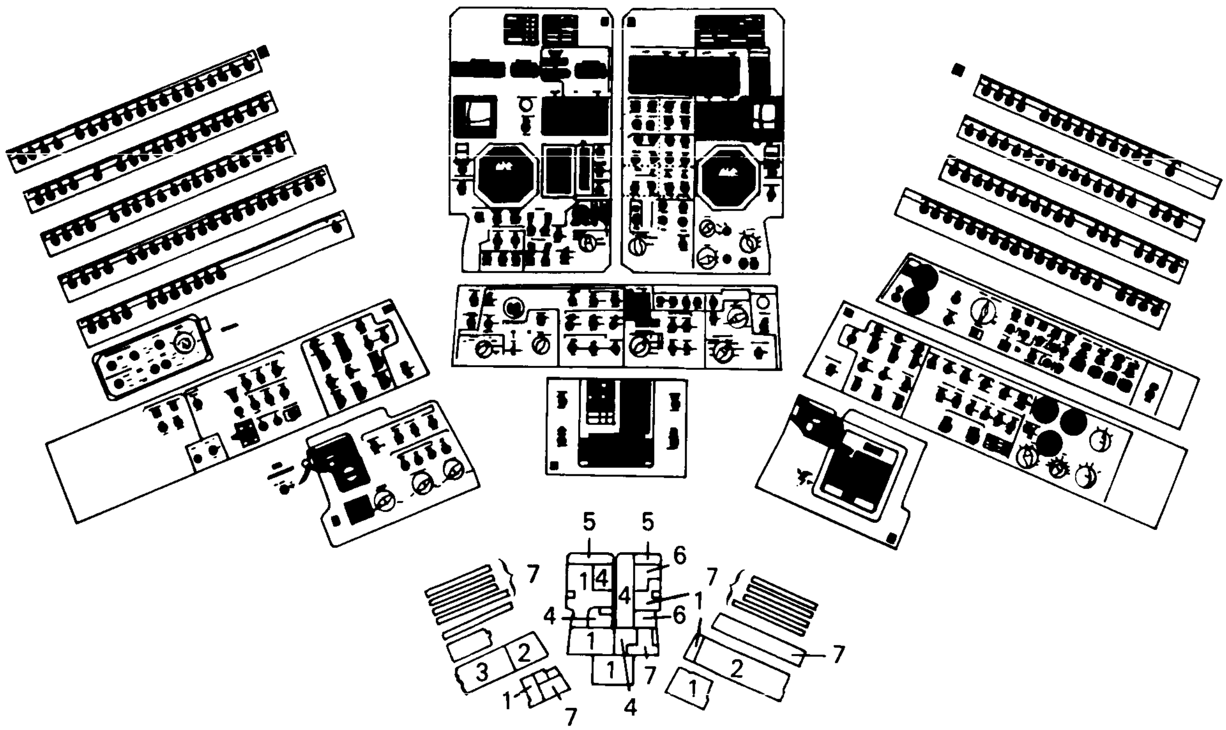


FIGURE 9.—Apollo command module display and control panel.



1. Flight control
2. Communications
3. Sequencing
4. Propulsion
5. Caution and warning
6. Environmental
7. Electrical

FIGURE 10.—Apollo lunar module display and control panel.

more extensively in diagnostic procedures than in nominal system reconfiguration.

The lunar module panel (Fig. 10) indicates many of the same points noted for the command module panels. Circular displays are used only for secondary parameters; unique devices, such as the flight director attitude indicator, the display and keyboard, and data entry and display assembly are most prominent. The large number of discrete control elements is related to the several configurations of the lunar module after launch; that is, to the parallelism of ascent- and descent-stage subsystems for electrical power, environmental control, and propulsion. The panel arrangement is typical for two-man, side-by-side flight vehicles. Each astronaut has the primary flight instruments located in the same visual scan area with a window. The commander on the left has access to the flight-control and propulsion systems; the lunar module pilot on the right has access to the alternate flight-control system, the abort guidance assembly, and the sustaining systems.

One of the most significant aspects of the lunar module displays is the importance of the caution and warning system. This system is substantially more complex than that in any other spacecraft because the lunar module is either in powered flight (landing, ascent, and rendezvous) or in a dormant state (while the crew sleeps or is absent on the lunar surface) during its active life. Because these mission characteristics allow the lunar module crew little time to monitor many subsystem functions, the caution and warning system and the Mission Control Center via telemetry act as a third crewmember to perform this status monitoring function.

The Skylab command module displays represent only minor modifications from the Apollo configuration, but the controls and displays in the remainder of the modules are a significant departure from previous spacecraft. For example, Figure 11 shows the controls and displays for the Apollo telescope mount. This panel, located in the multiple docking adapter, provides for control of the solar telescopes and instruments located on the mount. While this panel is of the same order of complexity as the Gemini controls and displays, its purpose is to acquire scientific data, not to conduct flight operations.

Notable characteristics of the panel are: use of cathode-ray tubes to display telescope views and amplitude-time plot of x-ray activity; extensive use of digital displays; and relatively low proportion of data displayed to those telemetered. Again, the types of displays reflect advances in spacecraft technology, such as cathode-ray tubes being conditioned to endure launch vibration and acceleration environments. Digital displays are required to provide adequate scale resolution for the parameters of interest.

The fraction of data displayed to ensure proper data acquisition is a small proportion of those data required for eventual analysis. This reflects the program and flight planning emphasis on using flightcrew time to acquire data, with data reduction and analysis to be performed on the ground. A certain amount of data analysis will be made during the mission to allow evaluation of achievement and to replan further data acquisition. The design logic of this console is the same as that for the flight controls and displays. The objective is to provide a capability for autonomous spacecraft operation, which, in this case, is supplemented by ground-based data analysis

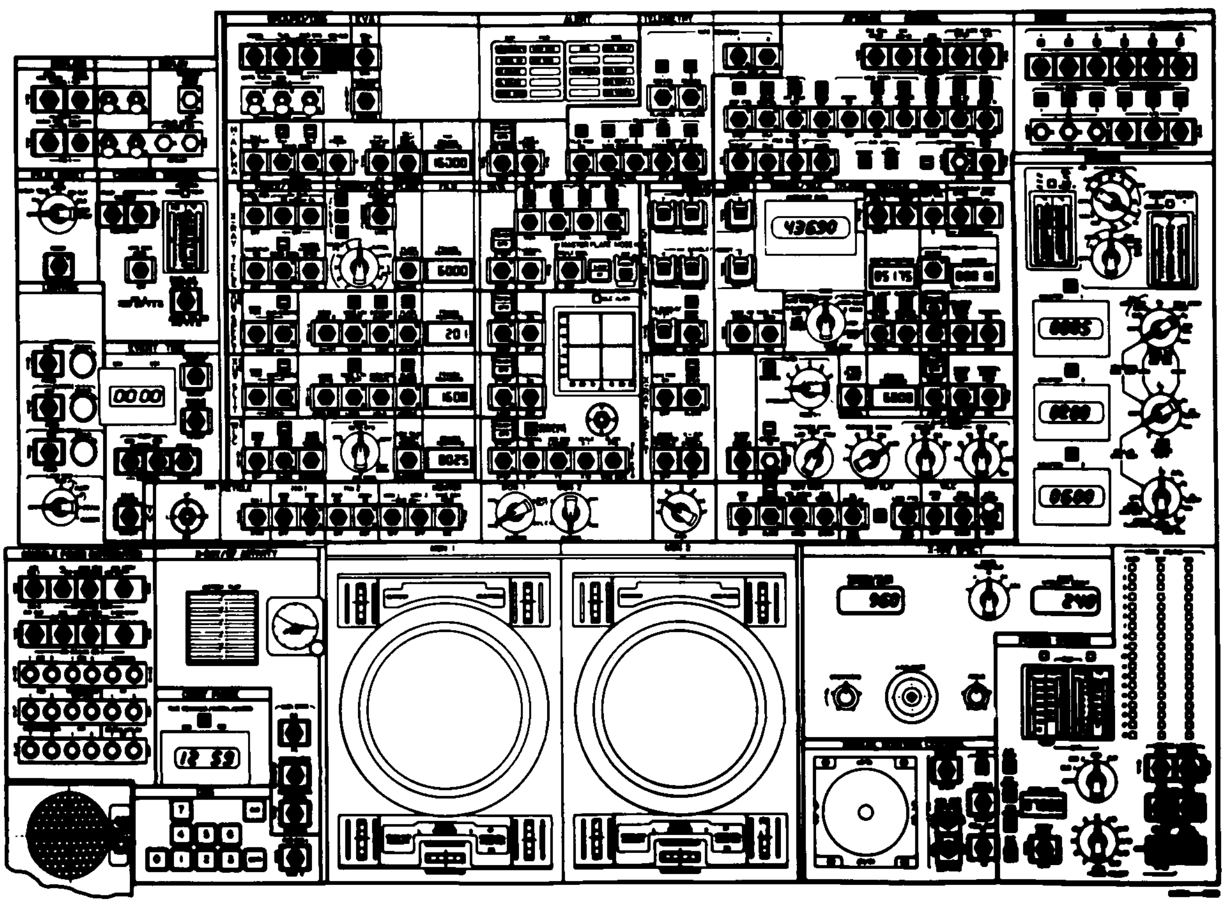


FIGURE 11.—Skylab Apollo telescope mount displays and controls.

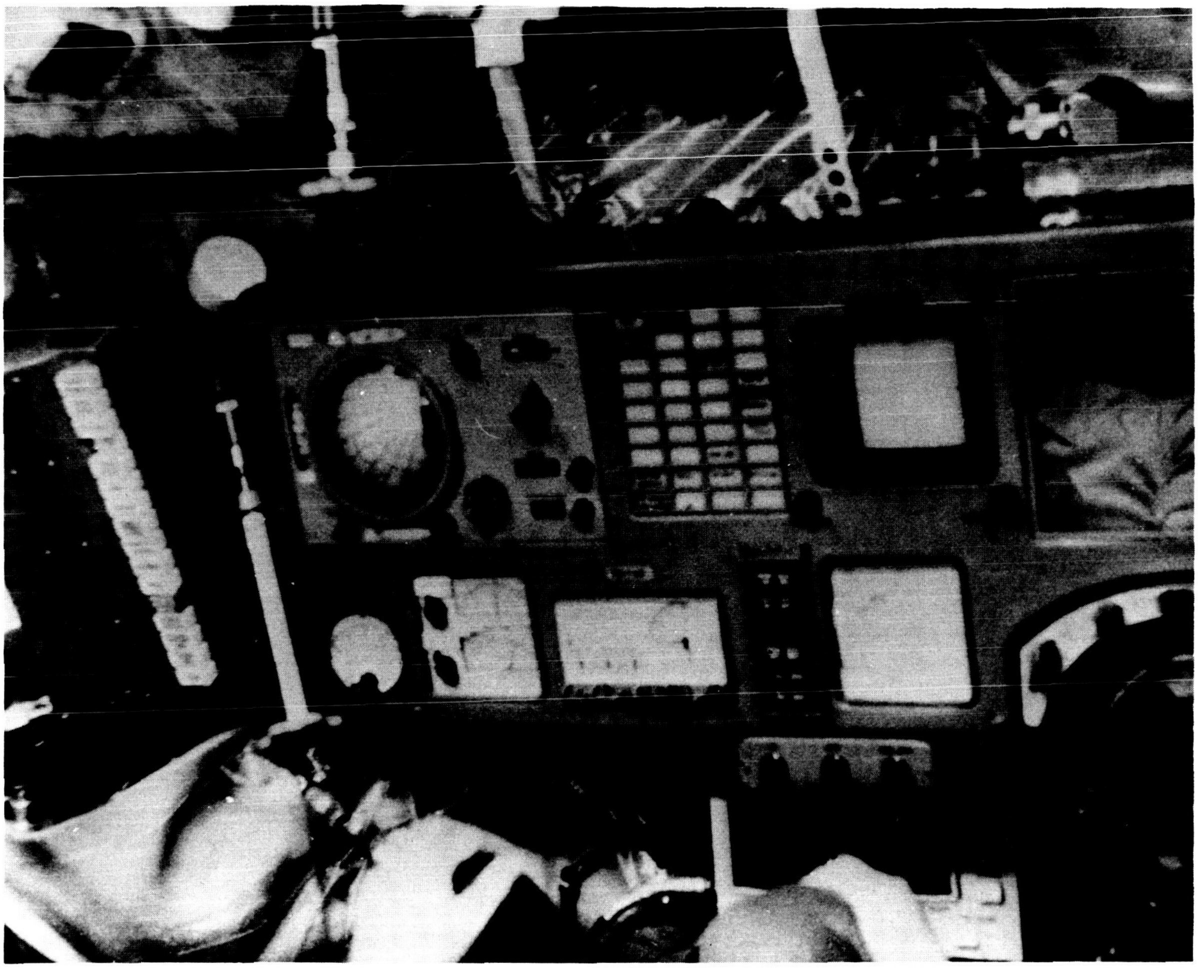


FIGURE 12.—Soyuz display and control panels.

and up-link command to enhance effectiveness and reliability.

The bulk of controls and displays in the orbital assembly is used for experiment operation and control, which is shown in Table 5. The operational instruments are used primarily for housekeeping; that is, maintenance of thermal and habitable environments and control of consumables such as water, oxygen, nitrogen, and electrical power.

The magnitude of this trend to increase scientific operations relative to flight systems is evident from the number of work stations and panels in the orbital assembly modules. The large number of panels reflects the number of experiment installations in each of the various modules. The numbers in Table 5 indicate that each panel is small and devoted to operational controls for the experiment. Data for experiments other than the Apollo telescope mount are returned to the ground primarily by voice link during the mission, and by written forms, film, and magnetic tape at the end of each crew visit.

For all spacecraft, the degree to which the flightcrew can be assisted by the ground in system monitoring is indicated by comparing the number of available measurements displayed with those telemetered. The crew and the ground share a common set of parameters; that is, those parameters critical to crew safety and the correct execution of powered flight maneuvers. The ground also has access to a large number of sensors not displayed to the crew, as well as access to data on a continuous basis that is accessible to the crew only as a discrete event. The ground-based flight control team can maintain continuous time histories of parameters, never needs to time share parameters on a display, and has independent trajectory data available from ground-based tracking that are not directly available to the crew. Also, ground-based personnel can size their team to the task at hand and afford to assign controllers to particular functions without the need for time sharing their attention among several functions. Because of these advantages, both analog and discrete data not furnished the crew are telemetered to the ground, and data that are time-sampled by the crew are monitored continuously. The ground has primary responsibility for detecting all gradual degradation failure modes, for example, gyro drift. Sampling rates are selected as a function of the dynamic variability of the parameter and the resolution required for flight control decisions.

Through the spacecraft and experiment status information conveyed by this telemetry, the Mission Control Center monitors the spacecraft for the crew while they sleep or address themselves to scientific observations and experiments. The telemetry data allow both the flightcrew and Mission Control Center to confirm the conditions of all spacecraft systems and assure that proper procedures are being followed. These data are also used to aid the crew in replanning the flight to take advantage of unexpected opportunities or recover from the failure of a particular instrument or previously planned experiment.

The unique control devices and displays are primarily associated with flight control of the spacecraft. They are the most complex of the control and display elements and can be typified by a description of the primary guidance and navigation system display and keyboard.

The Apollo primary guidance and navigation system's display and keyboard is the most complex and powerful of the unique crew interface elements (Fig. 13) [3, 22, 40]. It displays the status of the computer, inertial systems, and program within the computer. With this device, the crew can monitor program status and activity, and sequence and initialize the systems as desired. Communication between crew and system is conducted in terms of a set of program blocks identifying specific functions such as preflight operations (0X), monitoring launch (1X), and lunar module rendezvous (7X). The second digit identifies specific program activities within each major set. Within each program block, a set of two-digit verbs and nouns specifies actions to be performed and the object of the action, including the data to be entered into the calculation or to be displayed during the calculation. The computer can also drive the flight director attitude indicator sphere and error needles to provide analog displays. Figure 14 illustrates characteristics of a typical program element; in this case, the program for executing a command module maneuver to change orbital parameters by using targeting information furnished by the ground-based navigation system.

When the computer program requires a crew management decision about the acceptability of results or the need for new input data, the crewman is queried by flashing the verb and noun displays. This two-way communication between crew and computer is quite complex, requiring approximately 10 000 key strokes to complete all elements of a lunar landing mission. Approximately 40% of all crew training for a lunar landing mission is required to master the system. In this system, as in the others described, much of the complexity derives from providing crew access to a very low level of function. To guard against procedural errors, on-board data are provided to reinitialize erasable memory if an error occurs, and the probability of error is reduced by training each crewman to a high level of proficiency and assigning to each specific mission phase operations.

Another class of crew activity, related to control and display, is effected by crew observation of exterior objects through either the windows or the optical systems used to aline the inertial reference systems. In these activities, the crew has the task of recognizing complex patterns and providing either direct steering commands or input data to the automatic systems. The crew performs such functions in docking, rendezvous targeting, erecting and alining the inertial plat-

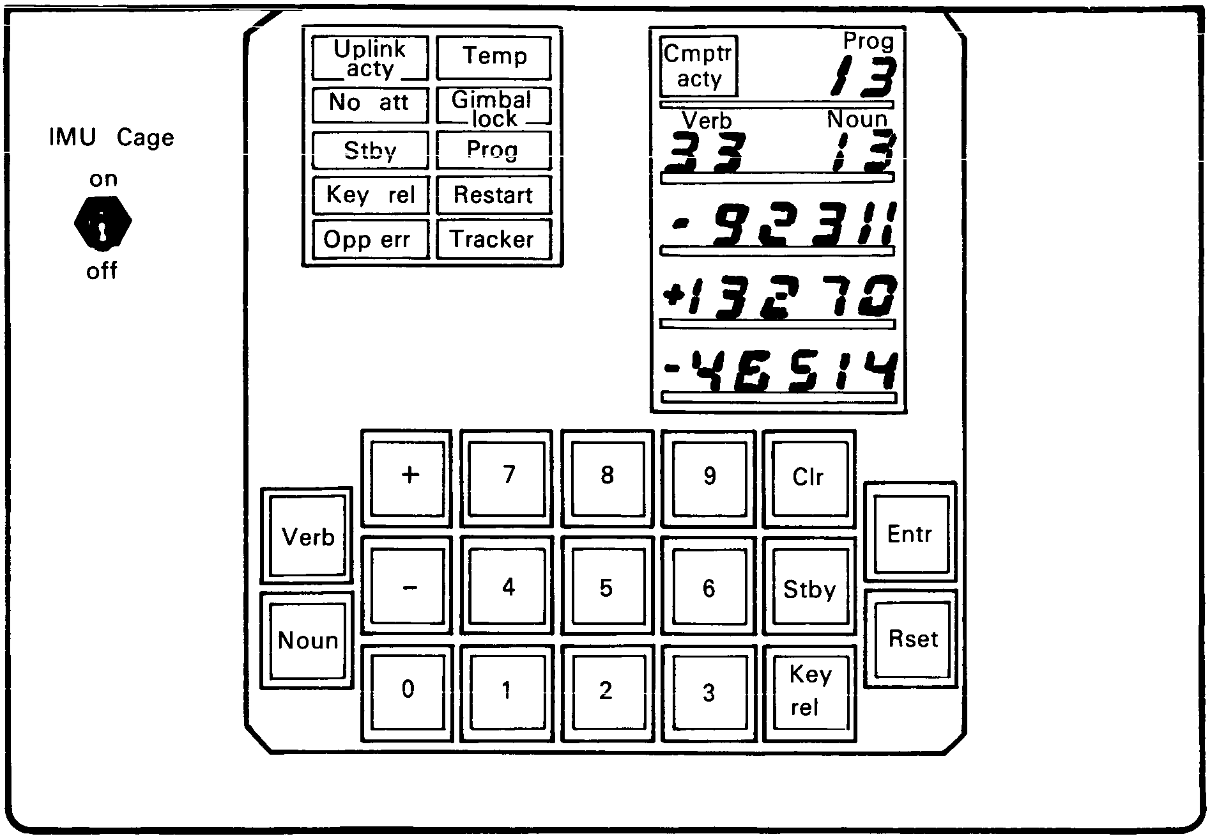


FIGURE 13.—Guidance and control system display and keyboard.

forms, aiming scientific instruments, and landing the lunar module.

The view from the lunar module as it approaches lunar landing and the system used during this maneuver are shown in Figure 15. The display and keyboard of the primary guidance and navigation system displays the elevation and lateral angle of the target point. If the target is not a suitable landing point, in the pilot's judgment, he can redirect the system to a more acceptable target by input of the coordinates of the desired site. The computer will then retarget. Alternatively, the crewman can take over and perform the complete maneuver manually. In this and other uses of the crew's primary senses as part of spacecraft information acquisition, there is no way to perform the function without the crewmen.

The Soyuz control panels (Fig. 12) illustrate several notable differences from US spacecraft. The main console consists of a central panel and two identical side panels. The side panels, one accessible to each crewman, are the master sequence controls and present a vertical column of switches and annunciators activated in accordance with the mission phase and system configuration desired.

The central console contains displays shared by the two crewmen. The navigation indicator, an Earth globe, displays latitude and longitude, period of rotation, daylight and dark periods, and nominal landing point. The caution and status panel indicates subsystem status. The cathode-ray tube is used to display systems performance data and as a monitor for a television camera located on the longitudinal axis. The television scene is used for Earth viewing, rendezvous, and docking. System status values also can be displayed on this tube. A rear screen projection panel displays procedural data; when each function is completed, that inscription becomes dim. A digital data entry device allows the crew-

P30-External Delta V Program

Purpose:

1. To accept targeting parameters obtained from a source(s) external to the CMC and compute therefrom the required velocity and other initial conditions required by the CMC for execution of the desired maneuver. The targeting parameters inserted into the CMC are the time of ignition (TIG) and the impulsive ΔV along CSM local vertical axes at TIG.
2. To display to the astronaut and the ground certain specific dependent variables associated with the desired maneuver for approval by the astronaut/ground.

Assumptions:

1. Target parameters (TIG and ΔV(LV)) may have been loaded from the ground during a prior execution of P27.
2. External Delta V flag is set during the program to designate to the thrusting program that external Delta V steering is to be used.
3. ISS need not be on to complete this program.
4. Program is selected by DSKY entry.

Selected Displays:

1. VO6 N33	
Time of ignition for external ΔV burn	OOXXX. h OOOXX. min OXX.XX s
2. VO6 N81	
Components of ΔV(LV)	XXXX.X ft/s
3. VO6 N42	
Apocenter altitude	XXXX.X nmi
Pericenter altitude	XXXX.X nmi
ΔV	XXXX.X ft/s
4. V16 N45	
Marks (VHF/optics)	XXbXX marks
Time from external ΔV ignition	XXbXX min/s
Middle gimbal angle	XXX.XX deg

CMC=command module computer
Delta V=thrust applied to change orbital ephemeris
ISS=inertial subsystem
DSKY=display and keyboard
CSM= command and service module

FIGURE 14.—Typical guidance program.

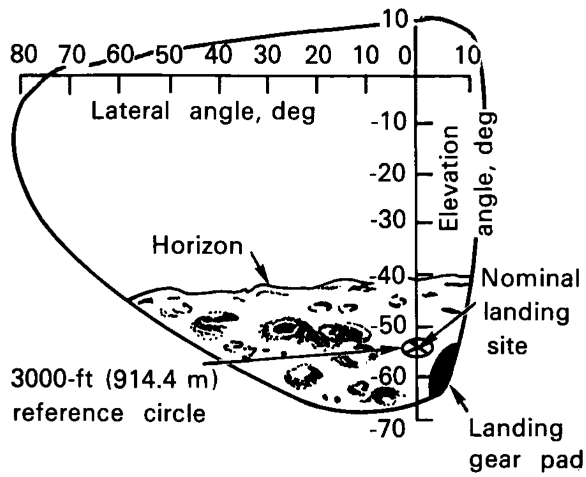


FIGURE 15.—Landing area perspective as seen by the lunar module pilot during final approach.

man to program the automatic system for the orientation and magnitude of maneuvers. Electrical power system performance, event timers, and radar range and range rate indicators are arrayed to the left of the periscope viewing screen. The periscope optics can be rotated to view the Earth beneath the spacecraft, the Sun, or a target vehicle; the peripheral field of view includes the visible horizon.

These displays and controls reflect the same reliance on ground-based navigation and flight planning assistance as US spacecraft and are adequate for all Earth-orbital operations of maneuvering, rendezvous, and docking. The most notable differences from US spacecraft are reliance on programed sequences in the management of subsystems, and absence of large numbers of discrete controls for malfunction isolation. The lesser volume occupied by the displays and controls contributes to the greater habitable volume in Soviet spacecraft.

MISSION EXPERIENCE

The crew's role has become increasingly complex and diversified as flight experience has increased. The early Mercury, Vostok, and Voskhod flights tested man's ability to endure in space and matured to demonstrate the potential value of Earth observation systems,

Maneuver	Reference	Time maneuver initiated h: min, G.c.t.	Control mode	Auto fuel, lb	kg	Gyro switch position
—— 1	Window	01:41	FBW-low	0.39	.18	Normal
— — 2	Periscope	01:50	FBW-low	0.32	.15	Free

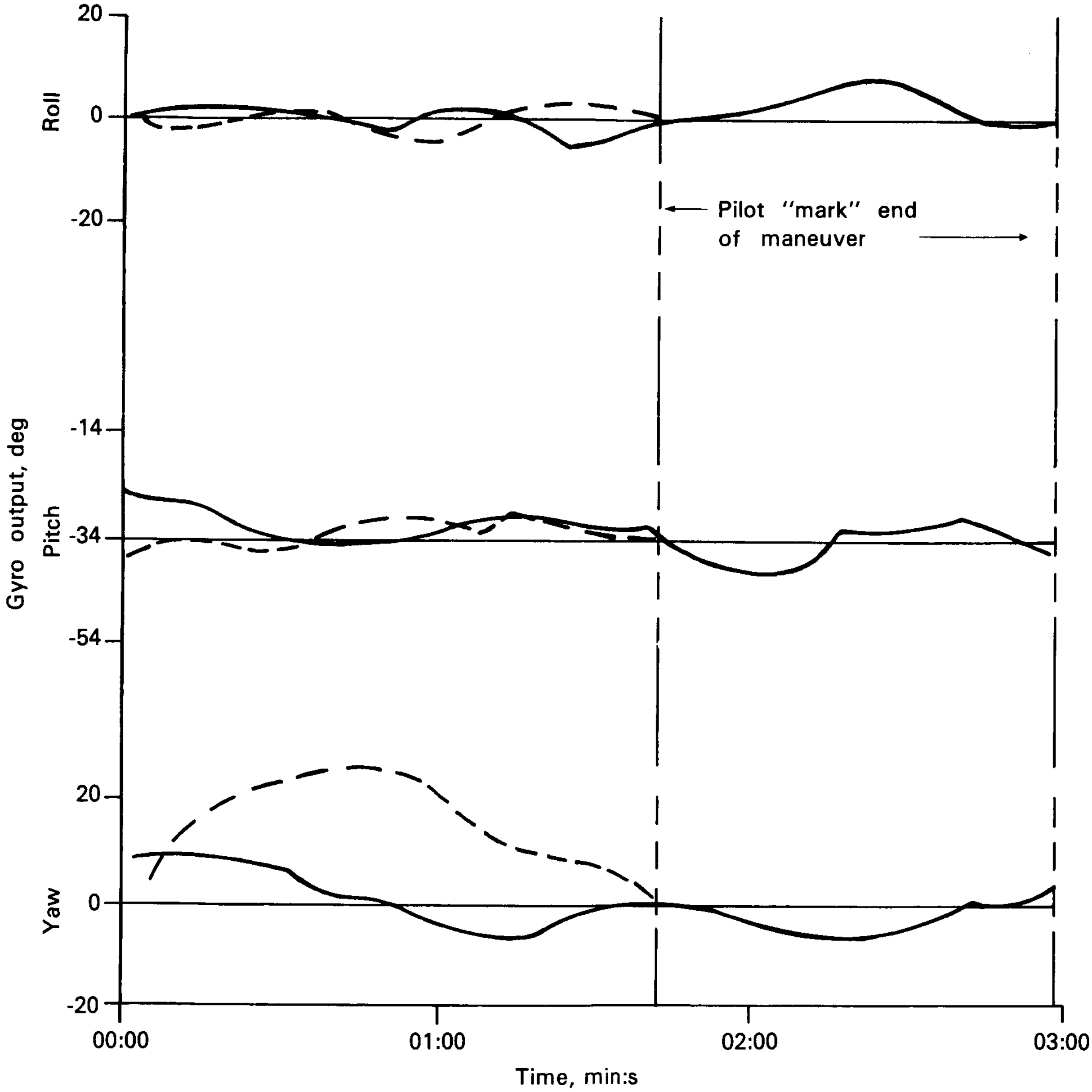


FIGURE 16. — Mercury attitude maneuver.

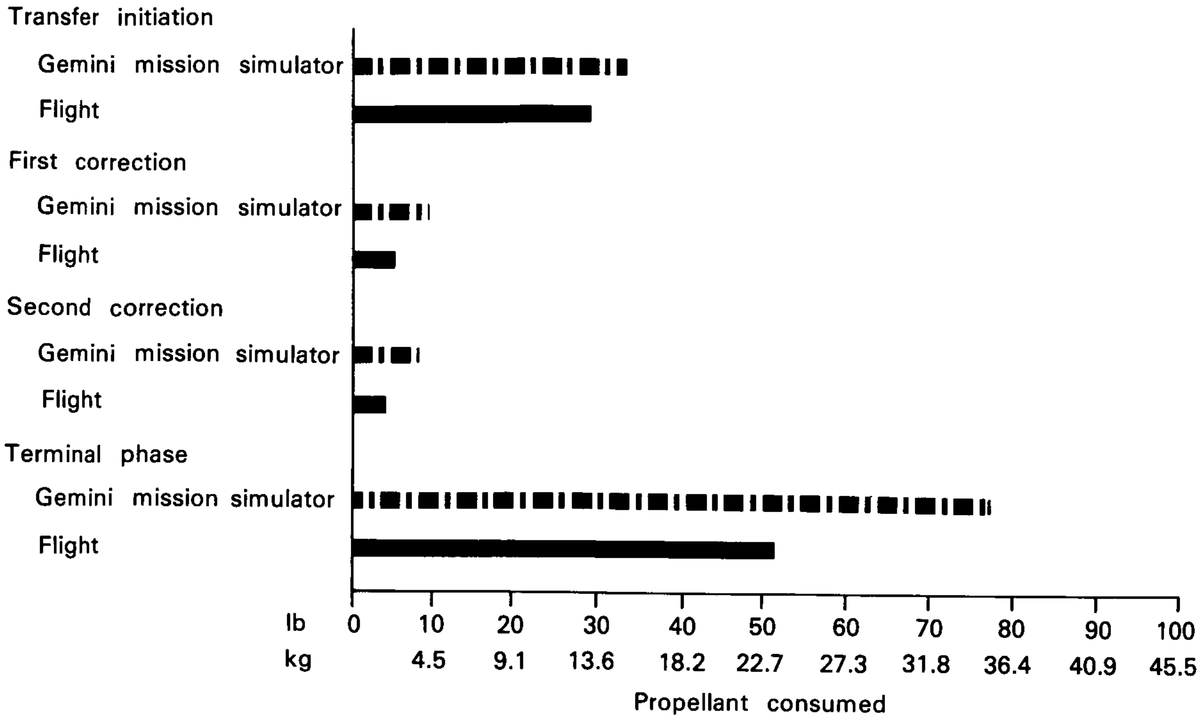


FIGURE 17.—Gemini spacecraft maneuver.

man's ability as a scientific observer, and the capacity of the crew to overcome substantial system failures and return the spacecraft to Earth. The Gemini Program demonstrated not only several rendezvous techniques, but also the ability to conduct simple and meaningful experiments. On the Gemini 8 mission, the crew successfully handled an unexpected and potentially catastrophic failure in the attitude control system. Each Apollo mission has been substantially more complex in both operational and scientific objectives. In this program, again, the Apollo 13 crew proved the capability to return to Earth safely even after a major system failure. The Skylab crew repair of equipment extended the life of the spacecraft and restored to operation several scientific instruments. In the Soviet space program, Soyuz and Salyut missions similarly demonstrated that the crew can perform critical operational duties in maneuvering spacecraft and operating complex scientific instruments. Such a record indicates that man contributes substantially to space systems.

Performance of the crew in the flight environment reflects the effect of extensive training in preparation for the mission. Figure 16 illustrates a typical comparison of Mercury crew performance in flight and during training. The maneuver is smooth, end conditions are precise, and control fuel cost is near optimum with less than 10% of the automatic system requirement [39]. The fuel saving is possible because in some cases the crew can select lower maneuver rates and more efficient sequences than the automatic system. Similar data for rendezvous maneuvers of the Gemini 9 flight are illustrated in Figure 17. Again, the consistency of performance is noteworthy. The propellant consumption in flight was less than that during simulation because the mission differential altitude was only 22.4 km (12.1 nmi) while the simulation data were gathered at a differential altitude of 26.8 km (15 nmi) [46]. The crew relies on the computer to calculate magnitude and direction of major maneuvers but controls final station keeping and docking directly.

Docking and Lunar Landing

Crew performance in the Apollo missions is illustrated by the execution of two critical maneuvers: docking and lunar landing. The docking maneuver normally is performed with the control system configured so that spacecraft attitude is held within a band of $\pm 0.5°$ in all axes, while the pilot controls closure velocity and lateral and vertical displacement manually. Table 6 shows the relationship of several significant parameters as reflected in the system specification, measured during piloted simulation tests, and estimated from telemetered data and crew reports for 10 Apollo missions. Clearly, flight performance is quite precise. The system capability is dictated by contingency modes not yet experienced in any flight. Simulation data include degraded system modes of operation and show increased variability in execution of the maneuver. The greatest variance in performance for degraded modes of control does not appear to be in the docking performance parameters, but in the time required and the propellant used to execute the maneuver. Both these values vary significantly as a function of the degree of control system degradation. Ample contingency propellant is available for critical lunar docking; neither the lunar nor the transposition docking are time critical.

The lunar landing also illustrates the combination of manual and automatic system control modes. During descent, the crew can select a manual descent mode by which they can control vertical and horizontal velocity while the autopilot provides an attitude hold. Figure 18 shows specification performance limits of the vehicle structure in terms of the velocity at touchdown that the landing gear can attenuate; that is, 3.05 m/s vertically at 0 m/s horizontally and 2.13 m/s vertically at 1.22 m/s horizontally. The ellipsoids centered at 1.83 m/s vertically represent the probability region of touchdown conditions. These probabilities are based on simulation of many landings with system performance varying within specification limits, and manual control based on instrument displays.

The flight points in Figure 18 represent Apollo lunar landings. The point plotted for the lunar landing training vehicle shows the average landing condition for a set of training flights. That landings executed on the Moon are softer than those simulated is not surprising. Even with blowing dust obscuring the surface near the time of touchdown, the pilot obtains significant information not available in simulations. Flight provides real proprioceptive and visual cues that are absent or incomplete in simulations. Finally, and perhaps most importantly, the flight maneuver is *scored* by the crewman on how gently he can execute the landing when he has arrived at a suitable touchdown location. In the simulation, the most readily obtainable performance measurements are the time and the propellant remaining as soon as acceptable conditions are attained. The margin reflected in these values becomes the index of success. The difference in the simulation and real flight situations appears to bias the results in different directions. Consequently, simulations are characterized by a positive rate of descent at landing probe contact, while flight landings are characterized by a near-zero rate of descent at probe contact and by a short delay in cutting off the descent engine after probe contact is established.

Crew Reliability

Demonstration of a high degree of predictability of crew reliability has been another facet of mission experience. A major simulation of the Apollo mission was conducted to assess potential reliability of crew performance [17, 34]. This simulation reflected the configuration of the spacecraft as nearly as possible, illustrated routine and most demanding procedures, and used as test crews personnel who met many criteria for astronaut selection. Several were, in fact, later selected for the astronaut group.

Study results indicated that crew performance could be expected to be very good. Procedural reliability varied from 0.94 to 0.98 as a function of mission phase or of the particular crew considered. Two of the crews were not given feedback about their performance during training, and their error rate was higher than that of the three crews who were given such information. Astronaut crews have always been furnished

TABLE 6.—*Spacecraft Docking Maneuver Characteristics*

Characteristic	Design envelope	Average of simulation results	Average of mission results
Closure rate, cm/s	0.3–30.5	10.4	6.89
Lateral displacement, cm	30.48	6.10	3.94
Lateral displacement rate, cm/s	0–15.0	.91	--
Rotational rate (any axis), deg/s	1	.06	--
Rotational misalinement, deg	±10	.9	1.12

feedback on performance during training. Conclusions from the study were:

1. Mission time-dependent performance in simulation increased variability rather than effecting any absolute change in performance.
2. Variations in constancy of workload appeared to be more important than peak workload as a factor in crew performance against the criteria that were used.
3. The criticality of "error" gave indication of no significant deviations in the performance of discrete task elements but could become significant in such integrated error tasks as manual nulling of steering errors in trajectory guidance.

The conduct of such studies is very difficult. Selection, and especially training, of test crews is necessarily much less rigorous than it is for flightcrews. Flightcrew training includes participation in many systems definition and development activities and in information acquisition opportunities of their roles in the management structure. It is even more significant that such simulations cannot make predictions, but can only mimic the influence of real-time purposive behavior.

A substantial artifact in all simulations is that they must establish readily accessible criterion measurements to produce quantitative and repeatable performance data so that design, procedure, or training decisions may be made. When properly selected, the character of these measurements is such that they bear direct relationship to a real optimum solution; however, by virtue of the simulation mechanization, the relationship is often a secondary measure of successful "real world" performance. It is not intended to find fault with such endeavors, but merely to note an inherent limitation that is particularly significant as the human "purpose-dominated" element is introduced.

This factor is most conspicuous in discrete element performance, as it is measured to establish a "reliability" number in the study noted. For a criterion, the checklist must be the standard. The difficulty with such a standard is indicated by noting that 17% of the switching errors by crews is attributed to lack of clarity in the checklist. Even after correction for clarity errors, the standard must remain because it is readily counted. Such a measure, although neatly quantitative, is hard to weigh in terms of significance because many such errors are of no consequence or are recognized and reversed by the crew. To note such deficiencies is to note that few laboratory tests are as complex as the real event.

Analysis of selected samples of flight telemetry for several missions has furnished data comparable to those from simulation studies. The switching error rate was very low; reliability, as measured by compliance to the checklist, was 0.996. All errors noted were promptly detected and corrected by the crew without ground comment. The bulk of errors occurred during keying operations of the display and keyboard of the primary guidance and navigation system.

In another analysis of these data to establish crew workload, the information processing rate during the lunar landing was estimated at 3.90 bits/s with most of the data flow being the lunar module pilot's callouts of descent rate and altitude to the commander. Because this is the period of highest crew activity during the mis-

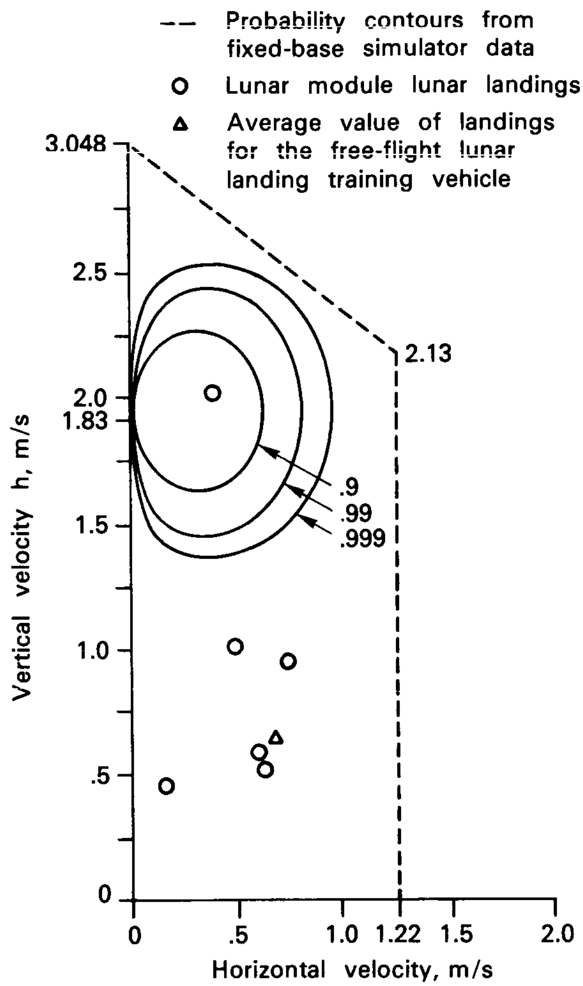


FIGURE 18. —Lunar landing performance.

sion, this information processing rate represents a maximum to be expected. Less demanding maneuvers are characterized by rates between 1 and 2 bits/s.

These data substantiate the observation that crew performance is very reliable. All errors observed were indifferent in consequence and detected and corrected promptly by the crew. Perhaps the error correction effectiveness is more noteworthy than the exceptionally low rate of error incidence.

Scientific Observations

Man's unique contribution to the scientific objectives of space missions is less readily quantified but not less significant. Both cosmonauts and astronauts have made significant scientific observations since the very first flight, and this facet of their activity has increased markedly as basic operational systems and procedures have developed during the decade 1960–1970.

The simplicity of early spacecraft and test character of the missions limited early scientific activity to observations on the crew's performance, and observation, and photography by the crews. Crew activity indicated that the human could and did effectively adapt to space environment, not encounter any significant sensory disturbances, and perform effectively under the stresses of the missions as psychologically stable individuals.

Phenomena observed during early flights included weather patterns, refractive distortion of the Sun at sunrise and sunset, presence and altitude of the night airglow, layered structures in the Earth atmosphere, and geologic and geographic structures. These crew observations were supported by photographs that permitted later, more extended analyses.

During all orbital flights, synoptic terrain photography has provided useful products for both geologic and topographic mapping. Photographs of the oceans under various angles of solar illumination indicated sea states as a function of glitter. Both the observed resolution and that apparent in photographs was greater than many anticipated.

Star sightings made during both day and night viewing conditions included identifications down to 5.95 magnitude at night and 4.00 magnitude at day. Meteors, auroras, and other satellites also have been observed.

In addition to these observations, experiments were conducted on biologic specimens (sea urchins, frog eggs, and white blood cells); effect of spacecraft passage on ion flow; and effects of micrometeorite impact on prepared samples [5, 29].

The major manned scientific missions have been the Apollo lunar surface explorations, Apollo lunar orbit observations, Skylab solar, medical and earth resources observations, and Salyut astronautical and electromagnetic fields experiments. The eight Apollo missions to lunar orbit and the six lunar surface explorations have been notably successful. Crew observations provided the basis for selection of photography, instrument observations, and geological samples. The productivity of subsequent analyses has been markedly improved by supplementary notes and priority selection provided by the crew. Among significant observations made by crews are the degree to which color variations in the lunar surface are most pronounced at low sun elevation, prevalence of breccia formation, detection of light flashes from several regions (even though these could not be located to specific coordinates), and similarity of the near and far sides of the Moon in the detailed characteristics of geological units.

On the Soyuz 11-Salyut mission, cosmonauts operated an astronautical telescope and performed an electromagnetic fields experiment. Success in demonstrating high-frequency secondary electron resonance in space and acquisition of spectrograms of Beta Centauri and Lyra were attributable to the same crew efficiency in operating space experiments as in operating the spacecraft. The ability to control experiments and react to the character of the data being acquired significantly improved the final data and experimental results [3].

The Skylab experience embodied two unique new elements: extended operations on orbit of a complex man-operated scientific facility for medical, solar, astronomical and terrestrial observations; and the capability to revisit this facility modifying the crew skill complement and instrument complex. Crew intervention not only sustained the facility, but also sustained the operations and modified the original character and purpose of the observing instruments. The three visits added new instruments and new observing protocols. The science skills of the crewmembers augmented by ground-based facilities and teams of scientists fostered new methods of operations. The timing of Comet Kohoutek was fortuitous in that it provided a unique opportunity to test this capability.

While it is too early in the assessment of data collected on this mission to characterize its scientific value, it is clear that properly selected and trained crews can contribute to the reliability and productivity of scientific facilities, as they have to flight systems.

Clearly, the techniques of exploiting man's capability in the operation of flight systems, mechanisms for the exploration of space, are well understood. It is not equally clear that there is a body of information or theory adequate to expolit his capability in confronting the challenging problem of how to productively explore this new space domain or exploit its unique opportunities to assess man and his environment effectively. The problems before us are not how to use man effectively in managing systems to predetermined ends, but in how to supplement his unique intellectual functions in exploring these new frontiers of man's inquiry into his own nature and that of the universe of which he is a part.

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Part 5

COMBINED EFFECT OF SPACEFLIGHT FACTORS ON MAN AND ANIMALS; METHODS OF INVESTIGATION

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Chapter 17

COMBINED EFFECT OF FLIGHT FACTORS[1]

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The body is subjected throughout life to innumerable stimuli of various kinds and intensities—mechanical, physical, chemical, biological, and mental. Many stimuli (environmental factors, various stresses, and so forth) rarely act on the body individually, but are encountered as a combined, complex influence. For example, when a spacecraft enters the denser layers of the atmosphere, the astronaut is simultaneously subjected to acceleration, vibration, noise, heat, changes in the ambient gas medium, and emotional stress. These factors act on a body that has been exposed for some time to limited space, weightlessness, increased radiation, and reduced motor activity. This combined effect is noted in any phase of space flight; because of the number of peculiarities related to flight specifics, the interrelationship and interdependence of the factors making up the combined effect are more clearly expressed than under ordinary, terrestrial conditions. This determines the approaches and principles used in the study of biologic effects of spaceflight factors and development of means and methods for protection or treatment against their adverse influence under flight conditions. Consequently, the problem of the combined influence of spaceflight factors is one of the key problems of space biology and medicine.

Many works are concerned with this problem. They are, however, mostly descriptive and explain qualitative changes in individual organic functions under the influence of combined flight factors. Indeed, few experimental studies have established the quantitative dependence of the body's reactions under these conditions; a few investigations have been made on the influence of combined factors on man's work capacity. Finally, most studies have dealt with simultaneous or successive effects of two or, quite rarely, three factors. Particular note should be given to publications on results of experiments in flight. Their significance is diminished for a number of reasons (to be discussed later), since the results for the most part, can be evaluated only as reaction to flight conditions as a whole, without distinguishing any single factor or combination of factors as responsible for the observed reaction. The problem of the influence of combined factors is a pressing one; and it has not been sufficiently studied.

The opinion of Murray and McCally [86] can be readily agreed to: the reasons for insufficient study of this problem are related to a number of causes limiting the required experiments. First,

[1] Translation of, Kombinirovannoye Deystviye Faktorov Poleta, Volume II, Part 5, Chapter 17, *Osnovy Kosmicheskoy Biologii i Meditsiny* (*Foundations of Space Biology and Medicine*), 76 pp. Academy of Sciences USSR, Moscow, 1974.

planning the experiments is extremely complex. The possible number of combinations and permutations of even a few factors is tremendous. Second, these studies require special complex apparatus (test stands) unavailable in most laboratories. Finally, since numerous experiments must be made to obtain reliable data, the cost is great. A significant hindrance is that a general theory is lacking to explain the basic principles of simultaneous or successive influence of combined factors on the body, as well as the lack of models of their action. Such models would be of theoretical interest, also of practical significance for manned flight support.

The results of certain experimental investigations of the combined influence of various flight factors on the body—vibration, acceleration, ionizing radiation, altered gas media, and so forth—are discussed in this chapter. An effort is made, using specific examples, to show the dependence of an effect on the force and nature of the factors, intervals, and sequence of their application; to estimate the significance of the initial functional state of the body (reactivity) for the final reaction to combined influence. Certain mechanisms of the modifying influence of various factors on the organism's reactivity are revealed. The possibility of using mathematical models and the prospects and most important trends in investigation of the combined influence of flight factors are also discussed.

EFFECTS OF COMBINED ACTION OF FLIGHT FACTORS ON THE BODY

Analysis of available data indicates that the effects of combined action may differ significantly from effects caused by each factor individually. The final effect, its magnitude, and direction depend on the force, sequence, and duration of application of factors and their nature [19]. The indicator (test) is significant, which is used to estimate the magnitude and direction of the effect, as well as the form, volume, and initial level of its functional activity.

In types of interactions, factors may be mutually additive, synergistic, or antagonistic. It is possible that the effect of the interaction is not revealed by tests. With an additive interaction, the effect of a combination is equal to the sum of the effects of each factor individually. With a synergistic interaction, the combination of factors will yield a greater effect than the simple sum of each factor's effect. With an antagonistic interaction, the overall effect is less than the sum of the individual effects. The factors related to flight dynamics will be considered.

Acceleration

Under actual flight conditions, acceleration may be combined with weightlessness, hypodynamia, vibrations, temperature variation, effects of penetrating and microwave radiation, altered gas medium, and other factors. The direction and extent to which these factors change the organism's resistance to acceleration effects have been described in experimental data.

Acceleration and hypodynamia. Hypodynamia, resulting from extended bed rest or immersion in water, causes a reduction in the organism's resistance to the effects of transverse acceleration [9, 63, 64, 85]. The dependence of acceleration tolerance on the duration of hypodynamia has also been studied. Criteria to evaluate human tolerance to acceleration were: changes in maximum tolerable acceleration; shifts in indicators of the basic physiologic functions; and the time required to restore them during the aftereffect. The results of these studies are presented in Figure 1, which indicates that tolerance for these factors following 3 d bed rest was unchanged when compared to the initial level. A gradual reduction in acceleration resistance began after 7 d of hypodynamia; following 15–20 d bed rest, the reduction averaged 2.4 g. This reduction had not changed by the 60th day. Initial acceleration resistance for all test subjects was restored between 17 and 50 d following the end of 2 months' hypodynamia.

Analysis of the physiological reactions showed that, in spite of the lower value of maximum tolerable acceleration following hypodynamia, a higher level of physiologic shifts were observed in most cases. For example, the data in Figure 2 show change in pulse and respiration rates for one test subject under acceleration before and after 20 d of hypodynamia. These indicators were significantly higher following hypodynamia than in controls, indicating greater stress of the

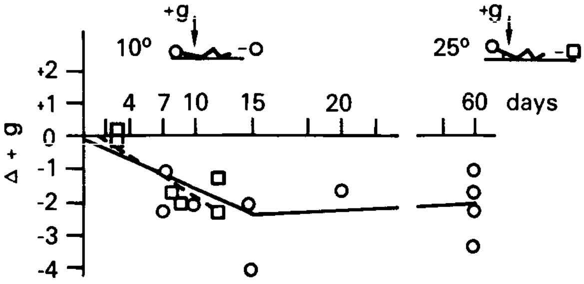

FIGURE 1.—Change in tolerance to transverse accelerations as a function of hypodynamia duration [64]. o: Individual differences at maximum tolerable acceleration with seat-back angle at 10° from horizontal. □: Same as o with angle at 25°.

body's compensatory-adaptive mechanisms in response to acceleration following extended hypodynamia. The authors concluded that two phases of the organism's changing reactivity to acceleration develop during hypodynamia. The first, lasting 15 to 20 d, is characterized by gradual reduction in acceleration resistance and increased manifestation of the organism's reactions. The second is a stabilization phase when the body's reaction and acceleration tolerance remain at the level achieved after 15 to 20 d hypodynamia. In other words, there is adaptation to long-duration (up to 2 months) hypodynamia.

The main mechanisms of reduction in the body's resistance to acceleration under the influence of hypodynamia are obviously related primarily to reduced hydrostatic blood pressure and disruption of vascular tone regulation. These reactions are based on increased excretion of electrolytes through urine [64, 76] and decreased content of biologically active substances such as serotonin [59], acetylcholine [62], adrenaline, and noradrenaline [107] in the body. A satisfactory correlation has been established between the phase of adaptation under the influence of hypodynamia and the degree of electrolyte excretion.

Acceleration and ambient temperature. The combined influence of acceleration with high or low temperature has been studied both in animal [24, 46, 50, 102] and human experiments [23, 51, 69, 77, 103, 113]. While the number of works concerned with this problem is relatively small, the results are in agreement, permitting a definite conclusion: high temperatures reduce, and low temperatures increase the body's resistance to accelerations. Burgess presented data [22, 23] on the drop in resistance to positive accelerations under the influence of high temperature and hypoxia; he evaluated acceleration tolerance on the basis of peripheral vision loss, and cited tests on the work capacity of test subjects. Figure 3 shows the reduction in acceleration resistance under various cabin air temperatures. A reduction in tolerance of 1 g at an air temperature of 83°–89° C (181°–192° F) was observed. Coordination was decreased, and in the

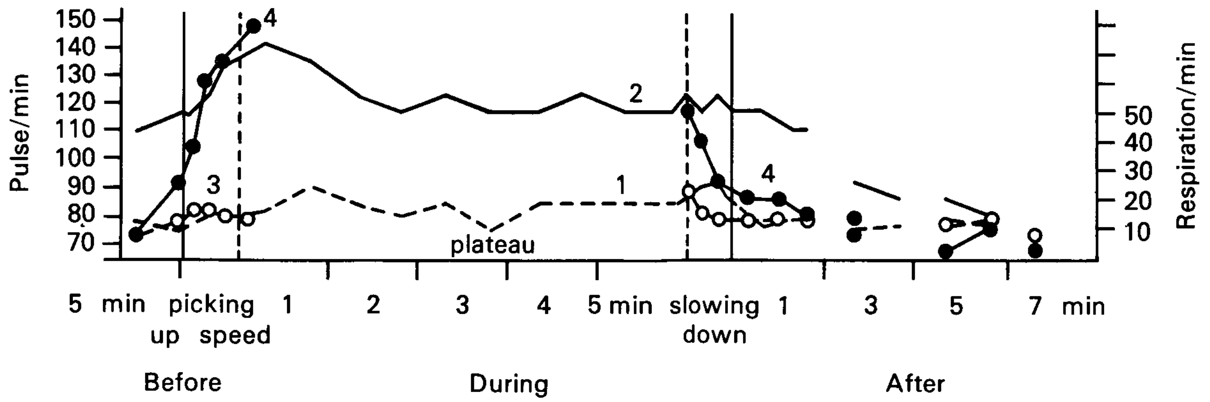

FIGURE 2.—Change in heart and respiration rate frequency before, after, and during acceleration with test rotation and after 20 days of hypodynamia (test subject B) [63]. 1: 1 h before hypodynamia (heart), 2; 1 h after hypodynamia (heart), 3; 1 h before hypodynamia (respiration), 4; 1 h after hypodynamia (respiration).

solution of relatively simple problems, the number of errors increased. In general, the mechanisms causing reduced acceleration resistance under high temperatures are related to dehydration [51,69, 103] and reduction of vascular tone [113].

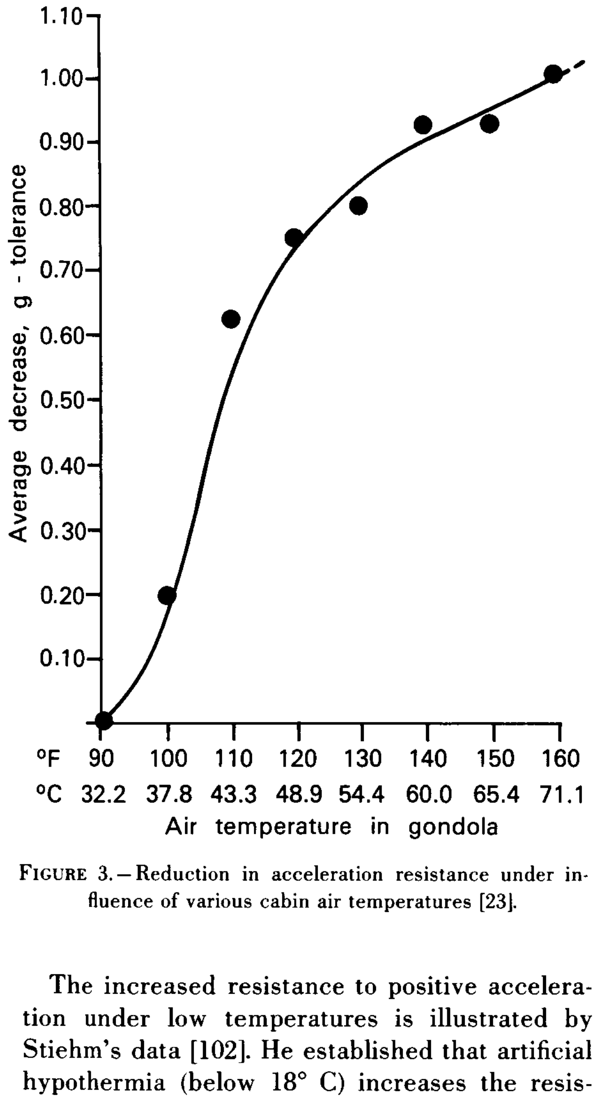

FIGURE 3.—Reduction in acceleration resistance under influence of various cabin air temperatures [23].

The increased resistance to positive acceleration under low temperatures is illustrated by Stiehm's data [102]. He established that artificial hypothermia (below 18° C) increases the resistance of rats to acceleration of 30 g and higher. The maximum effect of hypothermia was noted at 40 g, when survival time of an experimental group was 236% greater than in controls (Fig. 4). His explanation of the increased resistance to this type of acceleration (head-pelvis) is that hypothermia decreases oxygen uptake in tissues, allowing better toleration of brief anemia which develops in the brain under positive acceleration. The increased resistance, it can also be assumed, is related to hypothermia facilitating economical consumption of macroergic compounds, particularly by such organs as the brain and the heart [46].

Acceleration and ionizing radiation. The combination of acceleration and ionizing radiation is of interest. There are many possible combinations of these factors; when acceleration is the leading factor and radiation is the factor changing the organism's reactivity to acceleration, this combination has long been of concern to the authors of this chapter. In series of experiments [7, 31, 32, 33, 97], the reactivity of an irradiated organism to critical acceleration values has been studied. An attempt was made (based on the survival rate) to establish the dependence of this effect on the radiation dose. This method of investigation provides a general concept of the animal's reaction during the application period of the extreme stimulus and permits quantitative evaluation of this state. An extreme stimulus can reveal latent, unstably compensated mechanisms not revealed with weaker stimuli.

In Figure 5, showing results of the experiments, the general direction of the curves is almost the same for all radiation doses. The animals' resistance to critical acceleration increases 1–2 d following irradiation and reaches its maximum on the 5th or 6th day. Resistance decreases by the 7th day, and mortality even exceeds somewhat the mortality of the control animals. Reduction in the animals' resistance to acceleration during this period coincides with the start of death for animals irradiated with doses of 700 and 850 R. In the 4–5 d following irradiation, at least for doses of 500 R and lower, the period is perhaps a critical break time, when the pathological process either starts to decrease or continues to develop. All the body's protective forces are obviously mobilized at this time, increasing the acceleration tolerance of the irradiated animals. Data are relevant that indicate the animals' resistance to mechanical trauma [97] and hypoxia [54, 106], which is increased during the latent period of radiation sickness.

Data on the acceleration tolerance of mice irradiated with 850 R (Fig. 5, curve 4) permit the assumption that at higher doses, increased acceleration resistance would be observed earlier. Further investigations show that animals' degree of resistance to acceleration depends on the radiation dose, and this dependence can be represented by a hyperbolic equation [33, 97].

Vibration

Vibration, like acceleration, is related to the flight dynamics of spacecraft and influences the organism during the lift-off and descent. Thus the combined effect of vibration with acceleration, hypoxia, altered temperatures, and ionizing radiation is significant.

Vibration and acceleration. The combined influence of vibration and acceleration has only sketchy coverage in the literature. The effectiveness of a limited number of these factors in combination has been evaluated, considering parameters of the influence, intervals, and sequence of application of factors. However, the data obtained so far are useful. Vykukol [109] shows the results of acceleration on the human's resistance to vibration, factors found to be additive. Acceleration increases the body's rigidity and reduces its shock-absorbing properties, which helps to increase transmission of vibration energy to the internal organs. An antagonism during the interaction of vibration and acceleration was detected by Clarke et al [28]. In a study of the influence of these factors on certain indicators of an operator's work capacity, it was established that while vibration reduced visual work capacity, acceleration increased it. A comparison of these two studies shows that even when the same factors are interacting, evaluation of the final effect may depend to a great extent on the test used.

Vibration and hypoxia. The combined influence of vibration and hypoxia, studied by Shevchenko [99] and Megel et al [80], provided significant results from experiments with rats. Both an additive and an antagonistic effect were found with the combination of vibration and hypoxia; the antagonistic effect was noted in such indicators as oxygen uptake and skin temperature

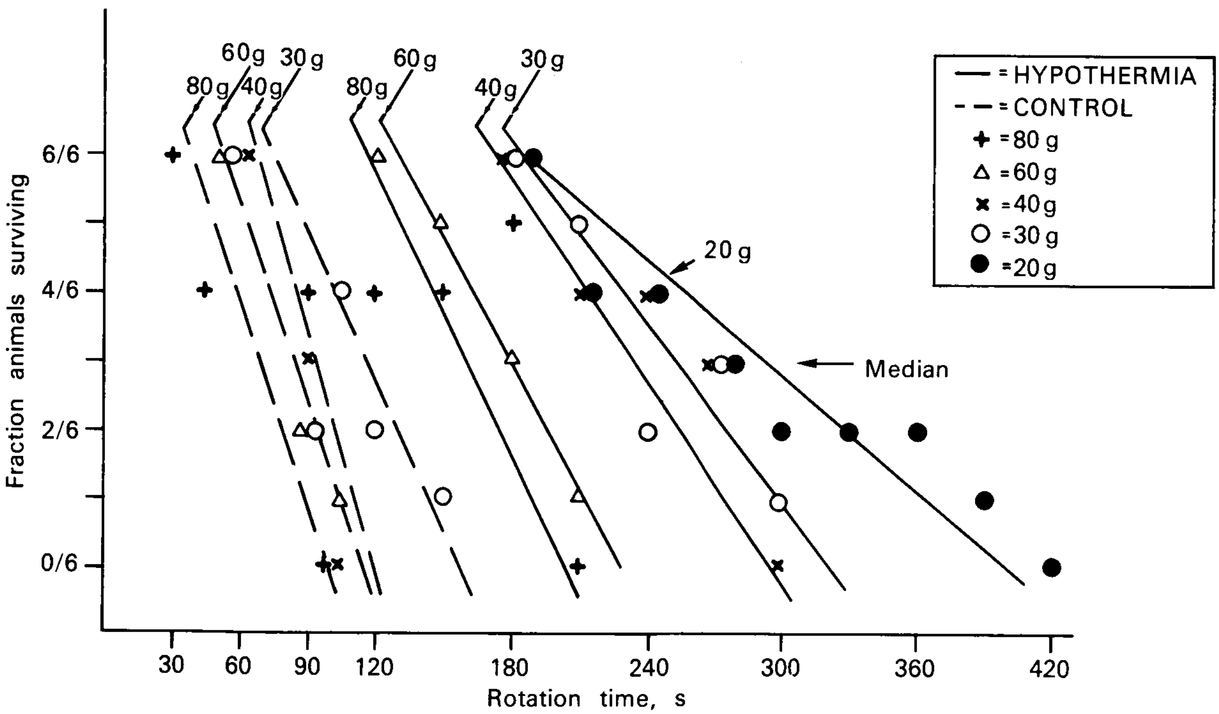

FIGURE 4. – Comparative data on survival rate of rats under influence of positive acceleration at normal and reduced temperature (15° C) [102]. Mean time 680 s. Rotation (20 g) of control rats (3/6) not shown in figure.

restoration following cold load. It was also concluded that the combined influence of vibration and hypoxia caused a reduction in the organism's resistance to acceleration. Megel et al evaluated the combined influence of vibration and hypoxia based on the animal mortality rate: at altitudes less than 6000 m, mortality resulting from vibration did not differ from that recorded at sea level; but at altitudes over 6000 m, mortality increased as a function of altitude. Some results of Megel's work are shown in Figures 6 and 7, indicating that the effect in groups with combined application of factors proved significantly greater than the effects of each factor individually. The significance of reduced partial oxygen pressure in the combined influence effect is also evident. Autopsies on the experimental rats showed extensive hemorrhaging in lung tissue, which may have been the direct cause of death.

The effects of vibration and high or low temperatures [52, 58, 79, 89], and of vibration and noise [18, 38, 53, 65, 112], have been studied in greater detail.

Vibration and altered ambient temperature. In an analysis of the interaction of vibration and thermal stress, the effect of the combination depends on various factors:

- nature and force of stimuli
- duration and sequence of their application
- nature of the tests (shown in a number of examples)
- stimulus topology, i.e., whether the stress has a local or general effect on the body.

The effect of stress is significant principally for vibration, ionizing radiation, and heat and cold, which has been illustrated [58, 79].

Kandror and Talivanova [58] studied the com-

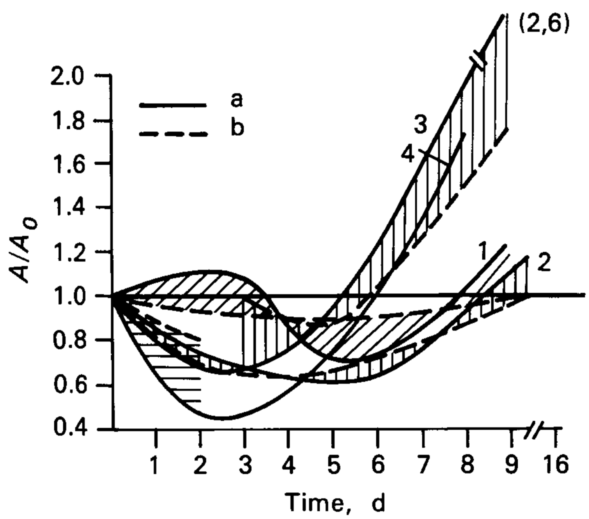

FIGURE 5.—Acceleration tolerance of irradiated mice [31]. A: Death of experimental animals, %. A_0: Death of control animals, %. 1: 250 R, 2: 500 R, 3: 700 R, 4: 850 R. a: Centrifuging, once. b: Centrifuging, twice.

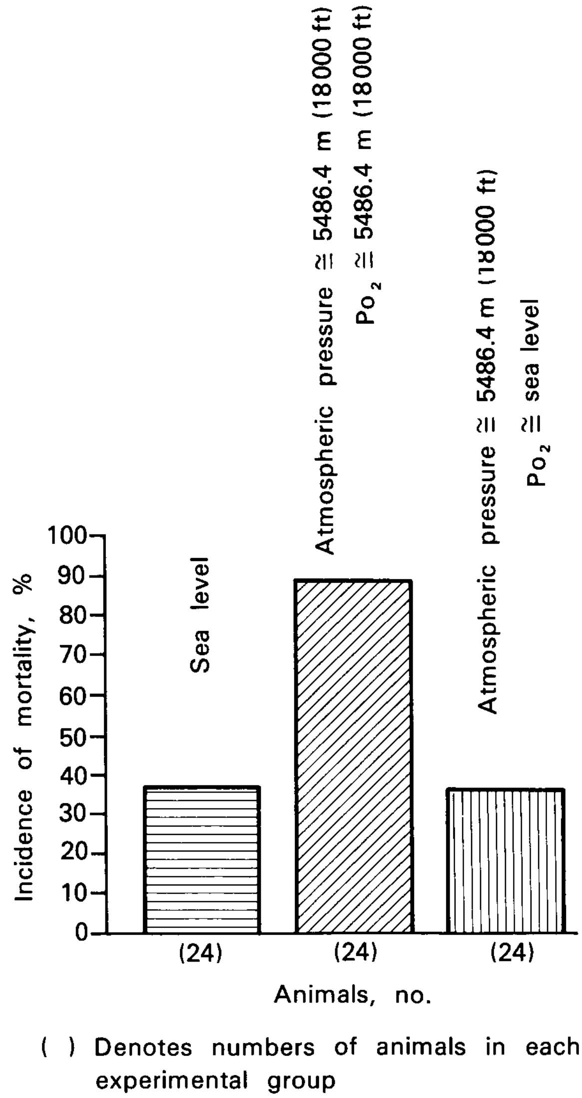

FIGURE 6.—Number of rats that died under influence of vibration (60 Hz–15 g) at sea level, at simulated 6000-m altitude, and at 6000-m altitude with partial oxygen pressure corresponding to that at sea level [80].

bined influence of local vibration and local heat on the peripheral circulation of humans. The peripheral circulation was evaluated by occlusion plethysmography and capillaroscopy. It was shown that vibration (50 Hz, amplitude 0.7 mm, 60 min) decreases the volume and rate of blood influx and efflux, and decreases the number of functioning capillaries and turbidity of the capillaroscopic background. Heat application during vibration (heating the contact surface from 40° to 43° C) reduced or eliminated the vasoconstrictive effect of vibration, where thermal dilation of vessels effectively counteracted the constrictive influence of vibration. The factors were antagonistic. However, the conclusion is correct only for the effects of local vibration on the tone of peripheral vessels and should not be extended to other points of application or to the factor's overall influence.

In experiments on rats, Megel et al showed that vibration and heat have a synergistic effect when applied to the entire body. The animals' resistance to the combined factors was evaluated, based on survival rate, hematological indicators, biochemical changes in blood, and macroscopic and histological changes in internal organs. Synergism, as an influential factor, has been pursued in a number of cases by means of com-

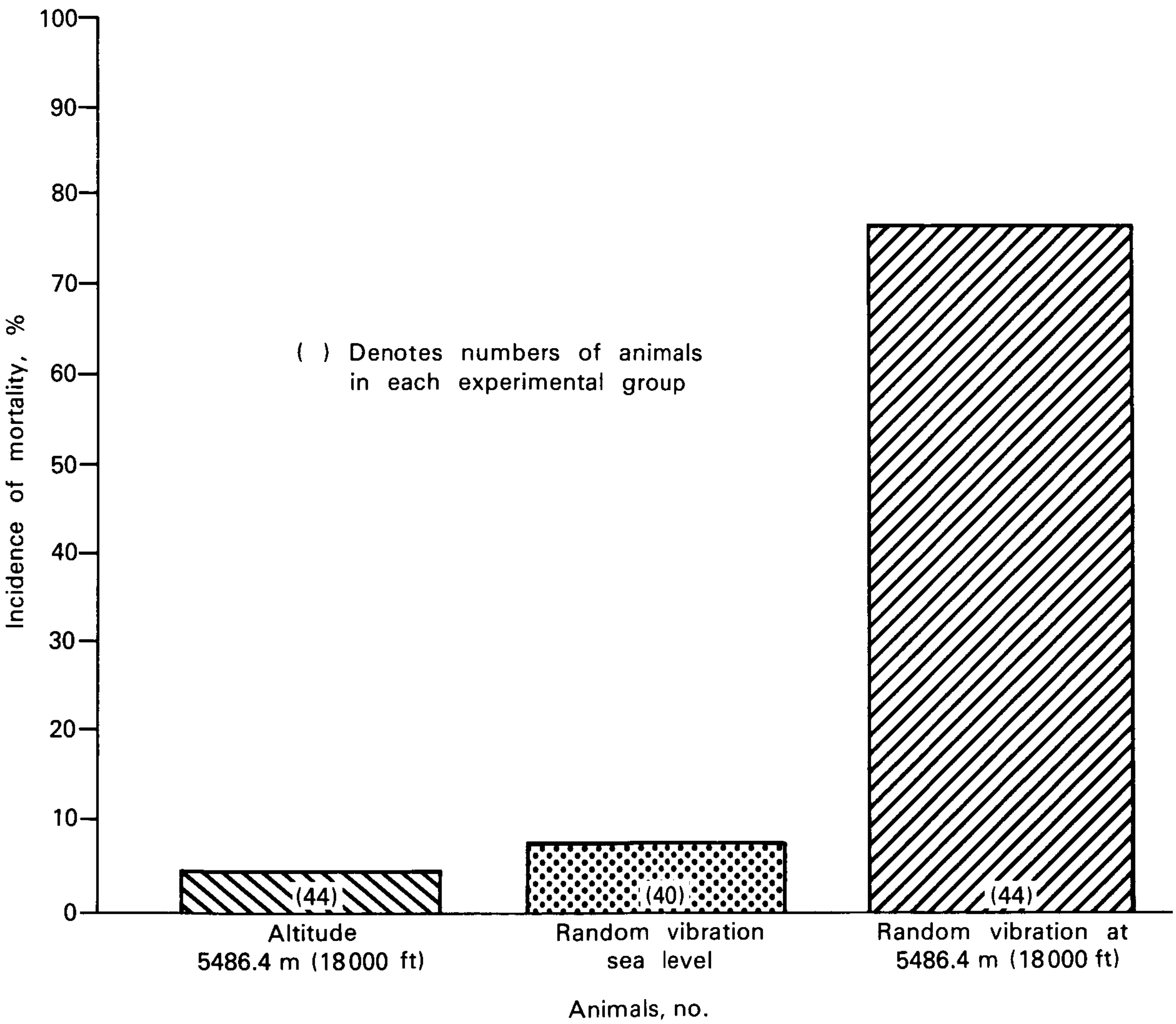

FIGURE 7.—Number of rats that died under influence of altitude alone (6000 m). Effects of vibration at sea level altitude, and the combination—vibration and altitude [80].

monly used, highly reliable tests. For example, while heat alone (46.1° C, 20 min) did not cause death in rats, and vibration (5–800 Hz, 17.5 g) caused the death of 7.5%, a group exposed to the combined influence of these factors showed a mortality rate of 65%. More manifest changes in a group that received application of combined factors in comparison to the effects of each factor individually were detected on the bases of such indicators as hemoglobin level, percentage of hematocrit, content of glutamic oxaloacetic transaminase (GOT), and weight of the adrenals, kidneys, and heart (Figs. 8 and 9). Some changes recorded following application of heat and vibration are reversible. For example, 24 h after the effects ended, the hemoglobin level, hematocrit percentage, and kidney weight returned to the initial values; but the GOT content and weight of heart and adrenals remained high.

The possible mechanisms of reinforcement of effects observed with the combined action of different factors should be mentioned. Vibration can cause damage to liver, kidneys, lungs, heart, and other organs, which Megel demonstrated by the increased content in serum GOT. The increase in hemoglobin level and hematocrit percentage may be related to displacement of liquid from blood vessels to tissues under vibration

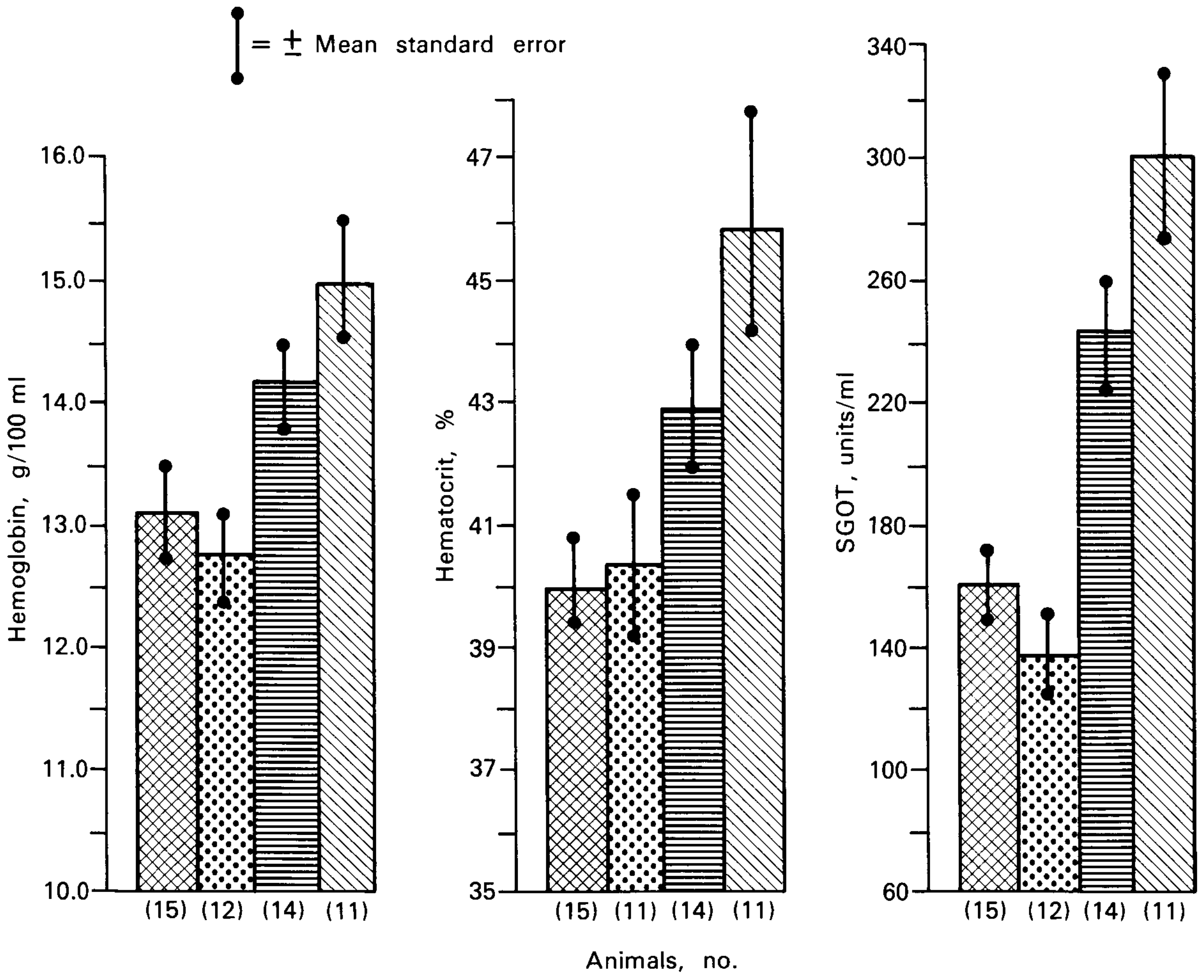

FIGURE 8.—Change in hemoglobin, hematocrit, and serum glutaminooxaloacetic transaminase 30 min after exposure to vibration, heat, and their combinations. Rats with limited mobility used as controls. 1: Control. 2: Heat. 3: Vibration. 4: Heat and vibration. Parentheses show number of animals in groups.

influence. The same influence mechanism on these indicators may be the basis for action of the thermal stressor. Fluid redistribution under the influence of vibration is probably one of the main reasons for increased weight of the organs. The data indicate convincingly that the hypophysis-adrenal system is involved in reaction to the combined influence of the factors. The rapid increase in kidney weight may result, to some extent, from the influence of the antidiuretic hormone (ADH), which is liberated from the posterior lobe of the hypophysis as a result of the stress. ADH stimulates liberation of adrenocorticotropic hormones (ACTH). The increased adrenal weight immediately after the combined influence is retained, even 24 h after the action, may be explained by the prolonged effect of ACTH.

The experiment of Megel et al [79] should be highly rated. However, their assertion cannot be given concurrence that the effect of the combined influence of vibration and heat on the survival rate cannot be predicted on the basis of information on the effectiveness of each of the factors.

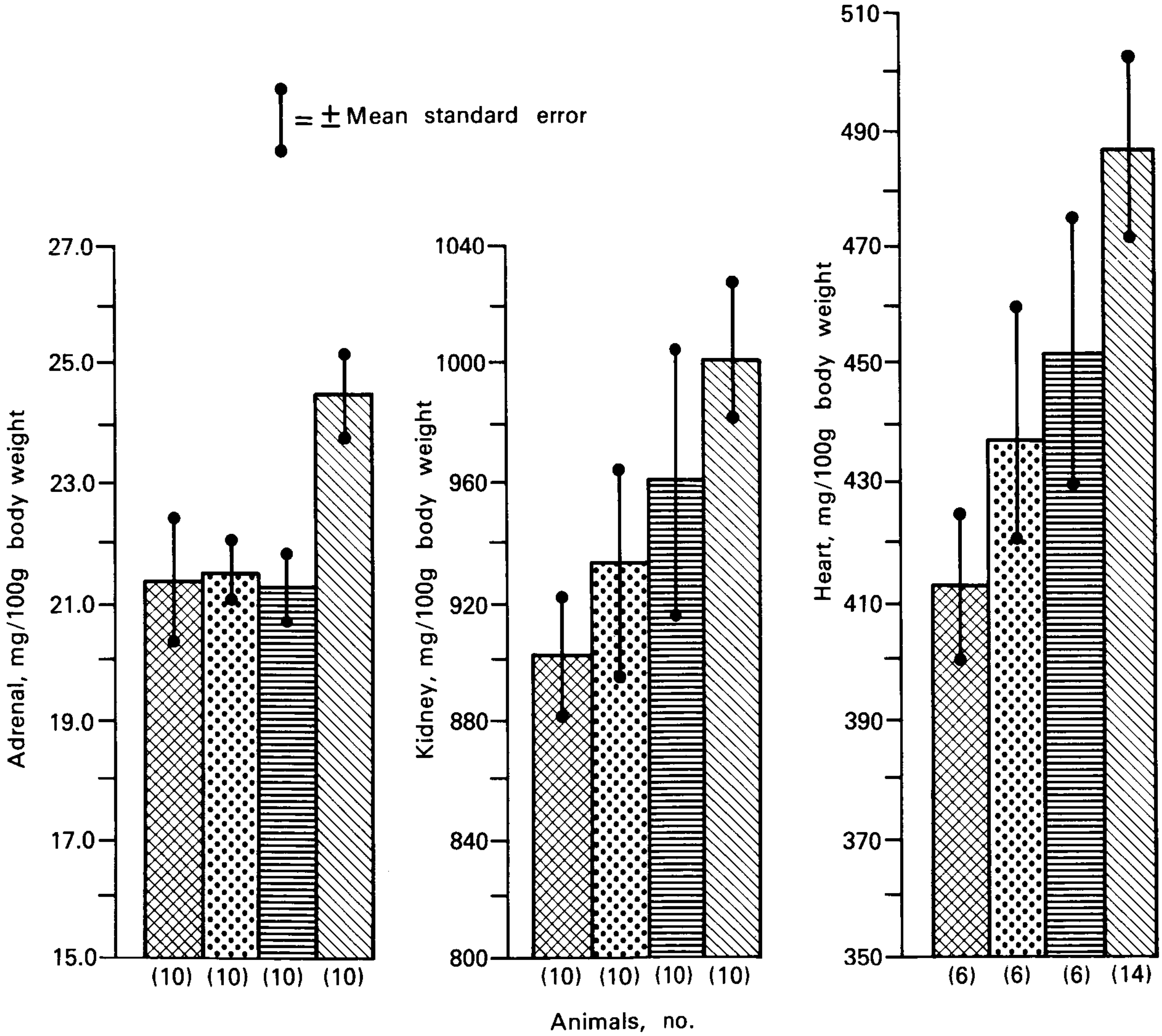

FIGURE 9. – Change in weight of adrenals, kidneys, and hearts of rats 30 min after exposure to vibration, heat, and their combinations. Rats with limited mobility used as controls [79]. Symbols same as in Figure 8.

An approach and formula have been presented [36] for satisfactory predictions of combination effects in many cases, including that of Megel et al.

Investigations on the combined influence of vibration and noise on men and animals should be considered briefly. The combination of vibration and noise has no significant effect on either physiological indicators (heart and respiration rates, number of eosinophils, and so forth) or on work capacity (tracking in two dimensions, and so forth) of test subjects [39, 53]. If combination effects arise, they are additive in nature [53]. This additive effect of combined vibration and noise has also been established by other studies, in particular, on the immunobiological processes in dogs [65], and on the hormone-producing function of the hypophysis in rats [18].

Ionizing Radiation

Ionizing radiation, regardless of the version of its effects that are in mind, must be analyzed only in interaction with other factors. Thus, in flight, changes in the body's radiosensitivity under the influence of nonradiation factors and changes in the body's resistance to these factors [49, 100] can be expected. Consequently, prediction of the course and results of the radiation reaction (damage) requires various data. Factual information should be at hand on the mechanisms of ionizing radiation interaction with at least the primary nonradiation stressors, and on the quantitative dependence of the combination effect on aspects such as power and application sequence of various factors.

In investigations cited in the literature, various methodological approaches were used which allowed evaluation of the reaction of an individual organ, cell, system, or of the entire organism to the combination of ionizing radiation and nonradiation factors.

Ionizing radiation and vibration. The effects of the combined influence of ionizing radiation and vibration have been estimated on the basis of genetic tests. In experiments on lysogenic bacteria *E. coli* [94], vibration used both before and after irradiation significantly increased radiation damage. However, vibration applied before irradiation intensified slightly the radiation damage, and vibration applied after irradiation did not change the influence of radiation (number of induced cells). Parfenov, in experiments with *Drosophila* [90], used a broad spectrum of genetic tests—dominant lethal mutations in males and females, crossing over in males, and primary nonseparation of sex chromosomes in females. He established the possibility of producing a weak antagonistic effect of the combination during vibration application before irradiation, and an additive effect by applying vibration after irradiation. Antagonism in the factors' interaction is explained in that vibration, while retaining its own damaging influence, can facilitate chromosome placement, favoring restitution of those split by the ionizing radiation and hindering their recombination.

Various cytogenetic studies were made of bone marrow cells and testicles of mice under the combined influence of vibration in various types of penetrating radiation [13, 14]. Several versions of the combined influence of the dynamic factor and ionizing radiation were studied, differing in strength, nature of stimuli, and intervals between them. The vibration influence on the radiation reaction was evaluated by determining the mitotic activity of cells and a count of various types of chromosomal restructuring. Results showed that vibration in all versions studied reduced the effects of radiation, which was manifested as decreased frequency of true chromosome restructuring and, particularly, of fragments. The data are partially presented in Figure 10, which shows that the maximum effect of the dynamic factor was recorded when it was applied before irradiation.

Pathomorphological changes in the hemopoietic organs of mice under the combined influence of vibration (60 Hz, 60 min) and ionizing radiation (protons with E = 660 MeV, 855 rad) were studied in detail [48]. Similar to the preceding experiment [14], the combination effect depended on the interval between applications and sequence of influencing factors. There was reduction in radiation damage in those animal groups where the interval between effects did not exceed 1 d. This effect was manifested by a smaller amount of myelopoietic tissue death in spleen and bone marrow, and earlier restoration of all types of hemopoietic cells. An increased interval between effects to 3 d caused a weakening of the antagonistic effect.

When vibration was applied after irradiation, the factors interacted synergistically, in other experiments. Animals exposed to the combined influence exhibited more severe damage of hemopoietic tissue and a notable weakening in reparative reactions, compared with groups exposed to vibration and radiation individually. The synergism was most clearly expressed when the dynamic factor was applied 5 d after radiation. The lymphoid tissue was particularly damaged. During restoration, extensive foci of necrosis were detected in bone marrow and spleen. Restoration of volume and cellular composition of spleen follicles was slower, and differentiation of cell forms in bone marrow and their maturation were retarded.

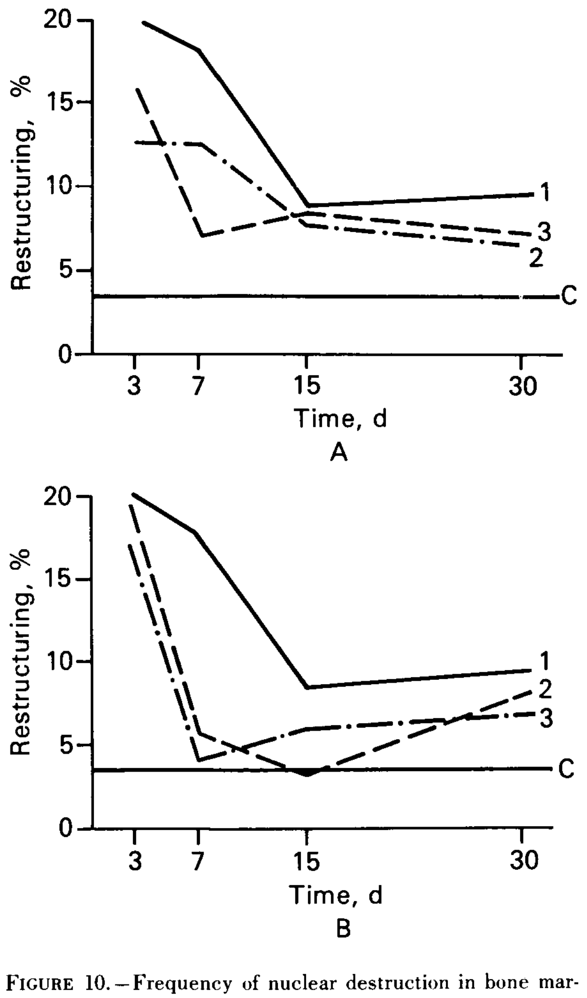

FIGURE 10.—Frequency of nuclear destruction in bone marrow cells of mice under influence of dynamic factors before (A) and after (B) irradiation [14]. 1: x-rays. 2: 700 Hz vibrations with subsequent irradiation 24 h later (350 R). 3: Acceleration 10 g with subsequent irradiation (350 R) 24 h later.

The combined influence of vibration and ionizing radiation on various functions of the central nervous system (CNS) was studied by various investigators [11, 12, 66, 70, 71, 72] who showed convincingly that vibration may significantly change CNS reactivity to radiation, and that the mechanisms of this dynamic factor's modifying influence are complex and varied. The application of vibration before whole-body γ-irradiation has a protective influence on the oxidative processes in brain tissues. When both irradiation and vibration were applied separately, it caused depression of the oxidative processes. However, when these two factors were applied together, the effects were not additive. For certain periods, the effect of the combined influence was less than that of radiation alone.

The combined influence of vibration and radiation caused significant disruptions in the functional state of the reflex arc of the defensive flexor reflex, according to Kuznetsova. This is manifested as changes in excitability thresholds and the length of the latent period of this reflex. Reactions to stimuli sometimes included parabiotic phases. Livshits et al [70] showed that under the combined influence of vibration and x-rays (50 R), the conditioned reflex activity changes during the first week reproduced the vibration effect in all details. During the next week, an unclear tendency toward summation and combination of the effects of both factors was observed. The dominant influence of vibration during the initial period following irradiation and its dependence on the radiation dose were also noted in other works [4, 5, 6, 11, 47, 72, 74].

In studies (particularly those of L'vova [73, 74]) on the combined influence of vibration and ionizing radiation, emphasis was placed on the use of such integral indicators as survival rate, mean survival time of animals killed (SKA), change in animals' body weight, and specific tests on reaction of the hemopoietic system. Experiments on mice, rats, and dogs showed convincingly the primary dependence of the combination effect on the strength and sequence of applying stressors.

Antagonism was noted in groups where the interval between application of the dynamic factor and irradiation was 4 h or 1 d; synergism was noted when the interval was reduced to 2 h or increased to 5 d. When vibration frequency was increased to 700 Hz, the modifying influence of vibration was also changed. For example, when vibration at this frequency was applied 1 d before or 5 d after irradiation, the damage became more severe instead of reduced, as was observed for 70 Hz vibration. In other words, antagonism was replaced with synergism following change in vibration frequency (Fig. 11).

In experiments of L'vova on the effects of repeated application of vibration and one-time irradiation, the interaction in all versions studied was synergistic. Thus, the factual material reliably indicates the possibility of significant change in the reactivity of the organism to radiation under the influence of vibration, which finally influences the course and outcome of radiation reactions (damage). The effect of the factors' influence may be either additive, synergistic, or antagonistic. Finally, the effect of the combined influence may not appear.

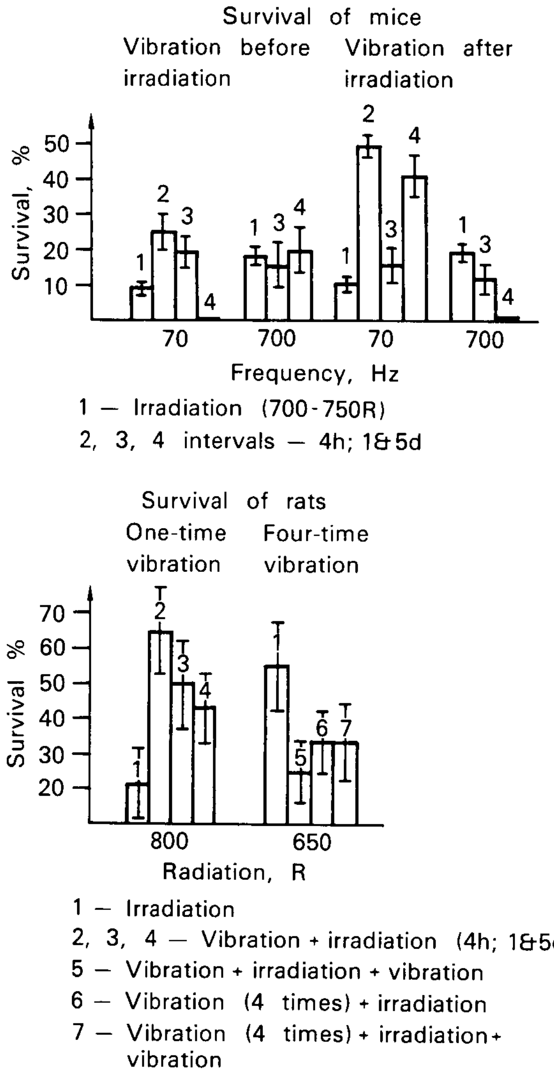

FIGURE 11.—Influence of combined effects of vibration and ionizing radiation on survival rate [73].

What, then, are the possible paths and mechanisms of this unique modifying influence of vibration on the radiation reaction? Vibration, acting on the organism through the central nervous and endocrine systems, possibly changes the organism's functional state, increasing or decreasing the activity level of various organs and tissues, including those that are radiosensitive. This is the indirect path. However, it cannot be ignored that there is direct influence of vibration on cells of the hemopoietic organs, intestinal mucous membrane, and on other organs which undergo functional changes. This has been confirmed by experimental data. Vibration can significantly change the functional state of the nervous system, causing, for example, reduction in cerebral cortex activity and general defensive inhibition [71]. Vibration can also cause depression of oxidative processes [72]. This stressor increases the function of the hypophysis-adrenal system [48, 97] and the content of the body's biologically active amines [8, 91].

Change in the hemopoietic system's functional state under the influence of vibration and consequent change in its radiosensitivity are significant. A limited list of changes in the hemopoietic system from vibration influence includes the reduction in mitotic activity of cells in bone marrow and spleen, increase in adhesion of chromosomes in various stages of the cellular cycle [14], increased death rate of lymphoid cells in the spleen [48], and neutrophilic leukocytosis, lymphopenia, eosinopenia, and thrombocytopenia [74]. These changes must influence the hemopoietic system's sensitivity to radiation and in the final effect to the combined influence of the two factors.

Changes in the quantity of leukocytes, lymphocytes, and eosinophils in the peripheral blood of dogs were noted when the animals were subjected to the influence of vibration, γ-rays, and their combination (Fig. 12). In dogs subjected to the combined influence of the factors, the reaction of these indicators differed significantly 2 and 4 h after irradiation compared with reactions in groups subjected to only vibration or only radiation. These indicators and others of change in the hemopoietic system's functional state correlate satisfactorily with an integral indicator such as survival rate [4, 7, 74] and convincingly show the hemopoietic system's significance in the mechanism of the combined influence of vibration and radiation.

Ionizing radiation and acceleration. In various versions of experiments with one-time application of ionizing radiation and acceleration, the effect observed was dominantly antagonistic. Acceleration is a "protective" agent, reducing the organism's reaction to radiation influence. Signs of reduced radiation effect under acceleration influence have been noted with various methods of investigation: cytogenetic [14, 45], histological and pathomorphological [35, 48], biochemical [1, 4, 91], hematological and radiobiological [1, 4, 9, 32, 56, 61, 68].

Curves of mice mortality have the same S-shape with one-time application of combined acceleration and irradiation (depending on dose), as with radiation alone. Processing these curves by trial method showed that with combined acceleration and irradiation, $LD_{50/30}$ is 100 R higher than with radiation alone. Rat experiments showed that acceleration in combination with radiation did not significantly change the value of LD_{50} [114].

Acceleration and irradiation may act synergistically. It was shown in particular that with relatively short intervals (5 min to 2 h) between the application of acceleration and radiation, acceleration can reinforce radiation influence. Figures 13 and 14 show that with combined application of acceleration and radiation, the $LD_{50/30}$ for rats is approximately 50 R lower than when radiation is used alone. When the two factors are applied together, the dogs' reactions (in regard to lymphocytes and eosinophils) are more strongly expressed than when either factor is used individually. Only synergistic effects have

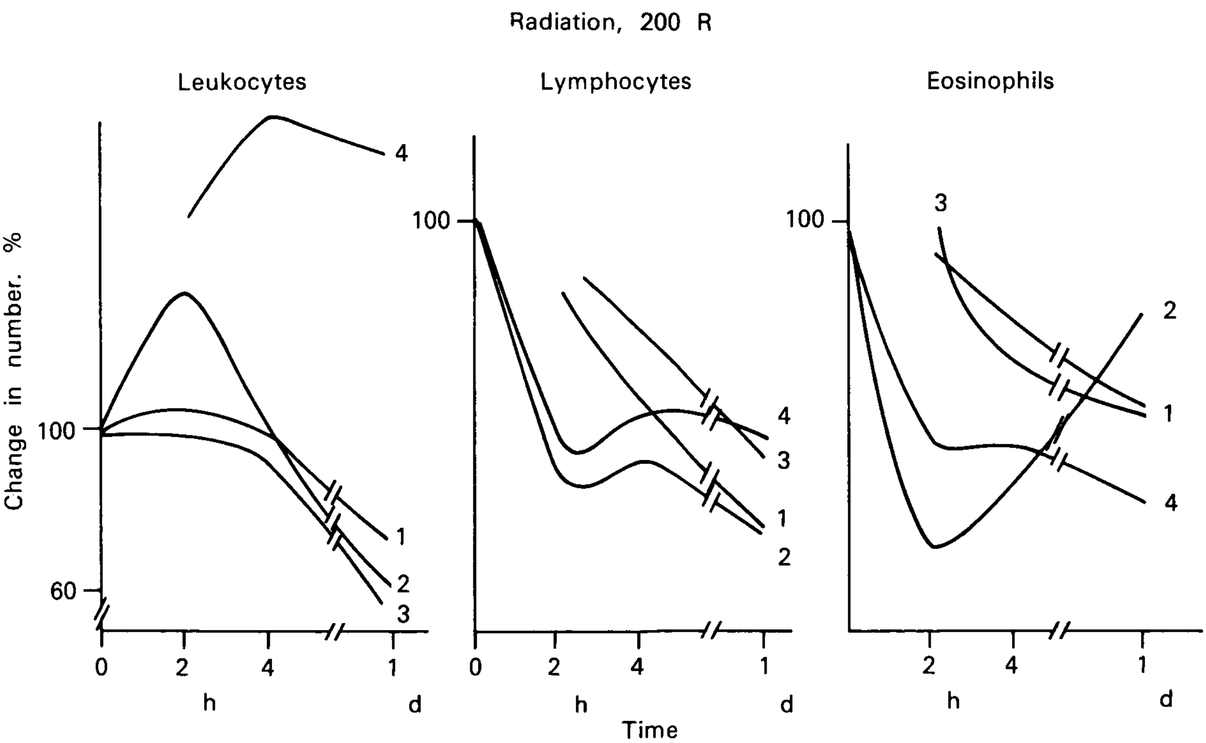

FIGURE 12.—Change in number of leukocytes, lymphocytes, and eosinophils in peripheral blood of dogs subjected to combined vibration and γ-rays [74]. 1: γ-radiation = 200 R. 2: V + γ-radiation = 200 R (for 1 h). 3: V + γ-radiation = 200 R (for 1 d). 4: Vibration.

been observed so far with repeated application of acceleration and radiation. The increase in radiation damage under acceleration influence has been noted based on such indicators as survival rate, survival time of killed animals (SKA), and rate of reparation processes [25, 43, 61].

The general aspects of mechanisms of the modifying influence of acceleration on radiation effects are related primarily to the hypoxia that arises under acceleration influence in various body organs and tissues, including those that are radiosensitive. The reduction in oxygen uptake, for example, by tissues of spleen or bone marrow may account for their increased radiation resistance. Furthermore, hypoxia (particularly in the hypothalamus area) can cause mobilization of adaptation mechanisms (changes in content of serotonin, ceruloplasmin, and so forth), or lead to formation of the specific hemopoietic factor, which also influences increased radiation resistance [97]. The role of nervous mechanisms related to the development of extreme inhibition in cerebral cortex cells and simultaneous deinhibition of subcortical centers cannot be excluded [70, 71, 110].

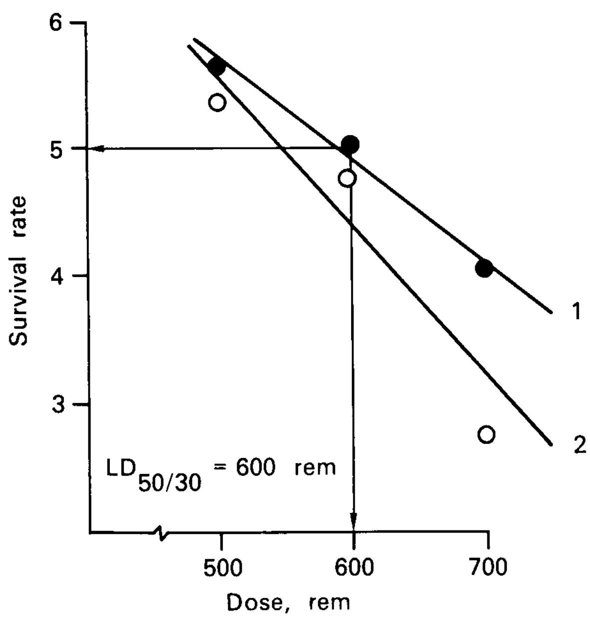

FIGURE 13.—Influence of combined effects of acceleration and γ-rays on survival rate of rats [97].

Finally, Zharova et al [115] studied the survival rate and remote (up to 2 years) reactions of the hemopoietic tissue of mice under the combined influence of transversely directed acceleration (10 G_x, 15 min) and x-rays (400 R). Significant differences were revealed only in the 5th month after exposure. By this time, of animals subjected to the combined influence, 90% died; the group exposed to x-rays alone suffered 65% mortality; while those exposed to acceleration only were alive. Leukemoid reactions, which are difficult to differentiate from true leukoses, were more frequent in mice subjected to the combined influence of the factors than in other groups of animals. These data indicate that the direction and magnitude of effects depend also on the period of time that elapses following the application of the factors.

Weightlessness and Ionizing Radiation

Biological experiments aboard Soviet and US spacecraft (Sputnik 2–5, Vostok, Voskhod, Discoverer 17 and 18, Gemini 3, and Biosatellite II) have been reviewed in detail [5, 18, 35, 41, 57]. The data indicate overwhelmingly that it is not possible to segregate the effect of radiation in combination with weightlessness from the complex of flight factors.

The most successful experiment on the combined influence of weightlessness and ionizing radiation was that on Biosatellite II. Its ionizing radiation source permitted a relatively heavy radiation load to be used on various biological objects, and strict control of the load. A significant shortcoming was the brief flight time (45 h) and, consequently, determination of the weightlessness influence. In experiments on *Drosophila melanogaster*, irradiation during flight led to greater mortality, and a greater percentage of chromosome restructuring and sex-linked recessive lethal mutation in actively growing and metabolizing objects, than were evident in various terrestrial control objects. It was assumed that these developments resulted from the interaction of radiation and weightlessness [88]. The action of these two factors in combination was also considered the cause of an increased number of specimens showing anomalous development of thorax and wings [20].

In an experiment with the plant, *Tradescantia paludosa* [101], synergism in the combined influence of radiation and weightlessness was revealed by the quantity of abortive pollen and dead microspores, and various nuclear anomalies. These are indicators that weightlessness influences the cell spindle apparatus, causing various mitotic disorders, which was first established by using bone marrow cells of mice [13] and on microspores of *Tradescantia paludosa* [40].

A less clearly expressed influence of flight conditions and, primarily, weightlessness on the effects of radiation was detected in experiments with *Tribolium confusum* [21], lysogenic bacteria [78], and other biological objects. In analyzing the material, the authors justifiably show great caution in evaluation of the effects of weightlessness and its combination with radiation. The findings on Biosatellite II require confirmation with similar, but longer experiments for further study of the combined influence of weightlessness and radiation.

Ionizing radiation and SHF-band radiation. The combined influence of ionizing and SHF-band radiations is studied in two areas—experimental and hygienic. Investigations are concentrating on combined effects of ionizing radiation and, particularly, SHF radiation, because of increasing use of equipment which generates electromagnetic fields at various frequencies on spacecraft and stations.

Data on the mechanisms of biological effects of ionizing and microwave radiation indicate that these radiations in combination can act as synergists or antagonists, which is confirmed by experimental material. In experiments on rats, the influence of continuous microwave radiation reinforced the effect of γ-rays, while pulsed microwave radiation weakened their effect [92]. This was determined by the mortality rate of the experimental animals; it should be emphasized that the animals were exposed to microwaves before exposure to γ-rays. The effect of the combined influence of microwaves and ionizing radia-

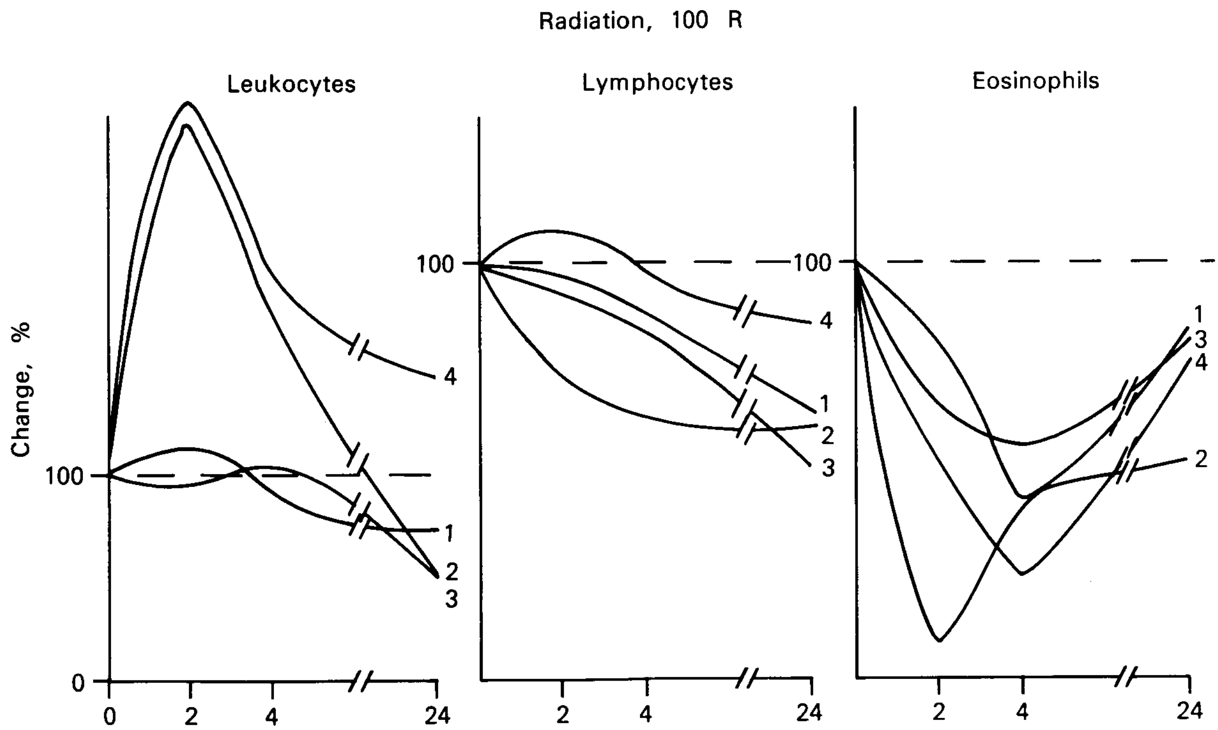

FIGURE 14.—Change in leukocytes, lymphocytes and eosinophils in peripheral blood of dogs subjected to combined acceleration and γ-rays [61]. 1: γ-radiation = 100 R. 2: P + γ-radiation = 100 R (2 h). 3: P + γ-radiation = 100 R (24 h). 4: P = 8 g 30 min.

tion depends on the sequence of application of both factors [83, 84, 96, 104]. The use of microwaves before ionizing radiation weakened the organism's reaction to the radiation, while use of microwaves after the radiation reinforced it. Synergistic effects during the action of SHF radiation and γ-rays were obtained by the authors of this chapter with Tikhonchuk [37]. The combined influence of the factors was estimated on the basis of mortality ($LD_{50/30}$) and SKA, changes in weight, and certain hematologic tests.

The data, partially presented in Figures 15 and 16, indicate that preliminary exposure to an SHF field makes radiation damage more severe, which is clearly seen in displacement of the $LD_{50/30}$ and dynamics of the changes in neutrophil and lymphocyte content. The greatest effect was observed in the SHF radiation application with ppm = 100 mW/cm^{-2}. Combined application of the two factors reduced $LD_{50/30}$ by 200 R and significantly decreased neutrophil and lymphocyte content as compared with the influence of γ-rays alone. Finally, from clinical examinations of persons working under exposure to SHF and soft x-rays firmly, it is concluded that the effects of these two harmful factors generally reinforce each other [27, 60].

Ionizing radiation and hypoxia. A review of studies on the combined influence of ionizing radiation and hypoxia requires an evaluation, if only general, of possible effects of this combination, since there is great probability of body exposure to these stressors during space flight.

Conclusions from available works are:

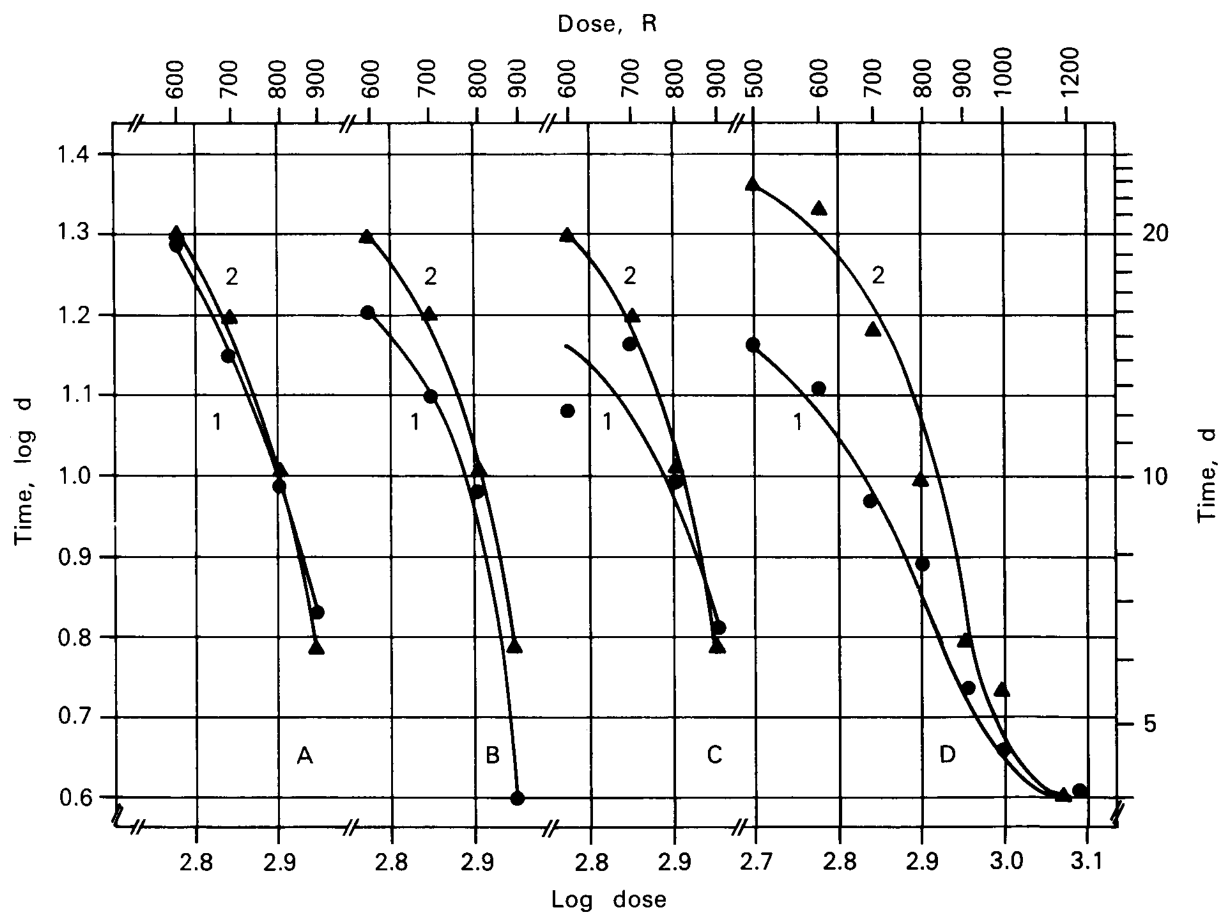

FIGURE 15.—Mean survival time of mice that died, as a function of radiation dose [37]. 1: SHF + γ-radiation. 2: γ-radiation. A, B, C, D: 10, 20, 40, and 100 mW cm², respectively.

Acclimatization to hypoxia can significantly increase the body's resistance to the effects of ionizing radiation [15, 106].

The "protective" effect of hypoxia is manifested during one-time application of this factor by starting with acute hypoxia before irradiation in the presence of ordinary oxygen [24, 67], and is particularly effective in dealing with hypoxia [106].

The factors here interact as antagonists.

Reports in the literature on the influence of hypoxia following irradiation are contradictory, which probably results from the period of radiation damage during which hypoxia and radiation application mode are combined.

Hypoxia applied 13 to 25 d after irradiation (each day 18 h/d for 30 d) slightly increases the survival rate; but when applied 1 to 4 d after irradiation, hypoxia increases mortality [87].

While the mechanism of the "protective" effect of hypoxia was discussed under the combined influence of ionizing radiation and acceleration, it should be added that the positive influence of repeated application of this factor between the 2nd and 3rd weeks of radiation sickness may be related to some stimulation of the hemopoietic organs.

QUANTITATIVE METHODS OF EVALUATION AND PREDICTION OF FLIGHT FACTORS' EFFECTS

The basic purpose in establishing methods to estimate quantitatively the influence of the combined action of stress factors during space flight

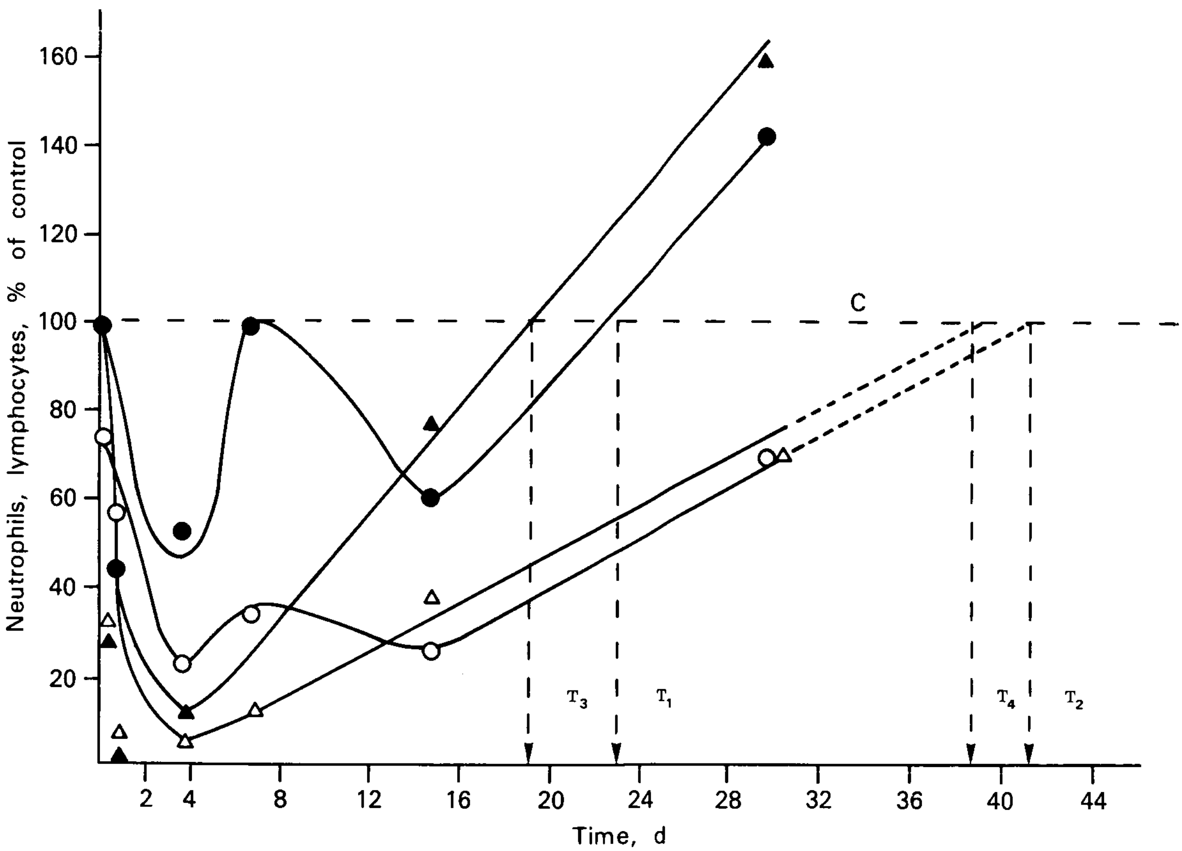

FIGURE 16.—Changes in number of neutrophils and lymphocytes in mouse blood. ●: γ-radiation alone (neutrophils). ○: SHF + γ-radiation (neutrophils). ▲: γ-radiation alone (lymphocytes). △: SHF + γ-radiation. T_1, T_2, T_3, and T_4: periods of full recovery, respectively. C: level of biological control.

is to enable prediction of both direct and remote results of this influence. This would be significant for timely development of preventive measures and effective medical monitoring in space flight. This is not a particular problem of space biology and medicine but relates to astronautics as a whole. The possibility of comparatively precise quantitative (although probabilistic) prediction of the influence of combined effects of spaceflight factors on crewmembers will also allow quantitative estimation of spacecraft requirements (since a crew is aboard) and the fail-safe functioning of the entire bioengineering complex (crew plus on-board systems). Designers will thus be provided with needed information to plan flight systems and the spacecraft.

Material has been accumulated on applying quantitative mathematical methods to investigation of the combined influence of flight factors. Dean et al [38, 39] used dispersion analysis methods in work on the combined influence of factors. Antipov and Davydov's factoral-analysis plans have been successful in predicting the influence of a radioprotector on survival rate under conditions of uneven irradiation, and in interpreting data of Megel et al [36, 79, 80] on the combined influence of vibration, hypoxia, and high temperatures. However, this is only a first attempt in seeking approaches to solving the problem.

The key to the solution is probably in the creation of adequate mathematical models of biological systems subjected to the combined influence of stress factors. Similar models are designed with certain initial prerequisites for the prediction of the development of the state of the model system as affected by time. The pragmatic value of heuristic methods of prediction must not be ignored. In this work, the professional skills and intuition of a team of experienced medical experts is combined with the capabilities of rapid information from modern computers. The value of these methods at the present stage in solving medical monitoring problems (particularly in monitoring individuals' states) is generally recognized. However, this does not eliminate the need for developing and improving formal algorithms for prediction based on statistical and dynamic simulation models.

Experimental study of the effects of combined action of factors, the traditional form of investigation of medical doctors and biologists, will not become less important as quantitative mathematical methods are introduced into medicine and biology. On the contrary, experience with mathematical biology has shown that the identification of models, without which their intelligent application is not possible, requires expanding the volume of experiments. However, the variety of work by experimenters, difference in methods used, arbitrariness of selection of factor levels applied, frequent duplication, and so forth, greatly reduce effectiveness in the study of this problem.

Quantitative Description of Stress Factors' Influence on a Biological System

The development of effective methods of quantitative description of the influence of various stressors on individual physiological systems and the body as a whole, the combined influence of a number of stress factors, as well as prediction of these factors' aftereffects for the biological system being studied, require a transition from verbal characteristics to precise formalized description. This applies not only to construction of a mathematical model of a biological system (detailed below) but also to assignment of the stressor actions. A characteristic such as the intensity of an action (radiation dose, acceleration amount, and so forth), which is easily interpreted and usually readily measurable, is widely used. Nevertheless, assignment of an action in a number of even relatively simple situations by means of a single scalar parameter is not complete enough. Other characteristics of the factor must be considered (e.g., not only intensity but also spectral composition of radiation, and so forth). The greatest difficulties are in assigning the action's time structure.

In an analysis of the time structure stressor actions, the first step is to differentiate between two main types of action (mode of factor application); these differ in relationship between duration of application time of the stressor to the biological system, and duration when reaction of the system to the factor is observed and studied. The first type is when the stress factor acts over a period substantially less than the observation period of the system. The second is when the factor is applied throughout the observation time or at least a significant portion of this time.

The difference in principle between these two modes of stressor actions is that in the first, the biological system, once displaced from its initial state, returns to it or shifts to another stable state without the stressor. Thus, changes in the biological system are either attenuating reactions to the initial stimulus or processes for which stress factor application served as a starting mechanism. In the simplest case, when the stress factor is applied for a very short time compared to the characteristic time of the system reactions, the time structure of factor application is insignificant. Only its intensity is significant. The second case shows essentially the system's adaptation to a continuously applied stressor. It can be said, using an analogy from mechanics, that the first action mode of stress factors generates "free" oscillations of the biological system, which are observed. The second generates "forced" oscillations. The specific features of a number of stressors allow their application in only one of these two modes (if limited to examination of stressors), which are compatible with the adaptative and restorative potential of the biological systems.

The expediency of differentiating between these two basic types of time structures of stressor actions is obvious, since it allows more precise, logical experiment planning, involving observation of the biological system's restorative processes after the stressor's action or adaptation processes. Many actual situations where the body (or functional system) is subjected to the combined influence of a number of factors can be interpreted as a combination of elementary processes belonging to one of these two main types. In these cases, the concept of the observation period of the system should be refined. This quantity, of course, cannot be arbitrarily selected. The natural scale for it is the characteristic time of change and other processes typical of that system, or for complex systems, for that system's level in which the stress factor's reactions are essentially concentrated.

Iberall and McCulloch [55] present a scale of time constants for man: nerve processes (0.3 s), chemometabolic processes (3 s), neurohumoral processes (3 min), hormonal processes (7 min), primary circadian rhythm (1 d), behavioral reactions (10 d), and so forth. The value of time parameters characterizing the responsive reactions and their modification is informative in that not only can judgments be formed concerning the degree of a stressor's influence but also those systems in which the stressor is basically concentrated can be determined. As examples, a number of investigations can be cited on the organism's postradiation restoration [2, 17, 30, 82, 95] and the influence of toxicological and pharmacological agents, acceleration and vibration [32, 35, 43].

For the entire organism in mice (survival rate test), the half-restoration period following acceleration is ca 3 h and following injection of cystamine, 1.5 h. However, when these two factors are combined, the half-restoration period is extended to 24 h and more [34, 35]. The additional application of acceleration and vibration increases the half-restoration time following the radiation factor from 4–5 d to more than half again as long [30, 43]. The periods required for half-elimination of the stressor reflect the hemopoietic system's restoration rate, primarily damaged by the radiation factor, as well as that of the cardiovascular system, primarily influenced by acceleration. Cystamine elimination is apparently determined by the detoxification rate in the parenchymatous organs (liver, kidneys).

Synthesis of Models of Biological Systems

The problems in constructing models to describe dynamics of biological systems, including models to analyze and predict adaptation and restoration processes following the combined application of a set of stressors, are properly considered to be among the most pressing and complex problems of modern science. Numerous researchers have been interested in this problem since the beginning of the century, and there have been endless publications; but significant results continue to be relatively rare and, unfortunately, have never been integrated into a single, well-ordered discipline such as mathematical physics. All of the basic difficulties of mathematical biology have not been overcome, despite claims to the contrary, but some scientists are unnecessarily pessimistic. Rashevskiy, for example, has said that "the current level of development of physics is possibly still insufficient to explain the basic biological phenomena, and, therefore, we are fully justified in raising the question of whether new physical laws might be required for this purpose" [93]. However, in disagreement with this view, the development of biology and all its current successes (particularly in molecular biology) are related to the extensive introduction of methods from the exact sciences into biology on the basis of known basic regularities. Also, passive waiting for the discovery of special laws in the exact sciences applicable to the life sciences would prove fruitless from the purely practical standpoint.

The true reason for difficulties encountered in introducing methods from the exact sciences into biology is related to the basic difference which, from the standpoint of the general theory of systems [81], is between animate and inanimate objects. The description of any natural object always involves a hierarchical structure. However, the relationship between structure levels for inanimate objects is usually relatively weak, which allows problems to be broken down into a number of tasks, each relating to a single level. For example, in solving problems of engineering thermodynamics, it is possible in the first approximation to ignore the atomic and molecular properties of substances and to utilize heat capacity values and kinetic constants as phenomenological parameters. This situation is rarer for biological systems because of the close relationship between hierarchical levels. For example, biochemical processes in muscle tissue determine the tonus of the neuromuscular apparatus and the entire organism's state as a whole.

The relationships between levels of a biological system are rich and dynamic, hindering use of the standard method of breaking down problems and analyzing models of processes at one level separately, and of considering the influence of neighboring levels by means of effective values of the model's parameters. An example which partly confirms this is the comparative success of quantitative methods of analysis of biological systems in the investigation of hereditary structures and population dynamics; i.e., at the two extreme poles of the space-time scale of hierarchical levels, where the relationship between neighboring levels is less intimate than between the tissue and system levels and, correspondingly, the system and organism levels.

The greatest successes in construction of mathematical models to analyze the stress factor's influence have been achieved (not accidentally) in radiobiology. Here, within certain limits, methods can be used which do not consider the true damage mechanism to the tissues of body systems, but rather replace it with an effective model. For examples see Blair's hypothesis [17], Dankov and Logofet's model [29], and others.

Nevertheless, the only intelligent alternative is continuation of tenacious, persistent, and painstaking work on the synthesis of mathematical models of biological systems. This problem, the reaction of the organism and its systems to the combined influence of stress factors, has a reasonable chance for successful solution.

The standard method for constructing a functional model of any biological system is the synthesis of a model according to which the initial system is assumed optimal. There can be no doubt that the initial system is in some sense truly optimal, since otherwise it would probably have been eliminated during the course of natural selection. Unfortunately, it is difficult to formulate an obvious criterion for natural selection. Thus, the study of a biological system's reaction to a certain stimulus is frequently complicated not only by the uncertainty that the optimal criterion selected is adequate to the specific situation, but also by uncertainty that the selection will be correct under different conditions. Selye's concept [98] is fruitful in this connection: the general adaptation syndrome confirms the presence of nonspecific components in the organism's reaction to a broad and varied range of stress situations. A certain generality about the body and its systems' reactions to stressors facilitates construction of a single method of quantitative description of combined application effects of stressors.

There are presently two basically different approaches to the solution of this problem; a comparative discussion of these approaches will follow in the remaining sections of this chapter.

Construction of Regression Multidimensional Models and Methods of Experimental Planning

The use of statistical methods in biology, compared to other branches of mathematics, has a more ancient tradition and apparently has yielded the greatest results, which, in turn, have had a stimulating influence on the development of the methods. Fisher's creation of dispersion analysis [44] is an obvious example. Problems that are traditional for statistics are those that require an estimate of the comparative significance of various factors which go together to produce a measurable effect, as well as problems of regression analysis—determining the dependence of the mathematical expectation of a measurable random quantity on a certain argument.

The selection of experimental planning methods is important to the problem of the combined influence of factors. The problem of planning, at its inception in the 1920s and 1930s, was considered one of averaging the influence of unmonitored factors. Experiments were fully randomized, so that by treating the results with dispersion analysis methods, it was possible to distinguish clearly the influence of the unmonitored factors. Subsequently, a more general statement of the problem was used—the experimental plan was composed to allow the minimum number of measurements to be used to determine, in the set of permissible levels of factors, the functional dependence between the factors studied and the quantitative characteristics of the effect caused by their action. Since in most cases, the form of the functional dependence is assumed known with an accuracy based on the parameters, the problem is essentially one of estimating regression coefficients with certain fixed properties (ϕ—optimal plans generate an information matrix with the greatest value of the determinant; the covariation matrix of an A-optimal plan has the smallest value, and so forth).

Thus, construction of regression models by means of the widely developed methods of experimental planning is one possible and promising method of investigating the problem of the combined influence of stressors. A group of authors in a study of automation of medical monitoring in space flight [111] predicted use of multifactor and multidimensional models in space medicine and biology. However, this trend is far from universal and has its basic limitations. First, even with a small number of factors, the need to consider the interaction time structure in even trivial situations increases the problem's dimensionality so much that solution is difficult even using modern computers. Second, the number of experiments necessary to construct a response surface with the proper accuracy (particularly when extreme points of this surface are sought) frequently exceeds the possibilities of biomedical studies. It is not always possible to observe the initial prerequisites on which the method of multidimensional regression analysis is based (for example, error-free measurement of independent variables). Also, practice has shown that multidimensional regression analysis is sensitive to such disturbances; when these disturbances are present, it is rarely possible to produce significant results. Finally, statistical models basically describe the relationship between an influence and the final effect, frequently without revealing completely the causal mechanism and dynamics of interaction of stressors and the biological system.

These reasons indicate that the role of regression models is limited in constructing a theory on the combined influence of stress factors, even though it is quite possible to effectively utilize these models in certain specific situations. A particularly successful example of the application of statistical methods is the work of Dean, McGlothlen, and Monroe [38, 39].

Dynamic (simulation) Models of Biological Systems and the Homeostatic Concept

The most traditional and natural means of describing a dynamic system mathematically is assignment of the correspondence between the set of input actions and observed variables by means of an operator, the structure of which reflects the combination of causal relationship in the system. The construction problem of such a functional model for a biological system was formulated by Lyapunov [75]. Conditions for successful synthesis of the mathematical model require a set of elementary processes (events), which, it is hoped, can be formalized to the extent required and give precise identification of the set's characteristics. This definition, in basic terms, and the conditions which follow from it are valid for a much broader class of situations. However, the construction specifics of models for biologic and other systems (economic, social) compared to systems studied in physics and chemistry consist basically of difficulties in observing these conditions. The richness and abundance of relationships in biological systems prevent precise axiomatic segregation of elementary objects and their types of interactions, and identification of values describing their parameters.

The difficulty in constructing biological system models (as discussed in earlier sections) means that less rigid requirements, from the standpoint of their adequacy and completeness, must be used than in mathematical physics, for example. The study should also be limited to the requirement of a reasonably good description (simulation) of at least certain processes in the system which are essential in each case. A good example is the description of radiation damage to the set of identical elementary systems [3]. The model allows a meaningful interpretation of the parameters of γ-distribution, indicating the number of elementary systems damaged without revealing many significant aspects of the internal mechanisms of the organism's reaction to the stressor in question. Radiobiology, together with population dynamics, is the area of biology where the greatest success has been achieved in the application of mathematical models. Other works of interest to space biology and medicine should be pointed out [2, 10, 17, 30, 36, 82].

The specifics of the problem in question, the combined influence of stress factors, are such that in most cases of practical interest it is necessary to study the factors' effects on the organism's tissue and basic functional systems and, correspondingly, compose simulation models of the biological processes in the given substrates. The most adequate mathematical apparatus in this case is a system of differential or (particularly considering the need for digital computer modeling) difference equations. Thus, the possible states of the organism can be interpreted as points of a certain vector space in which the occurrence of physiological processes is represented by trajectories. Simple mathematical considerations show that the operator mentioned at the beginning of this section, which describes the biological system's structure of relationships, must be nonlinear. The biological importance of this is that it allows adequate interpretation of the existence of many stable states or states of regular cyclical change of physiological parameters in a biological system. This characteristic feature of the class of simulation models in question was determined, based on purely physiological considerations as early as 1937 [105].

The difficulties in identification and analysis of nonlinear systems encountered in nature are well-known. In this case, they are increased by variation of parameters of the model under the influence of external action. The summation influence of various factors on the reacting substrate can change its lability, functional mobility, and so forth, and thereby basically transform the substrate's reaction to the primary stimulus [108]. The problem becomes extremely complex if the practical difficulties are added, in particular, the insufficient formalization of the symptom complex of physiological and pathological states. Nevertheless, there are examples of successful application of simulation models in space biology and medicine, not only in radiobiological but also physiological aspects.

One possible approach to the construction of a general simulation model for investigation of the combined influence of flight factors is the homeostatic concept in combination with Selye's concept of the general adaptation syndrome [98]. The homeostatic concept was used by Svirezhev to predict the state of crewmembers' organisms during space flight. It was assumed that the stress factors' effect could be described in the time interval by multidimensional vector $A(t)$, of which the components $a_i(t)$ are functions describing the stress factors' intensity and time structure. The state of the biological system could be represented in a certain space of observed characteristics X. The homeostatic concept assumes that, in the state corresponding to the physiological norm, the values of X are localized in a rather narrow area which may be expanded slightly by natural biological variability for the groups of systems studied. For stress actions not too high in intensity, and which are compatible with the system's adaptation potential, there is a homeostatic curve—a trajectory in X, significant variations from which indicate pathology of the process observed. In phase-space terminology, the physiologically normal state is a certain focal point for the area of stability, filled with a trajectory terminating in it. This is the homeostatic curve.

The use of this model, in combination with heuristic prediction methods, has yielded positive results in medical support and monitoring for a number of flights, and has considerable promise as well for constructing a theory on the combined action of stress factors.

Further development and improvement of the dynamic model of the general adaptation syndrome should include refinement of the boundaries of areas corresponding to states represented as "alarm," "resistance," and "exhaustion" [98]. Variation of qualitative composition of the complex of stressors, intensity of their levels, and the time structure of the actions make it possible to estimate the sphere of applicability of the basic statements. It was upon these that the model's synthesis was based, including the general adaptation syndrome hypothesis.

In addition to the development of general dynamic models, there has been fruitful work on the creation of models simulating particular cases of stress factor application. These models have a more limited range of application but reflect the regularities of processes occurring in specific situations more deeply and completely.

Another possibility cannot be excluded. That is the effective study of biological systems by combining models which relate to various aspects of the phenomenon studied, but merging to yield a complete description of the phenomenon within the framework of a certain concept similar to the principle of complimentarity.

Summary

The experience accumulated by space biology and medicine convincingly proves the pressing nature of the problem of the combined influence of factors, in its complexity and variety. The investigation both of specific mechanisms of the interaction of specific combinations of stress factors and of the general regularities of their combined influence, as well as the development of the most precise possible quantitative methods for prediction of effects arising under the influence of these factors are not only important general biological problems, but also of primary interest for solving a number of important practical problems in astronautics. The synthesis of methods to predict reliably the results of combined application of stressors under various spaceflight situations will greatly aid technical projects for future spacecraft. It will become possible to determine requirements for the arrangement and structural specifics of spacecraft. This will apply also to their life-support systems.

The production of quantitative characteristics relating the evaluation of the crewmembers' conditions to levels of intensities and parameters characterizing the time structure of stressor actions will allow optimal versions of plan decisions to be selected. High reliability will be assured of crewmembers' work as elements of a single man-machine complex with intelligent requirements placed on the technical equipment. The usefulness of a successful solution of the problem of the combined influence of factors cannot be overestimated in the development of methods of preflight training, preventive medicine, and postflight rehabilitation of astronauts, as well as algorithms for medical monitoring and control during the flight.

The many examples presented indicate that an influencing factor may stimulate reactions which are defensive-adaptive in nature and increase the resistance of the organism or an organ to the effects of other stressors. From the standpoint of the general adaptation syndrome theory, increased resistance during stress provides the necessary resistance of the organism to the effects of stimuli of another nature.

However, the so-called cross resistance in a number of cases was not observed, but rather "cross sensitization," in that the development of resistance to a given agent is not accompanied by a reduction, but rather by an increase in sensitivity to another factor.

Even though a significant part of the reactions to a combination of stressor actions which have been studied can be interpreted from the general adaptation syndrome (which is doubtlessly fruitful), there is an abundance of specific effects related to specific reaction mechanisms, which, in turn, are related to the tropism of the stress factor for a given biological system. For example, it can be assumed that the stressor's influence in many cases is transmitted through the autonomic nervous pathways to various tissues and organs, including the medullary portion of the adrenals, which secrete epinephrine and norepinephrine. Similarly, a stressor may act on the posterior segment of the hypophysis and stimulate secretion of vasopressin, which has a significant influence on the cardiovascular system.

A simple listing of possible mechanisms of combined factor influence emphasizes the complexity of the problem. Still more complex is the development of reliable models for reliable quantitative prediction of effects.

Combined research in a number of countries would have a highly fruitful and stimulating influence in developing adequate mathematical models of the combined influence of stressor actions on biological systems. This is particularly true for the organization of experimental work. Selection and coordination of standard conditions for experiments, a search for common criteria for evaluation of effects observed, and other similar measures would permit comparing the experiment results of different researchers, and make possible the intelligent allocation of research tasks. International cooperation in planning experimental work would greatly increase its effectiveness.

The interpretation of the experimental data is possible both within the framework of statistical description by means of multifactor and multidimensional regression models, and by means of portrait models simulating the causal mechanism of the most important regularities of the process observed. However, the most meaningful and promising results should be expected from the construction of analytic and algorithmic models of the process in question. Thus, attention must first be given to the construction of models of the influence of specific combinations of factors characterizing actual flights, and to models of the nonspecific influence of individual factors, in order to reveal the general regularities of reactions to their combined influence.

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Chapter 18

METHODS OF INVESTIGATION IN SPACE BIOLOGY AND MEDICINE: TRANSMISSION OF BIOMEDICAL DATA[1]

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A distinctive feature of space biology and medicine is the requirement for telemetric methods in collecting scientific information, providing medical monitoring during flight, and solving diagnostic and prognostic problems. Physiologists encountered for the first time, in manned space flight, the need for strict conformity of the volume of information transmitted with the carrying capacity of telemetry channels. It became necessary to design new data-measuring systems and to program their operation. Selection of the most suitable investigative methods for medical monitoring of man in space became of prime importance, to make appropriate modifications to the chosen methodologies, and to extract the maximum amount of information about the organism's physiologic systems from these space experiments.

Biomedical information was first transmitted from a spacecraft to Earth during the flight of the dog, Layka, in the second Soviet Earth satellite. Thereafter, a wide spectrum of physiologic methods for examining and monitoring the organism during space flight was tested in Earth orbiting physiologic laboratories in the second and third Soviet spacecrafts. From these experiences, a system of remote medical monitoring was developed for the first cosmonaut, Yu. A. Gagarin. The Mercury program laid the foundation for subsequent comprehensive biologic measurements in manned orbital flights.

Development of manned space flight poses new and increasingly complex problems for physicians and biologists. No other area of scientific endeavor has such dynamic goals, techniques, and observations. There is also a close link between practical constraints and development of a research capability in space science and space exploration [32, 85, 86]. In this matter, investigative methods are of utmost importance, specifically in obtaining information on reactions of the living organism to the combined factors of space flight. Longer and more distant flights make it imperative to solve problems of forecasting the astronaut's physical condition, and to develop new approaches to monitor the activities of crewmembers, based on the concept of the spacecraft

[1] Translation of, Metody Issledovaniya v Kosmicheskoy Biologii i Meditsine. Peredacha Biomeditsinskoy Informatsii. *Osnovy Kosmicheskoy Biologii i Meditsiny*, pp. 1–86, (*Foundations of Space Biology and Medicine*), Vol. II, Part 5, Chapter 2, Moscow, Academy of Sciences USSR, 1973.

as a totally autonomous system [68]. For this reason, automated recognition of physiologic and medical status is a pressing requirement at the present stage of development of space biology and medicine.

PHYSIOLOGIC MEASUREMENT SYSTEMS IN SPACE RESEARCH

Information about an astronaut's condition during space flight reaches Earth via three channels: radiotelemetry, television, and radio communication. Radiotelemetry is the principal method of transmitting physiologic parameters recorded in the form of oscillograms. Television monitoring permits examination of the astronaut's motor activity, posture, facial expression, behavior, and activities. The study of radio conversations permits evaluation of his verbal activity, adequacy of answers, accuracy of reports, and intellectual level. For this reason, all flight data, including radiotelemetry, television, and radio dialogue, must be analyzed for comprehensive assessment of the astronaut's condition.

The set of devices that permits physiologic readings on a spacecraft includes sensors and electrodes, physiologic radioelectronic equipment, instruments for accumulating and processing data, devices for transmission of information from spacecraft to Earth, and, finally, ground-based equipment for receiving, decoding, and recording. This entire arrangement could be called a "physiologic measuring system" [18].

The data acquisition system is the first element in the physiologic measuring system. It converts physiologic measures into electric signals, or it transduces bioelectric potentials. Special sensors or electrodes are needed to meet these two objectives. Development of sensors and electrodes for use in space flight presents some difficulties. The sensor must continuously operate for long periods with stable operating characteristics during and after exposure to vibration, acceleration, and various atmospheric factors (increased temperature and humidity, decreased barometric pressure). Because it cannot be replaced in case of malfunction, it is imperative to constantly search for new methods of recording physiologic reactions, design better types of sensors, and pay careful attention to placement of sensors on the subject's body. While the inconvenience of some examinations is brief on Earth, during flight it becomes an ever-present factor. Sensors and electrodes should not hamper the astronaut in his work, nor lead to discomfort. This applies equally to animals, since discomfort elicits restlessness in them, as well as increased motor activity, which can affect the results of physiologic examinations.

The placement of sensors and electrodes on the test subject (man or animal) involves special problems. Most sensors and electrodes must be applied at specific points, and even minor shifts may substantially distort the tracings. In animal studies, a solution to this difficult problem was implanting electrodes under the skin or in the muscle, using special surgical techniques to assure exact placement of the sensor (for example, bringing out the dog's carotid to a skin flap to measure arterial pressure), or even implanting sensors in the animal's chest cavity. It is a considerably more complex matter to position and immobilize sensors and electrodes on the human body. At present there are many proposals for pasting electrodes and sensors on the skin, sewing them into clothing, inserting them in the physiologic orifices (rectum, nose, mouth) and even imbedding them under the skin. A description follows of different types of sensors and methods for immobilizing them.

Physiologic Data Recording Equipment

The equipment for recording physiologic data on-board a spacecraft presents several substantial differences, compared with such usage on Earth. These differences relate, on the one hand, to weight, size, and electric power constraints; on the other, to specific conditions under which the equipment must operate. Feasibility of recording specific indices in flight is determined by characteristics of data acquisition channels; these characteristics must conform to the physiologic characteristics of information for which a specific channel is intended. To determine the quantity of information, the total number of signals possible under these conditions must be known, and the probability of appearance of each. To simplify the concept, all signals will

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be considered equally probable. As the measurement unit for quantity of information, the unit choice of two equally probable states is taken. In a digital transmission system, information (H) is measured in binary units per second (bits), according to the formula

$$H = n \cdot \log_2 m$$

where H is the quantity of information in bits/second; n is the rate of transmission, and m is the number of equally probable possible states.

The quantization rate or number of points transmitted per unit time must be twice the maximum signal frequency (the sampling theorem of Kotel'nikov and Shannon) for undistorted transmission of the signal over a radio channel. This thesis is one of the most important in communications theory, and as applied to physiologic data, permits determination of the sampling rate required for unambiguous transmission via a digital signal channel (Table 1).

Each digital radiotelemetry channel is designed to transmit a specific maximum quantity of information. The channel carrying capacity is also determined in binary digits per second. The ratio of the quantity of information that is transmitted over the channel without distortion to the total channel capacity is called the coefficient of useful signal channel operation. The smaller the channel capacity, the higher the coefficient of useful operation for a given signal sample rate.

The choice of methods for examining man and animals on spacecraft and satellites is closely related to problems of acquiring and transmitting biological data. There are broader opportunities for using diverse methods in flight experiments with animals. For this reason, such experiments furnish not only scientific information but also evaluate the effectiveness of different sensing methods for later transfer to manned spacecraft. Since the second Soviet satellite was launched with the dog Layka, there has been a revolution in biomedical instrumentation. Many medicophysiologic measurements which are now routine both on Earth and in space became feasible solely through the application of technologic advances that originated in space research. However, increasingly we encounter significant restrictions in the use of important methods during flight. Recently there has been an impressive increase in medicophysiologic data acquisition for research and medical monitoring [43]. Secondary use of some monitoring systems for investigative purposes is growing in importance.

Table 2 summarizes monitoring and examination methods, outlining acquisition and transmission of data, and some of the principles in physiologic measurement systems on Soviet and US spacecraft and satellites. Three directions can be distinguished in development of physiologic methods for manned space flight:

1. Search for methods, development and testing of systems for medical monitoring of astronauts in flight (Vostok 2 to 5 space satellites, Mercury, Apollo);
2. Development of systems for automated physiologic experiments in space (Cosmos 110, Biosatellite III);

TABLE 1.—*General Estimates of Physiologic Signals Bandwidth and Carrying Capacity of Radiotelemetry Channels Transmitting Such Information*

Physiologic parameter	Frequency spectrum, permissible top limit	Quantization level	No. discrete readings		Data quantity	Carrying capacity required
	Hz	% accuracy	time	amplitude	bits/s	bits/s
Electrocardiogram (ECG)	50	5	100	16	400	500–600
Electroencephalogram (EEG)	100	5	200	16	800	900–1000
Electromyogram (EMG)	500	20	1000	8	3000	3500–4000
Pneumogram (PG)	4	25	8	4	16	20–25
Thermogram (TG)	0.005	0.5	0.1	256	0.1	0.1–0.2

TABLE 2.—*Biomedical Data Acquisition and Transmission on Spacecraft and Satellites*

Spacecraft and satellites	Launch year	Physiologic measurement methods	Distinctions of on-board medical equipment and biotelemetry systems	References
2nd Soviet Earth satellite	1957	Electrocardiography, pneumography, arterial oscillography, actography	Equipment was turned on with a program device	[34]
2nd–5th Soviet spacecraft-satellites	1960-1961	Electrocardiography, pneumography, phonocardiography, sphygmography, electromyography, actography, arterial oscillography, body temperature reading, seismocardiography	Commutator for successive measurement of slowly changing parameters, electrocardiophone	[11, 13]
Vostok spacecraft	1961-1963	Electrocardiography, pneumography, seismocardiography, kinetocardiography, electrooculography, electroencephalography, galvanic skin reflex	Placement of preamplifiers in cosmonauts' clothing; multipurpose use of amplifier channels	[18, 90, 91]
Mercury capsules	1962-1965	Electrocardiography, pneumography, arterial pressure and body temperature readings	Automatic arterial pressure reading, system of ECG and impedance PG tracing using common electrodes	[71, 93, 110, 111]
Voskhod spacecraft	1964-1965	Electrocardiography, pneumography, seismocardiography, electrocardiography, electrodynamography, motor acts of writing	Distinction of two units: medical monitoring and medical examinations; special medical monitoring panel upon going into orbit	[18, 108]
Soyuz spacecraft	1967-1971	Electrocardiography, pneumography, seismocardiography, body temperature	Special medical monitor panel for recording body temperature and pulse while going into orbit [space]	[78, 116]
Gemini spacecraft	1966-1967	Electrocardiography, impedance pneumography, arterial pressure and body temperature phonocardiography, electroencephalography	Use of special on-board tape recorder for medicophysiologic parameters	[6, 47, 55]
Cosmos 110, simulated Earth satellite	1966	Electrocardiography, sphygmography, seismocardiography, aortic pressure	Electric stimulation of receptor zones of carotid sinus using a programed stimulator; automatic administration of pharmacologic agents	[81]
Apollo spacecraft	1968-1972	Electrocardiography, impedance pneumography	Upon exit on the moon's surface, pulse rate was retranslated in the lunar modulate and through its telemetry system to Earth	[29, 31, 32, 55]
Biosatellite III	1969	Electrocardiography, impedance pneumography, electroencephalography, changes in blood pressure by catheterization of pulmonary vessels, arterial and venous system, brain temperature with implanted sensors, study of behavorial reactions	Automatic analyzer of calcium, creatine, and creatinine in urine; special biotelemetry device with 10 channels operating at an access speed of 100/s and one "slow" channel (10/s)	[2, 3, 70]
Salyut orbital station	1971	Electrocardiography, pneumography, seismocardiography, kinetocardiography, sphygmography of femoral artery, arterial pressure by tachooscillographic method	On-board tape recorder to record investigative information; special unit of investigative [research] equipment	

3. Development of systems for medico-physiologic examination of the human organism in space (Voskhod, Gemini, Soyuz 1).

The block diagrams in Figures 1, 2, and 3 illustrate the biotelemetry systems of Vostok 3, Voskhod 1, and the artificial satellite, Biosatellite 3, as examples of the construction of physiologic measurement systems. In manned flights, especially in the early stages, attention was focused on medical monitoring. The development and testing of research equipment was of secondary significance until recently. However, with increased duration of flights, prognostic information is becoming increasingly necessary. To obtain such information, broader programs of physiologic measurements will be needed and most importantly, in-depth mathematical analysis of flight data and addition of necessary tests of functional capacities.

METHODS OF CLINICOPHYSIOLOGICAL EXAMINATION IN FLIGHT

Methods of Examining the Circulatory System

Electrocardiography. To record the ECG in the course of space flight, it was necessary to develop an essentially new technique. This was characterized by absence of interference with astronauts performing their flight assignments; absence of skin irritation or discomfort in studies lasting many days; adequate diagnostic value in the data; and absence of distortions in records during conversion and transmission to Earth. All this necessitated special research to develop electrodes, select placement points for them, and find means of providing long-term immobilization [5, 8, 96, 119].

The chief prerequisites for surface electrodes in long-term monitoring are: (1) reliable mechanical attachment, and (2) reliable electric contact [36]. Additional difficulties are raised by such factors as the presence of contact potentials between the surface of a metal electrode and the electrolyte in which it is dipped, the need to reduce resistance between the electrode and skin, and to make the input impedance of the signal amplifiers as high as possible. Ideally, the input impedance of the amplifier should be infinite, and that of the electrode system very low. Then, changes in resistance occurring in the "electrode—skin" system with body movement would not affect the potentials at the amplifier input generated by the contact potential battery. The amplifier should serve as an electrostatic measuring instrument in relation to the electrode system that is insensitive to any current from other tissue generators or electrode-electrolyte batteries.

Progress in developing electrodes can be illustrated from the Mercury, Gemini, and Apollo programs. The liquid electrode developed for the Mercury project consisted of a silicone rubber ring that supported a disk-screen of stainless steel with 40 holes (Fig. 4, A). After the electrode was placed in the space between the steel disk and the skin, electrolyte was added. However, these electrodes produced much interference in flight when the astronaut moved [62], probably due to polarization. For this reason, in the Gemini flights, the design of the electrodes was much improved by use of a pure silver disk with an anodized surface [37]. The ECG electrodes for the Apollo flights differed in that a hard plastic cap was used to enclose silver-silver chloride electrodes.

Low interelectrode resistance is important in assuring prolonged interference-free ECG recording. For this purpose, different pastes and methods for treating the skin are used (cream, soap, finely ground pumice, or a mixture of alcohol and ether). For the Mercury program, a paste was developed that did not irritate the skin for 48 h. In its latest modifications, 0.5% propyl-p-hydroxybenzoate was added as an antibacterial agent. The paste method was used to immobilize the electrodes on the skin (during the flight of Yu. A. Gagarin and all US flights) or they were taped on.

During the flight of G. S. Titov, the electrodes were either pasted on (as in the MX lead) or taped (as in the DS lead) [8, 91]. Subsequently, a complete change to the tape system was made on Soviet spacecraft. This system includes a chest belt with built-in silver electrodes of 18–20 mm diameter, with grooves for the paste, and two straps crossing over the astronaut's chest and attached to his back. There are rubber segments in the belt that help to provide good contact between the electrodes and the skin.

Two bipolar chest leads resulted from experimental research, which were named MX and DS [91] and chosen for the Vostok spacecraft. The advantages include minimum levels of interference from electromyographic potentials, convenient attachment of electrodes, and high diagnostic effectiveness. In the MX derivation, the electrodes are placed on the midline of the chest at the level of the manubrium and xiphoid process, and the DS lead is along the midaxillary line on the right and left, at the fifth intercostal space level. Thus MX is referable to the sternal group and DS to the axillary group of leads, according to Roman [96, 97].

The system of electrode placement in the Mercury project consisted of three electrodes for two ECG leads. Subsequently, a four-electrode system was developed. In the Gemini flights, the DS electrodes were also used to record the impedance pneumogram (Figs. 4 and 5). There is no doubt that a search for convenient electrodes and placement points for electrocardiography during space flights should continue. For example, a very promising electrode model proposed in the GDR could be mentioned. Three disks of 20–30 mm diameter are placed 5–10 mm apart on an insulating plate. The outside disks are active, and the middle one ("Earth") serves to diminish interference from surrounding equipment.

The "spray-on" electrodes proposed by Roman

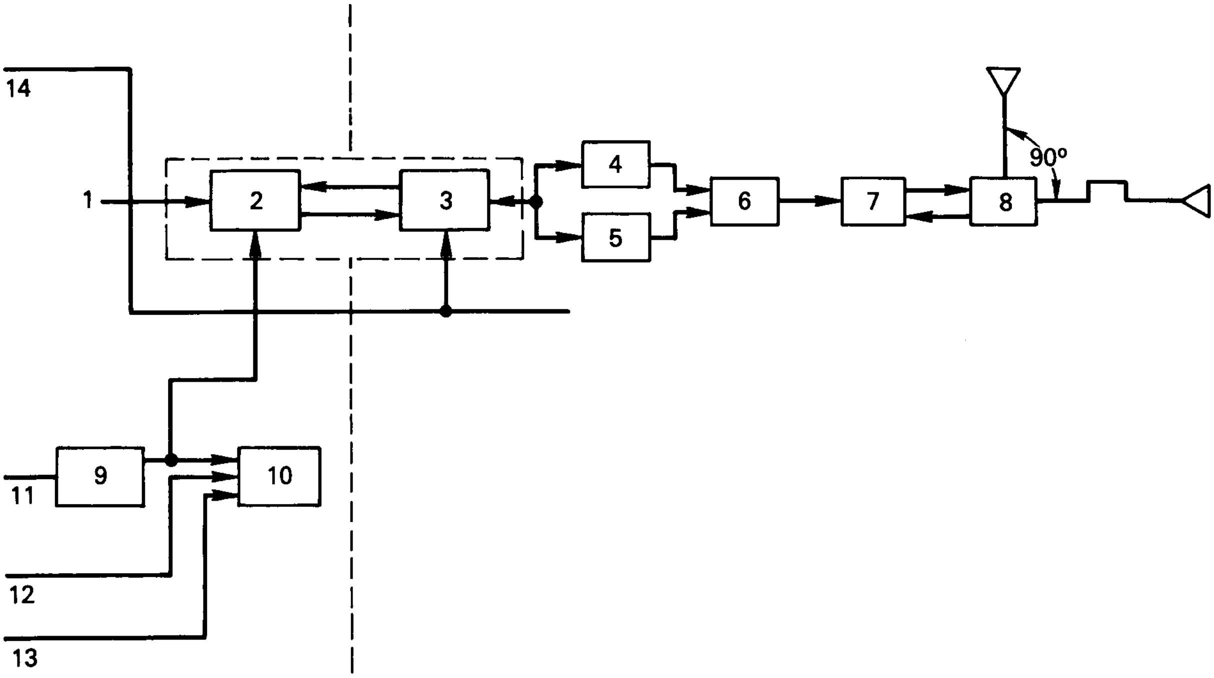

FIGURE 1.—Block diagram of the biotelemetry system of Biosatellite III.
Legend: (1) experimental data
(2) 65-channel switchboard
(3) 65-channel decoder
(4, 5) telemetric transmitters at a frequency of 136.68 mHz
(6) coaxial switch
(7) duplex
(8) command and telemetry antenna system
(9) mechanical switch
(10) biomedical analogue printer-tape recorder
(11, 12, 13) experimental and engineering data
(14) time mark

[96] are of great interest. Such electrodes consist of metal and cement dust which, along with solvent, is applied to the skin using a special sprayer. The sprayed-on electrode is about 1 mm thick and 19 mm diameter. A fine wire is used to derive biopotentials. The mean interelectrode resistance is about 70 kohms. Three types of electrodes to record electrocardiograms for 30 d or more are proposed [95].

1. Electrodes with lithium chloride used without paste and mounted on a belt system: interelectrode resistance is about 15 kohms; an amplifier with a

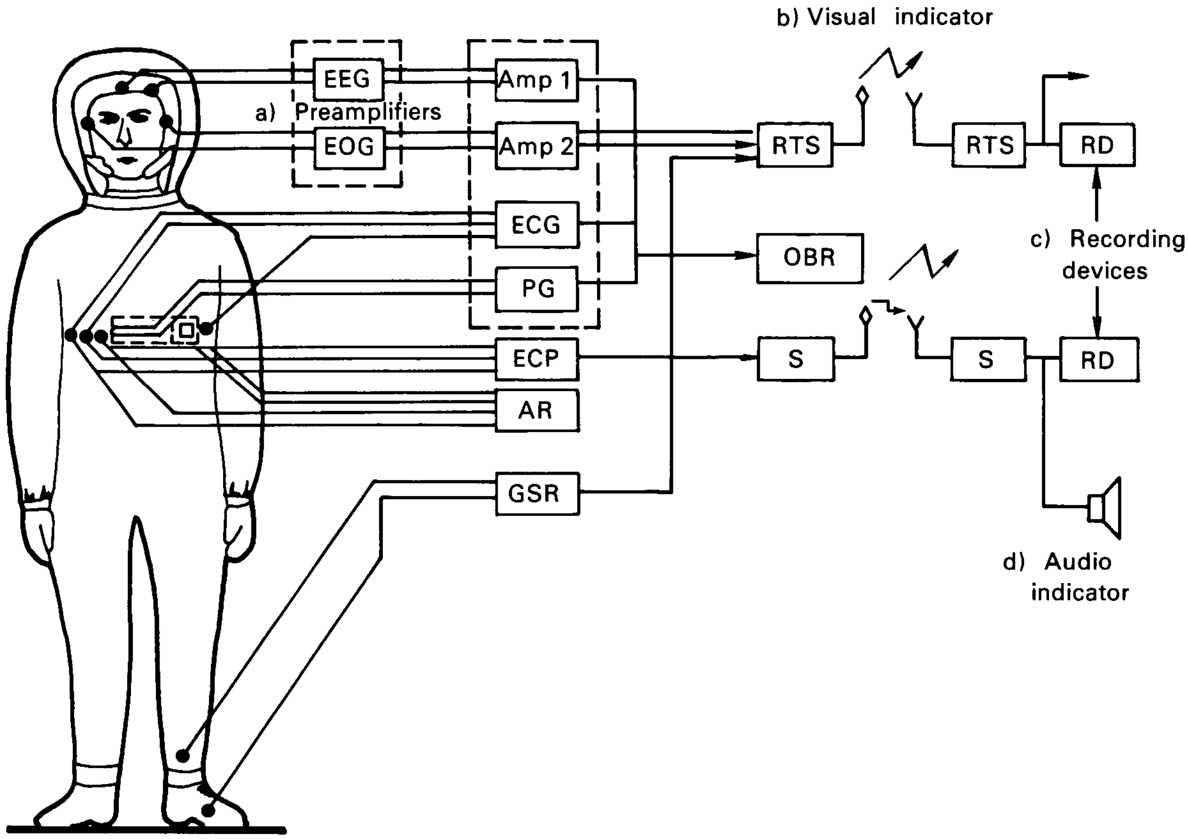

FIGURE 2.—Block diagram of Vostok 3 telemetry system.

EEG, EOG, preamplifiers for EEG and electrooculogram recording
ECG, amplifier for ECG recording
Amp–1, Amp–2, ECG amplifiers used to record EEG and EOG
PG, amplifier for pneumogram recording
GSR, system for recording galvanic skin reactions
ECP, electrocardiophone, system for current transmission of pulse rate using the "signal" (S) transmitter
AR, autonomous recorder for pulse and respiration rate while landing
OBR, on-board recorder
RTS, radiotelemetry system
RD, recording device
S, short-wave transmitter and receiver "signal"

bandpass of 2–50 Hz and an input resistance on the order of 1000 megohms is used.

2. Subcutaneous electrodes: stainless steel and tantalum wire clips, 6 mm long, were used; as early as 3 d after implantation, discomfort disappears; interelectrode resistance reaches 50 kohms.

3. Insulated electrodes consisting of aluminum disks covered with a thin insulating layer: resistance between the skin and electrode is over 30 000 megohms; a special circuit is used with a field-effect transistor connected to the electrode inside a grounded screen.

To improve the clinical quality of ECG recordings, some authors propose an amplifier with

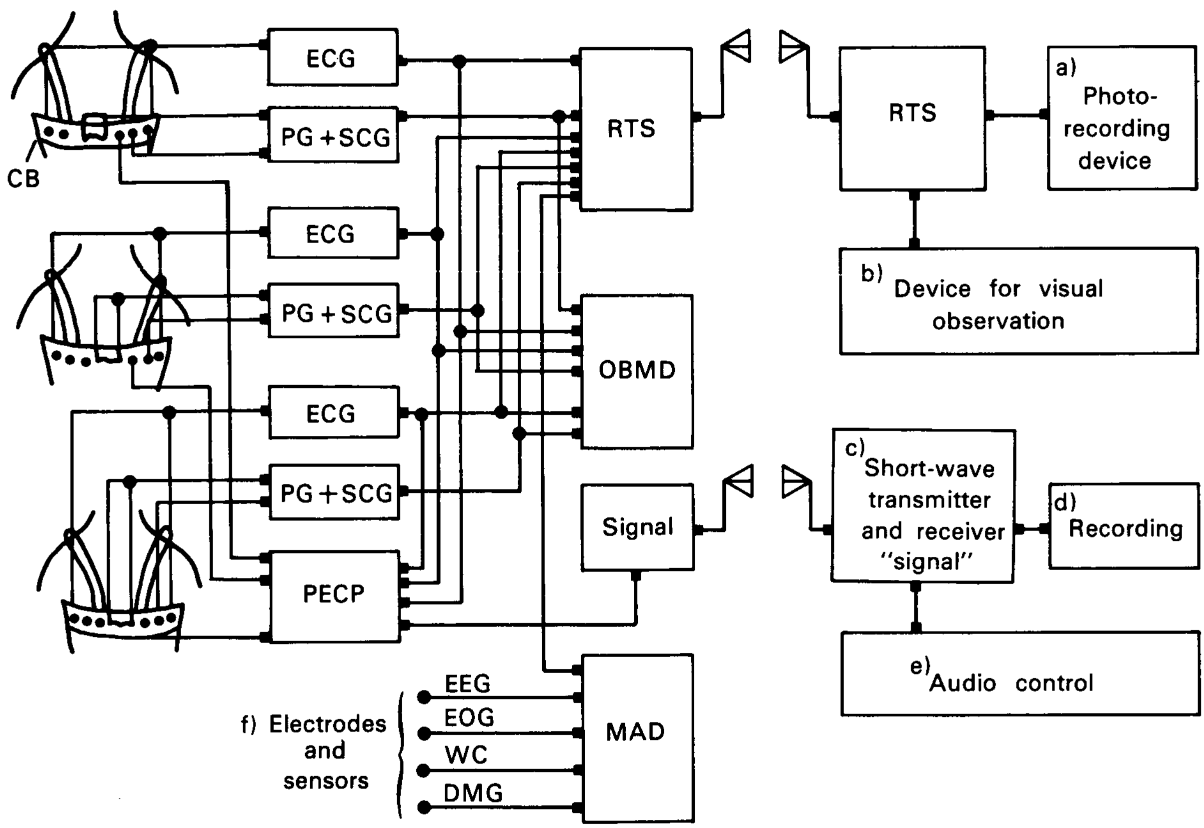

FIGURE 3.—Block diagram of Voskhod 1 biotelemetry system.

ECG, amplifier for ECG recording
PG & SCG, amplifier for recording seismocardiogram and pneumogram on the same channel
CB, chest belt
MAD, medical amplifying device to record on the same channel the EEG, electrooculogram (EOG), dynamogram (DMG), and writing coordination (WC)
OBMD, on-board memory device
RTS, radiotelemetry system
PECP, pneumoelectrocardiophone for transmission of pulse and respiration through the "signal" transmitter

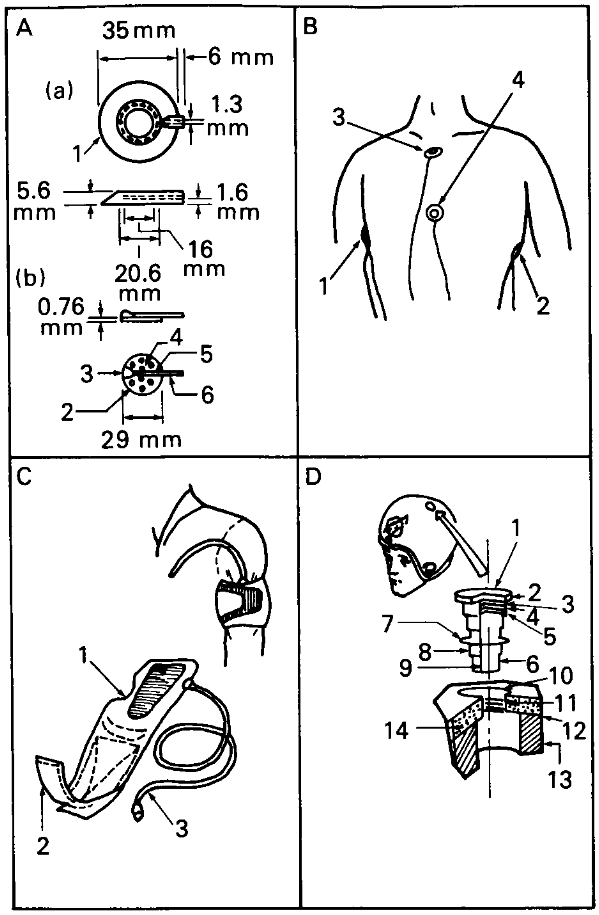

FIGURE 4.—Electrodes and sensors in the Mercury and Gemini programs.

A improved electrode for ECG recording
- (a) electrode casing
- (b) electrode disk
- (1) silicone rubber
- (2) thin disk of pure silver anodized with silver chloride
- (3) coating
- (4) perforations
- (5) wire attachment
- (6) outlet wire

B placement of electrodes for ECG recording
- (1, 2) DS lead electrodes
- (3, 4) MX lead electrodes

C cuff for arterial pressure measurement
- (1) nylon casing
- (2) Velcro covering
- (3) pneumowire of neoprene rubber

D design of NASA-Azimuth electrodes installed in the cosmonaut's helmet to record the EEG
- (1) plastic ring
- (2) silver contact
- (3) silver chloride
- (4) pressed silver powder
- (5) fire-polished glass disks
- (6) acetylcellulose sponge
- (7) rubber ring
- (8) silastic insert
- (9) electrode paste
- (10) amplifier's metal contact
- (11) outlet wire
- (12) electrostatic screen
- (13) plastic covering
- (14) silastic insulation

a limited frequency bandwidth. Roman [96] indicates that restriction of the high-frequency response to 100 Hz does not influence the clinical information in the tracing; with a limit of 50 Hz it leaves the ECG virtually unchanged; with a limit of 25 Hz some distortion occurs. A low-frequency cutoff at 0.2 Hz does not reduce clinical usefulness. The effect of muscular interference as related to different amplifier bandwidths was investigated by Freiman et al [39]. Optimum results were seen in a channel with interference, in which maximum signal/noise ratio was obtained by adjusting the frequency bandpass.

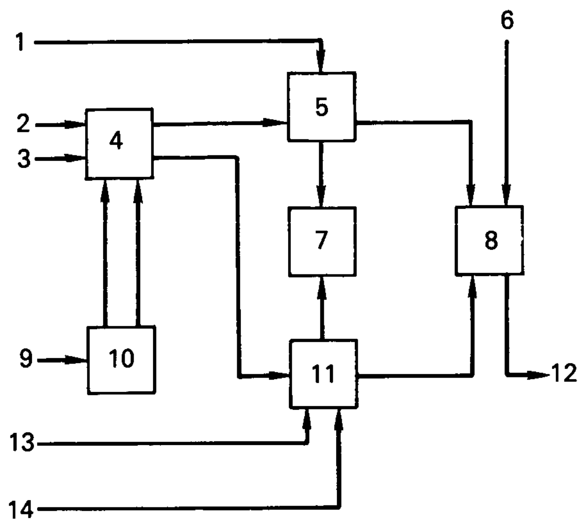

FIGURE 5.—Block diagram of control system for biochemical automatic device for urinalyses during flight of Biosatellite 3.
(1, 2, 3, 13, 14) inputs of time marks (1 min, 5 min, 1 h, 24 h)
(4) timer (control system of timing sequence of commands)
(5) device for calcium analysis
(6) telemetry on-switch
(7) suction pump
(8) data storage [collection] system
(9) sample collecting command
(10) urine sample control
(11) creatinine analysis device
(12) telemetry output

Phonocardiography. The value of phonocardiography in a cardiologic examination is that it permits objective registration of the volume of sounds, their phase correlations, and a number of variable cardiac cycle characteristics. Since astronauts are a specially screened and trained group without pathologic heart murmurs, it is useful to concentrate on recording heart sounds. A special method developed and named "integral phonocardiography" [27] consists of picking up the low-frequency envelope of audio frequencies, by detection and integration of the output signals of the phonocardiographic amplifier. Radiotelemetry channels with considerably smaller capacity can be used mostly to transmit the "integral" curve than to transmit an ordinary phonocardiogram. The method of "integral" phonocardiography was used in flight experiments with animals on the second and third Soviet satellites.

Phonocardiography was used by US researchers in the Gemini 4 flight [103]. Phonocardiograms were recorded on both crewmembers using miniature microphones weighing 7 g attached to the chest with special paste. A preamplifier was installed in the space suit. Phonocardiograms were obtained on-board on a tape recorder, then retransmitted, and the data analyzed on Earth.

Seismocardiography. Electric and sonic phenomena associated with cardiac contractions do not furnish information about the ultimate results of cardiac activity, such as the force, rhythm, and rate of blood ejection from the ventricles into the large arterial trunks, or how the heart fills during diastole. Ballistocardiography is one investigative method of these functions. However, it is practically impossible to use its clinical variants in space flight. For this reason, a special modification of ballistocardiography was developed and named seismocardiography (SCG) [22]. In essence, this involves registration of the third and fourth derivations of the dorsoventral (or longitudinal) ballistocardiogram. The principle of sensor operation is based on translation of chest wall pulse movements into oscillations of an inert (seismic) mass, elastically connected to the object being measured. The first sensors were tested in flight experiments with animals.

The seismocardiographic complex consists of two distinct parts (cycles): systolic and diastolic (Fig. 6). The amplitude of each cycle is directly related to the magnitude of cardiac contraction in a given phase. The decay time is related to the time relations between these forces. Since the frequency of oscillations of the seismic mass proper is rather high, respiratory excursions and other slow body movements have virtually no effect on the tracing; there are only some variations of amplitude with respiration on the tracing. As a rule, good tracings are obtained only when the subject is at complete rest. The SCG sensor was first used in tests on humans during the Vostok 5 and 6 flights [21]. The seismograms were recorded on the same telemetry channel as the electrooculogram which was feasible because of the different frequency spectra of the processes. Subsequently, on Voskhod and Soyuz spacecraft, seismocardiography became one of the continuous medical monitoring methods.

Kinetocardiography. During the flight of G. S. Titov, a sensor in the form of a miniature microphone with a one-transistor preamplifier [11] was used to record the kinetocardiogram. The tracing thus obtained characterizes local chest wall vibrations and permits evaluation of cardiac cycle phases, as well as coordination of right and left heart contractions. The pickup was placed in the apical pulse region and attached to the inner surface of the chest strap. Vibration of the chest wall was recorded in the frequency range 10–20 Hz. The defects in the electromagnetic sensor were its low sensitivity and the impossibility of transducing vibrations in the frequency range of the order of 1–5 Hz. For this reason, efforts were subsequently made to develop kinetocardiographic pickups using piezo elements [20].

Arterial pressure measurement. Methods of measuring arterial pressure are usually classified as direct and indirect. Direct methods were used in flight experiments with animals (Cosmos 110 and Biosatellite III). A system with pulsed delivery (heparin) was installed on Biosatellite III to improve patency of implanted catheters. Four catheters (two venous and two arterial) made it possible to obtain reliable information about blood pressure dynamics. Sensors, in the form of ordinary electric bridges, were used; one leg of the bridge changed parameters, depending on pressure on the sensor diaphragm.

To record arterial pressure in astronauts, indirect methods used were oscillography (USSR) and audio (USA). Arterial oscillography is based on recording pressure fluctuations in a cuff depressing a vessel. Tachooscillography (method

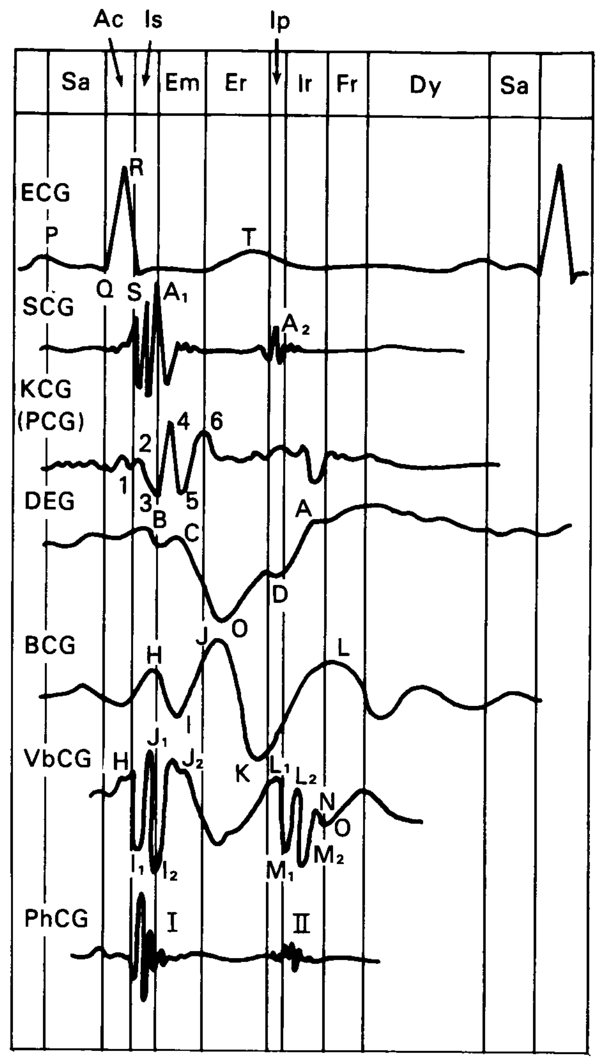

FIGURE 6.—Samples of cardiosignals recorded in space flight (ECG, PhCG, SCG, KCG) and under experimental conditions (VbCG, PCG, DEG, BCG).

ECG, electrocardiogram
SCG, seismocardiogram
KCG, kinetocardiogram
(Sa) atrial systole
(Ac) phase of asynchronous contraction
(Is) phase of isometric contraction
(Em) phase of maximum ejection
(Er) phase of reduced ejection
(Ip) protodiastolic interval
(Ir) phase of isometric relaxation
(Fr) phase of rapid filling
(Dy) phase of slow filling
BCG, ballistocardiogram
PCG, perimetric cardiogram
VbCG, vibrocardiogram
DEG, dielectrocardiogram

of Savitskiy [98]) records the velocity component of oscillations. The audio method is based on recording sonic phenomena (Korotkoff sounds) at the arterial compression site using a microphone. The oscillatory method, first tested during the flight of Layka, was then used in experiments on the second and third Soviet spacecraft-satellites. A compressor cuff placed on the carotid exposed in a skin flap was used to measure the animal's arterial pressure. Since the cuff is small (about 3 cm^2), an automated plunger device was used to create pressure in it; this device is a metal cylinder with a carefully ground plunger. The size of the cylinder was such that a pressure of up to 220 mm Hg was created in the cuff with each plunger stroke. The pressure in the cuff changed linearly and was converted into tension by means of an electric micromanometer.

During the flight of Voskhod, B. B. Yegorov, cosmonaut-physician, took arterial pressure readings on crewmembers, using an ordinary sphygmomanometer. Maximum and minimum pressures were determined by auscultation of Korotkoff sounds. In the Mercury and Gemini flights, an automatic sphygmomanometric system was used with an audio method to determine pressure [71]. In the first orbital flight of J. Glenn, there was no automatic pressure device and the astronaut pumped air into the cuff with a bulb. An automatic pressure device was used in all subsequent flights, where a pressure of 220 mm Hg was reached in 30 s. Special safety features lowered the pressure if it held at more than 60 mm Hg for over 2 min. Cuff pressure dropped at a linear rate from 220 to 60 mm Hg by means of a special pressure regulator. The microphone was in the lower part of the cuff, which turned out to be the most effective from the standpoint of sensitivity and noise-proof quality of the measuring system (Fig. 4, B). The pressure curve and arterial phonooscillogram were recorded on the same telemetry channel. A miniature piezo microphone was developed, 3.5 cm diameter and 0.5 cm thick, with significantly reduced interference.

Sphygmography. Carotid sphygmograms were recorded on dogs during the third and fourth Soviet spacecraft-satellite flights. For transducing carotid pressures, the casing of the cuff was enclosed. Instead of a rubber cuff, a tubular sensing element filled with graphite or piezo crystal was used. A bridge network was devised for the graphite transducer. The bridge capacitance in the RC network formed a simple low-frequency filter, limiting the frequency band and thus lowering the interference level. Due to the solid contact between the pickup element of the sensor and vessel, the cuff sphygmographic sensors produced very stable tracings. Movement of the animals and even vibration had little effect.

Development of new methods of studying blood circulation in space flight. Electroplethysmography is one of the promising techniques in space cardiography. It is known in two variants: rheography, developed in 1945 by Poltzer, Marco, and Holtzer, and dielectrography, devised by Atzler and Leman [17]. In both, readings are based on use of high frequencies, but with rheography changes in ohmic components of complex resistance in living tissues are examined primarily, while with dielectrography the capacitance component is considered.

For man, electroplethysmography is probably the only method, acceptable in space flight, of studying blood supply to the brain. Work in the field of intracranial electroplethysmography (rheoencephalography) resulted in development of radiotelemetry systems to study blood supply to the brain [74]. More recently, a phase-sensitive circular detector has been used, which removed the chief disadvantage of rheoencephalography—nonlinearity of voltage-ohmic characteristics near the balance point of the bridge [74]. Diagnostic importance is attributed to thoracic and abdominal rheography [18]. A method of chest rheography has been developed using additional electrodes inserted in the astronaut's chest strap. Recording the rheogram of the pulmonary artery appears to be a useful application.

The need for continuous contact between the electrodes and skin limits the area and duration of application of this technique, in spite of the definite practical value of rheography to examine central and peripheral circulation. For this reason, attention was concentrated on investigation of contact-free techniques, in particular, dielectrocardiography. Two types of instruments have been developed [42]; the first is based on the principle proposed by Atzler and Leman [17], where the generator operates at a frequency of 8 MHz. The output tank circuit or "secondary circuit" is inductively coupled to the generator, and the patient's tissues connected to it form the capacitance. Changes in amplitude of generator oscillations due to changes in behavior of current in the primary tank circuit are recorded. Changes in the resistive component of the secondary circuit affect this behavior more than changes in capacity. Thus, this system primarily records changes in resistive losses in the tissue capacitance, rather than changes in dielectric constant. To record the true dielectrocardiogram, an instrument was developed, based on the principle of frequency modulation with a sensitivity of 1 mV/0.001 mF upon recording on any electrocardiograph. Figure 5 illustrates a dielectrogram tracing in the region of the fifth intercostal space along the anterior axillary line. Because the electrodes can be placed in the clothing, without skin contact, this is a promising technique for wide use in prolonged space flights for both medical monitoring and research purposes.

Vibrocardiography is a promising technique to study cardiodynamics. This method, developed by Agress et al [9, 10], is a variant of ballistocardiography and low-frequency phonocardiography. A sensitive piezomicrophone and amplifier system with a frequency band of 2–2000 Hz are used. Vibrations are recorded from a point in the fourth intercostal space, 2 cm to the left of the sternum. A 1–2 cm shift of the microphone does not affect the shape of the tracings. Ferruginous pastes are used to eliminate friction between the pickup and the skin. The polarity of the tracings is indicated by the convention that outward movement of the chest wall produces positive deflections. The vibrocardiogram is described by the same indices as the ballistocardiogram waves (Fig. 5): H corresponds to the start of isometric contraction, L to opening of the semilunar valves, and L_2 to closure of semilunar valves. A formula has been proposed for indirect estimation of the stroke volume from the vibrocardiogram [9]. This formula was derived by comparing vibrocardiogram data to the results of estimating minute volume by the dye dilution method (coefficient of correlation: 0.90).

A method of perimetric cardiography (PCG) was developed in order to obtain information about the cardiac cycle phases. It is based on recording microfluctuations in the chest perimeter by means of a pickup installed in the chest strap [24]. In a simplified variant of this technique, a carbon respiration pickup was used (resistance: 1.5–3.0 kohms), as well as a differentiating RC circuit, and electrocardiographic amplifier. The PCG is recorded during breath-holding. The structure of the curve corresponds to that of the acceleration kinetocardiogram (Fig. 5).

Ultrasonic Doppler cardiography [107] is promising for use in long space flights. This technique is based on recording reflected ultrasonic oscillations, the frequency of which are distinct from transmitter frequency, and the faster the object moves, the greater this distinction (Doppler effect). Furthermore, the frequency-amplitude characteristics of the reflected signal depend on the acoustic properties of the medium and changes in tissue density at different phases of the cardiac cycle. To obtain information about the phase relations of cardiac contractions, a noninterference method of ultrasonic Doppler cardiography was developed which permits examination of man's cardiac activity during physical activity. Quality of the tracings is as good as the ECG recorded in the Nebov leads. The pickup is a piezo element—a cylinder of 12 mm diameter and 6 mm thick—attached by means of an elastic belt in the region of the fourth or fifth left intercostal space. A system has also been developed and tested for radio transmission of the ultrasonic Doppler cardiogram using a miniature radio transmitter worn by the subject [60].

Considerable attention is being given to developing methods of studying peripheral circulation. Work is in progress at the Stanford Research Center on a direct force method of measuring arterial pressure [92]. A transducer was created which measures arterial pressure according to movement of the skin surface above the artery. The artery is assumed to lie on a hard base with elastic walls, surrounded by homogeneous tissue. The mathematical model of the measurement system is based on the assumption that distended and constricted tissues can be represented as linear springs. The pickup is 1.5 mm wide and 6.5 mm long. At a pressure of 40 mm Hg, it was necessary to measure a force of 5.5 g which, with deviation of up to 3 mm, elicited a deformation of 1.8 kg/cm. When the sensor pressure was reduced, it was found to be sensitive to inertia of movement of the transducer itself, as well as extremely thermosensitive. Further development of this technique resulted in a pickup to measure small forces with a shift close to zero, using a lever dynamometer system with feedback. A laboratory prototype of the instrument has been constructed with a Hall effect transducer. One of the main advantages of the direct force principle of measuring blood pressure is that ideal, absolute calibration is possible. The main problem is to place the transducer correctly on the artery.

Another method of indirect measurement of arterial pressure makes use of a pickup located on the ear, with recurrent squeezing of the helix [111]. This pickup consists of a corrugated ring and blood pulsation detector which measures the fluctuations in transparency of the capillary bed to infrared light. Control experiments showed that the technique is very accurate and presents no inconvenience to the patient.

Methods for studying vascular tonus are of particular interest. A valuable method for studying peripheral circulation, including venous tonus, is that of Arinchin [16], which is based on recording volumetric changes in the extremity with gradual elevation of pressure in a cuff worn proximal to the region examined. The degree of elevation of the plethysmographic curve serves as a measure of venous tonus. Step-by-step pressure elevation is a more accurate method.

External Methods of Examining the Respiratory System

In the course of preparations for flight experiments on the Vostok spacecraft, different sensors were tested for pneumography, including those based on piezoelectric effect, wire potentiometers, and tensiometric circuits. All were found unsuitable, due either to large size or the need to develop special amplifying and measuring circuits. From the standpoint of simplicity and economy, a graphite sensor was found the most suitable; it consists of a rubber tube filled with carbon granules (microphone type). When unstretched, such a sensor has a resistance of 100–500 ohms. When stretched, the resistance increases to several thousand ohms. The sensitivity of the pickup can reach tens of ohms per millimeter of displacement. To measure respiration during space flight, the carbon sensor is attached in the chest belt in a manner so that it would be distended along with the rubber segments of the belt during respiration.

The contact sensor is another device for pneumography. It is based on opening and closing an electric circuit by means of a microswitch controlled by a plastic capron [2] cable. The contact sensor operates whenever there is a change in direction of movement of the plastic capron cable which is attached to the chest belt at the opposite end of the rubber section in the belt. Square pulses are recorded, which correspond to inspiration and expiration. From a reliability standpoint, the contact sensor is preferable to the carbon, since its operation is not impaired when the initial tension of the belt is altered.

A special belt with both carbon and contact sensors recorded respiratory excursions in animals. Elastic inserts were sewn into the belt so that an increase in perimeter of the dog's chest in inspiration and a decrease in expiration elicited extension or contraction of the rubber tube containing carbon granules. The design of the belt included techniques to standardize the tension of the tube against its resistance.

Different methods were used to record respiration in US space studies: pneumography (rubber tube with copper sulfate solution), pneumotachography (variant with heated thermistor attached in the form of microphone in the flow of exhaled air), and impedance pneumography (measurement of electric resistance of the chest). According to a number of authors, the respiratory changes in impedance with the electrodes in the sixth intercostal space, on the right and left, along the mid-clavicular line, are proportional to

[2] Capron is the Soviet equivalent of nylon.

magnitude of pulmonary ventilation [57]. There are reports of a miniature impedance pneumograph to be placed in the astronaut's clothing [73]: the dimensions are 13 × 56 × 94 mm; it weighs 125 g. To reduce the number of electrodes on the astronaut's body, special bandpass filters have been developed which permit using the same electrodes to record the ECG and impedance pneumogram. The filters are tuned to the frequency of the pneumograph generator and connected to the input of the ECG amplifier [37, 44].

There are advantages to the impedance pneumography method, compared with other methods that do not use face masks, since it makes possible quantitative estimation of pulmonary ventilation. However, it is not suitable for lengthy studies, thus the possibility of recording respiration by dielectrography merits attention. A miniature transistorized instrument has been developed which records changes in value of the reactance phase angle, in the capacitor formed between the electrode plates by a chest segment [41]. The generator has an operating frequency of 8 MHz; one of the plates is mounted on the back of the chair, and the other is the "ground." Thus, respiration is recorded without contacts. This development of a high-frequency method for recording the dielectrocardiogram has prompted efforts to use it also for quantitative estimation of lung volumes. In such use, the electrodes, in the form of foil plates, are sewn into the subject's shirt.

Methods of Examining the Vestibular System

After vestibular and vestibulosensory disorders were discovered during the flight of G. S. Titov [91], physiologic measures were included to characterize the functional state of the vestibular system. Special tests were developed providing for alternate coordination and load tests [42, 90], which included evaluation of spatial orientation with eyes closed and open, a series of head and body bends and finger-to-nose tests, determination of ability to perform fine coordinated acts (writing, drawing with eyes open and shut). To assess different reflex changes due to vestibular stimuli, it was very important to make a complex evaluation of all the other parameters recorded: ECG, respiration, and EEG. Electrooculography was added to the telemetry program, starting with the flight of A. G. Nikolayev.

There are considerable methodologic difficulties in performing electrooculography in prolonged space flights. Thus, it is virtually impossible to use nonpolarizing electrodes. It is not possible to assure reliable contact between electrodes and skin, when they are placed at predetermined points for long periods. Thus, it was necessary to develop a method of recording electrooculograms under specific conditions. In the first two flights, silver electrodes were used, mounted in plastic spring inserts firmly connected to the helmet. The electrodes made close contact with the skin, in the region of the zygoma, near the external angles of both eyes. Eye movements to the right and left elicited both biopotentials related to eyeball movement and action potentials of facial and oculomotor muscles. The potential level was 50–100 μV. This made it necessary to use a preamplifier with a gain of about 20. AC amplifiers were used, so that the electrooculogram was recorded as the first derivative, i.e., a velocity curve [11].

A method was subsequently developed to record the electrooculograms with detachable electrodes, located in the immediate vicinity of the external angles of the eyes, and connected to amplifiers by means of snaps on the helmet. This method furnished better tracings, but required preliminary instruction and training of astronauts.

Subthreshold electric stimuli have also been proposed [116], to study the sensitivity of the vestibular system, in addition to suprathreshold stimuli. Electric stimulation of the vestibular apparatus was used as a diagnostic test by the cosmonaut-physician, B. B. Yegorov, in studies on Voskhod.

When examining the vestibular system, body and head movements are also taken into consideration, as well as movements of the eyeballs. Special sensors in the cosmonaut's helmet [118] can be used for objective recording of such movements. Head movement studies are important in determining the accuracy of vestibular test performance, as well as in evaluating reflex reactions to stimulation of the vestibular system. Special tests were performed in the Vostok flights for the purpose of evaluating coordination of movements, which included writing tests consisting of drawing various geometric figures with eyes open and shut. Analysis of different autonomic reactions, such as pulse and body temperature [77], is important in assessing the condition of the vestibular system. Effects of vestibular stimuli on electric potentials of the stomach have been shown [58]. Since vestibular dysfunction is associated with diverse autonomic and coordination disorders, development of special tests for automated examination of vestibular functions may evolve along lines of measured loads with recording and processing of parameters such as: rhythm of cardiac contractions, motor reactions, and galvanic skin potentials.

Methods of Examining the Central Nervous and Musculoskeletal Systems

Investigation of man's working efficiency is of primary importance in order to solve the practical problems of manned space flight. Problems pertaining to guiding a spacecraft can be solved only on the basis of optimum choice of data characteristics of the "man-machine" system with the necessary coordination of voluntary movements.

The interfaces between the astronaut and spacecraft systems are of both scientific and practical interest. It is important to determine the effect of spaceflight factors on neural information processing. Thus, weightlessness is associated with a decreased flow of afferent impulses, a circumstance which aggravates hypodynamia and relative isolation. Processing of information in the astronaut's central nervous system and performance of previously learned, skilled motor acts can also change under the unique conditions of space flight. The practical aspect of this problem is ultimately related to the astronaut's ability to carry out purposeful action and, in particular, performance of processes involved in controlling the spacecraft.

The flights of Soviet and US astronauts indicate that man can perform in space, all the complex operations involved in guiding the spacecraft: preparing for docking, moving from one spacecraft to another, performing assembly work, astrophysical observations, photography, and others. However, operations take more time in space than on Earth, and are more tiring [108].

Capacity for purposeful activity is closely related to the condition of the nervous and muscular systems. The first investigations of these systems were partially made during flight experiments with animals. Actography and electromyography were used. Subsequently, the content of radio conversations, television data, and analysis of entries in the spacecraft log were used to evaluate astronaut activity. Electroencephalography (EEG) was an important method for studying the condition of the central nervous system.

Actography. Motor activity in space flight can be studied by television data, as well as from incidental occurrence of mechanical artifacts in some physiologic tracings, for example, EEG or seismocardiogram.

For the study of motor activity in animals, two types of pickups were used. One consisted of a potentiometer controlled by a nylon string connected to the dog's clothing. Three such pickups, installed in different parts of the cabin and recording the animal's movement along three perpendicular axes, furnished information about the animal's spatial position and motor reactions. However, this was not sufficient to investigate the magnitude of effort, so a different type of sensor [117] was developed, built into cables that attached the dog to the cabin floor. These contact-potentiometric sensors were switched on only when the cable was extended, and their resistance changed in proportion to the force applied.

Analysis of movements compared the actograms to the television image. From combined evaluation of all data, it was possible to gain an idea about the animal's behavior in a weightless state. Telemetric actogram recording is also of some value in assessing other indices, since it demonstrates artifacts related to the animal's movements.

Dynamography. Force exerted on a wrist dynamograph was chosen as a test muscle load for programed medical examinations. Such a load can be used whatever the space limitations, and with the appropriate setting of squeeze rate and force, it is possible to obtain information about the time and force relations in the act of movement coordination and about the cosmonaut's physical fitness.

An electrodynamograph was developed to record dynamograms which has a linear scale over a range to 50 kg. Both force and endurance, as well as fatigability, can be examined with the electrodynamometer. Endurance studies were made on the time of maintaining an effort equal to half the maximum effort, or of the ratio of force executed at the start to the magnitude at the end of a set interval, during which a close-to-maximum exertion was maintained. Ergography was used to study fatigue. The subject was assigned a rate and force to maintain (on an arbitrary basis). Fitness was then evaluated on performance over a specific interval.

The dynamograph test was added to the flight program on the Voskhod spacecraft. The problem consisted of squeezing a wrist electrodynamograph [28] for 1 min, rhythmically, with the same force and duration. All cosmonauts showed some changes in the dynamogram during flight. Thus, this first experience with the dynamograph in flight was successful and demonstrated some of the characteristic aspects of a coordinated work load in weightlessness.

Recording motor acts of writing. During the flights of the Voskhod series, an effort was made to evaluate movement coordination in weightlessness, based on handwriting. For this purpose, the cosmonauts' entries in the spacecraft logs were analyzed by handwriting experts. It was concluded that in a weightless state, there are deviations in handwriting [66]. For this reason, a method was developed for objective recording of motor acts involved in writing, with telemetric transmission of data. A special induction-type instrument was designed and added to the onboard equipment of Voskhod [18].

The device consists of two wooden (or plastic) platforms, firmly connected to four flat, fiber glass springs. These platforms can move only in the direction perpendicular to the plane of the spring. A permanent magnet and induction coil are attached to opposite platforms. If a sheet of paper is placed on the top platform of the instrument and a letter or digit written on it, the movement of the pencil is transmitted to the platform and causes it to move. As a result, an induction current is generated in the coil, proportional to the rate of pencil movement and to the sine of the angle formed by the direction of movement of the platform and direction of pencil movement. An ordinary ECG channel is used to record the signals. The data obtained with this device during the Voskhod flight revealed a number of deviations of writing movement coordination. Oscillogram analysis of the time required to draw a double spiral showed average increases of 51% when writing with eyes open, and 17% with eyes closed. Impairment of stereotyped movement was also observed. Motor skills involved in writing the number 6 and in drawing were less impaired than more complex movements, which can be attributed to the greater degree of automatization in the former. Subsequent development of techniques to record writing motor acts was related to attempts to quantify some psychologic tests [28] and to create new types of sensors [12, 18].

Electromyography. Experience in telemetric electromyogram recording was gained during flight of the third Soviet satellite-spacecraft. To transmit the relatively high-frequency signals of muscular biopotentials (up to 500 Hz) through the telemetry channels, "integral" electromyography was used which consists of detection and integration of amplifier output signals. The method of integral electromyography furnishes data about EMG changes during movement and static loads which, combined with the actogram, could be used to describe the motor acts of animals in flight. The theoretical substantiation of integral electromyography ensues from the following considerations. The EMG parameters are determined by the quantity of motor units active at a given moment, frequency of discharges in each, and degree of synchronization thereof. With isometric contraction, the area under the EMG integral curve is proportional to the force of contraction, but in actual measurement this relationship does not hold, due to greater synchronization of motor units at high-force levels. For moderate and average loads, the mean amplitude is a measure of force and the mean frequency a measure of load. Thus, the integral EMG with measured loads permits investigation of the fatigue process, and in the case of spontaneous activity, it permits evaluation of mean expenditure of energy, which has a direct bearing on the study of energy metabolism.

The first myographic research in flight had the goal of comparing the level of spontaneous muscular activity under normal, increased, and decreased gravity. Since the animal's head participates actively in all motor reactions (exploratory, alimentary, protective), the electrodes were implanted in the region of the splenius cervicis muscle. To obtain control tracings, a 2–2.5-kg weight was suspended from the dog's head. This was associated with static muscular tension which was well-recorded by the method.

Electroencephalography. The differences in electric activity of the brain in calm waking, sleeping states, and intensive mental work are well-known. In the USSR, the EEG was recorded during the flights of Vostok 3, 6, and Voskhod 1, while the cosmonauts were working actively, during communication with ground bases, and while performing various work operations. In the US, EEGs were recorded on F. Borman, while awake and asleep, during the first 55 h of his flight in Gemini 7.

Several methodologic problems had to be solved to record the EEG under spaceflight conditions: secure contact between the electrodes and scalp for several days; choice of the most effective, and most interference-free EEG leads from the standpoint of medical monitoring; placement of electrodes in the space inside the helmet in a manner so as not to elicit discomfort or difficulty in working [53, 54, 56, 69, 122]. In solving these problems, different variants of EEG examinations were tested. EEG recordings were made from different points on the skull, monopolarly and bipolarly, with investigation of reactions to opening and shutting the eyes, and rhythm assimilation. A study was also made of the interference-free quality of tracings while blinking, clenching the jaws, turning the head, and moving hands and body. Soviet investigators chose the "forehead-occiput" lead. To assure reliable prolonged contact between the electrodes and skin, contact pastes and depilatory agents were used. Electrodes similar to those used for ECGs, along with a Perlon washer-liner, were mounted on the inner surface of the helmet. The wiring was sewn under the lining and led out to a common connector. This system of biopotential derivation was tested in experiments lasting many days and yielded good results.

Special preamplifiers were developed to permit recording the EEG through existing ECG channels in the on-board equipment. The use of preamplifiers worn by the cosmonaut, aside from purely technical advantages, is also significant in improving the interference-free quality of the EEG channel. EEGs recorded on the cosmonaut during flight reflect blinking and motor activity. When analyzing tracings, it is important to carefully select segments free of interference, or to insure that automatic analysis techniques are capable of recognizing recorded segments impaired by movement artifacts.

In EEG studies of the Gemini 7 flight, US investigators used two pairs of electrodes which consisted of silver chloride disks in small plastic caps, filled with electrode paste and attached to the scalp by glue. Flight EEG data were recorded on a special magnetic tape recorder with a 7-channel, 100-h recording capacity. The scalp was first treated to remove superficial layers of epidermis. At the site of the electrodes, depressions in the helmet lining assured comfort during lengthy recordings. In this experiment, attention was concentrated on evaluation of sleep states. Two consecutive 20–s segments of the tracing were analyzed every 2 min during sleep periods; while the astronaut was awake, 30–s segments were analyzed every 10 min. Data evaluation was by computer analysis (see below).

Electric resistance of skin. Two methods of recording galvanic skin reactions have been tested: by recording electric potentials of the skin (Tarkhanov) and by recording electric resistance of the skin (Ferre). Both methods yield similar results. Galvanic skin reactions are considered to indicate the pilot's alertness and

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consciousness. Various emotions—excitement, fear, terror—may be clearly detected by this method, so that it is recommended in many space research telemetry programs.

Two types of instruments were developed to record galvanic skin reflexes in flight. One measured absolute skin resistance and slow changes therein; the other recorded only fast oscillations of resistance. On Vostok 4 and 8, the former type of instrument was installed, and on Vostok 5 and 6 the latter type. The electrode problem turned out to be quite complex; it was necessary to provide for lengthy recording of skin resistance. However, errors were observed even in brief tests, due to increased interelectrode resistance, resulting from impaired contact and polarization phenomena. It was also necessary to preclude discomfort because of prolonged attachment of electrodes on the skin. Under spaceflight conditions, it was necessary to record continuously for several days. Electrodes similar to those used in electrocardiography, proper treatment of the skin, and choice of appropriate paste solved this problem. The electrodes were placed on the plantar and calcaneal surfaces of the cosmonaut's foot and immobilized with an elastic bandage.

The nonspecificity of galvanic skin reactions makes it imperative to compare them constantly with other physiologic indices, to the radio conversation record, and to the television image. It is difficult at present to assess the value of this method for medical monitoring, and more experience must be gained in recording spontaneous and induced reactions under different stress situations.

Efficiency studies. Under spaceflight conditions, the diversity of the astronaut's activities furnishes extensive material to evaluate his work efficiency and medical fitness. Radio contact, entries in the spacecraft log, special observations, procedures pertaining to spacecraft maneuvering—docking, extravehicular activity, reentry procedures—all of these professional steps characterize the astronaut's efficiency.

Investigation of tension and fatigue processes in the astronaut is of practical value only if it is possible to obtain immediate on-line results. This would permit taking steps, such as reducing workload, reassigning duties, and adding stimulators, to minimize a further predictable decline in efficiency.

In evaluating the cosmonauts' work, consideration is given to the results of psychophysiologic measurements, including verbal responses during flight, accuracy in performing different operations and time spent on them, and data obtained from television monitoring of work movements [20, 48]. The simplest behavioral problems can be studied on animals. Thus, television observation of dogs on the second and third Soviet satellite-spacecraft resulted in several important conclusions concerning the capacity of the animal organism to perform purposeful acts in weightlessness.

Special investigations were conducted on the US Biosatellite III [5]. A monkey was trained to solve two problems: to perceive a symbol presented and to find a similar one, and a visual-motor problem for coordination of arms and eyes. For the first problem, the animal viewed a panel having five windows (one in the middle and four at the periphery). First, any one of four symbols (square, triangle, circle, cross) appeared for 5 s in the central window which was then extinguished. Twenty s later, all four symbols appeared in the four outer windows. The monkey had to pick out correctly the symbol in the outer windows which it had been shown 20 s before.

The second problem was based on using two concentric rings around a circular screen. The outer circle had a cone-shaped opening of 12 mm diameter, and the inner one had a microswitch, which, when the rings were corotated in the same direction, coincided with the opening for less than 1 s. The disks rotated at speeds from 60 to 100 rpm. The monkey had to observe the coincident position of the ring and opening and depress the button at the moment they coincided. In both problems, the monkey was rewarded with food tablets for correct solutions. A computer was used to control panel signals and to record test results [49].

Biologic Analysis of Body Fluids

Thorough investigation of reorganization mechanisms for neurohumoral regulation under unique conditions would not be possible without biologic analysis of the organism's fluids. Urinalyses and blood tests are extremely important to diagnose a number of illnesses. Under spaceflight conditions, there are difficulties with such problems. Without dwelling on the blood, urine, and saliva tests presently performed (specimens collected before and after flights), discussion will center on the system of automatic urinalysis used during the Biosatellite III flight [5].

Urine was collected from the monkey using a silicone rubber catheter implanted in the bladder. The automatic urinalysis instrument was 30×17×13 cm, weighed 6.8 kg, and used 6.5 W power. The instrument contained all necessary reagents to perform 450 analyses in 30 d. Calcium, creatinine, and creatine levels in urine were estimated. Analysis was made in a clear cylindrical container, and the chamber was transilluminated with light of appropriate wavelength for each analysis. Fluorescence was used in the calcium analysis, and creatinine color absorption in the creatinine test. The container was filled and emptied with a plunger. A pump also washed out the chamber after completing the analysis and delivery of calibration solutions. Two milliliters was the maximum volume of urine for an analysis. The photoelectric cell signal, proportional to the concentration of the element analyzed, was encoded as a binary signal to the data processing subsystem, then to the telemetry system of the spacecraft. Figure 6 illustrates the functional diagram of the automatic urine analyzer. The logic control circuit is the command center of the instrument; its principal element is a timer that receives daily and hourly signals from the spacecraft instruments, and generates successive commands for two analyzers at 0300, 0900, 1500, and 2100 h. Each successive command controlled the corresponding valves, pumps, and devices throughout the measurement cycle, including the final encoding of output data in the telemetry system.

It is presently planned to install automatic urine, blood, and saliva analyzers on orbital stations, such instruments being in the design or development stages. Studies are in progress also on the processing of different biochemical indices, in order to determine which methods of gathering and analyzing information are most effective under spaceflight conditions [53].

ANALYSIS AND EVALUATION OF DATA

Automation of Medical Measurements

The broadening of research problems and need to increase reliability of medical monitoring are related to the increased quantity of data subject to transmission from spacecraft to Earth. At the same time, diagnostic and prognostic problems arise, the solution of which requires increasingly complex methods of data analysis. In this connection, automation of medical and physiological measurements and use of electronic computers are acquiring considerable significance in space medicine. At present, development in this direction involves two aspects:

> development of on-board systems of automatic data analysis, and use of computer technology to process telemetry data on Earth.

In considering the possibility of transmitting the maximum quantity of data through channels with limited capacity, the first awareness should be of theses in information theory; in particular, those branches dealing with optimum coding methods. In the ECG, for example, it means dealing with a periodically strictly repetitive process (with the exception of extrasystoles). If only the necessary useful information is extracted from the data, 10 or 100 times less capacity will be needed in the telemetry channels than for transmission of the original data [21]. An algorithm of extreme bounds or limiting conditions has been proposed, which consists of determining the positive and negative extremes and development of a code characterizing the ECG type. The authors propose using the method of extreme bounds for ECG transmission via telemetry channels with small capacity, with computation of the main intervals in the tracing, and transmission of a series of numbers, the first indicating the type of curve, and the following numbers the values of the intervals. For complete transmission of the ECG, six numbers are required, instead of the 100–200 with direct quantization.

Many authors [61] have tried to describe the ECG using a minimum number of measurements. For example, it has been suggested that the ECG be approximated to the Fourier sine series [18], in which case, 20 readings would reproduce the ECG form with an accuracy of 1–2%.

Principles have been developed for coding electromyograms and EEGs for transmission, on the same telemetry channel, of data from four biopotential leads. The coding principle consists of determining the frequency and amplitude characteristics of the process and shaping signals that reflect these characteristics [83].

An automatic logic device evaluates the set of parameters according to assigned criteria. These devices operate on a "rigid" program which is determined by the design of the instrument. Different types of automatic logic devices are described in the literature [61].

McLennan's [69] was one of the first designs for an on-board automatic device. His system outputs to the telemetry channel information about the physiologic condition and efficiency of the astronaut. It operates on the principle of a scanning device to review all data coming from the astronaut, followed by binary selection for each channel and formation of an arbitrary signal (code) using simple logic systems of the "and" and "no" type.

Electronic digital computers offer totally new opportunities to formulate and solve problems of medical monitoring, diagnostics, and prognostics in space. The present level of medicophysiological knowledge already permits the designing of on-board diagnostic devices. Moreover, their level of technology makes them quite reliable and provides for appropriate size and weight indices.

Experience has been gained in using electronic computers to analyze biomedical data in clinical physiology. The first steps have been made in the use of computer technology to solve specific problems of space medicine. Three mathematical methods of analyzing data from space flights will be discussed; these examples pertain to neurophysiologic and cardiologic investigations.

Computer analysis of EEGs. To analyze the sleeping state during space flights, computer analysis was made of EEGs taken on astronaut F. Borman on Gemini 7. Telemetry data were recorded on magnetic tape, then analyzed in the Space Biology Laboratory of the University of California.

Analysis methods were developed on the basis of searches for correlation among EEG, attention, and psychologic tension [1, 4, 6, 7, 120]. Auto- and cross-correlation, as well as auto- and cross-spectral methods were used. The coherence function was computed as the statistical measure of correlation between different biopotential regions of the scalp at each frequency:

$$\mathrm{coh} = \{[\mathrm{Avet}(PP' + QQ')]^2 + [\mathrm{Avet})PQ' + QP']^2\}/SS'$$

where coh is the coherence function; Avet is time averaged value; P, Q, and S are input values of digital filters according to phase squared with an axis at a frequency of f. P', Q', and S' result from second channel filtration. Analyzed data were displayed on special plots with time plotted on the X-axis, frequency on the Y-axis, and coherence levels as a Z-axis modulation (shading from white to black). Contour lines joined points of identical coherence level. In this way, a continuous map was constructed, covering several hours of data.

To obtain initial data on normal values and to characterize individual EEG records in different states, astronaut candidates were examined [109]. Tracings of good quality were obtained from 200 subjects tested in perceptual and learning tasks using a programing device. A data file was made up for 50 of 200 subjects, with reference both to rest and to selected sleep periods. As a result, a spectral plot was obtained, from 0 to 25 Hz, for each part of the scalp (Fig. 7).

Contour plots with results of processing spaceflight data were made for two consecutive epochs, each 20 s, every 2 min during sleep, and for two epochs, each 30 s, every 10 min when awake. These data were compared to control EEGs of F. Borman, including the data in the "norm file" and those obtained in simulated flight. With this method it was shown that 1 min before lift-off, the plotted area of intensified θ-rhythm merges with increasing oscillations in the α- and β-rhythm zones, which relates to great concentration and orienting reactions. Immediately before and after lift-off, the density of EEG voltage increased by about 10 times in many areas, as a reaction to marked nervous and physiologic excitement. These increased densities then slowly diminished in the frequency band above 10 Hz within the first 30 min of flight. From other experimental studies on EEG coherence in physiologically and psychologically stressful situations, high levels of coherence in the 3–9 Hz range at the end of the first orbit can be explained as consistent with a relaxed state after strong psychic emotions.

Mathematical analysis of heart rhythm. Mathematical analyses of a dynamic series of RR intervals in the ECG were made in recent years by Soviet researchers in experimental physiology, clinical practice, sport medicine, and space medicine [18, 43]. The sequence of intervals was postulated to be a random stationary process with the property of ergodicity [83]. From data obtained by different authors in studies of sinus arrhythmias, it can be concluded that there are mechanisms directly influencing the sinus node in autonomic regulation, as well as mechanisms that control cardiac rhythm by central regulation at cortical-subcortical levels.

The sinus node is a sensitive indicator of changes at all control levels. Fluctuations in cardiac rhythm with respiration are related essentially to disturbances in self-regulating systems, whereas nonrespiratory fluctuations reflect influences of central, mainly neuroendocrine, systems [88]. It would therefore appear that a series of ECG intervals should contain information about the state of each regulatory system, as well as on the nature of interactions among them [89].

The feasibility of evaluating neurohumoral regulation of circulation from cardiac rhythms and of drawing conclusions about the state of the entire organism is particularly important to space medicine, where the volume of physiologic data transmitted from spacecraft to Earth is limited.

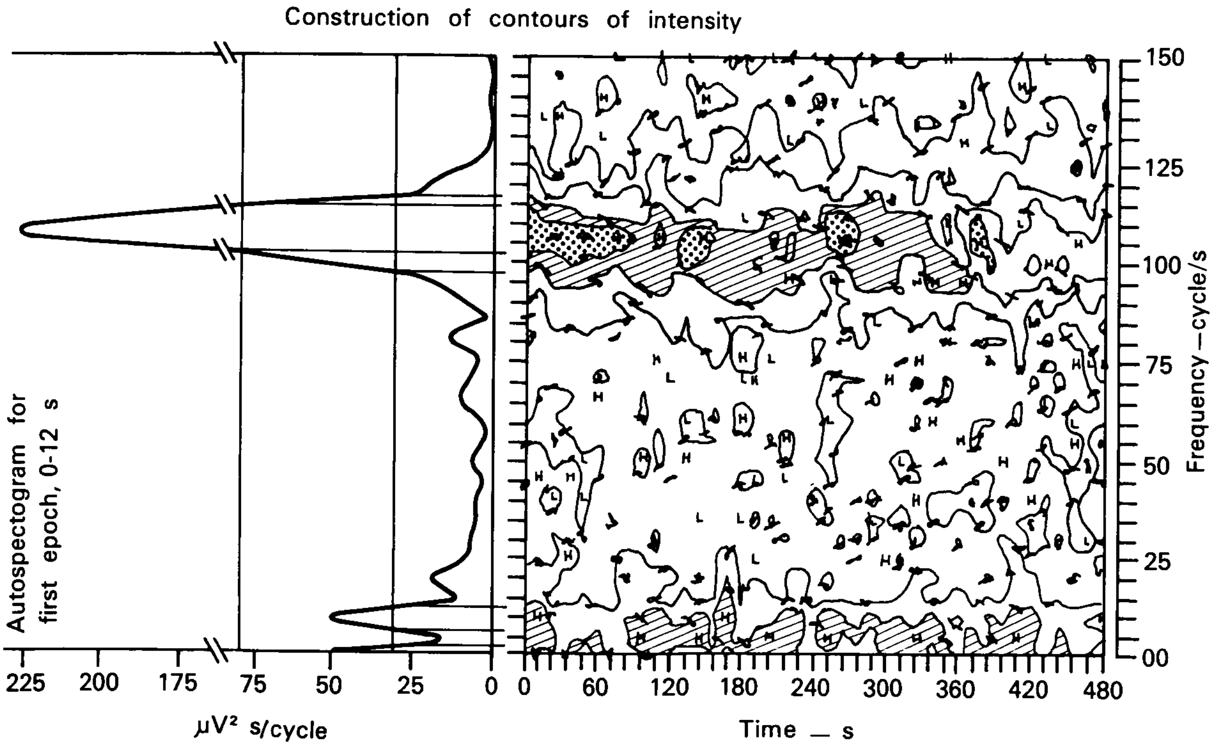

FIGURE 7.—Results of computer analysis of the EEG. Construction of intensity contours (on right) and autospectrograms for the first 12 s of recording (on left).

Segments for analysis were selected from telemetry tracings of ECGs or SCGs [seismocardiograms] and included 100–120 cardiac cycles. This sample size was determined to be sufficiently reliable statistically because within the framework of a single telemetric communication session, such a volume of data could always be distinguished from a background of noise related to both technical reasons and motor activity of the cosmonaut.

Four methods were used to analyze dynamic series of RR intervals: histography, autocorrelation, spectral analysis, and cardiointervalography.

Histography, or variation pulsimetry, demonstrates the law of distribution of the index in question. The type of distribution and type of variation curve are related to the state of the autonomic nervous system.

The autocorrelation function was calculated to demonstrate the internal structure of the process. The more homogeneous the dynamic series of RR intervals under study, the slower autocorrelation functions will reach zero, and the more stationary the process. A nonstationary process shows a sharp drop of correlation coefficient to zero, even after the first shift. Decentralization of control leads to intensification of respiratory arrhythmia, and the autocorrelation function, which rapidly reaches zero, then indicates the presence of periodic respiration. In a state of tension (work, emotion) a very slow drop of autocorrelation function is observed. The process becomes more stationary and respiratory periodicity levels off.

The presence of periodic fluctuations in the process under study can be demonstrated on the cardiointervalogram or autocorrelation function; however, spectral analysis is the most effective for quantitative evaluation of different periodic components [89].

Investigation of slow waves of cardiac rhythm is of great interest; apparently, they relate directly to the activity of neuroendocrine regulation mechanisms. Cardiointervalography is the simplest method of demonstrating such rhythms. Compression cardiointervalography—time summation for 10, 30, and 60 beats—was used to smooth out respiratory waves. This demonstrates waves with periods of 30 to 150 s [89].

Diagnostic and prognostic value of such an analysis was confirmed in a cardiac rhythm study of operators performing monotonous work. It was shown that appearance of marked slow waves (30–100 s) was one of the early signs of mental fatigue and preceded an increase in number of errors made in the operator activity [18]. Onset and intensification of slow waves could be attributed to "disinhibition" of subcortical structures as a result of development of extinction inhibition at cortical levels.

These methods of mathematical analysis of cardiac rhythmicity were used to process data obtained during Soviet spacecraft and satellite flights. Variation pulsimetry was first used to assess the condition of cosmonauts V. F. Bykovskiy and V. V. Tereshkova [83].

The first experiments in the use of autocorrelation analysis of cardiac activity were performed by Venttsel and Voskresenskiy, and Chekhonadskiy [83], to analyze data on the Voskhod flight. It was established that along with respiratory variations of cardiac rhythm, there are also slower fluctuations with a period of 70–80 s. During flight, there was a tendency toward longer periods of slow waves and a longer time for extinction of the autocorrelation function to zero. These changes are interpreted as an increase in centralized control of cardiac rhythms. From spectral analysis of slow waves in cosmonauts [86], activity of central regulatory mechanisms was found greatest during the first orbit. From autocorrelation and spectral analysis of cardiac rhythms, it was established that there are individual types of autonomic regulation: they were normotonic in V. M. Komarov, vagotonic in K. P. Feoktistov, and sympathicotonic in B. B. Yegorov.

During the long flight of Soyuz 9, variation pulsimetry demonstrated changes related to emotional stress (1st, 15th, and 19th d of the flight) and readjustment of regulatory systems (12th d), when only the amplitude of the distribution mode increased. Other statistical indices were unchanged. The emotional changes on the 1st and 19th d are understandable, marking the start and end of flight, and the 15th day was apparently one of emotional tension since on this day V. N. Nikolayev and V. V. Sevastyanov surpassed the prior record set by the crew of

Gemini 7 for length of time spent in space. Variation pulsograms obtained while the cosmonauts slept are of some interest. It can be concluded from the pulsograms that along with deep sleep when there is a marked prevalence of vagal tonus, there are times of "intense" sleep when the variation pulsogram presents sympathotonic features. Sympathotonic episodes are characteristic of rapid-eye-movement (REM) sleep associated with dreaming. Figure 8 illustrates samples of variation pulsograms in different functional states.

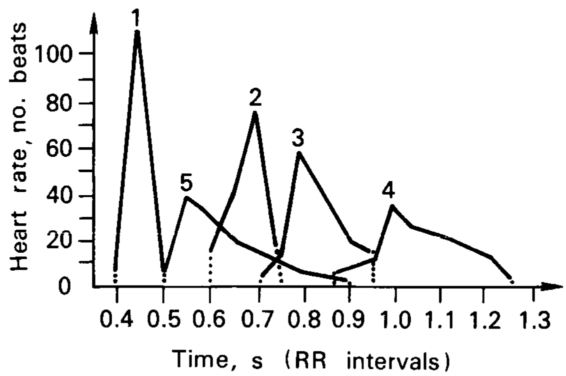

FIGURE 8.—Statistical characteristics of cardiac rhythm with different states of the organism (histograms).
(1) overstress
(2) stress
(3) normal
(4) sleep
(5) transitional process

Spectral analysis of the seismocardiogram. Seismocardiography is one of the derivatives of dorsoventral ballistocardiography (BCG) and bears information about oscillatory phenomena associated with cardiac contraction and shift of blood masses to the major vessels. The cardiovascular system comprises a series of oscillators generating oscillations of different frequencies and amplitudes. The ballistocardiogram reflects pulse fluctuations of the body's common center of gravity. Techniques of kinetocardiography and vibrocardiography permit recording local oscillations. Seismocardiography differs in that it shows, differentially, the fluctuations of the entire chest wall without picking up, as does ballistocardiography, body movements as a single system. Thus, it can be assumed that in seismocardiography, oscillatory processes are mostly related to heart activity proper [118].

SCG spectra were studied using a method developed under the guidance of Professor V. A. Zverev as applied to BCG analysis. The logarithms of the spectra are studied by means of an optical analyzer. From 2–3 to 8–10 cardiac SCG complexes are analyzed, with a resolution of up to 0.1 Hz. SCG spectra can be interpreted by analogy to BCG spectra, since they reflect the same phenomena, the only difference being that there are no oscillations in the SCG spectrum that are related to the actual frequency of the

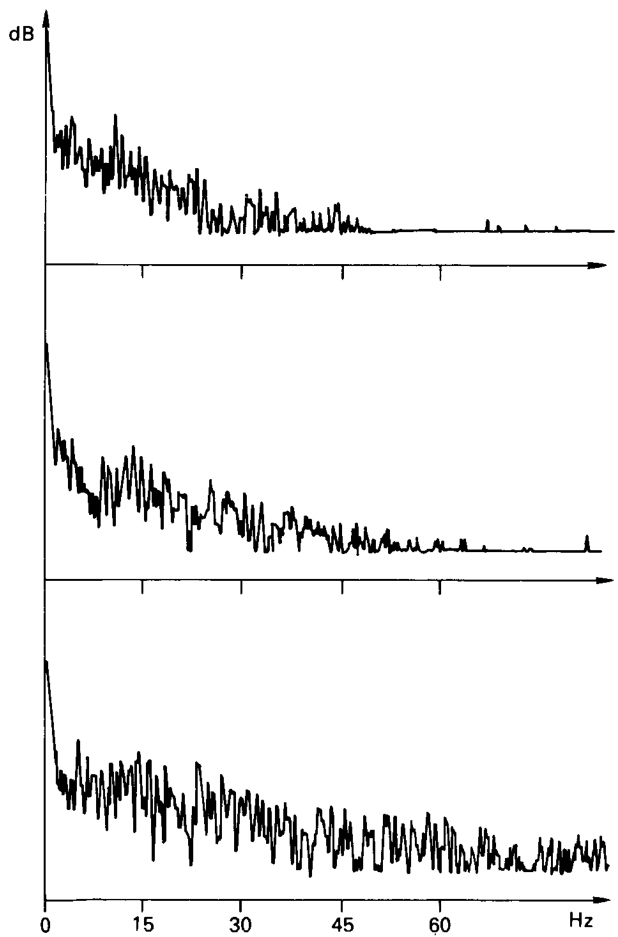

FIGURE 9.—Spectral analysis of seismocardiogram. Salute 1 orbital station, cosmonaut G. T. Dobrovol'skiy.
(a) 3rd orbit (1st day)
(b) 243rd orbit (15th day)
(c) 326th orbit (20th day)

"Earth-ground" system (5–6 Hz). This permits interpretation of the correlations between the first and second spectrum harmonics and width increases relative to impairment of normal correlations between the right and left heart parts. In progressive mitral stenosis, characterized by gradual development of pulmonary hypertension, with an increased load on the right ventrical and a relative underload on the left one, a predominance of the second harmonic over the first is observed. The width of the spectrum increased from 14 ± 0.7 Hz, which is normal, to 18 ± 0.4 Hz (P 0.001). These changes correspond to greater changes in the ballistocardiogram [119].

Figure 9 illustrates the seismocardiographic spectra of cosmonaut V. A. Dobrovol'skiy, Salute 1 orbital station commander, on different flight days. When compared to spectra from the prelaunch period and first flight day, there was subsequently a gradual broadening of the spectrum from 25–30 to 45–50 Hz, and some drop in amplitude of the first harmonic. Since spectral seismocardiography data constitute the only information about changes in the state of the heart and pulmonary circulation during flight, such data should be considered of prognostic value.

Questions of Medical Monitoring and Diagnostics

Analysis and evaluation of data obtained during space flights are directed toward solving problems of medical monitoring, diagnostics, and prognostics. Medical monitoring at present is based on on-line evaluation of telemetry, television, and radio communication data. Attention is focused primarily on the cosmonauts' general well-being and condition, and their degree of efficiency. Aside from vestibulovegetative disorders, specific manifestations of the effect of weightlessness on the human organism have been subtle and incompletely observed. Consequently, criteria for evaluation of the physical condition of cosmonauts and decisionmaking are based on the usual clinical conceptions. On the basis of practical problems, these states of the subject can be proposed: normal, stress, threatening, and critical [48]. Such a classification is quite arbitrary, but permits development of a system to identify states from relatively concrete signs that can be obtained during flight.

When developing diagnostic algorithms applicable to on-board conditions, a number of factors must be taken into consideration: nature of initial information, means of expressing it for input to a machine, methods of analyzing and evaluating data, and others. The choice of parameters to be monitored is of the utmost importance. It has already been stated that the problem generally involves minimizing input data without diminishing diagnostic effectiveness. Final choice of parameters depends on duration and objectives of the flight, type of spacecraft, and composition of the crew. The theoretical aspects of choosing a set of parameters for medical monitoring in space flights are based on criteria of need and adequacy of parameters (including analytical methods). These serve to diagnose changes in the main physiologic functions and efficiency of cosmonauts attributable to flight factors, provide the possibility of predicting later reactions, and differentiate between physiologic and pathologic states, including identification of specific reactions [78]. A specific monitoring problem in flight may be cited: the investigation of altered neuroendocrine regulation and degree of stress. Correlations may be determined between indices from deviations from normal values or from expected relationships. For a quantitative evaluation of effects of different factors on the physiologic indices under study, covariance analysis may be useful.

The development of basically new methodologic procedures is imperative, in particular, "no-contact" systems of gathering data, methods for examining the internal medium of the organism, and appropriate examination programs to back up long space flights [85]. There is need to develop rapid methods of gathering necessary data, while algorithms are needed for rapid transfer of commands using the on-board computer.

Development of on-board automatic data processing systems will open the way, first of all, to back up on-line medical monitoring, by transmitting summarized computer data to Earth via narrow-band telemetry channels, as well as using data independently on-board the spacecraft.

We concur completely with authors who indicated that it is not possible to diagnose an illness by means of an on-board computer [114]. It can only be a question of identifying dangerous conditions and reporting them promptly. Programs for processing medical data on-board a spacecraft could vary, depending on the capability of on-board computer devices, availability of additional equipment, and data volume [56]. In choosing automation systems, the data processing scheme will be of the utmost importance. Conditions that must be taken into consideration in regard to an on-board computer are: (1) data are acquired directly from the cosmonaut; (2) the computer capabilities may be limited in operation speed and in memory, although current computer developments show a rapidly changing state of the art for both; (3) in solving problems pertaining to on-line monitoring, it is necessary, at the same time, to provide for transmission of partially processed data to Earth through a narrow-band communication channel. The first problem that arises here is addressing data to the computer. Regardless of whether the data stream is in the form of pulses or quantized values of the parameter in question, it is converted into a series of numbers stored in the buffer memory of the computer. These data can subsequently be analyzed in three ways [21]: (1) display by typical clinicophysiologic analysis techniques, as for example, in isolation of specific ECG intervals and waves; (2) bionic; and (3) mathematical-statistical.

The first of these directions refers to methods of amplitude and period analyses, since the most common method today is determination of time intervals and wave amplitudes of different oscillograms with calculation of indices and indicators. Clinical methods for these analyses are not complicated. However, from the standpoint of the computer programer, this is the most complex form of analysis, since exact identification of different waves and intervals on the tracing is required. Actual demonstration of definable amplitude and time indices often becomes a most complex logical problem.

The bionic approach is related to the problem of pattern recognition. The machine simulates the activity of an experienced specialist who determines the nature of deviations or makes a diagnosis according to the appearance of the curve alone, without making any calculations. Similar to a physician, the computer compares data submitted to the standards stored in its memory. The standard closest to the curve under study is retrieved and its number reported to the doctor.

The mathematical-statistical method of analysis consists of calculating a number of strictly mathematical indices and functions. This is an unfamiliar form of analysis for a physician, but the most adequate for the computer. Experience in histographic, autocorrelation, and spectral analyses of a dynamic series of cardiac cycles of other physiologic data, including electroencephalograms, has revealed that mathematical analyses are adequate to estimate physiologic differences. The latter would have required extensive examinations to be identified by the usual techniques and most probably would have escaped detection without such sophisticated analyses. Thus, on the basis of mathematical analysis, it was possible to prepare the algorithm for monitoring the cosmonaut's condition with only one parameter available: rhythm of cardiac contractions [18, 88].

These analysis methods for medical data can also extend to physiologic processes recorded in both micro- and macrotime intervals. It is possible to obtain new and effective diagnostic criteria in this manner, provided that due regard is paid to statistical constraints in dealing with short data epochs.

Considerations in Predicting Man's Condition in Space Flight

Problems pertaining to prediction of the physical condition of cosmonauts are acquiring increasing urgency in view of longer flight durations. However, it turned out that the solutions were very complex, because of inadequate concepts of the mechanism underlying pathologic shifts in the organism's status, that might be specifically attributable to weightlessness. Several investigators have voiced the opinion that it is impossible to predict human endurance on prolonged space flights on the basis of existing techniques and knowledge [65, 97]. Indeed, it is not possible to use the traditional approach to prognostication in clinical practice and physiology, when the condition or illness whose course and outcome must be predicted has been observed many times at different stages in development. Unlike terrestrial conditions, the adverse states and changes that must be predicted have yet to be observed in space, with the possible exception of motion sickness. Thus, there are not yet any facts to design a predictive system for expected pathologic states.

Demands of practice dictate, in some cases, an empirical approach to prognostication. For example, the results of the Gemini and Apollo flights were used to predict satisfactory tolerance of astronauts to the Moon [37, 46, 47]. In the physiology of stress factors there are only isolated attempts to predict development of some reactions and conditions: considering initial data or analyzing the dynamics of the ongoing process in thermal collapse [105], decompression [101], and operator activity [100]. The forecasts of Dietlein [37], as applied to long space flights, merit attention. In 1964 he described a scheme of possible development of symptoms for flights of various durations.

Three types of methods for forecasting man's condition in prolonged space flights can be distinguished at present.

1. Methods based on using experience and intuition of highly qualified specialists emerging as experts. These methods have been developed in the area of scientific technologic forecasting and named heuristic, since they are used under conditions of high levels of uncertainty [51, 84]. During the Salyut orbital station flight, a variant of heuristic forecasting was used involving expert evaluation. Good correlation was obtained between predicted and actual parameters of the medical monitoring system, which indicates that it is purposeful to continue developing this line of research.
2. Methods based on functional characteristics of a series of measurements on which prognosis is made, and of correlations between them. Differential equations of discrete algorithms are used to approximate data as a function of time. Mathematical methods permit short-term prediction of dynamic processes and of their progression as applied to problems of space medicine. They are of great scientific and practical interest.
3. Methods based on knowledge of physiologic concrete laws governing the function to be used in estimating prognosis. This category is most attractive to space medicine, since it opens the way for broad practical use of knowledge accumulated to the present about man's reactions to stressing factors.

Two variants of forecasting systems being developed in the USSR and USA will be discussed on the basis of the last category.

Investigative (research) prognosis [20]. Since a system cannot be built for predicting expected pathologic states within the framework of existing scientific knowledge about the effects of spaceflight factors on the living organism, the concept of a standard prognosis cannot apply to solutions of this problem. However, there is another approach to prognosis, called investigative or exploratory, which is the way one of the founders of modern forecasting, Erikh Yanch, defines the difference between these approaches.

> Investigative forecasting starts with the base of knowledge available at the present time and is directed toward the future, whereas normative forecasting first assesses future goals, requirements, and needs, and then proceeds in the opposite direction, toward the present [112].

The working hypothesis of exploratory prognosis proceeds from the well-known thesis that tonic activity in regulatory systems, including the sympathoadrenal system and cerebral mechanisms of regulation, are common to all adaptive reactions of the organism in response to stress factors. This leads to mobilization of protective systems that assure the necessary end effect

[15] by initiating action in an orderly sequence and, in some cases, ahead of the pathologic development process. Excessive demands on regulatory systems may lead to breakdown and appearance of pathologic syndromes of illnesses. Consequently, the stress [tension] state could be viewed as the state typical of the first developmental stages of any pathology, and it could be adopted as the base in investigative prognosis. The presence may be noted of both positive and negative vectors of this state as projected into the future. In introducing the arbitrary term, "vector of state," it may be defined as a measure of impairment severity and tendency to develop a specific state of the organism. Thus, the research focus was to find criteria that would permit detection of a tendency to change in the stress state, in the direction of overstress or normalization, i.e., to determine the vector of state. It should be noted again that the stress state does not imply emotional or physical stress alone, but also the changes in regulatory mechanisms that are associated with any readjustment of a functional system to a new reaction level. Such changes can be either specific or nonspecific; the latter are mostly referable to the sympathoadrenal complex.

The search for prognostic criteria, i.e., fine indices of current condition and tendencies toward change in physiologic functions, proceeded on a hypothesis postulating that all states undergo four stages [87]:

1. Temporary functional nonconformity;
2. Impaired information flow;
3. Impaired metabolism;
4. Structural disturbances.

Consequently, to solve prognostic problems, it is useful to investigate the level of temporary disorganization, since changes at this level precede informational, energetic, and structural disturbances.

Thus, the proposed method of prognosis is based on two principles:

1. Determination of tendencies toward change in stress state in the direction of overstress or normalization;
2. The search for prognostic criteria on the level of temporary function disorganization.

The difference between standard and investigative prognosis is illustrated in Figure 10. On the abscissa is shown the scale of states and state vectors corresponding to the prognostic principles adopted in clinical practice or proposed for space medicine.

On the ordinate are shown the various levels of organization of a living system: time–information–energy–structure. The diagonal arrows show that the prognostic criteria should be opera-

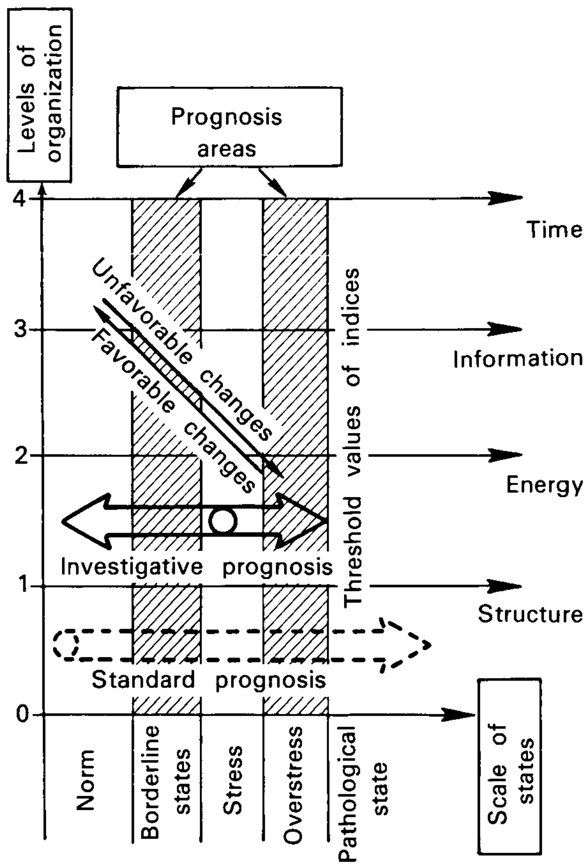

FIGURE 10.—Diagram of investigative prognosis in space medicine.

tive primarily in the prognosis areas that correspond on the one side, to borderline conditions between normality and stress, and on the other side, to overstress at certain informational levels and energetic change.

During task performance, techniques were used to obtain information about the state of neurohumoral regulation and the circulatory system. Only methods that had been either previously tested or could be used in the future for direct, on-board readings on a spacecraft were selected. The choice of prognostic criteria was based on indices of temporary [or time-related] organization of functions. Two types of fluctuating processes in the organism were investigated: circadian (with a period close to 24 h) and cardiac-respiratory rhythms (periods of 0.5 to 10 s).

Circadian periodicity was studied from pulse rate, body temperature, and sodium concentration in mixed saliva [25]. The last parameter is related to the condition of the sympathoadrenal system and may be viewed as an adjustment index of the organism's control systems to a set rhythm of work and rest; and as a tension degree indicator of function regulating mechanisms [25]. Cardiorespiratory rhythms were studied by mathematical analysis of a running series of RR intervals on the ECG with construction of histograms and autocorrelation functions (see above). Changes in the statistical characteristics of cardiac rhythms are an important index of sympathoadrenal system activity and state of neurohumoral regulation of the circulatory system [88]. Factors simulating some of the spaceflight conditions were used in trial studies.

Studies were made of the adaptive reactions of the human organisms to experimental hypokinesia, artificial and natural time shifts, antiorthostatis, and combinations of these factors. A series of studies, used to form certain conclusions, included investigation of the normal variation range of the indices chosen, development of models of different states, and investigation of adaptive reactions to these experimental factors.

The conclusion was reached that determination of individual adaption types and evaluation of the organism's functional reserve are important in predicting probable pathologic changes, in addition to determining the severity and direction of stress reactions.

For on-line evaluation of normal, disturbed, and stressed states, the statistical characteristics of cardiac rhythm (M, Mo, AMo, Δ, X), data on sodium levels in mixed saliva, indices of function synchronization, and circadian parameters can be used. Trends involving a massive decline in all these indices (for AMo—a rise) is prognostically unfavorable, and indicates development of overstress in regulatory systems, which could lead ultimately to regulation breakdown, severe debilitation, and appearance of specific syndromes.

As an example of this, in Figure 11 is shown the variations of pulse, body temperature, and sodium concentration in saliva during a 64–h sleep-deprivation experiment [23]. Compared with control levels, during the experimental period there was a decline of mean 24–h salivary sodium level and marked function desynchronization. Recovery to control state was still incomplete even after 3 d.

The length of recovery for different factors is one of the functional reserve indices of the organism. Significant debilitation eliciting regulatory disturbances is manifested by an inadequate reaction to tasks. The amplitude of daily fluctuations of different parameters can also serve as a good indication of functional reserve, since it reflects the organism's response to routine "natural load," the change in environmental conditions. It is useful to use the difference between measures of function at rest and during activity as the amplitude index of daily fluctuations. A daily adaptivity index (PSad) has been proposed, defined as the percentile ratio between the 7 and 11–h difference in value of the parameter to the initial 7–h value [23].

The characteristics of the organism's regulatory systems must be known in order to establish the individual type of adaptation. Just as Pavlov described the properties of major nervous functions at the cortical level by their force, balance, and lability, it would be useful to develop analogous criteria for systems implementing interaction between the organism and environment. Thus, types of adaption may be classified according to lability of function in systems important for brief and long flights. The extreme types, ranging from sluggish to highly responsive, are notable, respectively, for faster or slower readjustment of the organism to a new level and rhythm of activity. Various manipulations will test lability of physiologic systems including postural adaptation, physical work loading, and administration of pharmacologic agents. The transition rate of the organism to a new level of function, or recovery rate of the initial level, are measured. In tests with shifts through time zones, the sluggish adaptation type, in contrast to the flexible, is characterized by slower synchronization of circadian and other biological rhythms [23].

In the antiorthostasis test, individuals with good flexibility of regulatory systems were characterized by a greater range of changes in cardiodynamic parameters during adjustment to a new functional level. The passive ortho-test performed immediately after orthostasis was usually well-tolerated by such individuals. When using the "phase plane" method to analyze types of adaptation, tolerance to orthostatic tests could be forecast according to the "area of regulation" (region circumscribed by the phase trajectory of the system of parameters under study) and vector of transition (magnitude and direction of the segment of the phase trajectory in the first minute after switching the subject from antiorthostatic to orthostatic position). A small area of regulation and large transition vector are prognostically unfavorable [23].

Thus, prediction of the organism's condition if exposed to physical and psychological stress, from the standpoint of biomedical prognosis, now permits establishment of a number of effective criteria that evaluate the direction of the adaptive process, severity of stress state, individual type of regulation, and functional reserves of the organism.

Clinicofunctional approach to prognosis. The changes in functional state of the organism under spaceflight conditions could be viewed as quantitative and qualitative shifts relating to changes in functional reserve and defense capabilities. This is in reference to detection of early and minor changes in different systems and organs in the course of extensive and diversified examinations. Scientists at Beckman Instrument Co. have postulated that the reserves of the organism can be evaluated by monitoring the liver, endo-

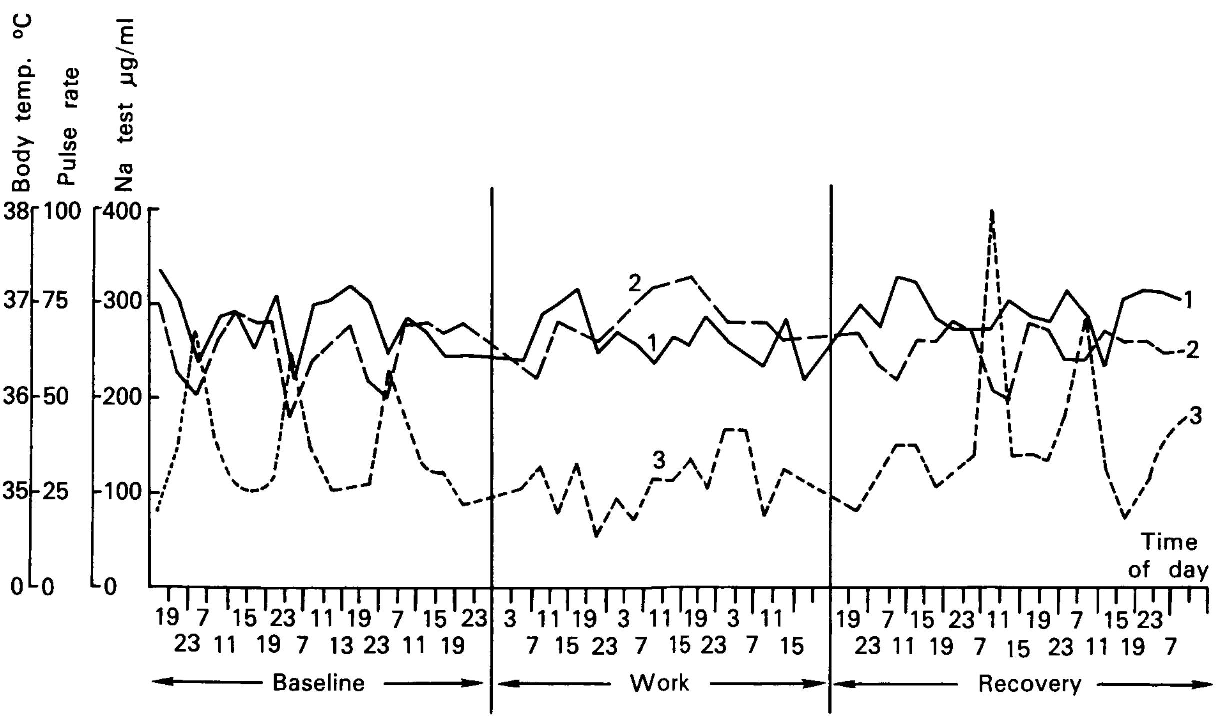

FIGURE 11.—Dynamics of pulse (1), body temperature (2), and saliva sodium (3) in experiment with 64 h sleep deprivation.

crine, and hemopoietic systems, to which all metabolic and stressor changes are related. The defense capabilities of the organism and its susceptibility to stress can be assessed by estimating the globulin level, the state of the leukocyte system, determination of phagocytes and leukocytes, as well as microbiologic studies. The problem is to detect microsymptoms of changes that are not symptoms, per se, of illness and that appear long before onset of illness [50]. It is assumed that the true picture of the changes can be detected only through intensive sequential examinations involving many readings and comparing them to the initial data.

Based on this concept, Beckman Instrument Co. with Lockheed Corp., under the guidance of NASA, developed a system of biochemical and hematologic analyses in space, including collection and storage of biofluids and adaptation of a number of clinical techniques to spaceflight conditions. These techniques have been applied in the Skylab program. In gathering initial data, it is planned to devote special attention to investigation of circadian rhythms and fluctuating phenomena in different systems of the organism. A series of tests is being developed to demonstrate primary responses to stress. Importance is attributed to metabolic studies, in particular to changes in blood sugar and calcium.

In developing a system of prognostic readings in space, specialists consider it imperative to collect blood at specific intervals, but not too often. Emphasis is on examination of natural fluids: sweat, saliva, and tears. Special attention was given to the study of salivary gland secretion. Special techniques have been developed to collect and automatically analyze salivary secretion with telemetry of the measurement results. Saliva will be examined in a daily cycle with estimation of potassium, sodium, calcium, and albumen. Globulins, proteins, glucose, and lipid components will be measured in blood. The pH, proteins, and glomerular filtrate will be examined in urine. An automated biochemical analysis system has been developed, with manual input of material, and automatic analysis with output of the results in a special code to the on-board digital computer.

Extensive and diversified studies are being conducted on Earth to obtain data on the range of normal variations and prognostic value of gathered data [100]. It is planned to obtain 400–500 parameters from each individual, including biochemical and hematological measurements, examination of respiratory, digestive, nervous, and cardiovascular systems, and anthropometry. Newly developed techniques will also be used, such as examination of salivary secretion (Fig. 11). Individual variability of the parameters will be investigated by taking readings several times a day. It is planned to conduct such extensive examinations twice a year.

Thus, the system of prognostication being developed in the US is directed toward demonstration of negligible, subclinical, early changes in systems and organs by means of diversified automated examination. The area of prognosis is referable to borderline states between normal and stress. The search is directed from normal to subclinical shifts characterizing the functional reserve and protective capabilities of the organism. On the diagram pertaining to forecasting principles (Fig. 10), this clinicofunctional approach could be viewed as the first stage of clinical prognostication which ends in the area of borderline states. It should be noted that this approach, in essence, is analogous to the concept of mass screening for early detection of premorbid states.

DIRECTIONS AND TECHNIQUES FOR FURTHER IMPROVEMENT OF PHYSIOLOGIC MEASURING SYSTEMS IN SPACE

The methods of examination and problems of transmitting biomedical data, being developed at present by space medicine, are the foundation for future research with regard to medical backup of long flights on orbital stations and interplanetary craft.

Lovelace and Schwichtenberg indicate that the farther man is from Earth, the more difficult it is to assure his safe existence and return [65]. For this reason, reliable medical monitoring and collection of physiologic data on the effects of interplanetary factors on man are becoming important [51].

The participation of a physician as a crewmember is one of the chief distinctions of the physiologic data-measuring system on an interplanetary craft. Many studies [30, 65] discuss the need for inclusion of a doctor in interplanetary expeditions. The long duration of an interplanetary flight and availability of a doctor in the crew, as well as use of on-board systems of automatic processing and storing of data make it imperative to develop new principles in the design of physical measuring and data systems. In the first place, there is need to define the chief problems that are to be solved by physiologic readings on the interplanetary craft. At least four such areas can be defined.

1. Periodical on-line medical monitoring by the on-board physician, at different phases of flight.
2. Routine general physical examinations of crewmembers by a dispensary system to evaluate their health and gather scientific information on the effect of factors inherent in long interplanetary flight on the physiologic functions of man.
3. Medical examinations performed for the purpose of in-depth monitoring of different systems and organs, and to diagnose illness that might occur during flight.
4. Transmission to Earth of the principal results of all the above physiologic measurements.

Medical checks on an interplanetary craft should be made periodically, on a scheduled basis, as well as extemporaneously, when there is a possibility of dangerous deviations in the physical condition of crewmembers. It is impossible to anticipate all such situations in advance. Some may be cited: repair work involving extravehicular activity, significant increase in radioactivity, malfunctions in air-conditioning and heat-regulating systems, and slowing down the craft for maneuvers and landing. Under such conditions, the necessary sensors and electrodes are applied by the doctor (or the cosmonaut himself), and the proper on-board equipment is turned on (the intracabin telemetry system is used). The data should be displayed in a summarized form (and, if the doctor so wishes, in their primary form) on a specially equipped medical panel. At the same time, these data should be stored in a memory device, then transmitted to Earth in abbreviated form during a scheduled communication session.

Many studies [11, 14, 73, 80] deal with development of in-cabin telemetry. Some of the essential specifications for such systems [18] are:

1. Equipment carried by the cosmonaut should be of minimum weight and size, and should offer maximum continuous operating time without changing the power pack.
2. A good quality recording of monitored physiologic parameters should be provided while the cosmonaut is active or when he is in any of the compartments of the spacecraft.
3. The system of electrodes and sensors should not hamper the cosmonaut in his activity and should not cause discomfort when worn for any length of time.

Several multichannel biotelemetry systems have been developed for acquiring and transporting data in the spacecraft cabin, including an eight-channel system using pulse amplitude modulation (PAM) [80], a number of systems with frequency modulation of audio subcarriers [11, 13], a modulation system with separate carrier frequencies for each channel [18], a miniature biotelemetry transmitter on a tunnel diode [102], systems with power supplied by an artificially created electromagnetic field [74], with biological power supply [64, 75], and others.

Routine, dispensary-type, medical examinations of the crew should be comprehensive in order to assure prompt detection of even minor health deviations and to obtain sufficiently complete scientific information. A definite set of techniques, standardized and tested in advance, with a wide range and concrete program, will permit the use of reliable algorithms for primary automatic processing of data on-board the spacecraft. A special reference "library" will also be needed for evaluation of the examination results. Even if it is assumed that such examinations would be made only once a month, storage of records accumulated during the entire flight would pose a complicated problem. For this reason, this problem should first be investigated jointly by physicians and engineers, to determine the extent of preliminary data processing both for storage on-board the craft and for transmission to Earth.

Special medical examinations may be included in those planned in advance in the event of specific changes appearing in different organs and systems, or physiological readings taken for research purposes may be used. Examinations may also be initiated to determine the condition of crewmembers who develop a set of symptoms not yet known on Earth.

The lack of continuous communication between an interplanetary spacecraft and Earth, the small volume of medical information transmitted, the impossibility of rendering assistance from Earth (with the exception of consultation)—make it necessary to consider in detail the possibility of morbidity among cosmonauts during long flights, and methods of diagnosis and treatment under these specific conditions [90, 113]. It must be borne in mind that while a cosmonaut may be considered absolutely healthy at the start of a flight, and his reactivity does not differ in any way from that observed on Earth, as time passes his reactivity may change under the influence of flight conditions. Such factors as prolonged isolation and hypodynamia diminish the defense properties of the organism. Environmental factors in interplanetary space may also have an adverse effect on the cosmonaut's organism. Vasil'yev [104] showed that weightlessness and hypodynamia lead to decrease in orthostatic and vestibular stability, increased infection sensitivity, decreased acceleration and physical-load tolerance, and altered reactivity of the organism to pharmacologic agents.

Illness during an interplanetary flight can be classified in one of these groups: (1) illness due to living conditions (hygienic environment, diet, routine, psychologic factors); (2) illness due to effects of interplanetary space factors (cosmic radiation, electromagnetic fields, weightlessness); (3) pathology related to endogenous factors (autoinfection, impaired nervous and endocrine regulation). The concurrent effect of several factors can apparently elicit complex, serious pathologic forms not known on Earth. New nosological entities may also appear, due to the effect of cosmic factors not yet known.

The approach to morbidity among interplanetary crews from the standpoint of probability of onset of different diseases is extremely important in planning both diagnostic procedures and therapeutic care. Thus, it is certain that the probability of pneumonia or appendicitis during a long flight is greater than that of other illnesses. The possibility of rather frequent disturbances of coronary circulation is not ruled out, since flight tension and living conditions can affect blood supply and metabolism in the myocardium.

In investigating morbidity during interplanetary flights, broad use would be made of the varying probability of illness concept. In a given set of environmental conditions, obviously, the probability of some diseases increases and of others, decreases. Thus, in dietary disturbances, there is a greater probability of alimentary dystrophy, avitaminosis, and others; under the influence of cosmic radiation, there is greater probability of radiation sickness. If the diversity of pathologic forms and the course of illness is also considered, what is observed will depend on concomitant disturbances referable to living conditions or appearance of adverse external factors. Complex mathematical analysis is clearly required here, with the use of modern computer technology.

Design of diagnostic systems on a spacecraft has inherent specifics related to these factors: (a) volume of memory and speed of on-board computer devices are limited; (b) the most diverse data in the most diverse form are to be transmitted to the diagnostic system (oscillograms, directly from man, digital data, complaints and coded data, and others); (c) number of probable diagnoses is quite large; and (d) sets of symptoms may appear that are not yet known and cannot be anticipated in advance.

Difficulties involved in developing a general purpose diagnostic system on an interplanetary spacecraft could be reduced, to some extent, by preparing special reference microfilm, as well as providing for solution of special diagnostic problems on the computer on board according to programs that could be developed, if necessary, by mathematicians on the craft, with physician participation. Nor should it be forgotten that consultant aid from Earth is available, but this is related to the next problem, that of transmitting data to Earth.

In interplanetary flights, there is a limited supply of power on board the spacecraft. Moreover, the greater "astronomical" distances may limit wideband and prolonged radio communications. It has been assumed that the capacity of telemetry channels and time of transmission will be hundreds of times smaller and limited exchange of information between spacecrew and Earth. However, greatly expanded data bandwidths (tens of kilobits/second) have now been proven at interplanetary distances in US unmanned spacecraft and give promise of much better biomedical data transmission capabilities for manned interplanetary missions.

It is difficult at present to perform the necessary calculations on needed data bandwidths. However, difficulties may remain in transmitting large quantities of medical oscillographic data. Apparently, coded, summarized data will be the chief means of data exchange with Earth. For this reason, a start should be made now to work on a new "code language" to express all necessary medical and biological data and concepts that may be required in interplanetary flight.

Space medicine should have acquired the necessary means for exchanging information between countries widely separated on the Earth's surface, just as there is an international exchange in other fields of scientific endeavor. Also to be kept in mind is the possibility of and the need for automatic distribution of codes used by the on-board computer for transmitting data to Earth after each scheduled and unscheduled clinicophysiologic examination.

Thus, the system of diagnostic readings on an interplanetary spacecraft will differ appreciably from the systems as known today. The comparative characteristics of three types of physiologic measurement systems (for brief and long space flights, and interplanetary spacecraft) are given in Table 3.

TABLE 3.—*Characteristics of Physiologic Measurement Data Systems for Different Purposes*

Short flights (up to 5 d)	Long flights (up to several mo)	Interplanetary flights
During flight all sensors and electrodes are on the cosmonaut	Only a minimum number of sensors and electrodes for medical monitoring are on the cosmonaut; most are applied by him for brief examination periods	Sensors and electrodes of medical monitoring system and all other sensors applied by the on-board physician
Cosmonaut is wired to on-board equipment	In-cabin radio links are used for medical monitoring	In-cabin radio links used for medical monitoring
On-board medical equipment is controlled automatically from Earth or on-board programed computer	Manual control in addition to automatic and programed	Physician controls the equipment
Physiologic data are recorded only during periods of direct communication with landbased centers	Bulk of physiologic data recorded and stored during periods without communication to ground, with subsequent automatic transmission of all data to Earth	Data recorded by on-board devices with storage in processed form; only a small part of summarized data transmitted to Earth
Physiologic data are transmitted in the form of oscillograms	Physiologic data transmitted only partially in oscillogram form; most data are transmitted in digital and summarized coded form	Physiologic data transmitted to Earth only in summarized form

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Problems of diagnosing dangerous states should be closely related to solving problems of rendering medical care on board spacecraft. Rapid identification of pathologic states has the goal of speedy rendering of aid, which should be qualified and effective. In interplanetary flight conditions, both diagnostics and care must be automated. Immediate emergency care, for example, delivery of oxygen to one of the compartments, could be given either by depressing the proper button on the physician's panel or automatically, on the basis of generating the appropriate command by the computer that is performing on-line medical monitoring. The latter deals with a typical example of biologic control for the purpose of rendering therapeutic care. Orbital space station flights should be one of the important stages in solving the above problems. During such flights, new investigative methods and promising systems of automatic processing and transmission of biomedical data can be tested. Man's prolonged stay on orbital stations will undoubtedly furnish valuable scientific information about the regulating mechanisms of functions in weightlessness, and allow a more concrete approach to the solution of problems in medical monitoring, diagnostics, and prognosis in interplanetary flight.

Thus, the promising directions of developing methods for physiologic and medicobiologic measurements in space are related to flights on orbital stations and interplanetary craft. This broad gamut of tasks and problems requires deeper analysis of experimental material and, on this basis, further development of space medicine methodology. There must be continued development of collection methods to automatically process diagnostic and prognostic data. Research in these directions should definitely be focused not only toward solving specific problems of space medicine, but also toward concurrent development of medicine and public health care on Earth.

In conclusion, it should be mentioned that use of the principles of normative prediction in research is now making steady progress. Such principles are used in current work in the US and the USSR on orthostatic tolerance prediction using lower body negative pressure (LBNP). A number of methods have also been developed in the USSR for prediction of motion sickness tolerance, and initial stages of mental fatigue for detection of early signs of heart maladjustment due to right-sided congestion, and others. The cardiac rhythm mathematical-statistical indices and seismocardiographic data regularly monitored by the operational medical control system are used as predictive criteria. Further progress of the normative approach to medical prediction in space would be associated, first, with a widening of the range of on-board physiologic measurements, and second, with better understanding of individual crewmember response types.

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Chapter 19

BIOLOGIC GUIDELINES FOR FUTURE SPACE RESEARCH [1]

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APPEARANCE AND VOLUME OF PROBLEM—BIOLOGIC INDICATION OF SPACE AREAS

The first biologic experiments aboard high-altitude rockets and satellites had predominantly an applied scientific-investigative character. It was necessary to verify the ability of highly organized animals to withstand the effects of lift-off, orbital flight, descent, and landing of flight vehicles and to check the operation of life-support systems. These investigations proved the possibility of manned space flight, and subsequent flights of cosmonauts confirmed the well-founded evidence. A consequence of the immediacy of this practical scientific goal and its importance was that many continued to consider space biology an applied science concerned with providing support for manned space flight, and all experimental work in this area was directed toward determining biologic guidelines for new space research. The foundation of many initial such tests devolved (to a certain degree) from an intuitive striving of man to further verify his experiences, not from an attempt to master new ones.

The support of manned space flight, the importance of this problem notwithstanding, is obviously an incidental task for space biology. From the viewpoint of biology, space flight is primarily an instrument for studying fundamental problems, making it possible to study the nature and properties of living organisms by new, previously unavailable methods, and opening fields of investigation in which biologic theory is in no position to make trustworthy predictions.

New elements of the environment created by space flight are significant for biologists. These phenomena are: a prolonged state of weightlessness, weightlessness with ionizing radiation, absence of circadian rhythms, and finally, an increased radiation background of high-energy particles which cannot be simulated on the Earth's surface.

These four factors have three characteristics of exceptional biologic interest. First, the influence of these factors on biologic objects during space flight is continuous and practically unchanging. Second, terrestrial organisms throughout the entire history of their existence and evolution, have not encountered these influences. Third, exposure to these actions does not cause immediate death of the organisms, which permits varied and accurate quantitative experiments. Thus, the nature and properties of the basic environmental factors during space flight open a unique experimental approach to study cardinal questions of biological science: the role of gravitation in the appearance of life and realization of vital processes, determination of ontogenesis, and the autogenic nature of biologic evolution.

[1] Translation of, Biologicheskaya indikatsiya novykh kosmicheskikh trass (Vol. II, Part 5, Chapter 3, 90 pp., *Osnovy Kosmicheskoy Biologii i Meditsiny (Foundations of Space Biology and Medicine)*. Academy of Sciences USSR, Moscow, 1972.

Serious development of these problems is a matter for the future. The experiments conducted previously have dealt with more limited, although equally serious problems. Experimental biologic investigations in the upper layers of the atmosphere and in space have been conducted for more than 35 years, but the goals of these investigations have changed repeatedly with the appearance of new problems confronting science and mankind and, proportionately, with the increase in knowledge of space environment as well as in connection with practical requirements of conquering space.

Biologic investigations in space are divided into three distinct periods, according to which task is given priority. The third period of investigation is drawing to a close, and a new, fourth period is beginning. The first three periods could be examined within the framework of the problem of biologic guidelines for study of space. However, the nature and tasks of the fourth period are significantly more complex, which show that the earlier exploratory problems of biologic guidelines are outdated, their various aspects diverging into independent branches of space biology.

EVOLUTION OF GOALS AND METHODS IN BIOLOGIC GUIDELINES FOR SPACE RESEARCH

The first period of biologic investigation lasted from the early 1930s to approximately the late 1940s. These investigations were brought about and stimulated by two new scientific discoveries: ionizing radiation of cosmic origin on the surface of the Earth, and evidence of mutagenic activity of ionizing radiation. A hypothesis made in comparing these discoveries was that spontaneous mutations in living organisms are, in fact, not spontaneous, but result from exposure to natural ionizing radiation, which, consequently, must be a most important factor in biologic evolution. Investigations of the first period were not more than an experimental verification of this hypothesis and were carried out to explain the effect of cosmic ionizing rádiation on the evolutionary process.

The problem attracted the attention of many distinguished biologists, including Kol'tsov, Timofeyev-Ressovskiy, Nadson, Friesen, Müller, and others. Investigations in this field conducted on the Earth's surface yielded poor results. The questions concerning the genetic and evolutionary significance of cosmic rays were expected to be solved if experimental biologic material could be placed on the peaks of high mountains and on balloons ascending into the stratosphere. Such proposals were specifically expressed by Kol'tsov, Nadson, and Müller at the first All-Union Conference on the Study of the Stratosphere, held in 1934. Their hypotheses and investigations were supported by Korolev, a conference participant, who, throughout his life, devoted a great deal of attention to biologic studies in space.

The experiments were conducted on mice and certain species of arthropods, including *Drosophila*, on higher and lower plants, microorganisms, and cell cultures of mammalism tissues. The culminating point of the investigations of the first period was the genetic experiments conducted aboard the stratospheric balloons SSSR–1, BIS and Explorer 2, USA. The results proved negative as were the results of the majority of the other experiments. It was believed that cosmic radiation could not significantly influence the processes of biologic evolution, inasmuch as the mutagenic effects were not great. Later, however, this conclusion was reexamined, since the results of earlier experiments had been extrapolated without taking into account the period of maturation of embryonic cells and duration of the reproductive period. It is now generally accepted that in biologic species with a reproductive period measured in decades, a significant part of the mutations that accumulate in embryonic cells in a generation are caused by natural ionizing radiation. Man, of course, is one of these species.

These earlier experiments had great significance even though the results were negative. They attracted attention to the relationship between duration of the reproductive period and the magnitude of mutation load. There was also improvement in the concept about the nature of spontaneous mutations. Finally, experience accumulated in the autonomic exposure of biologic material in the upper layers of the atmosphere turned out to be exceptionally useful.

In the second period of biologic investigations in space, from the 1940s to the 1950s, attention was directed primarily toward an explanation of the biologic effectiveness of primary cosmic rays. Interest in the problem arose in connection with the gradual increase in the flight ceiling of aircraft and the anticipated appearance of satellites. Experiments were conducted with biologic objects placed in aircraft, balloons, ballistic rockets, and the first satellites. However, exposure was mainly achieved by placing test objects in balloons, the flight altitude of which had by that time reached 20–30 km, i.e., the upper boundaries of penetration of the heavy particles of primary cosmic rays. Furthermore, the flight duration of balloons and, consequently, the exposure time of experimental biologic material, had been increased to approximately 1 day.

The intensity of the experimental investigations increased significantly in the second period. Experiments were conducted on mice, hamsters, rats, guinea pigs, rabbits, cats, dogs, and primates. Numerous arthropod species were also studied, as well as a great number of higher and lower plants, bacteria, and viruses.

The specific nature of the tasks required the participation of many physicists—specialists in the interaction of high-energy particles. New methods of investigation had to be developed and used with the common, classical genetic and cytologic methods of analysis. In particular, the cytologic method was widely employed to record tracks left by heavy particles in nerve tissue, retinas, skin, and other mammalian tissues, following flights into the upper layers of the atmosphere.

Another method was to expose certain biologic materials in balloons—mammalian tissue cultures, arthropod eggs, seeds of higher plants—together with self-contained physical cosmic-radiation dosimeters, photoemulsions, and films. With this method, biologic objects were either impregnated with special photoemulsions or placed on sensitive film. This allowed simultaneous recording of the same cosmic-radiation particles passing through the physical and biological systems, determination of the type of particles passing through, and determination of the biologic effect evoked by them. Thus, a clear relationship was established between the two.

A method of calculating depigmented hairs in mammals proved quite useful for estimating the biologic action of primary cosmic radiation; this effect was produced by ionizing particles passing through the hair follicles. Inasmuch as the mechanism of pigment formation in hair is quite well-known, a conclusion could be formed concerning the number of cells which could be disrupted by one heavy particle of cosmic radiation.

The use of so-called phantoms had certain significance for determining the absorbed doses of cosmic radiation. Investigations with phantoms revealed an exponential decrease in the frequency of tracks left by heavy particles proportionate to the increase in the depth of the atmosphere.

Strictly speaking, the goals sought in the second period of biologic investigations in space were not achieved, and the corresponding tasks remained unfulfilled. The reason was not because the volume of investigations and methods used were inadequate or conducted in an unqualified manner. The explanation is found elsewhere. The goals simply could not be achieved; because with the inadequacy of scientific data in the more fundamental fields of knowledge, they had been incorrectly formulated. Recognition of this situation is one of the most important results of the investigations. However, this was not the only benefit. Frequently, in the history of science, investigations conducted in a purely applied field yielding results of no practical significance have made important contributions to theory and components of a more general scientific discipline. Thus, these investigations provided a better understanding of the effects of differences in linear energy losses of ionizing particles during their passage through living tissues. It was also possible to refine general concepts concerning the biologic action of ionizing radiations.

It became obvious that during a comparatively short stay in space, cosmic ionizing radiation cannot evoke biologic effects either in populations of embryonic cells of the organism or in populations of their somatic cells to an extent comparable with any standard radiation source with irradiation given in a single dose. Moreover, the biologic effects of cosmic radiation cannot be compared with x-ray or γ-ray irradiation in any significant dose range, without which, of course, relative biologic effectiveness cannot be determined.

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Cosmic radiation acting on individual cells causes changes that are different in character from those following exposure, for example, to γ-rays. However, in the organism as a whole, which consists of many billions of cells, and even more so in a population of organisms, the genetic effect of cosmic radiation during a comparatively short term in space cannot be detected since it is lower than the mutation level of noise.

The goal of the investigation, in the comparative study of the biologic effects of cosmic radiation, should consist in setting up standard genetic parameters in the populations of cells and organisms that would exist for a long period in an increased radiation background created by primary cosmic radiation. The time has not yet arrived for an experimental study of this problem; the technical capabilities for setting up the corresponding tests do not exist, and the processes within populations of organisms located in an increased radiation background created in laboratories and "terrestrial" types of ionizing radiation are far from fully known.

The third period of biologic investigations began in the early 1960s with the event of recoverable satellites. The basic goal was to study the effect of the state of weightlessness, both by itself and in combination with other outer-space and spaceflight factors, on the hereditary structures of the somatic and embryonic cells of various organisms. Experiments in this period, as well as those previously, were conducted on organisms of various taxonomic classification—from viruses to primates. Understandably, emphasis was on the study of the smaller and, consequently, lower species. A great many scientists, among whom were the most important contemporary biologists, participated enthusiastically.

An important scientific achievement of this period was establishing that the state of weightlessness does not, of itself, possess any mutagenic activity, and is not a mutagenic agent, at least in regard to genetic and chromosomal mutations. The practical and general significance of this discovery is: it became clear that mutations can be caused only by those agents in which the energy quanta or fluctuations are in the same order of magnitude as the levels of molecular energetic bonds. This view is now so obvious that it seems experimental verification should not have been required, although actually, its self-evidence is the basic result of experiments.

It was further demonstrated that, although weightlessness does not induce mutations, its action is not neutral for the ultimate frequency of mutations. This pertains primarily to mutations which appear because of double-hit or more complex mechanisms, inasmuch as weightlessness can affect the behavior of chromosomes in the intermediate stages between the occurrence of chromosomal breakage and fixation of mutations.

Interest increased during this period in study of the effect of an increased gravitational field upon the genetic mechanisms of cells and organisms. Corresponding experiments on numerous organisms confirmed a previously established fact, that gravity in excess of 1 g does not induce mutations, but does modify the rate of radiation-induced and, in all probability, spontaneous mutations. The direction and magnitude of the modifying effect in this case can vary, depending upon the means and order of application of agents, type of mutations, species of cells, and structure of cellular population exposed to the action.

Thus, this curious fact was revealed: both an increase and a decrease in the force of normal gravity generally have similar effects on the genetic systems of the organisms. Primary mutations in both cases are not induced, and selection and realization of existing primary mutation damages have a different character than under ordinary conditions. This means that the normal spontaneous mutation rate of organisms on the Earth, at least regarding certain types of mutations, is determined by the magnitude of the gravity force as well as other factors. Change in the force of gravity will cause change in the spectrum and rate of mutations, and consequently in the direction and intensity of the evolutionary process. This concept must be taken into consideration when experimental problems are related to the existence of a population of organisms throughout the course of several generations in space flights or on planetary stations.

The significance of altered gravity in the appearance of genome mutations has not yet been conclusively decided, i.e., its effects on disruptions in the genetic material which lead to the formation of aneuploidy and polyploidy. Mutations of this type arise by an entirely different mechanism than do gene and chromosomal mutations. While the latter are related to intra- and intermolecular restructuring of the hereditary substance, the former appear as the result of abnormal mitosis. Inasmuch as cell division is an oriented process related to the direction of the force of gravity, it is entirely probable that a change in it would have an effect upon that process. There has not yet been any precise experimental proof in this regard, although certain data seem to indicate that such an effect takes place.

The third period of investigations is at present far from complete. The scientific problems of this period will be exhausted only after a universal theory has been developed which describes the effect of gravitational fields on elementary biologic structures. Further work needed in this field is obvious: study should be made of changes in biologic structures in various states, determined by their unique properties and external effects from the influence of gravitational fields of various intensities. Complex biologic experiments during space flights for this purpose should be combined with the equally useful, but more inexpensive and simple laboratory experiments.

Tasks confronting investigators at the beginning of the third period of investigations still are not fully solved, but a new stage in the conquest of space places new problems to the fore. Theoretical and even experimental development of these problems has already begun, which signifies the advance of biologic investigations in space to the next, fourth period.

In general outlines, such are the problems and history of biologic experiments in space. The basic factual material obtained by investigators during the development and growth of new fields of space research will be discussed. Studies on vertebrate animals will not be included which are considered in detail in chapters devoted to physiology and related questions. During the experiments, biologic material was exposed in balloons, rockets, and artificial Earth satellites. Since the means of exposure determines certain characteristic features of the experiments (altitude and duration of flight, complex of active factors), the experiments will be examined according to the means of exposing the material, although this will disrupt somewhat the chronology in the presentation. The data obtained on microorganisms, on higher plants, and finally with animals will be examined separately, to provide better systemization and convenience for discussion.

INVESTIGATIONS DURING FLIGHTS OF BALLOONS AND HIGH-ALTITUDE ROCKETS

Experiments on Microorganisms

The first space microbiologic investigation in space was in 1935 aboard the Explorer 2, USA aerostat which reached an altitude of 25 km, 286 m—a record for that time. The investigation focused on the influence of conditions practically equivalent to open space on the survival of microorganisms. Spores of seven species of fungi were used. The material was placed in small quartz tubes, both ends of which were sealed with cellulose wadding. The tubes were affixed outside of the aerostat. In the course of the 4-hour flight the spores were exposed to low temperature, light rays, ultraviolet rays, low barometric pressure, and cosmic radiation. The viability of the spores of five species following the flight did not change, while there was a high death rate for spores of *Clostridium sporogenes* [14, 112].

Sounding the upper layers of the atmosphere by balloons with biologic objects aboard was resumed at the end of the 1940s. By this time, the flight altitude of balloons had increased to 35 km, i.e., the upper boundary of penetration of primary heavy cosmic particles. The duration of balloon flights and the exposure time of the material increased to 1 day. The investigators did not note any genetic changes during the exposure of neurospores in balloons [20].

The results of sounding the lower radiation belt by a rocket containing the vegetative fungus *Neurospora crassa* in project NERV were unclear in many respects [17]; the rocket ascended vertically to an altitude of 1900 km and remained within the limits of the radiation belt for 26 min. Mutations observed in the experimental material were 200 times more than in the control. The mutants turned out to be auxotrophic in terms of amino acids, vitamins, and purine and pyrimidine bases.

Physiologic disorders that were noted included inability of a majority of the cells of the experimental series (97%) to grow in a minimal medium. Adding amino acids, vitamins, citrate, succinate, ketoglutarate or organic acids to the medium increased survival and germination of the cells to various extents (from 16% to 100%). The low percentage (3.2%) of surviving cells was only slightly related to exposure to the flight factors, but was caused, primarily, by the cells drying out prior to being placed in milliporous filters. The result of drying was that 4.4% of the control cells survived. Temperature in the capsule did not exceed 45° C. Information concerning the radiation situation was not included in the report.

Experiments on the influence of conditions similar to those of open space were conducted by Hotchin and coworkers during flights of two balloons and two high-altitude rockets [62]. They used the poliomyelitis virus, the phage TI virus, and spores of *Penicillium* sp. and *Bacillus subtilis*. The balloons rose to an altitude of 35 km, the flights continuing for approximately 6 h. The altitude of the rockets reached 160 km. Outboard exposure of biologic subjects located on the surface of milliporous filters was provided by a special device on the outsides of the balloons. Part of the material was in the open, and another portion was screened by aluminum foil of 38-μm, thickness. The microorganisms were carried on the balloons during flights for 90 min in one case and 120 min in another. External exposure of the material during the rocket flights lasted 206 and 143 s at altitudes of 60–124 km and 82–160 km, respectively. Results of these experiments confirmed Stevens' data concerning short-term exposure to outer-space environments: high vacuum, ultraviolet, and cosmic radiation, as well as great temperature fluctuations (from +24° C to −75° C), are not specific lethal factors in regard to microorganisms during comparatively short-term exposures.

Another scientist, Mitchell, studied the microflora of a television camera which had been taken to the Moon in April 1967 by the Surveyor 3 spacecraft and returned to the Earth in November 1969 with the crew of Apollo 12. He observed that cells of *Streptococcus mitis*, located on the Moon for 950 d, were capable of growth in a nutrient medium after their return to the Earth [4]. Kemmerer considers that high vacuum and low temperature on the Moon surface led to freeze-drying of the streptococci, which accounts for their survival.

Experiments on Plants

A long-term experiment with air-dried barley seeds was conducted during the flights of balloons from 1953 through 1958 [40]. The experiments were accompanied by a photoemulsion control, which made it possible to take into account the location where the heavy particles hit the embryos. In the four generations obtained from the test seeds, 8539 plants were analyzed. In the descendants of 25 seeds with central impact, the plants had a decreased number of earlets and grains in the ears compared with the controls. The descendants of three seeds with central impact of heavy particles, in which chlorophyll mutants were detected, are of particular interest. Colored mutants, checked for three generations, stably transmitted the new character. In 18 seeds, edgewise impact of heavy particles into the embryonic cells was recorded. Curiously, sterility of the grains struck by heavy particles increased less significantly than with passage of γ-ray quanta.

Radish seeds were also exposed several times in balloons [104]. The control variants were kept in a chamber above sea level in the same pressure, temperature, and humidity conditions which obtained during the flights. The primary cosmic radiation to which the radish seeds were exposed in flight for a total of 251 h at an altitude of 24 km did not affect the germination and energy of sprouting. No differences were found in the dry and moist weights of the mature plants.

Onion bulbs, corn, and mustard seeds were placed aboard ballistic rockets launched in the USA from 1958 through 1960. The experiments were concerned not only with the effect of cosmic radiation on these subjects, but also with the effects of vibration, acceleration, and weightlessness. The method of conducting these experiments and their results have not been reported in detail. However, there were no genetic effects found in these vegetables [116].

Experiments on Animals

The first experiment was performed on *Drosophila* as early as 1935. Male *Drosophila* of the normal Nal'chik strain were put aboard the USSR-1-BIS stratospheric balloon which ascended to an altitude of 15 900 m; they were analyzed following landing for recessive lethals in the sex chromosome. The differences in frequency of lethals between experimental and control groups were not statistically significant. On the basis of this experiment, Friesen concluded that the role of cosmic radiation of evolutionary processes on the Earth was insignificant [41]. A similar experiment on *Drosophila*, leading to similar conclusions, was also conducted during the Explorer 2, USA, balloon flight [14, 64a].

Significant balloon launchings were carried out in the US, 1951–58, under Skyhook, Man-High, and Stratolab projects. A basic goal of investigations during these balloon flights was to study the biologic effectiveness of the heavy component of primary cosmic radiation. The cytotopologic method of investigation was employed; experimenters counted the number of tracks left by heavy particles in tissue sections of mammals which were carried alive in the flights. Nerve tissue, skin, and retina were primarily the objects of analysis, and mice, hamsters, rats, rabbits, guinea pigs, and cats were used [101, 102, 103, 104, 110, 111]. A significant number of experiments was conducted, although many flights concluded unsuccessfully. However, not in a single case was it possible to estimate successfully the effectiveness of cosmic radiation or detect its influence on the tissues. The authors concluded that the selected method was inadequate for studying the biologic effectiveness of cosmic radiation.

Mammalian and human tissues in vitro (usually skin tissue) were frequently exposed in the balloons. Usually there was parallel topical recording of the effect of cosmic radiation by the use of photoemulsions, which were saturated with transplants according to a method developed by Eugster and Schaefer [37, 93]. In certain cases, the skin transplants grew after regrafting to the donors. Skin transplants saturated with a photoemulsion proved an adequate method for recording the number of cosmic-radiation particles passing through them. However, the specificity of the biologic effect of the heavy component of cosmic radiation remained unexplained. In a number of experiments the observed effect was difficult to explain. Eugster, who placed the experimental material aboard a balloon and the control material in a tunnel or on a peak of Jungfrau, noted a stimulative effect of the flights on the cellular activity of the transplants [38, 39, 40].

The investigators who conducted the balloon experiments considered the most successful method that of recording depigmented hair in black mice which was developed by Chase. With this method, a difference was noted in every case between the experiment and the control [18, 19, 39]. Chase, taking into account the character of the effect and the cellular mechanism for pigment formation, considers that one heavy particle can disrupt as many as 50 or more cells. However, a certain number of depigmented hairs is always found in black mice, and with age, this number increases. Chase considers that the data obtained are in need of further verification and confirmation.

The eggs of the dwarf shrimp *Artemia salina* were used in many of the flights, with the viability of the eggs taken into account. In many cases, the experiments were accompanied by a photoemulsive control [37, 102, 103, 110, 111]. Death of the eggs was noted consistently as the result of direct hits of heavy particles of cosmic radiation. The results in one of the experiments were: following the flight (28–30 km), 100% of the eggs were dead; in the control kept underground (Simplon tunnel)—91%; and in the control kept on the Earth's surface—4%. Considering these data, it is difficult to agree that a significant fraction of the effect was caused by exposure to cosmic radiation.

Unprotected insect eggs were exposed at an altitude of approximately 15 km. The eggs of *Prodenia ornilhogalli* died, as is theorized, from cold. At the same time, the eggs of *Malacosoma americanum* survived [114]. In houseflies and fleas which were kept in the gondola of a balloon, no biological changes were noted after landing [113].

Pipkin and Sullivan [88], in 1959, proceeding from Müller's idea that the heavy component of cosmic radiation should cause chromosomal rather than genic mutations, used 10 761 larvae of

Drosophila in a corresponding experiment aboard a balloon. The flight lasted 16 h at an altitude of 24 km. The method made possible an alternating count of genic and chromosomal mutations arising from the identical genetic system. There were no differences with regard to both types of mutations. The authors, however, consider it possible that those chromosomal mutations which caused death of the larvae, were thereby eliminated from the count.

Male *Drosophila* were kept for 12 h at an altitude of 30 km in another experiment [90], and the dose of cosmic radiation was 0.25 mrad. The frequency of recessive lethals in the experimental flies did not increase in a statistically reliable manner and translocations were not detected; at the same time, induced frequency of dominant lethals was approximately 10%. The effect disappeared after 9 d, i.e., when the spermatogonia began to be exhausted. It is necessary to note that following the flight the male flies bred individually and copulations were recorded. However, it is difficult to concur that dominant lethals appeared under the influences of cosmic radiation.

An experiment with live mammals aboard ballons, in which genetic methods of investigation were employed, yielded a negative result [71]. Mice (35 females and 54 males) were in flight for 24 h at an altitude of 24–33 km. No differences between the experiment and control were detected with regard to fertility, fecundity, gonad cytology, cyclicity of gametogenesis, and life span.

When biologic experiments were conducted aboard balloons, emphasis was on the study of the effects of cosmic radiation, primarily by genetic methods. The effect, as a rule, was insignificant in its absolute expression, if there was any effect at all, independent of whether or not statistically reliable or unreliable differences existed between the experiment and the control. Thus, it was established that biologic and, specifically, genetic danger is absent during flights in the upper layers of the atmosphere, only when not dealing with extremely large populations.

Dosimetry of cosmic radiation using biologic methods under these conditions is exceptionally complex, because its doses and the resolving power of the most modern methods of investigation are at approximately the same level. When conducting experiments, it is also very difficult to distinguish changes due to specific flight factors from those caused by nonspecific factors. The latter are caused, as a rule, by the differences in the conditions of maintaining the experimental and control series, or exposure of the experimental series for a certain time to uncontrollable conditions.

Significantly fewer biologic experiments with animals were conducted during rocket flights than aboard balloons. In these experiments, there was a certain shifting of the center of emphasis of the investigations. A great deal of significance was acquired by the influence of other factors, in addition to cosmic radiation, which accompany rocket flight: vibration, acceleration, and weightlessness.

Launchings were made in the US, 1946–52, of the V–2 and Aerobee rockets with *Drosophila*, mice, and monkeys on board. Most of these launchings, however, from the viewpoint of biologic investigations, concluded unsuccessfully and the objects perished. Rocket flights with animals aboard continued, 1953–57 [60], but investigations with regard to biologic indication were seldom conducted during this period. The chief goals of the launchings were to develop hygienic requirements and to check life-support systems.

An experiment with the flour beetle, *Tribolium castaneum*, yielded negative results [106, 107]. The rocket was in flight 30 minutes and reached an altitude of 85 km. Viability of specimens in various stages from eggs to imagoes was unchanged. The increase in number of mutations was statistically insignificant; however, some of the mutations obtained were previously described.

The launching of US ballistic rockets with mice and monkeys aboard continued from 1958 to 1960. Egg cells and sperm cells of sea urchin and *Drosophila*, in addition to mammals, were included in a number of flights [3, 116, 120]. No significant genetic changes in the experimental objects were detected. There was, however, decrease in the viability of fertilized sea urchin eggs, but this result proved to be an artifact [120].

INVESTIGATIONS ABOARD SATELLITES AND OTHER SPACECRAFT

The number of genetic investigations in space increased rapidly with the development of satellites. The first such object, the second Soviet spacecraft-satellite, could be compared to Noah's ark. It carried 26 species of animals, plants, and microorganisms aboard, and many species were represented by several lines or strains. Particular attention was paid to the study of weightlessness and the search for indicators of the biologic risk in the complex of spaceflight factors in manned spacecraft.

Experiments on Microorganisms

Opinions concerning radiation background and influence of the complex of spaceflight factors have been based on tests. Results that were utilized included: postflight survival of microbial cells, spores, virus or phage particles; occurrence of mutations; level of phagoproduction in lysogenic bacteria; and change in the morphologic and physiologic-biochemical characters of the microorganisms. The experimental material exposed aboard satellites was in the form of cellular, spore, or phagous liquid suspensions sealed in glass ampules, and in sealed containers on the surface of milliporous filters or agar plates.

Lysogenic Strains

The most comprehensive investigations were conducted by induction of the prophage λ in the lysogenic strain *Escherichia coli* K–12 (λ). This strain is a convenient biological model which permits detection of small doses of radiation. Doses of less than 1 rad induce a detectable disintegration of the prophage from the bacterial chromosome; therefore, the lysogenic strain of the intestinal bacillus *E. coli* strain was used more frequently than other microorganisms. The bacteria were exposed aboard 12 spacecraft with flight durations varying from 1.5 hours to 3 weeks. When flight continued longer than 1 day, a slight but statistically significant increase was noted in phagoproduction in the experimental material. However, correlation between the magnitude of the effect and duration of spaceflight was not established, which is evident in Table 1.

The effect was higher in those experiments where it was recorded, than might be expected from the influence of cosmic radiation at the doses measured during the flights, and according to the character of the dose-effect relationship.

TABLE 1.—*The Effect of Spaceflight Factors on Phagoproduction of* E. coli K–12 (λ)

Spacecraft		Flight time (h)	Measured radiation dose (mrad)	Degree of induced phagoproduction	Literature sources
Spacecraft satellite	2	26	10	Did not exceed spontaneous level in the control	[126, 127, 128]
	4	1.5	—		
	5	1.5	—		
Vostok	1	1.5	0.6	1.0	[92, 123, 125, 129, 130, 131, 132]
	2	25	1.3	1.2	
	3	94	64	4.6	
	4	71	48	1.8	
	5	119	75	3.6	
	6	71	48	1.7	
Voskhod	1	24	75	1.2	[122]
	2	26	65	1.2	
Cosmos	110	22 d	36 rad	2.3	[121]
Zond	5	6.5 d	2 rad	1.9	[120]
	7	6.5 d	2 rad	2.0	

This effect was not considered an artifact, but to have been caused by the complex effect of cosmic radiation and other flight factors. In special laboratory investigations it was demonstrated that vibration itself does not induce phagoproduction, but on the contrary, inhibits it. At the same time, vibration increases the sensitivity of lysogenic bacteria to radiation. Therefore, the conclusion concerning the complex effect of spaceflight factors on lysogenic bacteria seems quite logical, but no hypothesis for explaining the mechanisms of this effect is proposed.

The use of radioprotectors β-mercaptopropylamine and cystamine, which block spontaneous phagoproduction in *E. coli*, significantly decreased induced phagoproduction in the flight series without affecting viability of the bacteria [92]. The flights of Zonds 5 and 7 did not affect the synthesis level of β-galactosidase in the intestinal bacteria; however, in the medium in which the experimental cultures were grown, a slight increase of colicin and disintegration of the sex factor from the bacterial chromosome were noted. Disintegration of the sex factor and auxotrophic mutations were also studied after the flight of Cosmos 368. No significant differences were found between the experiment and the control, relative to these indicators [72].

Experiments were conducted by Zhukov-Verezhnikov and coworkers in addition to a study of phagoproduction in *E. coli* K–12 (λ), with *Aerobacter aerogenes* 1321, *E. coli* B, *Staphylococcus aureus* 0–15, and *Clostridium butyricum* aboard both the second spacecraft-satellite and Vostok 1 and 2 spacecraft [124, 126, 127, 128, 130]. *C. butyricum*, in addition to spore suspensions, was exposed aboard the second spacecraft-satellite in bioelements especially adapted for growing microorganisms in flight. When the bacteria were seeded onto the nutrient medium during the space flights, no changes in their vital activity were observed. The viability and activity of the bacteria were evaluated according to the intensity of gas formation. Information regarding this was relayed to the Earth by telemetry. After the flight, the culture of fermenting bacteria did not differ from the control series either morphologically or biochemico-physiologically.

On these satellites, no effect of flight factors was observed with regard to the viability of 1321 and T–2 phage particles. Similar results were obtained after exposure of the tobacco mosaic and influenza viruses aboard the second spacecraft-satellite [59].

The frequency of appearance of biochemical mutations in *E. coli* following flights aboard satellites did not change. At the same time, space flights induced dissociative forms which differed from the original bacteria with respect to colony morphology, increased mutability, and biochemical properties [68]. An attempt to induce dissociative transitions and auxotrophic mutants in *Bacillus brevis* spores exposed during the Voskhod 1 flight yielded negative results [87].

Analysis of a large volume of experimental material did not reveal any effects of spaceflight factors on natural microflora in the cabins and in Apollo 7–11 manned spacecraft. The microorganisms taken for study from various locations in the cabin, from cosmonauts' body surfaces, and from their waste products did not differ morphologically or physiologically from the control variants [12].

During the flights of the Gemini satellites, experiments (which were a continuation of earlier investigations carried out on balloons and rockets [61, 63]) were conducted on survival of DNA and RNA viruses in several species of microorganisms. These experiments confirmed that the space environment is not a specific lethal factor for terrestrial microorganisms.

Algal and Fungal Strains

During the flight of Vostok 2, a significant portion (up to 50%) of yeast haploid cells died in those cells sensitized with low concentrations of oleic acid. The flight had no effect on the diploid or the nonsensitized haploid cells [70]. This test was repeated during the flight of Voskhod 1. The result for the diploid cells was completely confirmed, whereas with the haploid cells the results were contradictory: in one experimental series the effect occurred and in another, it was absent.

The results of the yeast experiments were remarkable in two respects: they demonstrated that sensitizing biologic objects can be useful in increasing the decisiveness of tests, and that additional difficulties are created when analyzing the effect which has appeared.

In three space flights (2, 3, and 5 spacecraft-satellites), the survival of spores and certain characteristics of mycelium growth were studied in four strains of actinomycetes. The second spacecraft-satellite carried *Actinomyces streptomycini* Kras λ and −3, and *A. erythreus*, strains 2577 and 8594. The spores of strain 2577 contain large nuclear elements and are resistant to ultraviolet radiation. The spores of strain 8594 have small nuclear structures and are sensitive to ultraviolet radiation. Survival of the spores increased 6 times in the radio-resistant spores, but decreased 12 times in the radiosensitive strain. Spores of *A. aurantiacus* LSB–2201 were placed aboard the fourth and fifth spacecraft-satellites. In both experiments, 76% death of the spores was recorded. Clear stimulation of the growth of mycelia was observed in all strains studied, after termination of the flight. There were no clonal-morphologic changes [52, 67].

No significant influence of flight factors was found aboard the second spacecraft-satellite, with regard to changes in basic physiologic processes in *Chlorella:* growth, development, and photosynthetic activity. Immediately after the return of the specimens to Earth, a significant number of destroyed cells and decrease in photosynthesis were observed. However, after undergoing 6 days of culture under ordinary laboratory conditions, the experimental variants did not differ from the controls [94].

A detailed genetic study of *Chlorella* exposed to space flight was conducted by Shevchenko et al [98] during flights of Cosmos 109 and 110 [98]. Survival of cells, frequency of mutations, and processes of sporulation were studied. The space flight did not influence the parameters under study. For example, aboard Cosmos 110 the survival rate of cells of the strain LARG–5 was $97.0 \pm 1.4\%$, and in the control, $89.0 \pm 1.53\%$. The frequency of mutations was, respectively, 0.25 ± 0.06 and 0.25 ± 0.09. The results of the experiments in both flights coincided, even though the dose of radiation aboard Cosmos 109 was several times smaller than that aboard Cosmos 110.

In the study of sporulation, no differences were detected between the experiment and the control in strain LARG–1. In the remaining four strains, a delay in the first mitosis was observed; however, toward the end of the second sporulation this physiologic effect vanished and sporulation was not delayed in any of the strains. The conclusion was that prolonged exposure to spaceflight factors does not cause significant changes in the vital activity and mutation process in strains of *Chlorella* studied.

Similar conclusions were reached by Vaulin et al after the same tests on strains LARG–1, LARG–2, and LARG–3 of *Chlorella* during the flight of Cosmos 110 [117]. These strains of *Chlorella* were also used in experiments during flights of Zonds 5, 6, and 7 and Soyuz 5. The Zond 5 flight caused significant decrease in viability of cells, increase in mutability, and stimulated anomalies in sporulation. The results of the Zonds 6 and 7 experiments were quite contradictory. Aboard Zond 6 a statistically significant decrease in survival of cells was observed (91.9 ± 0.07 in the control and 80.2 ± 1.78 in the experiment). The mutability of cells did not change. The flight of Zond 7 did not affect the survival of the cells, but had an antimutagenic effect (0.82 ± 0.11 in the control and 0.57 ± 0.06 in the experiment) [2, 118]. The reason for these contradictions in the experimental data is not clear so far.

In *Chlorella* experiments aboard Discoverer 17 [16], differences in cell survival of the experimental and control series were not detected. The reproduction rate and the mutation process also were unchanged. This satellite also carried spores of *Clostridium sporogenes.* The experimental spores responded poorly to incubation in a warm solution of caramelized sugar. Their survival was approximately 3%; decreased survival of nonincubated spores was also noted.

Spores of both *Clostridium sporogenes* and *Neurospora* were studied aboard Discoverer 18. The effect of incubation in caramelized glucose was significantly weaker (survival 88%). The flight of Discoverer 17, however, occurred during a solar flare, and the biologic objects were subjected to a dose of 20–33 rad, basically protons.

These microbiologic experiments in space, conducted according to the practical requirements of astronautics, sought to explain the effect of cosmic radiation and weightlessness on living organisms. The results demonstrated that flight conditions do not cause any serious changes at the cellular level. The data obtained in the microbiologic experiments, together with those of experiments on higher plants and animals, guaranteed man's safety during space flights in the orbits investigated. Although these microbiologic investigations were useful for the goals of astronautics, their theoretical value is significantly less. The investigations did not answer, and indeed could not answer, questions of how weightlessness and flight factors affect metabolism, mitosis, growth of microbe populations, induction of mutations, and so forth, because of inability to employ adequate methods of investigation. When corresponding techniques were used, because of uncontrolled conditions in conducting the experiments, results were obtained which could not be duplicated. In a number of experiments, the means of exposing the material did not permit determination of the effects which appeared; the experimental variants were under conditions which excluded an active physiologic state and normal metabolism of the cells.

Microbial Populations

The use of normally metabolizing microbe populations in space investigations would significantly increase the value of the experiments by making it possible to study the true reactions of the microorganisms. An experiment which answered this requirement to a significant degree was conducted aboard the Biosatellite II where cultures of amoebae, infusoria, bacteria, and neurospores were exposed. The experiments were conducted so that the organisms were in a physiologically active state for 44 h 54 min of the space flight; they metabolized normally, grew, and reproduced in the nutrient media. A source of γ-rays emitted by strontium 85 made it possible to study individually the biologic effect of weightlessness together with various doses of radiation.

In an experiment with bacteria, lysogenic strains of *E. coli* C600λ/λ and *Salmonella typhimurium* BS-5 (P-22) were used [75]. Both strains do not adsorb "their own" phages and differ in their rate of growth and frequency of prophage induction. An important feature of these experiments was that the analysis was performed on the descendants of bacterial cells which had undergone several divisions during orbital flight and were several generations removed from the stress effects of the launch. The descent process was not reflected since the cells were in a steady growth phase when tested. The effects were evaluated by these criteria: (1) growth of the bacteria—number of viable cells, (2) density of free bacteriophages, (3) formation of bacteriophages induced by viable cells, and (4) ultrastructure of the cells. Bacterial strains with differing rates of growth were useful methodologically; by the time of descent, the *Salmonella* culture had reached a steady phase of growth, while the culture of *E. coli* was in a stage of exponential growth.

The density of bacterial populations in the flight series was higher than that of the control series. The explanation was that the increased density resulted from an increase in growth rate of the bacteria in flight, as well as the effect of weightlessness which distributed the bacteria uniformly throughout the medium. Because of this, the nutrient substances were more completely and effectively used. An interesting observation is difficult to explain at present: density of the *Salmonella* populations of the flight series irradiated with 645 R was higher than that of the nonirradiated *Salmonella*. The increase in density of bacterial populations was linked partially with temperature conditions and partially with more effective restoration of cells damaged by radiation under conditions of weightlessness. Another explanation is that γ-irradiation induces radiation mutants which, under conditions of weightlessness, have a selective advantage over cells of the original strain. It is also possible that this is not induction of mutations, but rather physiologic stimulation, which leads to an increased growth rate of cells.

Ultrastructural study of the bacterial cells by electron microscopy did not reveal differences between the control and experimental series. Statistically significant data were obtained only for *Salmonella* with regard to induction of phagoproduction. The amount of free P-22 was lower both in the irradiated strains and in the nonirradiated experimental variants than in the control. This result indicates that spaceflight factors do not enhance induction of phagoproduction, but inhibit it. It is hypothesized that such inhibition is related to an increase in prophage repression. The observed effect can also be linked with destruction of certain processes during formation of the mature P–22 phage from the prophage.

Prophage Induction

The results of this experiment on the induction of prophage contradict data obtained by Zhukov-Verezhnikov et al. Possible reasons for this difference are that these results can be compared only arbitrarily, since they were obtained by different procedures. The Zhukov-Verezhnikov group used a method that was developed for actively metabolizing intestinal bacteria to determine the phagoproduction of lysogenic bacteria [73]. This procedure is very accurate and usually permits the induced effect of radiation in doses of 1 rad and even less to be determined. Since the experimental cultures were kept in sealed ampules from the moment of their removal from the laboratory until their return, under conditions permitting the lysis of the bacteria, the number of viable cells should have varied from experiment to experiment. This makes a comparison of results more difficult. Additionally, the procedure does not allow an exact count of the number of free phage particles, since the lysogenic strain used in the experiments adsorbs free phages; the adsorbed phage loses its infectious activity and cannot be counted. Determination of prophage induction only among the surviving cells cannot completely represent the effect of spaceflight factors on the degree of phagoproduction of the entire bacterial population, since in such a case the total phage output (i.e., number of free phage and phage particles produced by the viable bacteria) is not taken into account.

The special experiment with *E. coli* in the 2-day flight aboard Soyuz 12 was designed to explain the lack of correspondence in the results obtained by Zhukov-Verezhnikov and Mattoni. The microorganisms were contained in a special instrument which allowed active multiplication in conditions of weightlessness. The instrument was controlled by the cosmonauts; a button pressed at a set time opened a connection between the cultures of microorganisms and the sterile nutrient medium. Analysis showed that the number of bacterial cells increased by 4 to 5 orders during the experiment. The increase in the control, maintained under similar temperature conditions, was approximately the same. It was also established that weightlessness had practically no effect on the processes of genetic recombination, repair, and mutagenesis in the bacteria.

Phagoproduction of the lysogenic bacteria was higher in the test than in the control in approximately half the vessels. Disparities between the test and the control for some of the vessels were statistically significant when the materials were processed by traditional microbiologic methods. There were no differences when the material was pooled; and significantly, the individual vessels and the cultivation techniques were almost identical. Thus, phagoproduction on Earth and in conditions of weightlessness were the same. There are then no real differences between the results of Zhukov-Verezhnikov and Mattoni. The apparent differences were brought about by dissimilar procedures in the tests and by the fact that to evaluate the data from the "space" tests with microorganisms, it is necessary to increase substantially the criteria of statistical significance.

During the flight of Cosmos 605, vegetative fungi were used for the first time to analyze the action of weightlessness on living objects. Conidia of four fungi species were implanted on a solid nutrient medium where they reproduced during the flight. Differences were established between the test and the control: conidia of *Aspergillus* were contaminated in the control apparently through procedural errors, and not in the test. The test *Mucor* sporangia were half as large as the controls. More intensive spore formation was observed in the *Helminthosporium.* Micelia cushions in *Nyctalis* were five times larger in the test than in the control. At the same time, the dimensions of the fruiting bodies decreased 1.5 to 3 times, and in a number of cases, embryos of the fruiting bodies were formed. Weightlessness then apparently does not affect reproduction of vegetative fungi, but their morphogenesis under the force of gravity and in weightlessness are different. The relative simplicity of these fungi and their sensitivity to changes in gravity will clearly make them the "superstars" in future biologic investigations in space.

Chromosomal Aberrations

Although an increase in the phagoproduction of the experimental bacteria is statistically significant, the causes of the increase can vary because of spaceflight factors or conditions of storing and transporting the material, which frequently are not controllable. Experiments in space should be conducted in strictly controlled conditions to avoid confusion in comparing data obtained by various authors and from repeated experiments by one group of investigators. Another example is useful here. A group of US scientists in Gemini 3 and 11 spacecraft experiments obtained inconsistent results on the effect of weightlessness and radiation on cell cultures [1, 10, 11, 91, 93]. Leukocytes of human peripheral blood were exposed aboard Gemini 3 without irradiation and with β-irradiation in a dose up to 180 rad with 32 P decay. A postflight study of the frequency and type of chromosomal aberrations showed no differences in the frequency of multiple aberrations (rings, dicentrics) between the experiment and the control. The frequency of single-strike aberrations was almost two times higher in the irradiated flight series than in the controls. The conclusion was that there is a synergistic effect of radiation and weightlessness on the appearance of chromosomal aberrations. These experiments were repeated aboard Gemini 11; but the results were not the same. No differences were detected in frequency of chromosomal aberrations of all types between the experiment and control series.

Gemini 11 also carried spores of *Neurospora* aboard. A count was made postflight of inactivated spores, induced direct mutations, and the adenine locus [95, 96]. There were no differences between the irradiated and nonirradiated flight and control series. The conclusion indicated absence of the synergistic effect of radiation and weightlessness with regard to genic mutations, inactivation of spores in *Neurospora*, and chromosomal aberrations in the leukocyte culture [23].

A similar experiment with *Neurospora* conducted aboard Biosatellite II used heterokaryotic neurospores obtained from two different haploid strains that contained a series of genetic markers [97]. Survival of the vegetative spores and induction of recessive lethal mutations throughout the entire genome and in two adenine loci were studied. The effect of radiation on frequency of chromosome breakages and genic mutations was determined. In the laboratory and aboard Biosatellite II, spores were kept on the surface of moist filters in five special packages placed so that four received doses of radiation at 500, 1000, 2500, and 6000 rad. The spores in the fifth package were not irradiated. No differences were revealed in frequency of mutations in the nonirradiated material either on-board or in the laboratory. The low frequency of spontaneous mutations indicates absence of a mutagenic effect of weightlessness or of any other spaceflight factor. The radiation experiment demonstrated that the dose-effect curves for survival of heterokaryotypic conidia and curves for induction of recessive lethal mutations in specific loci were identical in the experiment and control. An analysis of the frequency of lethal mutations in the entire genome did not show differences between the irradiated flight series and the laboratory series. Hence, weightlessness itself does not have any mutagenic effect in *Neurospora*, and the radiation effects under conditions of weightlessness are the same as on Earth. The absence of differences in the frequency of recessive mutations (point mutations or chromosomal mitosis) and in the frequency and type of complementary reactions was confirmed at the molecular level in the spectrum of point mutations in the control and experimental variants.

The effect of weightlessness during the flight of Biosatellite II was studied also on the amoeba *Pelomyxa carolinensis* [36, 89]. The experiment did not reveal any differences in the rate of mitosis in the amoebae during or after flight. Nuclear mitosis in the state of weightlessness was synchronous, as in the control. Survival of the control and experimental series was identical.

The material obtained on microorganisms is difficult to interpret uniformly. However, most of the data seems to indicate that weightlessness does not significantly affect growth, development, cellular or nuclear mitosis, and mutagenesis in single-cell organisms, and that weightlessness also does not modify the radiation effect. This conclusion agrees with available hypotheses on the subject [108]. However, the results on the phagoproduction of lysogenic bacteria are clearly not subordinate to this conclusion.

Experiments on Plants

Effect on Dry Seeds

Most investigations on the effect of spaceflight factors on plants have been carried out with seeds. Seeds are convenient for this purpose because metabolic processes are greatly suppressed, and the nuclei in the cells of meristem tissue are predominantly at one developmental stage—interphase. Chromosomal aberrations appearing under the influence of this factor or any other are accumulated and maintained up to germination of the seed. Nuclear damage can be counted in the first mitotic fissions, which occur in various parts of the plant at a certain stage of germination.

Radiosensitivity

The selection of seeds particularly at the beginning of the investigations, took into account their radiation sensitivity, since cosmic radiation is one of the major factors that will affect the structure of the plant cell in flight. Thus, aboard spacecraft-satellites 2 and 5, and Vostok 1, air-dried seeds of two species were exposed which differed strongly in their radiosensitivity—the Welsh onion and *Nigella*. Sensitivity of the onion to x-rays is nine times greater than sensitivity of *Nigella*. With such differences, it was hoped that an accurate characterization of the biologic effectiveness of cosmic radiation could be made. However, a cytologic analysis of the chromosomal disorders in the cells of shoots did not reveal a difference between these species, and no differences were found between the experiment and the control [67, 100].

Seeds of several other plant species, also aboard these flights, have been well-studied genetically, and differ with regard to radiosensitivity [52, 67]. The seeds studied were two types each of peas and corn, and winter wheat. The percentage of chromosomal disorders increased in the rootlets of all five species. However, this increase was statistically significant only in winter wheat and γ-resistant peas. Multiple breakages were noted in certain cells of the pea which indicated chromosomal damage by a single heavy particle. The radiosensitivity of the plant organism could not be correlated successfully with the magnitude of the effect, but the pea seeds radioresistant to γ-rays showed a high percentage of chromosomal damage. It is improbable that there was no relationship between sensitivity to γ-rays and cosmic radiation. Rather, the dose of cosmic radiation to the seeds in flight was inadequate to reveal the differences.

Air-dried seeds of PPG–186 winter wheat and peas were again exposed on subsequent flights of Vostok 3 and 4 satellites [66, 99]. No statistically significant increase in the number of chromosomal restructurings was detected; however, after the Vostok 3 flight, a tendency toward an increase in aberrations was observed. The summary data on the pea and wheat seeds aboard all satellites up to, and including, Vostok 3 demonstrated a significant difference in vulnerability of the cell nucleus in comparison with the controls. For both species, there was no correlation between length of flight and presence of the genetic effect. The experimental and control material differed in the types of chromosomal reconstructions. In the experiment, restructurings of the chromosomal type predominated; while in the control, the chromatid type was dominant. The increase of chromosomal-type restructurings was linked to the effect of certain flight factors on the interphasic nuclei of the embryonic cells. Of the 14 other species and types of seeds aboard Vostok 3 (rice, onions, garden cress, mustard, pine, cabbage, radish, beans, tomatoes, carrot, lettuce, beets, wheat, peas), only the pine and bean seeds were cytologically analyzed [24, 54, 78]. The experimental groups in both species showed a tendency toward increased chromosomal aberrations.

A general predominance of chromosomal over chromatid reconstructions was also detected in all the experimental species on Vostok 5 and 6 satellites by means of cytologic analysis of anaphasic cells in the radicles of carrots, tomatoes, pine, beans, cucumbers, wheat, lettuce, and mustard [31]. In the controls, chromatid restructurings predominated over the chromosomal; a predominance of chromosomal recombinations over fragments was also noted. This experiment showed statistically significant differences between experiment and control, with regard to the number of damaged chromosomes, only in the carrots and tomatoes. Analysis of the seeds confirmed that the sensitivity of seeds to γ-rays does not coincide with sensitivity to spaceflight factors.

The results obtained here on genetic damage were similar to results that had been recorded in previous flights.

Air-dried seeds of the European spindle tree were also aboard the Vostok 5. Part of these were preirradiated with γ-rays of ^{60}Co at a dose of 10 curies [77]. In the series without preliminary irradiation, frequency of cells with abnormal mitoses differed significantly from the control. Preliminary irradiation of seeds did not alter the results of the spaceflight effect. Each factor made its own contribution to the total percent of chromosomal damage, i.e., their effect was additive. In the experiment with the spindle tree, pine, and wheat aboard Voskhod 2, no genetic effect was observed following their exposure in open space by cosmonaut A. Leonov.

Corn seeds were used during the flight of the Discoverer 32 satellite (27 h) and another US satellite (50 h) to evaluate the biologic effect of heavy particles of cosmic rays. These seeds were heterozygotic in regard to the factor which controls chlorophyll formation. A study was made of frequency of chlorophyll mutations in the somatic cells of the third and fourth leaves. Photoemulsion monitoring was used in this experiment. A slight but statistically reliable increase in frequency of mutations was noted which coincided with the result expected based on calculated data [23].

Seeds on Zond 4 and 6 automatic stations which circumnavigated the Moon were Odessa–17 barley in natural and induced dormancy and Moscow–122 barley seeds in both radiosensitive and radioresistant forms [64, 76]. The genetic effect of combined exposure to spaceflight factors and γ-irradiation depended on the irradiation dose and physiologic state of the material. Under the same conditions (normal dormancy of seeds, radioresistance), an additive character was observed as a result of exposure to two factors; and in the others (induced dormancy, radiosensitivity, low dose of irradiation), irradiation increased the effectiveness of spaceflight factors.

Following the flight aboard Zond 5, pea seeds previously stored for several years and with low germination capacity revealed the "revival" phenomenon which is a high survival rate of old seeds in the experimental series compared with the control [43]. This phenomenon was also detected in old pea seeds after their flight aboard Cosmos 110 [25, 45].

Mutagenic Sensitivity

Crepis seeds flown aboard one of the Soyuz spacecraft for 6 d showed a slight but statistically significant increase in damage of the nuclear structures [35]. Seeds processed with ethylenimine after the flight showed a higher mutagenic sensitivity than the control; the spectrum of mutations was displaced toward reconstitutions of the chromosomal type. Barley seeds flown aboard the same satellite showed increased chromosomal damage [42]. The increase was not the result of chromosomal-type restructurings, as noted in most investigations, but rather consisted of individual fragments, multiple breakages of the chromosomes, and exfoliation of the chromosomes.

According to Dubinin's analysis of the *Crepis* and barley seeds, the conditions of space flight per se do not alter the chromosomal structure; nevertheless they make possible the appearance of potential changes in the chromosomes and increase their sensitivity to the effect of another mutagenic factor.

Lettuce seeds, preirradiated with a 10-krad dose of γ-rays, which had various levels of spontaneous and induced mutagenesis, were sent up in the Cosmos 368 satellite. The unirradiated seeds with a low level of spontaneous mutation showed an accelerated mutation process as well as decreased mitotic activity of the fissioning cells. In the irradiated seeds, no differences with regard to this indicator were detected between the variants. Both the unirradiated and the irradiated seeds with a high level of spontaneous mutagenesis were more sensitive to the effect of spaceflight factors. The postradiation effect of spaceflight factors (Cosmos 368) did not have a modifying effect on radiation damage of the Kapital variety of pea seeds [115].

Data concerning nuclear damage in the shoots of the various types of seeds and species are contradictory. Damage of the genetic structures is found in some objects on board and not in others. Genetics effects noted in one flight frequency are not repeated in another; the reasons for this disagreement are difficult to explain at present. It is sometimes thought that the differences primarily are due to dissimilar original physiologic states of the seeds and, consequently, to dissimilar reactions to the spaceflight factors. Inaccuracies in methodology are also considered the reason.

As an example of this, the fixed material of the experiment and the control could be in different stages of primary mitoses, which would infer the observation of dissimilar material. The production of mutations in primary mitoses, proportional to the growth of radicles, changes after irradiation or during exposure to chemical mutagens. Therefore, it is important to evaluate chromosomal changes in shoots not fixed at the same time point in primary mitoses, but fixed throughout their entire cycle at certain time intervals. Not all species of seeds sent into space, however, have a determined duration of cellular cycle and its various phases, which is necessary for correct positioning of the material.

Cells in the dry seeds of various plant groups are usually at the interphase stage; however, seeds can differ in mitotic phases at this stage, and the appearance of restructurings of various types is determined by the chromosome structure in these phases. This is probably the reason for chromatid restructurings having been observed in some cases and chromosomal restructurings in others.

The correct understanding and interpretation of the results of the experiment require knowing how the natural mutation process occurs in seeds, and taking into account the influences of temperature, humidity, and growth. The natural mutation process was not studied in many of the species sent into orbit.

Effect on Processes of Growth and Development

An effect was noted on the processes of growth and development of plants during the exposure of air-dried seeds aboard satellites. This effect was found partially by accident, during an explanation of genetic effects, and through certain experiments for which this goal was specifically set. Stimulation of germinating capacity and energy of sprouting of seeds was detected during germination of the Welch onion and *Nigella* aboard spacecraft-satellite 2 and Vostok 1 [67, 100]. An especially clear effect was observed in radioresistant species of *Nigella*. The stimulating effect was not considered related to the effect of radiation (since it should have been more strongly pronounced in the radiosensitive onion), but rather it was related to the effect of some other flight factors, or, possibly a complex of such factors.

Similar results were obtained on peas and wheat aboard these same spacecraft [66, 67]. An increase in the sprouting energy of the pea seeds occurred without change in the mitotic index, while in wheat it occurred with a decrease in the mitotic index. In spacecraft-satellite 5 where generally there were no mitoses in the pea radicles, the sprouting energy was higher. Stimulation of the growing radicles is connected with cellular distention.

After Vostok 3, 4, 5, and 6 flights, strain PPG–186 wheat showed a tendency toward stimulated growth [54, 55]. After 10 days, wheat shoots sprouted their first leaves from coleoptiles, while in the control plants the leaves were still within the coleoptile. Following flight with another type of wheat—the Krasnozernaya or red-grain—aboard these same spacecraft, a suppression of sprouting energy and germination capacity was noted [64]. Phenologic observations on growth and development of plants during the vegetative period did not reveal significant differences between the experiment and the control.

In the investigations with seeds of the European spindle tree, a special task was to determine the reasons for postflight stimulation. Spindle tree seeds are distinguished by a special characteristic—they sprout slowly and with great difficulty; this characteristic was used to determine whether spaceflight conditions stimulate germination of seeds or hasten the shift from the dormant to active state. This interesting problem was not solved since the seeds did not sprout, and the experimenters had to use other means to force them to grow, which made analysis of the results difficult [77].

A broader analysis of the stimulating effect was conducted on onion bulbs flown aboard Cosmos 110 [29]. Sprouting of the experimental and control material was observed for 10 days after flight. Data were collected for germination, sprouting energy, number of chromosomal restructurings, mitotic index, and sizes of cells in various zones. In the experimental samples, sprouts appeared significantly earlier and their growth was more energetic. Cytologic investigations to explain the reasons for the stimulative effect did not yield convincing results. The percentage of chromosome damage was higher than in the control and the disorders were most frequent in the last days of sprouting, i.e., after passage of several cell generations.

Mutagenesis

The mechanism of long-term mutagenesis, discovered by Dubinin, is manifested here. Potential changes can occur during a long period through a series of DNA syntheses and appear after several cell generations. This type of potential change underlies the effect of alkylating mutagens and radiation.

Stimulative effect on the bulbs was also observed after other flights [43]. It did not depend upon flight duration or total dose of cosmic radiation; thus, it is concluded that the stimulative effect is not the result of exposure to radiation and weightlessness, but rather is related to other factors or a combination of spaceflight factors.

Growth and development stimulation in lettuce plants after being flown aboard Cosmos 110 led to a significant increase in productivity of the plants [5, 45]. The yield of green mass increased 50%, dry weight 15%, and vitamin C content 21%. Stimulation was also observed in bean seeds and in garlic bulbs aboard the same satellite. At the same time, in an experiment with cabbage leaves and radishes, reliable differences were not found in growth and development of the experimental and control plants, nor was there noticeable change in the quantity of dry matter. Doses of ionizing radiation aboard this spacecraft against a background of other flight factors proved adequate for stimulating the growth processes of radiosensitive garlic, onions, beans, and lettuce, but not for such radioresistant plants as cabbage and radish.

A pronounced stimulative effect on germination and sprouting energy of barley seeds was observed during the Voskhod 2 flight. In the control, 42.85% of the seeds germinated, and in the experiment, 68.57%. The experimental seeds sprouted significantly earlier than the control, and the growth of shoots was accelerated [76]. Sprouting wheat seeds, 65-hour-old coleoptiles, aboard the Biosatellite II were longer than those in the control [56], a difference thought to be related to accelerated growth of the experimental plants after return to Earth.

A tendency to increased germination capacity and sprouting energy in nonirradiated material was observed in the flight variants of lettuce seeds with a low level of natural mutagenesis aboard the Cosmos 368 satellite. In the irradiated seeds, growth processes were unchanged. In nonirradiated seeds with a high level of spontaneous mutagenesis, the flight variant showed a tendency to decreased sprouting energy and germination.

Thus, a stimulative effect observed following space flights in most of the plants was reflected in accelerated growth and development processes, and occasionally in increased yield. In certain cultures, only a tendency to stimulation was noted, while in several cases there was suppression. At present, it is not possible to know which flight factor causes stimulation, since the effect of each factor individually on the growth processes has not yet received adequate study.

Ionizing radiation causes stimulative effects after irradiation of seeds with low, as opposed to lethal doses of radiation; radiostimulative doses for various species of plants fluctuate from several hundreds to thousands of roentgens. These are fairly large doses, on the order of mrad and several rad, which living objects encounter during space flights. Thus, it is improbable that the stimulative effect is linked to cosmic radiation action. Nor is stimulation of growth correlated with flight duration and radiation dose; based on radiostimulation data, it is improbable that such doses in combination with other flight factors can cause stimulation of the growth processes. Possible incidental factors, such as temperature during flight and its change at certain stages of the flight, are agents affecting the growth processes.

Effect on Vegetating Plants

The effect of space flights has been studied on actively metabolizing plant organisms, in addition to dry seeds. One whole plant and several cut plants with racemes, *Tradescantia paludosa* and Sack's clone No. 5, were aboard various USSR spacecraft. Microspores of *Tradescantia*, widely used in radiation genetics, are convenient for investigating the effect of various agents on the cell nucleus. The first postmeiotic fission occurs over a long time, the duration of separate stages of the cell cycle having been well-studied. The cells of the anthers in a single bud mature relatively synchronously, and knowing the duration when the separate phases occur in the microspores simplifies determining which stage of the mitotic cycle has undergone exposure. Microspores contain three pairs of large, well-stained chromosomes suitable for cytologic analysis by both the anaphasic and metaphasic methods.

Cut stems with racemes of *Tradescantia* were placed aboard Vostok 3 and 4 spacecraft-satellites in special biocartridges. The first spacecraft was in flight for 4 d and the material was fixed 18 h after landing; the second was in flight 3 d and the racemes were fixed twice, prior to the spacecraft's descent from orbit and 48 h after landing. Counts of all types of chromosomal and chromatid restructurings in the metaphases and anatelophases (anaphase and beginning of telophase) in both experiments showed an increased percentage of restructurings compared with the control. A new type of aberration was also noted: spherical fragments which had not appeared either during exposure to ionizing radiation or chemical mutagens [6, 30]. The spherical fragments, the largest group of damage indicators, were found at all stages of the cell cycle. The spherical fragments were thought to result from breakage and isolation of parts of the chromatin in interphase or prophase during exposure to spaceflight factors. Complex chromosomal exchanges accompanied by this spherical fragmentation were also noted.

Mitotic Disorders

Five types of mitotic disorders, in addition to restructurings of chromosomes, were detected in the *Tradescantia* microspores. The primary disorders were nonseparation of chromosomes, 3- and 4-poled spindles, and changes in axial direction of the spindle.

Subsequent studies conducted on *Tradescantia* (Vostok 5 and 6, Voskhod, Cosmos 110) confirmed the earlier results (Vostok 3 and 4). Attention then turned to an explanation of which flight factors caused chromosomal restructurings, and which caused disorders of the mitotic mechanism, since quantitative differences between the first and the second were found after increased flight duration. For this purpose, cosmonaut V. Bykovskiy (Vostok 5) fixed portions of the material at timed intervals (1.5 h after launching, during flight, prior to descent). Material was fixed by cosmonaut B. Yegorov (Voskhod 1) prior to the spacecraft's descent and 2.4, 24, 48, and 120 h after landing [5, 26, 27, 28, 32]. Based on the data, it was hypothesized that chromosomal aberrations were caused by dynamic factors (vibrations and acceleration) and disruption of the mitotic mechanism by weightlessness.

One complete flowering plant was aboard Cosmos 110 satellite [5, 32]. In addition to the mitotic anomalies noted earlier, the cells were of abnormal size (some very small, some very large). The small cells, which did not exceed the dimensions of microspores, had separated during the collapse of the tetrad, and in many of them micronuclei could be seen. The giant cells had abnormal contours and contained one, two, or

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more nuclei. The photographs clearly show that the analyzed cells were not only in the postmeiotic stages, but also in various stages of meiosis. Frequency of chromosome restructurings did not differ noticeably from those recorded in prior flights, but the number of mitotic disorders was increased, and the number was greatest in that material in which the cells were in early interphase during the flight.

The microspores of *Tradescantia* plants aboard Zond 5 could not be analyzed due to the absence of buds suitable for investigation [43]. Cytologic examination of the cells of radicles in the fission zone did not reveal any differences from the control. Methodologic inaccuracies in the *Tradescantia* experiments and insufficiency of material for study in certain experiments complicated interpretation of the data. Thus, of 22 analyzed buds from two plants aboard Vostok 3 and 4, only one bud contained stages suitable for analysis of chromosomal disorders; however, the appearance of many forms of disorders, and not their numerical expression, was important. Absence of cytologic investigations of the cell stages in each bud preflight makes it impossible to link the observed disorders with a single mitotic cycle. Without such control, analysis of the results is complicated, especially after flights the duration of which exceeds the duration of the cell cycle.

Discussion of the data on material fixed at different intervals aboard Vostok 4 requires keeping in mind that the goal—differentiating the effect of dynamic factors from weightlessness—was not achieved by the first fixation. The active stage of the flight continued for several minutes, but the first fixation was conducted 1.5 h after launch. Consequently, the fixed material included microspores subjected to both the effects of dynamic factors and weightlessness. There was no complete isolation from the effects of other flight factors during either the second or third fixation. It is still too early to link the appearance of spherical fragments with dynamic factors, inasmuch as a disorder of this type was observed as an effect of increased temperatures on the dry seeds of *Crepis tectorium* [98]. The increased temperature at certain flight stages could affect the appearance of the indicated disorders in *Tradescantia* as well. Knepton experimentally vibrated *Tradescantia* microspores and found no spherical fragments [69]. Both temperature and vibration experiments on Earth must be set up and flight experiments must be conducted under strictly controlled conditions to discern the etiology of these disorders. Attention must also be given to the processes related to fixation of material in weightlessness. The complex combinations of physicochemical factors during the transition of the object from a state of normal gravitation to a state of weightlessness and during its stay in the weightless condition can significantly influence both the quantitative and qualitative characteristics of fixation.

Chromosome Aberrations

An important experiment on *T. paludosa* (clone 02–heterozygotic in raceme coloration) was conducted aboard the Biosatellite II [74, 109]. Plant cuttings with racemes were planted in a nutrient solution and placed in a container installed so that the buds were exposed to γ-radiation in a dose of 218 R, while the rootlets received doses from 125 to 285 R. Experimental and control plants were under a tungsten shield.

The basic goal was to determine the effect of weightlessness and other spaceflight factors on the frequency of spontaneous and radiation-induced chromosome aberrations and somatic mutations. The investigations demonstrated that the frequency of somatic mutations on the whole was not influenced by spaceflight factors, but in one case (a mutant with staminal hairs of a rose color) a statistically significant decrease in expression of the character was obtained, and in irradiated on-board objects a higher percentage of abortive pollen and stunted hair growth was found, indicating an increased effect of radiation during its interaction with weightlessness. Microspores were removed from the same buds both before and after flight to study their rate of development in flight. The results proved basically inconclusive due to the high percentage of microspore death in both flight groups. In the microspores at various stages of mitotic division or immediately following its completion, "ejection" of the Feulgen-positive chromatin into the cytoplasm was observed, possibly the result of nuclear membrane rupture. This effect could be linked to vibration, although weightlessness could play a part as well.

Data relative to the *Tradescantia* radicles show an absence of significant differences in frequency of chromosomal aberrations between the material in flight and the material on the Earth, both with and without irradiation. In all flight groups, disorders were observed in the function of the spindle (multinucleated cells and cells with an incorrect shape).

Such effects were not detected on Earth either during exposure to radiation or during rotation in the clinostat, so that a relationship between mitotic disorders and weightlessness was cautiously proposed. The possibility is not excluded, however, that spindle disorders can be linked with an increase in the effect of colchicine caused by spaceflight factors; this substance is used prior to fixing the rootlets.

During a study of the effect of weightlessness on the growth, morphology, biochemistry, and histochemistry of wheat shoots which had been aboard Biosatellite II, cytologic investigations were also conducted on the rootlet cells and the leaf coleoptiles. No differences were found between the experimental and control plants in the nuclear structure of the cells, and no mitotic disorders were recorded [21, 22].

These are the basic results of experiments with plants, a large number of which were conducted as biologic indication for space regions. Certain experiments could be assigned arbitrarily to this category with stipulations, because of a more concrete goal; however, these experiments were mentioned in the survey and discussion of the results in the interests of a complete presentation. The setting up of plant experiments had a more specific goal than a simple biologic indication of new space regions in that the work accomplished permitted accumulation of source material for certain branches of space botany. The results of the experiments could be characterized as contradictory and irreproducible. Nevertheless, they have a positive value, since in the absence of stable effects significant in character or in absolute magnitude, they provide additional evidence for conclusions concerning the safety of man during a comparatively short stay in weightlessness in the presence of irradiation by small doses of cosmic radiation.

Experiments on Animals

Tests on *Drosophila* in the Soviet satellite flights were widely used. The frequency of recessive lethal mutations in the sex chromosomes of the males was determined during flights of the second, fourth, and fifth spacecraft, Vostok 1, 2, 3, and 4, Voskhod 1, and Zond 5 [46, 47, 48, 49, 50, 51]. The experiments were usually conducted on two lines of *D. melanogaster* of both the highly mutable and mutation-resistant varieties. Where possible, the embryonic cells at the stage of mature sperm and spermatids were analyzed separately. A statistically significant increase in the frequency of recessive lethals was noted in three experiments—aboard the second and fourth spacecraft, and Vostok 1. A statistically reliable effect was absent in the other experiments. No correlation between flight duration and magnitude or presence of the genetic effect was observed. Cytologic analysis of the salivary gland chromosomes where the frequency of mutations was increased, showed that they were punctate. Exposing *Drosophila* at various stages (eggs, larvae, imago) did not change the character of the effect. The use of radioprotective 5-methoxytryptamine had no effect on frequency of mutations.

With regard to primary nonseparation of the sex chromosomes in male *Drosophila*, statistically significant differences between the experiment and the control were found in two cases [33, 34, 49]. Nearly significant differences were found in one experiment, but in another, no differences were noted. The greatest effect was during the Vostok 1 flight (duration 1.5 h), and was least during the Vostok 3 flight (duration 96 h). Thus, even a cautious hypothesis is improbable concerning induced nonseparation of chromosomes by weightlessness. Two interesting features were also noted during these experiments: the independence of the effect from the stage of gametogenesis, and the ratio of males to females characteristic of spontaneous nonseparation of chromosomes.

Eight experiments were conducted to determine the frequency of dominant lethal mutations in gametes of male *Drosophila* following space flights [9, 81, 83, 86]. In three, two lines of *Drosophila* were used; in nine instances mutability at the stages of mature sperm and spermatid-spermatocytes was analyzed separately. The most noteworthy results of these experiments are:

percentage of induced dominant lethals was positive and low in all the experiments;

correlation between magnitude of the effect and flight duration was absent;

frequency of lethals in the highly mutable line was somewhat lower than in the mutation-resistant;

the effect was greater in the spermatid-spermatocytes than in the mature sperm.

On the basis of additional laboratory experiments, it was concluded that the observed effect was due to decreased fertility of the males caused, primarily, by nonspecific spaceflight factors. Adequate bases are lacking for suggesting induction of noticeable frequency of mutations in the dominant lethal type during space flights [85].

Female *Drosophila* showed a high frequency of egg death following space flight. However, the effect was practically absent in experiments where females were fertilized prior to launch. Hence, the result was obtained not as a consequence of induction of dominant lethals, but rather was due to disruption of processes of sperm utilization caused by temperature shock [83].

A fourth type of genetic change recorded in *Drosophila* was crossing-over in the embryonic cells of males. In one of three experiments, a statistically significant effect was observed. The absence of the effect in two flights was explained by the fact that during analysis of the gametes, the stage of late spermatogony, in which crossing-over occurs in males with greatest frequency, was omitted. In laboratory investigations, crossing-over in male *Drosophila* can be induced by low-frequency vibration [1, 84].

During Vostok 3 and 4 flights, virgin female *Drosophila* were bred with males after the satellite was in orbit [82], demonstrating that copulation, ovulation, embryonal and larval development of *Drosophila* can occur normally under conditions of weightlessness. Morphoses of a nonspecific character appeared, the number differing from the control level which was statistically significant.

Cytogenic Considerations

Cytogenetic experiments with mice were conducted aboard the spacecraft-satellites 2, 4 and 5. After landing, a count was taken of chromosomal aberrations in the marrow and spleen. The first two experiments showed a statistically reliable effect, but the third, no effect [8, 9]. The effect was characterized by duration of its maintenance but in almost total absence of chromosome fragmentation. The changes were caused most frequently by adhesion and subsequent incorrect chromosome separation, not by breakages. A similar effect appears when animals are exposed to vibration [7, 58]. Test dogs Ugolek and Veterok aboard Cosmos 110 were studied postflight to determine the status of spermatogenesis. The flight did not significantly affect the spermatogenesis process although a few aborted spermatozoids were found. No flight effects on the production of offspring were detected [40].

Experiments on cultures of normal and pathologic human cells (the clone of HeLa cells, fibroblasts, cells of human amnion) during flights of the second, fourth, and fifth spacecraft-satellites, Vostok 1, 2, 4 and 6, and Zond 5 and 7, tested the cell survival of a single-layer culture on glass and their capacity for growth and reproduction upon return to normal conditions. In a number of experiments there were certain immunobiologic changes. In several experiments aboard Soviet satellites, the viability and ability of human and rabbit skin flaps to "take" were studied following exposure in space. The data indicate that skin flaps maintain viability [120, 126, 127, 128, 130].

Discoverer 17 and 18 satellite experiments demonstrated increased activity in the antigen-antibody reaction similar to that which appears during application of chemical mutagens and ionizing radiation. A similar effect was achieved with exposure to vibration. Cells of several human tissues were also exposed in the form of single-layer cultures: amnion, conjunctiva, synovial membranes, bone marrow, leukemic monocytes, and embryonic lung. There was degeneration and necrosis of a significant number of cells in both the experimental and the control cultures because of poor storage conditions. In the experimental material, multipolar mitoses were observed, as well as haploid, polyploid, and aneuploid nuclei with fragmented and decentric chromosomes.

The test for chromosome disorders in preflight and postflight examinations of cosmonauts can be considered a test for biologic indication of spaceflight regions [53, 57]. Crewmembers of Soyuz, Gemini, and Apollo showed a slight increase in frequency of chromosome aberrations following flight. This phenomenon differs in individual specificity and its significance and etiology are not clear at present.

Brief examination of insect experiment results conducted during the Biosatellite II flight is worthwhile. The experiments aimed to study the effect of weightlessness on various indicators, chiefly genetic, and to register radiation effects under conditions of weightlessness. Various lines of *D. melanogaster* and *T. confusum* (flour beetle) and *Habrobracon* (the ichneumon fly) were used in the experiments.

Genetic Tests

The genetic apparatus of *Drosophila* was analyzed by several tests which permitted observation of practically all known types of disorders in the genetic material of multicellular organisms. Studies of the weightlessness effect on spontaneous and radiation-induced somatic damage in *Drosophila* larvae yielded these results:

> Young larvae irradiated with 800 R in orbit had a higher death rate than larvae irradiated on Earth.
>
> The death rate of nonirradiated *Drosophila* larvae in space and on Earth, as well as in laboratory experiments using accelerations, vibrations and shock G-forces, was identical within the limits of standard error.
>
> Among those specimens which survived, no changes in duration of development were found in any of the groups or for any of the stages [79, 80].

When cytologic methods were used on the same material, the numbers of rearrangements and nonseparated chromosomes were counted in ganglion cells of larvae. Specimens irradiated in flight showed a statistically significant increase in chromosome damage. The nonirradiated material showed no significant differences between experimentals and controls. In specimens in terrestrial conditions subjected to mechanical effects, the frequency of chromosomal aberrations did not differ significantly from that in laboratory controls. In preparations of the specimens of nonirradiated and irradiated flight groups, photographs showed an evident incapacity of the chromosomes to separate correctly. Inasmuch as this effect was not detected in either of the terrestrial groups, but was in both of the experimental groups (irradiated and nonirradiated), weightlessness in itself can affect the character of the separation of chromosomes.

Translocations

A portion of the surviving males was bred with test females to determine frequency of translocations. In both flight groups translocations had formed but there were none in the terrestrial control groups. Translocations appeared at the extremely resistant stage of spermatogony. It was concluded that the interaction of radiation and weightlessness increases the frequency of *Drosophila* death in those exposed at immature stages and during active metabolism and mitosis. This effect is also observed during exposure to radiation alone, but is less pronounced and occurs more slowly. Death occurs at the later stages of development, usually at the pupa stage. Frequently death approaches unnoticed and is reminiscent of mature aging. This phenomenon, together with an increase in observed cytologic chromosomal aberrations following irradiation in flight, indicate that weightlessness augments in the radiation effect. The mechanism by which weightlessness increases induced radiation disorders apparently by influencing the process of reuniting broken chromosomes. This could indicate suppression of certain restorative processes in the cell, or a purely physical phenomenon — weightlessness — which permits spatial separation of the broken termini of the chromosomes, thus increasing a tendency to form bridges and translocations.

The presence of translocations in the flight material, including participation of the very small #4 chromosome, confirms the possibility of spatial separation of chromosomes. The explanation for this phenomenon might be sought at the molecular level, since reuniting chromosomal breaks required expenditures of energy. These results indicate an interaction between radiation and weightlessness manifested as increased instances of slowly approaching early death and chromosomal damage in specimens actively growing and metabolizing, compared with those irradiated on Earth. The experiments with *Drosophila* larvae also demonstrate that some spaceflight factor, probably weightlessness, is capable of influencing chromosomal mutagenesis in forming translocations.

During the flight of Biosatellite II, another experiment was conducted on the reproductive cells of *Drosophila* at the pupa and imago stages [15]. The procedure enabled detection of various genetic disorders: recessive lethal mutations, visible mutations in special loci, losses of the dominant genetic marker in the Y-chromosome, translocations, crossing-over in males, and nonseparation of chromosomes. One group of flies was exposed to continuous γ-irradiation in a dose of 1495 R in flight, another to acute x-ray irradiation in a dose of 4000 R prior to launching; and a third was not irradiated. Corresponding controls were set up on Earth.

The experiments were divided into two groups according to the types of cells in which the mutations appear. One type — mature sperm cells — were resistant to mutations. The second type — cells at various stages of maturation — was characterized by sensitivity to the induction of mutations which was varied and fluctuated with time.

In mature sperms located in fertilized females during flight, the frequency of sex-linked lethals, in comparison with the corresponding control, was on the boundary of statistical reliability. There were no significant differences for the nonirradiated speciments. Recessive visible mutations could be counted in four loci of the sex chromosome. In the "dumpy" locus in the irradiated flight group, the frequency of mutations was 4.5 times greater than that of the corresponding control. There were no differences between the other groups of the experiment and the controls. No reliable differences were detected in numbers of translocations; frequency of translocations in the irradiated flight group was lower than in the corresponding control.

Chromosomal Tests

Other results were obtained from analysis of reproductive cells in the process of maturation during flight. In female descendants of fertilized females of the nonirradiated flight group, nearly a threefold increase was observed in frequency of X-chromosome nonseparation compared with the corresponding control. Nonseparations occurred in cells of the ovarioles which were at various stages of maturation during flight. The loss frequency of Y-chromosome markers in males of the irradiated group, at the pupal stage during flight, was higher than in the control, and statistically significant. No differences were detected between the nonirradiated groups. The frequency of translocations between the X- and the Y-chromosomes was 3.5 times greater in irradiated immature embryonic cells of the males. There were no differences between the nonirradiated groups, and no reliable differences between the flight and terrestrial groups in frequency of crossing-over, recessive lethals, and translocations among autosomes.

Among the male descendants of males irradiated in flight, which had been also exposed to x-ray irradiation preflight (4 Ci), the frequency of loss of both markers of the Y-chromosome was lower than in the corresponding terrestrial group. A similar result was obtained in the same specimens for frequency of translocations between Y-chromosomes and the second pair of autosomes. There were no differences in frequency of translocations between the second and third pairs of autosomes. Interesting data were obtained on the activity of xanthine dehydrogenase. The activity of this enzyme was significantly lower statistically in the flight groups, both irradiated and nonirradiated. Xanthine dehydrogenase is a catalyst for many reactions including xanthine formation from uric acid [65].

Thus, in terms of mutations in the dumpy locus, a synergistic effect in the interactions of irradiation and spaceflight factors was detected among cells that were at stages of equal sensitivity during flight. In the cells which, during flight, were at various stages of differing sensitivity, synergism relative to chromosomal nonseparation in fertilized females was detected. In experiments with males irradiated preflight, radiation had an antagonistic effect with other factors. Obviously, in the experiments with *Drosophila*, radiation in space flight causes genetic effects that differ from the effects on the Earth.

The goal of the insect experiment aboard Biosatellite II with yellow mealworm beetles (*Tribolium*) was to investigate the effects of weightlessness, alone and in combination with γ-irradiation, on the somatic development of wings, on the embryonic cells, and the development of pupae [105].

Half of the young mealworm pupae on-board were subjected to a continuous dose of 950 R γ-irradiation, and the other half was protected from irradiation. Additionally, two-thirds of the pupae in each group were subjected to preliminary x-ray irradiation on Earth (1350 R), in order to conduct an experiment within the same range of doses at which massive damage would occur, i.e., so that the dose would correspond, as it were, to the "shoulder" part of the dose-effect curve. An identical control group of pupae was kept on Earth. Following return of the material to Earth, the duration of pupae development was determined, frequency of deviations from the norm in wing structure was tabulated, and cross-breeding experiments were set up to record the number of dominant lethals in oocytes and spermatocytes.

In the experimental group, a delay in the emergence of the imago from the pupae was observed, but it was thought that this was caused by decreased temperature during descent from orbit. Larvae molting and pupae survival were normal. The percentage of deviations from the norm in wing structure showed a statistically significant increase in the group that received preliminary x-ray irradiation and γ-irradiation on board, compared with the control group. Flight factors per se did not cause the changes. There was no change in the group that had only preliminary irradiation. Hence, the increase in frequency of anomalies was the result of simultaneous exposure to irradiation and weightlessness. Dominant lethals among female descendants also increased twofold in the irradiated group; females from the experimental group had 77% dominant lethals in comparison with 28% in the control. There was, therefore, also an increase in the radiation effect.

The laboratory data show that both females and males underwent embryonic cell irradiation at the early gonial stages, as did a certain quantity of their sensitive meiotic cells. The mechanism of wing damage is not exactly known, but indications are that it is a local somatic effect occurring during rapid development of the imaginal disks and related to chromosomal damage. This, and an increase in dominant lethality suggests that spaceflight factors, probably weightlessness, facilitate chromosome breakages and DNA damage or delay the restorative processes.

Gametogenesis

The experiment with the ichneumon fly (*Habrobracon*) aboard Biosatellite II investigated the appearance of recessive and dominant lethals, visible mutations, and partial sterility at various stages of gametogenesis [13]. These changes were analyzed at all stages of the life cycle. The insects received γ-irradiation R doses of: γ—2400, 1200, 600, 530, and 350. Some of the insects were irradiated with a dose of 2000 R prior to launch; none of the 558 specimens died in flight. For 2 d following flight, the males had orientation disorders in sexual conduct.

Summary data on all variants of the experiment indicate a significantly longer lifespan for females which had been flown compared with the terrestrial control. The radiation experiment with this fly demonstrates that space flight can either increase, decrease, or have no effect on the irradiation effect. The effects depend on the developmental stage of the specimens and the embryonic cells, as well as on the indicator being analyzed. Space flight did not have an effect on radiation damages in mature sperm. The sperm are quiescent, fully differentiated cells in which the systems of radiation do not react. An increased radiation effect was noted on the meiotic cells, which are quiescent cells but with functioning systems of restoration. In the mitotic cells and in cells at the stage between the last mitosis and meiosis, spaceflight factors weakened the radiation effect. The restoration system also functions in these cells.

The conversion of oogonia into oocytes is a complex process. The cells which form the sequential lines are metabolically active, but manifest varying levels of metabolism. With regard to fecundity and fertility, the reaction of these cells to irradiation and to various chemical agents varies. Consequently, it cannot be considered unexpected that cells at the stages of meiosis and mitosis react differently to spaceflight factors.

This hypothesis can be proposed on causes of the effects noted: first, various systems for repairing radiation damage can be active in the meiotic and mitotic cells. Spaceflight factors, by blocking the compensating systems in the cells and the stages of meiosis, can stimulate or cause the effects to be manifested in these cells at the mitotic stage. The possibility should not be excluded that the conditions of space flight may cause a slowdown in the cellular cycle in the cells at the mitotic stage, as a result of which the process of restoration occurs over a longer time.

Second, during weightlessness the broken termini of the chromosomes in meiosis can be further separated from each other, making their reunion more difficult, whereas the chromosomes in cells at a transitional stage or in interphasic oogonia are packed more closely together and reunite more easily. For such a hypothesis, it must be assumed that under the influence of spaceflight factors, separation or approach of the broken termini of the chromosomes occurs in cells of various types.

A third possibility is that processes of cellular metabolism under terrestrial conditions occur more intensively than under flight conditions. It can then be assumed that an increase or weakening in the radiation effect is linked with resorption of eggs, which are replaced by the broken gonial embryonic cells. The sperm, of course, remain uniformly viable in both conditions. These hypotheses cannot be viewed as mutually exclusive or equally possible, but they agree well with data obtained.

Reproduction

In view of the number of tests with insects performed recently, the experiments with *Drosophila* and *Tribolium* during the flight of the Cosmos 605 deserve attention. The basic purpose in using *Drosophila* was to obtain several generations which had developed under conditions of weightlessness. The test was designed to make it possible to distinguish partially, according to phenotype, the individuals of the first generations, which had developed under weightless conditions, from the individuals of the second generation. In addition, it was possible to consider the frequencies of morphoses, primary nondisparity of X-chromosomes in females, sex-linked recessive lethals in females and males, and the visible mutations. Nevertheless, great significance was not attached to the frequency of genetic and morphologic anomalies, with the exception of recessive lethals, because obtaining a large population of flies was not anticipated.

Four cultures of *Drosophila* were aboard; launch took place when the larvae were 3-days-old. The cultures after recovery contained approximately 50 F_2 individuals and approximately 150 F_1 individuals, and a total of 206 flies. No statistically reliable differences between the control and test in any one of the indices studied were found, including recessive lethals.

In the test with *T. castaneum*, it was difficult to calculate completion of the full cycle of development during the flight time. Therefore, the flour beetles were put aboard in different stages of development: eggs, young larvae, late larvae, prepupae, and pupae. It was hoped that transition from a lower stage of development to a higher one in weightlessness could be obtained. The results agreed with those anticipated: embryos developed into larvae; young larvae underwent 2 to 3 ecdyses; late larvae were transformed into prepupae and pupae; and prepupae were transformed into pupae. The survival of individuals in all groups, both in the test and in the control, was almost 100%. The tests revealed no dramatic anomalies in development during full completion of the life cycle. The development of centrolecithal egg cells of a holoblastic type (most insect egg cells are of this type), is not subject to the effect of weightlessness, or, in other words, is not determined by the force of gravity. It must be hypothesized, in the absence of a strict rigorous regionalization and full subdivision, disruption of the processes of convection, characteristic of the state of weightlessness, cannot damage development.

Two facts are obvious. These experiments show that the results of animal experiments, similar to experiments with microorganisms and plants, do not permit a single, exhaustive interpretation. The experiments with animals with regard to a biologic indication of new space regions have produced data supporting the possibility of comparatively short-term manned space flights. It is no less important that experiments conducted as biologic tests in space were an experimental foundation for space biology.

THE NATURE OF FURTHER INVESTIGATIONS

The next stage in the conquest of space poses fundamentally new problems. The theoretical and even experimental development of these problems has already begun. The transition of the investigations to the new period is linked with an increase in spaceflight duration to a point commensurate with durations of the ontogenetic development of multicellular organisms, their reproductive period, and lifespans. The increased duration of space flights will bring into the sphere of investigations practically all experimental biologic disciplines, thereby creating a reliable methodologic base for a broad section of biologic science—space biology. In the future, it will hardly be appropriate to speak of the biologic indications of space regions. Various trends of investigations in this field are being converted into fields of space biology which do not have an empiric, but rather a strict theoretic basis.

With comparatively brief flights, biologic objects have been studied primarily for mutability—phenomena of repair and recombination—and various other elementary processes in which changes have served as indicators of danger in the spaceflight regions traveled by man. Long flights allow posing and solving, in the experimental plan, any questions related to the influence of prolonged space flight and outer-space factors on the whole complex of processes in both individuals and groups of organisms and species.

Two basic problems of primary theoretical importance are advanced by space flights. The most important is the study of the influence of space flight and outer-space factors on the entire complex of processes which control the development of organisms. The essence of the problem is to explain the principles and characteristics of genetic expression in the phenotype in organisms of the basic taxonomic groups during their development in space from embryonic cells to pubescent stages. This will signify a change of central interest of genetic investigations in space from mutagenesis and survival to the biology of development and phenogenetics. The practical aspect of the problem evolves from the hypothesis that the meeting of certain organisms with new environmental factors (primarily weightlessness) not encountered during their development and evolution can cause widespread disorders of normal morphologic organization. Of particular interest are questions on the development of mutant organisms in space. In the absence of a phylogenetic base, there is a sharp decrease in the accuracy of channeling of development, and the reaction norms in mutants will change. Experimenting with the development of organisms in conditions of weightlessness will probably be an important fundamental method for investigating the mechanisms which control and regulate development.

The basic experimental method in the genetics of development, up to the present, has consisted in replacing the normal alleles of the genes by mutant alleles, as a result of which there is either a block or a change in the synthesis of certain substances. This permits establishing the concrete significance of these substances and of the corresponding normal genes in the development of the organism. A supplementary method in the genetics of development was to study the development of organisms with the same genotypes under various conditions. Changing environmental conditions is quite simple, and this method of investigation is widely employed. However, the force of gravity, the physical factor of the environment which is customary for the organism, can very likely be altered only according to the all-or-nothing principle.

The second basic task is to study the processes in populations and associations of organisms aboard spacecraft during long flights or aboard planetary stations. This task is a practical one. It is impossible to seriously pose the question of the creation of reliably and permanently functioning artificial ecologic systems without an explanation of the laws of microevolution of organisms in specific conditions: i.e., in a state of weightlessness, or in an altered gravitational field, in an increased radiation field, in a severely limited space, or in an unusual arbitrarily created ecologic environment [44].

Such investigations will also have more general significance. From another point of view, these investigations are nothing more than solving the problems of experimental ecology and science, which are necessary to understand the processes occurring in the biosphere of the Earth, and, to transform these processes for efficient use of the Earth's resources.

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